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International Journal of Medical Students
The International Journal of Medical Students (IJMS) is a peer-reviewed open-access journal (ISSN 2076-6327) created to share the scientific production and experiences of medical students and recently graduated physicians worldwide.

International Journal of Medical Students
Year 2024 - Volume 12 – Issue 3

EDITORIAL STAFF

IJMS

INTERNATIONAL JOURNAL *of* MEDICAL STUDENTS

The *International Journal of Medical Students* (IJMS) is an open-access, peer-reviewed scientific journal (ISSN 2076-6327) that publishes original research in all fields of medicine. The Journal was created in 2009 to share the scientific production and experiences of medical students (*i.e.*, MBBS students, MD students, DO students, MD/MSc students, MD/PhD students, etc.) and recently graduated physicians (<3 years into practice) from all over the world. Our objective is to be the primary diffusion platform for early-career scientists, using standards that follow the process of scientific publication.

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The *IJMS* also strive towards the training of a new generation of Editors and Peer-reviewers promoting different training strategies among our Editorial Team that includes the Web of Science Academy courses and the Committee on Publication Ethics (COPE) courses available to its members (*IJMS* is a member of COPE).

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IJMS INTERNATIONAL JOURNAL of MEDICAL STUDENTS

Editorial

Bridging Innovation and Education: IJMS Volume 12 Issue 3 and the 2024 World Conference on Medical Student Research (WCMSR)

Francisco J. Bonilla-Escobar,[1] Mihnea-Alexandru Găman,[2] Juan C. Puyana.[3]

As we continue to foster the growth of future medical professionals, the International Journal of Medical Students (IJMS) is thrilled to present this issue featuring a wide array of research that spans critical areas in healthcare, medical education, and clinical practice. Our journal's growing influence was recently recognized in *The Lancet Psychiatry Commission on mental health in Ukraine*, which cited a previous Editorial in its discussion of global efforts to advance mental health care in challenging environments.[1] This accomplishment underscores the journal's commitment to disseminating impactful research that addresses both current and emerging challenges in medicine.

We begin with "The Power of Story Slams: A Mixed-Method Analysis of Narrative Medicine,"[2] which explores how storytelling events can reduce burnout and enhance community among healthcare workers. This study demonstrates the value of narrative medicine in improving professional satisfaction and fostering better patient relationships. Another article, "Stress Levels and Coping Strategies in Medical Students,"[3] investigates the connection between stress levels and coping mechanisms, with findings that highlight the importance of promoting effective stress management interventions within medical training.

The lingering effects of the COVID-19 pandemic remain a focal point in healthcare research. "The Impact of the COVID-19 Lockdown on Cancer Referrals in Primary Care in the UK"[4] reveals a significant decrease in cancer referrals during lockdown, emphasizing the need to prioritize early detection post-pandemic. Additionally, "A Descriptive Analysis of Therapeutics in COVID-19 Patients and Media Influence"[5] examines how media coverage swayed treatment choices during the pandemic, calling for stronger collaboration between medical leaders and the media to ensure accurate public health information. Finally, a review on the "Effects of the COVID-19 Pandemic on Physical Activity in Children"[6] continues to shed light on the pandemic's impact in other areas of healthcare.

Antimicrobial resistance is also a crucial public health issue, as highlighted in "Assessment of Antimicrobial Resistance in UTI-Causing Microorganisms in Southern Punjab."[7] This study found that *Escherichia coli* demonstrated high resistance to antibiotics such as Trimethoprim-Sulfamethoxazole, stressing the need for culture-based diagnostics in guiding treatment. Meanwhile, "Improving Access to Syphilis Screening Among Unhoused People in Yolo County"[8] underscores the success of incentive-based screening programs in increasing healthcare access for vulnerable populations, achieving a notable 87.5% rise in syphilis screening.

In the field of pediatrics, "Evolving Patterns in Inpatient Pediatric Consultations to Allergy/Immunology"[9] explores shifts in consultation patterns, particularly with regard to immunodeficiencies and drug allergies. This study points to the increasing importance of T-cell receptor excision circle (TREC) screening and its impact on clinical decision-making. Another clinical review, "Vascular Anomalies Review of the Head and Neck for Physicians in Training,"[10] provides an in-depth look, from experts in the field, at vascular anomalies and stresses the importance of early diagnosis and multidisciplinary care, particularly in pediatric patients.

Medical education also takes center stage in "A Scoping Review on the Utility of Ultrasound to Visualize Bursae in Anatomical Dissection Courses,"[11] which advocates for integrating ultrasound into anatomy courses to enhance students' understanding of anatomical structures. Similarly, "Integrating Tendinous Pathophysiology Into Rotator Cuff Tears and Greater Trochanteric Pain Syndrome"[12] offers new insights into tendon pathophysiology, challenging traditional

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views and suggesting earlier non-surgical interventions for both shoulder and hip conditions.

Several case reports bring to light rare and challenging medical conditions. "An Atypical Sellar Mass - Sellar Tuberculoma in a Young Patient"[13] presents a rare case of sellar tuberculoma, an uncommon form of tuberculosis that mimics pituitary tumors. The case highlights the importance of early diagnosis and successful management with anti-tubercular therapy and hormone replacement. "Successful Subungual Glomus Tumor Removal"[14] provides another compelling case study, detailing the diagnostic process and successful surgical treatment of a rare benign tumor in the thumb.

Personal reflections on medical education are also featured. "Summer Surgical Elective in Hong Kong"[15] reflects on a medical student's elective experience in plastic and reconstructive surgery at Queen Mary Hospital, illustrating the educational value of international electives. "Innovating Against Odds: A Medical Student's Research Journey in a Resource-Constrained Environment,"[16] shares the challenges and triumphs of conducting research with limited resources, emphasizing the importance of mentorship and resourcefulness.

Public health efforts are explored in "VAXXED & BOOSTED: Increasing COVID-19 Vaccination Rates in West Greenville"[17] which highlights a successful community vaccination campaign aimed at overcoming vaccine hesitancy in a low-income area. Additionally, "The Shame Is Not Mine: Addressing Abuse of Power Dynamics in Medical Training"[18] presents a medical student's courageous and deeply personal reflection on mistreatment during a surgery clerkship, advocating for institutional reform and support for students facing such challenges.

Finally, in "Intricacies of Using Spaced Repetition Tools,"[19] a letter to the Editor, the author reflects on the benefits and challenges of using Anki for medical board exam preparation, offering practical insights for students striving to enhance their learning techniques.

The IJMS is pleased to provide this issue, which covers a broad range of research covering important topics in healthcare, medical education, and clinical practice, as we continue to support the development of future medical professionals. This selection of papers demonstrates the journal's dedication to offering varied, excellent material that tackles both present and future medical issues.

We are excited to announce the third edition of the World Conference on Medical Student Research (WCMSR), which will be held on October 26, 2024. More than 100 people from 40 nations will attend this event, which will highlight the best research from across the world. The presentations and discussions from this global platform are highly anticipated, and you can watch them live and participate on YouTube.

We hope that these papers will inspire and educate students, researchers, and healthcare practitioners around the world as we continue to support the next generation of medical professionals. We appreciate your participation in our efforts to increase medical knowledge and enhance healthcare for all.

References

1. Pinchuk I, Leventhal BL, Ladyk-Bryzghalova A, Lien L, Yachnik Y, Casanova Dias M, et al. The Lancet Psychiatry Commission on mental health in Ukraine. Lancet Psychiatry. 2024:S2215-0366(24)00241-4.
2. Stringer AD, Liu L, Marino J, Mupparapu A, Fergus A, Rosenberg N, et al. The Power of Story Slams: A Mixed-Method Analysis of Narrative Medicine Connecting, Encouraging and Comforting Healthcare Trainees and Professionals. Int J Med Stud. 2024;12(3):239-245.
3. Karanth M, Shenoy Basti AR, NC, Reberio C. Stress Levels and Coping Strategies in Medical Students and its Association with Salivary IL-6 Levels]. Int J Med Stud. 2024;12(3):246-251.
4. Whittle O, Bushby L, Chambers R, Gittens J. The Impact of the COVID-19 Lockdown on Cancer Referrals in Primary Care in the UK: Two Years On. Int J Med Stud. 2024;12(3):252-258.
5. Mathew AA, Mensah B, Cravero JC, Moffatt DC, Dongre R, Giang TK, et al. A Descriptive Analysis of the Use of Various Therapeutics in a Cohort of COVID-19 Patients and the Influence of Media Coverage. Int J Med Stud. 2024;12(3):259-266.
6. Ramirez A, Rapp AB, Santarossa S. Effects of the COVID-19 Pandemic on Physical Activity in Children: A Systematic Review. Int J Med Stud. 2024;12(3):311-333.
7. Anjum MM, Khalid F, Saleem R, Abdul Malik MAB, Rizwan M. Assessment of Antimicrobial Resistance and Susceptibility Pattern of UTI-causing microorganisms in Southern Punjab, Pakistan. Int J Med Stud. 2024;12(3):267-273.
8. Kupa J, Bruguera R, Agnoli N, Agnoli A, Melgoza L, Portnoy A, et al. Improving Access to Syphilis Screening Among Unhoused People in Yolo County, USA. Int J Med Stud. 2024;12(3): 274-277.
9. Wurst M, Brameli A, Krantz M, Peebles RS Jr, Khan Y, Stone CA Jr. Evolving Patterns in Inpatient Pediatric Consultations to Allergy/Immunology at an Academic Medical Center. Int J Med Stud. 2024;12(3): 278-283.
10. Allred CM, Zenner KB, Bonilla-Velez J. Vascular Anomalies Review of the Head and Neck for Physicians in Training. Int J Med Stud. 2024;12(3):284-293.
11. Margenfeld F, Zendehdel A, Tamborrini G, Polzer J, Naville M, Poilliot A, et al. A Scoping Review on the Utility of Ultrasound to Visualize Bursae in Anatomical Dissection Courses. Int J Med Stud. 2024;12(3):294-302.
12. Poole JR, Alaia E, Meislin RJ. Integrating Tendinous Pathophysiology Into Rotator Cuff Tears And Greater Trochanteric Pain. Int J Med Stud. 2024;12(3):303-310.
13. Jamali AM, Luhana R. Case Report: An Atypical Sellar Mass - Sellar Tuberculoma in a Young Patient. Int J Med Stud. 2024;12(3):334-337.

14. Made Bramantya K, Suteja RC. Successful Subungual Glomus Tumor Removal: A Case Report and Future Guidance on Diagnosis and Treatment. Int J Med Stud. 2024;12(3):338-344.
15. Ho M, Chow V. Summer Surgical Elective in Hong Kong. Int J Med Stud. 2024;12(3):345-346.
16. Rajakumar HK . Innovating Against Odds: A Medical Student's Research Journey in a Resource-Constrained Environment. Int J Med Stud. 2024;12(3):347-349.
17. Stamey T, Opelami o, Moye J. VAXXED & BOOSTED: Increasing COVID-19 Vaccination Rates in West Greenville, NC, USA. Int J Med Stud. 2024;12(3): 350-353.
18. Norman S. The Shame Is Not Mine: Addressing Abuse of Power Dynamics in Medical Training. Int J Med Stud. 2024;12(3):354-365.
19. Ghani A, Intricacies of Using Spaced Repetition Tools. Int J Med Stud. 2024;12(3):366.

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Original Article

The Power of Story Slams: A Mixed-Method Analysis of Narrative Medicine Connecting, Encouraging and Comforting Healthcare Trainees and Professionals

Amy D Stringer,[1] Lisa Liu,[2] Julia Marino,[3] Archana Mupparapu,[4] Anelisa Fergus,[4] Naomi Rosenberg,[5] Michael Vitez,[6] Brian Tuohy.[7]

Abstract

Background: Narratives convey information and emotion, evoke understanding, empathy, and connection. Healthcare professionals can use narratives to reduce burnout, benefiting them, patients, and colleagues. Story slams are narrative sharing events used for group reflection, providing an opportunity for participants and listeners to improve their well-being by processing complex emotions and identities. Story slams have traditionally been popular with creative writers and nonprofit organizations. **Methods**: Following a local event hosted by *The Moth*, the Temple University Lewis Katz School of Medicine (LKSOM) Narrative Medicine program hosted nine story slams over five years with 93 presenters including students and health systems staff. Through a mixed-method analysis, the authors examined the stories for thematic patterns and surveyed presenters to investigate how the experience had impacted markers such as job satisfaction, stress levels, and connection to patients. Eleven presenters were interviewed to provide additional information about the impact they experienced. **Results**: Patient-centered care, resilience, and the value of learning comprised over half of all themes presented. Following the event, many presenters experienced improved connections with patients, and everyone reported feeling neutral or increased satisfaction with their profession. The interviews conveyed participation, created a lasting impact, fostered a sense of community, and increased appreciation for diversity. **Conclusions**: Overall, story slams nourish humanity and promote diversity, enthusiasm, and encouragement. This study and others suggest that story slams are inexpensive and effective events that can help reduce burnout and provide academic medical centers with a way to restore and cultivate community among students, physicians, and staff.

Introduction

Stories convey information, understanding, insight, and wisdom while evoking emotion, compassion, and connection.[1,2] Stories are fundamental to medicine as patients communicate symptoms, feelings, and experiences to their provider. In turn providers relay vital information to patients and peers. Narrative Medicine aids healthcare professionals in understanding patients' conditions as it allows for a deeper comprehension of the patient's symptoms and diagnoses along with the impact their condition has on their lives, connecting providers to a shared mission that is focused on healing.[1,3] This approach to medicine strengthens the patient-doctor interaction by creating a relationship and increasing the provider's efficacy in addressing the patient's illness.[1,4,5]

Furthermore, Narrative Medicine can be used to help combat burnout, a state of depersonalization and demotivation that is widely experienced in the medical community.[6] Burnout among physicians is leading to increased negative patient outcomes, medical errors, and lower efficiency.[7] Today's conventionally cognitively and emotionally demanding practice environment often leads to exhaustion in many specialties and across levels of training and experience with the rate of resident physician suicide estimated to be as high as four hundred per year.[7-11] Although harmful and widespread, burnout is partially preventable; more consideration, options, and resources must be supplied to combat it.

Interventions - both physician-directed and at the organizational level – have attempted to increase mindfulness, enhance job satisfaction or performance, and reduce work volume.[12,13] However, a 2017 review found some methods to be too brief, not widely used, costly, time-consuming to implement, and ineffective.[14] Burnout is recognized as a problem, but with little information available about how to effectively address it.[15]

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***Figure 2*. Flow Diagram of Study Methodology.**

Recruitment	Story Slams			Thematic Analysis	Surveys			Interviews		
Email invitations were sent to students, faculty, and staff to participate in the annual story slam.	96 presenters performed a total of 114 stories to an in-person audience and/ or recorded on a video livestream.			93 stories were available by recording and analyzed thematically. Themes were defined by researchers as a group. Then, each story was independently analyzed by 2 researchers, who agreed on a theme for each. If novel themes	Secure surveys were emailed to presenters. 52 surveys were completed and analyzed.			11 of the 52 survey respondents agreed to a virtual interview.		
	Gander	**n**	**%**		**Gander**	**n**	**%**	**Gander**	**n**	**%**
	Male	39	40.6		Male	20	38.5	Male	4	36.4
	Female	57			Female	32	61.5	Female	7	63.6
	Total	96	100		Total	52	100	Total	11	100
	Tittle				**Tittle**			**Tittle**		
	Faculty / Attending	30	31.3		Faculty / Attending	21	40.4	Faculty / Attending	7	63.6
	Staff Member	11	11.5		Staff Member	2	3.8	Staff Member	1	9.1
	Medical Student	34	46.9		Medical Student	26	50.0	Medical Student	2	18.2
	PA Student	1	1.0		Pre-med Student	2	3.8	Pre-med Student	1	9.1
	Pre-med Student	3	3.1		Resident/ Fellow	1	1.9	Total	11	100
	Resident/ Fellow	6	6.3		Total	52	100			
	Total	96	100							

The incorporation of humanities into medical practice through the form of Narrative Medicine is therapeutic, ana potential avenue to aid in this dilemma.[16] Expressive writing exercises have improved post-traumatic stress disorder symptoms, depression, and global psychopathology symptoms in healthcare workers impacted by the COVID-19 pandemic.[17] Narrative-provoking interviews of resident physicians have been correlated with an improved sense of empathy for patients and treatment agency.[18] A family medicine residency program found storytelling to be an easily implementable and effective way to enhance physicians' long-term well-being.[19] All this evidence suggests that incorporating shared stories into a medical setting can be powerful.

Story slams are an example of a form of Narrative Medicine, originally created by the National Public Radio (NPR) program *The Moth* as open-mic storytelling events.[20,21] Story slams have been used by students and professionals in academic medicine as safe spaces to share their experiences in front of an audience of their peers. With the aim of decreasing burnout, LKSOM and other institutions, including University of Vermont's Larner College of Medicine (UVCOM), University of Massachusetts School of Medicine (UMSOM), University of Minnesota Medical School (UMN), and the American College of Physicians, have held these events for several years within their health systems and conducted post-event surveys of attendees with positive findings.[22-24] Research with an additional aspect beyond post-event surveys such as interviews of participants could permit more elaboration about the significance of their experience. This new source of data would allow for further analysis of the impact and aid in gathering information and suggestions for effectively implementing them across academic health systems.

Through a mixed-methods investigation that includes interviews, thematic analysis, and surveys, this research provides detailed information about the personal impact participation in story slams has on healthcare professionals and students. We aim to contribute further data to demonstrate the potential of story slams as an inspirational way to provide an effective and inexpensive avenue for reducing burnout and applying Narrative Medicine principles in busy medical centers. LKSOM hosted nine story slams between 2017 and 2022, with 93 individual storytellers. The intention of this study was to discover the themes that healthcare professionals presented and to learn how sharing stories affected them in a variety of domains, including empathy, patient care, physician wellness, humanity, listening ability, and sense of community. We sought to further enrich the argument for the role and value of story slams by obtaining a better understanding of the significance of these events for presenters.

Methods

Study Design and Sample

This was a mixed-method study involving survey response collection, thematic analysis, and semi-structured interviews with story slam event presenters. Presenters for each story slam were recruited through emails sent to faculty, staff, and students across Temple University Health System. All those who volunteered to present were both current and former students, faculty, staff, and physicians. (About the story slam: each event had a one-word theme (e.g. "strength") to provide direction. Presenters were offered a workshop to help craft their story, which could be read from notes or memorized. Stories were about five minutes long and the events were about 2 hours long. Presenters were introduced by name, brief biography, and the title of their piece. At the end of each event, the audience voted for favorites and the top three presenters received a small prize. Food was provided. The population of interest for this investigation was presenters, therefore attendees were not surveyed or interviewed. We evaluated 93 stories presented, analyzed 52 survey responses, and interviewed 11 presenters. A schematic representation of our methodology with demographic information can be seen in ***Figure 2***.

Table 1. **Themes Identified in Thematic Analysis.**

Themes	Definitions
Advocacy	Advocating for self, family member, or patient in a hospital setting; female empowerment
Burnout	Physical and emotional exhaustion
Connection to patient	Relating to a patient outside of medicine, e.g.: food, culture, music
Gratitude	Thankful for their experiences, remembrance of a lost one
Healthcare accessibility	Access to healthcare; EMR
Humility	Goal isn't to be a hero, but to be part of a team
Humor	Humor in medicine
Idealism	Being idealistic vs realistic
Injustice	Injustice within the healthcare system; social determinants of health
Patient-centered care	Compassion; treating patients as people; removing barriers to professionalism; good communication between doctor and patient
Resilience	Perseverance through difficult experiences
Self-care	Taking care of self; recognizing when to take a break
Self-confidence	Increasing confidence in provider ability
Self-improvement	Finding purpose; transformation; learning to take responsibility
Teamwork	Working in a team, amongst peers, allows for a better outcome
Value of learning	Class and student experiences; mentorship

Legend: The 16 themes identified from thematic analysis of 93 stories and how these themes were defined. This analysis was performed in 2022 at Temple University, Philadelphia, PA, USA.

Thematic Analysis

To develop a list of themes, ten stories were randomly assigned to each team member. One main theme was assigned to each piece, based on the subjective opinion of the stories content, a list of present themes was then compiled, and definitions were created for each theme. These original ten pieces were reviewed by a different member to agree or disagree on the presence of a theme based on these definitions. From then on, each piece was viewed by two team members and had a theme assigned from the created list. The definitions are shown in ***Table 1*** below. If novel themes emerged during the reviewing process, they were appended to the list. These definitions were refined as needed while reviewing stories.

Survey

We surveyed 96 participants via REDCap (Research Electronic Data Capture) (Vanderbilt, TN, USA), a secure web application for online surveys and databases, to investigate how the experience of presenting in a story slam had affected job satisfaction, feelings of community, sense of compassion, empathy and humanity, ability to listen, and interactions with patients. We asked if and how stress levels had changed, why they participated in the story slam, and how listening to other stories impacted them. For a confidence level of 95% and a maximum margin of error of 10% with a population size of 96, our target was a minimum of 49 completed surveys, we received 52 completed surveys. For data analysis, "Professionals" are defined as residents, attending physicians, nurses, and other staff, and "Students" are medical students from all four years of medical school training and post-baccalaureate students.

Interview Approach

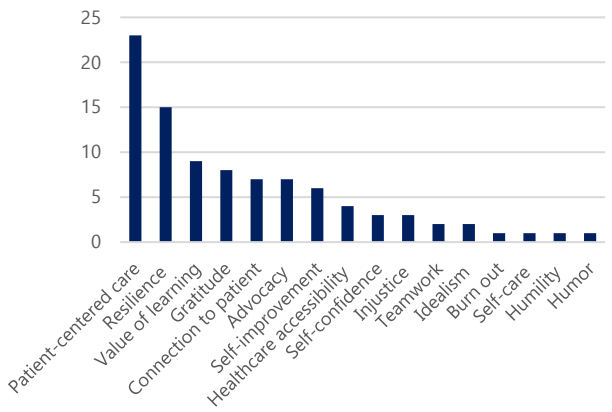
We conducted 11 virtual semi-structured interviews lasting approximately 30 minutes each to acquire additional information about the impact of participating in a story slam. One team member conducted the interview for each participant while another acted as a recorder. An interview guide was designed to provide structure and consistency between interviews. Interviews elicited participants' open-ended opinions and assessments of the value of the story slam event and each interviewers' responses are represented in the results. Ethical approval for exempt, minimal risk human subjects research was obtained. This project was approved on Aug 31, 2021 by the Temple University IRB, protocol # 28591.

Results

Thematic Analysis

Of 114 individuals signed up to present, four (3.5%) were absent and 17 (14.9%) did not have recordings. The remaining 93 stories were viewed, and 16 themes were identified as defined in ***Table 1.*** Patient-centered care was found to be the most common theme, representing 25.6% of the total. Resilience was second-most common at 16.7%, followed by the value of learning at 10%. These three themes together sum to more than half of all themes identified. See ***Figure 1*** for a breakdown of the total representation.

Figure 1. **Breakdown of the Story Themes.**



Legend: 16 themes found from 93 stories. Analysis was done in 2022 at Temple University, PA, USA.

Survey

In 52 completed surveys, about 94% experienced neutral or improved connections with their patients, and 67% felt improved satisfaction with their current profession or schooling. All professionals reported feeling neutral or increased satisfaction with their profession. 92% reported acknowledging that their patients are humans not defined by their disease experience. 90% reported spending equal or more time listening to their patients' concerns, with 44% reporting more time. 90% experienced an equal or increased feeling of empathy for patients, 40% reporting an increase. About 77% of respondents reported feeling equally or less stressed at work. At the end of the survey individuals reported why they participated; some shared that "listening to others' stories was healing" and "participating allowed [them] to relate to other professionals in medicine." They found the experience "rewarding and cathartic," and listening to others' stories evoked feelings of "humility, amazement, pride, excitement, connection, inspiration, and empowerment." Some claimed it helped to accentuate the humanity behind medicine and remind them why they chose this profession. These responses illustrate the role of story slams in improving well-being and fostering community.

Interviews

Several dominant themes emerged from the interviews: first, that participation had a lasting impact on the day-to-day life of the presenter; and second, that the events created a sense of community by uniting individuals within and across disciplines. In addition, interviewees reported that story slams increased their appreciation for diversity by exposing them to new perspectives.

Lasting Impacts

We found that lasting impacts were reported in a variety of ways, each unique to the individual presenters. One physician reported that his participation sparked his desire to write, resulting in the composition of autobiographical stories and reflections. Another faculty member who presented a story about a mentor who impacted her career as a woman in medicine later published her piece in a medical journal. After the event, one presenter was invited to speak at organizational and interdepartmental meetings and had her work published in a city newspaper. Another presenter was inspired to attend a creative writing class.

Commenting:
"I really loved the experience... I'm used to giving talks and lectures, but this was almost like stand-up comedy, and so it was very new to me and...it was the highlight of 2020...It was so revealing to me about my own feelings. It was kind of like this introspection...a safe place to explore and express my emotions."

These individuals not only went on to participate in further creative endeavors, but also gained an enhanced ability to reflect on their own experiences and present them to others. Participation in story slams encouraged introspection and thoughtfulness, and motivated these presenters to expand their public speaking and leadership experiences. The impact also appears to be enduring, with multiple respondents reporting effects several years after the event.

A Sense of Community

We found that a sense of community was fostered among presenters and their audience, bringing together practitioners of multiple disciplines and training levels. Some presenters directly connected with others during the event and recalled colleagues and classmates approaching them after the story slam to talk about their own experiences. One clinician said coworkers he had never met approached him for weeks after the event to thank him for sharing. These experiences provided many presenters with a chance to feel heard, recognized, and supported, which fostered a sense of comfort and belonging.

A Student Commented:
"I felt like everybody was rooting for me... You look in the audience and you see the connection that you have with people. You see them smile and laugh at your jokes; you see their heart literally full."

A Senior Doctor Commented:
"The idea of sharing stories... is healing. And it's connection. So often [physicians] look for validation and understanding. And storytelling does that. It connects us to one another. Watching others react to what we're sharing is where that validation occurs."

In addition to feeling connection, many individuals felt encouraged by their peers, decreasing feelings of isolation and burnout. Healthcare settings can often feel isolating, an effect which was amplified during the COVID-19 pandemic.[22]

One Clinician Noted:
"It's a reminder we're all in this together. Particularly in such a lonely time, the idea of building community and trust is really important. Honestly, it's the best. I've been here for 12 years. This has been the best experience for pulling people together that I've seen."

In addition, story slams have the potential to reach across generations, encouraging sympathy, empathy, community, and unity through the sharing of common experiences. One doctor, who had shared a deeply personal story about the death of his brother, said:

"A lot of our trainees have to sacrifice a lot of who they are as individuals in order to accomplish becoming a physician, particularly a good one. Dealing with personal grief and loss, while trying to do all this, is something that we all are doing and I figure there's a lot of suffering in silence and sadly there just probably isn't enough discussion. We all have lots of stories and we all learn from each other through those stories."

Another Presenter Emphasized:
"I think in both medicine and medical education, you do a lot of studying and working… Events like this break that up and force people to move from their computer… and enjoy the company of others, enjoy the stories of others… That inherently builds community. Sharing stories, sharing feelings, sharing perspectives allows people to remember that they're not alone… Coming together when the world is online and being separated, there's a lot of value in that… Medicine sometimes feels very clinical, very scientific, very cold… Telling stories… about people's feelings, about people's experiences, challenges some of those expectations."

Story slams help to relay the wisdom of senior physicians, who have already experienced the tolls and expectations of medical training, to students and other staff. Many medical professionals report that during medical training and practice, insufficient time is devoted to emotional processing - especially during training, when this emotional toll is profound.[23] By sharing intimate experiences with peers, healthcare students and professionals can begin this necessary emotional processing. There was an agreement among presenters that the experience restored them and helped them heal, and that they were inspired by shared vulnerabilities.

One Student Said:
"So many things are…stripping the humanity and subjectivity of medicine away. And I think storytelling allows us to restore that. There's a level of intimacy that you cultivate with an audience when you're sharing your work… and you're inviting people into your inner thoughts, your emotions, sometimes very vulnerable moments in your life."

Story slams provide opportunities for validation and connection between individuals across many disciplines, bringing together students, senior physicians, teaching faculty, nurses, staff members, technicians, and social workers. These shared experiences provide belonging, understanding, and stress relief among healthcare professionals and students, with great potential to reduce burnout.

Appreciation for Diversity

Story slams foster an appreciation for diversity in age, race, background, specialty, and experience level. Many presenters considered story slams one of the few times in a hierarchical profession when faculty, students, attendings, residents, and other staff could come together as equals. Older faculty appreciated students' stories as a chance to reflect on past experiences and rejuvenate their spirits. Post-baccalaureate students were able to share experiences about their transitions. Senior faculty shared wisdom: one relayed the challenges of taking care of a patient at the beginning of the AIDS epidemic:

> "[I wanted to] provide the audience with a perspective they had not heard, [such as] what you had to go through to get a patient taken care of… and contrast that with today… I think about [her] every time I offer a newly diagnosed patient with HIV a single-tablet option: "Take this and you will live for decades.""

Story slams are a valuable opportunity for presenters and audience members to hear stories from individuals in various stages of their careers.

Discussion

Participation in story slams significantly enhances the sense of community, connection, and humanity among medical professionals and students, which in turn improves patient care. Patient-centered care, resilience both in life and the healthcare environment, and the value of learning from our mistakes and peers are important topics for all professionals and students in healthcare. Our findings showed, bringing personal stories about these topics to an event during which they are shared contributes to a sense of belonging, community, and purpose. Moreover, they demonstrated that hearing the experiences of others informs us that we are not alone in our own experiences, providing comfort which leads to a reduction in feelings of isolation and despair, the core contributors to burnout.

The aforementioned institutions have been conducting story slams and have published results of post-event surveys. UMN found these events increased connectedness and fulfillment experienced by medical communities and personnel and that they are a way to positively impact wellbeing while fostering resilience and a sense of community throughout graduate medical education.[23,27] UVCOM's results indicated improved quality of work and reduction in feelings of burnout among healthcare professionals.[24] UMSOM's results demonstrated a decrease in emotional exhaustion and depersonalization, as well as an improved sense of professional development.[22] All of these institutions demonstrated the utility, impact, and importance of story slams. Our work builds upon these studies and found through our survey that story slams have the potential to reduce burnout, increase job satisfaction, improve job performance, and improve patient outcomes. Our responses indicate increased feelings of connection, decreased stress, and improved satisfaction with medical training.

Beyond the survey responses, further detail was provided by the testimonials of interviewed presenters, who were able to

elaborate upon the positive impact of participating in a story slam. These effects were not limited to storytellers; presenters recounted experiences of being approached by listeners, who often thanked them and wanted to further discuss what was shared, hence conveying a reduced sense of isolation and increased feelings of encouragement, creativity, community, unity, and connection.

Abstraction from our findings suggest that these inexpensive, simple events are powerful tools that can contribute to decreasing burnout in the academic healthcare community. Since 2017, LKSOM has experimented with annual or biannual events, which were optional to attend and had the added benefit of catered food. In 2020 and 2021, virtual events were held; in 2022, the organizers decided to return to an in-person event. We acknowledge that this study is produced by one institution, and results from events such as these can vary significantly and depend on many factors, such as attendance, educational level and demographic composition of participants, the number and size of institutions participating, and the atmosphere preceding and during the event. The measurement of impact from a survey or interview is potentially biased by the way the questions are phrased, therefore we attempted to control for this by using neutral language and a script for team members conducting interviews. It is imperative to keep in mind the intention of story slams is to bridge generations, disciplines, and professions, encouraging unity among participants. They bring people together, underscoring their humanity, helping them confront feelings of isolation, and creating a welcoming atmosphere. While other interventions may require weeks, multiple attempts, and involve complex coordination,[28] story slams are one-time events that are inexpensive and simple to plan and execute. Moreover, story slams have the potential to impact a large group with a single event, and to impact a diverse group of physicians and other medical community members. Instating these events regularly, either annually or more frequently, can provide these positive impacts not only immediately but also over time. For these reasons, we recommend their implementation in all academic medical facilities. Future research could focus on surveying and interviewing both presenters and listeners, in addition to creating a simple guide to be used by institutions interested in holding their own events.

The organizations that have implemented and analyzed the results from story slams have reported generally positive feedback and lasting impacts on their participants.[22-24,27] These studies together demonstrate wide applicability and the power of their implementation. Shared narrative events counter the traditional secrecy of generations trained the past, where there was an implication of weakness for seeking connection. Story slams can leave an impact that is personal and meaningful, reducing the feelings of isolation, despair, and meaninglessness characteristic of burnout.

Summary – Accelerating Translation

The Power of Story Slams: Connecting, Encouraging and Comforting Healthcare Trainees and Professionals sought to study narrative medicine events called story slams, for their effect on people within an academic medical facility. This was a mixed-method study involving survey response collection, thematic analysis, and semi-structured interviews with story slam event participants. We found that story slams are a means of nourishing those in healthcare, encouraging goodwill, community, and enthusiasm, and helping people feel valued. These one-time or annual events are inexpensive, simplistic, short-duration, and effective ways of decreasing burnout within the academic medical community, thereby benefiting not only physicians and staff but also the patients they serve.

References

1. Charon R. Narrative reflective practice in medical education for residents: composing shifting identities. JAMA. 2001;286(15):1897-902.
2. Zaharias G. What is Narrative based Medicine? Narrative Medicine 1. Canadian Family Physician. 2018;26:176-80.
3. Greenhalgh T. Cultural Contexts of Health: The Use of Narrative Research in the Health Sector. Copenhagen: WHO Regional Office for Europe 2016; Health Evidence Network Synthesis Report, No. 49.
4. Palandri F, Benevolo G, Iurlo A, Abruzzese, E, Carella AM, Paoli C, et al. Life for patients with myelofibrosis: the physical, emotional and financial impact, collected using narrative medicine-Results from the Italian 'Back to Life' project. Qual Life Res. 2018;27(6):1545-54.
5. Hurwitz B, Greenhalgh T, Skultans V. Narrative research in health and illness. London: British Medical Association Ed 2004.
6. Ji YD, Robertson FC, Patel NA. Universal Suicide Prevention for Health Care Professionals. JAMA Surgery; Letters. 2021;156(3):290-1.
7. Ward ZD, Morgan ZJ, Peterson LE. Family Physician Burnout Does Not Differ with Rurality. J Rural Health. 2021;37(4):755-61.
8. Bass PRR, Gena Castro. Burnout Pediatrician, heal thyself. Contemporary Pediatrics. 2018;35(06).
9. Center C, Davis M, Detre T, Ford DE, Hansbrough W, Hendin H, et al. Confronting Depression and Suicide in Physicians: A Consensus Statement. JAMA. 2003;289(23):3161-6.
10. IsHak WW, Lederer S, Mandili C, Nikravesh R, Seligman L, Vasa M, et al. Burnout during residency training: a literature review. J Grad Med Educ. 2009;1(2):236-42.
11. Pantaleoni JL, Augustine EM, Sourkes BM, Bachrach LK. Burnout in pediatric residents over a 2-year period: a longitudinal study. Acad Pediatr. 2014;14(2):167-72.
12. Thomas Craig KJ, Willis VC, Gruen D, Rhee K, Jackson GP. The burden of the digital environment: a systematic review on organization-directed workplace interventions to mitigate physician burnout. J Am Med Inform Assoc. 2021;28(5):985-97.
13. DeChant PF, Acs A, Rhee KB, Boulanger TS, Snowdon JL, Tutty MA, et al. Effect of Organization-Directed Workplace Interventions on Physician Burnout: A Systematic Review. Mayo Clin Proc Innov Qual Outcomes. 2019;3(4):384-408.
14. Panagioti M, Panagopoulou E, Bower P, et al. Controlled Interventions to Reduce Burnout in Physicians: A Systematic Review and Meta-analysis. JAMA Intern Med. 2017;177(2):195-205.
15. Shanafelt TD, Dyrbye LN, West CP. Addressing Physician Burnout: The Way Forward. JAMA. 2017;317(9):901-2.
16. Clarke LE, de Jong JD. The Value of Story in Medicine and Medical Education: A Chance to Reflect. J Learn through the Arts. 2012;8(1).
17. Procaccia R, Segre G, Tamanza G, Manzoni GM. Benefits of Expressive Writing on Healthcare Workers' Psychological Adjustment During the COVID-19 Pandemic. Front Psychol. 2021;12:624176.

18. Tait GR, Schryer C, McDougall A, Lingard L. Exploring the therapeutic power of narrative at the end of life: a qualitative analysis of narratives emerging in dignity therapy. BMJ Support Palliat Care. 2011;1(3):296-300.
19. Nutting R, Nilsen K, Walling A, Level E. Origin Storytelling in Faculty Well-being: A Pilot Study. PRiMER. 2021;5:15.
20. The Moth. The Moth: True Stories Told Live. Available from: https://themoth.org. Cited July 7.
21. Linett P. Interview: Ben Lillie on Science and the Storytelling Revival. Curator: The Museum Journal. 2013;56(1):15-9.
22. Silver M, Ohnigian S, Silk H, Ennis M, Savageau J. Med Moth: A Storytelling Platform for Improving Wellness in Medical Education. Int J Med Stud. 2022;9(4):300-3.
23. Olson ME, Smith ML, Muhar A, Paul TK, Trappey BE. The strength of our stories: a qualitative analysis of a multi-institutional GME storytelling event. Med Educ Online. 2021;26(1):1929798.
24. Francis Mtuke AG. Story Slam Rx: Is Connection to Personal Stories in Medicine an Antidote to Burnout. UVM Scholarworks 2022.
25. Sampaio F, Sequeira C, Teixeira L. Impact of COVID-19 outbreak on nurses' mental health: A prospective cohort study. Environ Res. 2021;194: 110620.
26. Ahmed I, Banu H, Al-Fageer R, Al-Suwaidi R. Cognitive emotions: depression and anxiety in medical students and staff. J Crit Care. 2009;24(3):e1-7.
27. Olson ME, Walsh MM, Goepferd AK, Trappey B. Sharing Stories to Build Resilience: Articulating the Common Threads That Connect Us. J Grad Med Educ. 2019;11(3):340-1.
28. Kleinpell R, Moss M, Good VS, Gozal D, Sessler CN. The Critical Nature of Addressing Burnout Prevention: Results from the Critical Care Societies Collaborative's National Summit and Survey on Prevention and Management of Burnout in the ICU. Crit Care Med. 2020;48(2):249-53.

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Original Article

Stress Levels and Coping Strategies in Medical Students and its Association with Salivary IL-6 Levels

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Abstract

Background: Medical students face ongoing stress during their training but have developed coping mechanisms. Stress alters various physiological processes, including pro-inflammatory markers like Interleukin-6(IL-6). The present study was conducted to assess stress levels and coping strategies in medical students and their association with salivary IL-6 levels. **Methods**: This descriptive study was conducted after obtaining institutional ethical clearance. A total of 76 consenting undergraduate medical students answered the Cohen's perceived stress scale and BriefCOPE questionnaire. Unstimulated saliva was used to assess salivary IL-6 levels using a Diaclone human IL-6 ELISA kit and the data obtained was analyzed. **Results**: Out of the 76 participants, 59(77.6%) were female and 17(22.4%) were male. Mild stress was reported by 9 students, moderate by 53, and severe stress by 14 students. Based on Kruskal-Wallis p test, most students used approach coping for stress of all levels. This active strategy involves problem-solving and future planning. Approach coping has shown better responses to adversity, physical health, and emotional responsiveness. Mild and moderate stressed students used acceptance, positive-refrain, and planning, while severe stressed students used planning, self-distraction, and self-blame. Despite the perceived stress, there were no significant differences in the salivary IL-6 levels among the three categories. **Conclusion**: 'Approach' coping was commonly used and linked to positive outcomes. Despite this, a number of students have reported to experience stress. Therefore, more effective strategies are needed to handle stress and demands of the profession effectively. Further research with larger samples is recommended to explore salivary IL-6 levels' relation to stress.

Introduction

Stress is defined as a state of psychological and physiological imbalance resulting from a disparity between situational demands and the individual's ability and motivation to meet those needs. It is the mental and physical response and adaptation by our bodies to actual or perceived changes and challenges in life.[1]

Students face different domains of stress including academic, interpersonal and intrapersonal stress, teaching and learning-related stress, social stress, drive and desire-related stress, and group activity stress. In the case of a medical student, the amount of stress in these domains is so high, making it the second most stressful academic course in India.[1] Acute stress results in decreased cognitive function, impaired attention, problem-solving abilities, and performance. Chronic effects of stress on the students increase the risk of cardiovascular diseases, type 2 diabetes mellitus, metabolic syndrome, depression, as well as suicide. Therefore, addressing stress-related psychological concerns is crucial.[2]

Different students have developed their own coping strategies. Coping with stress can be defined as the process of managing external or internal demands that are perceived as taxing on personal capacities and resources. Many coping strategies like effective time management, social support, and positive reappraisals have been broadly grouped as approach and avoidant strategies.[3]

With the start of the COVID-19 pandemic, there has been increasing levels of stress on the medical students. Being a novice to management and etiquette during a pandemic situation, there were concerns regarding the safety of family, friends, and oneself. Effectively adapting to virtual learning in contrast to the age-old classroom and bedside learning. All these factors were new stressors that had to be efficiently faced. This led the students to search for new coping mechanisms to effectively navigate such stressors and also develop the skill to face any such situation arising suddenly in future.[2, 3]

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Stress also has considerable corollary on the biochemical aspects of the body. Interleukin-6 (IL-6) is known to be altered in many diseases with studies associating marked rises in levels of IL-6 with psychological stress and depression.[4] Any stressor that has a negative effect on the central nervous system can stimulate the production of IL-6, initiating various peripheral immunological responses. Different compartments of the immune system can react differently to the stressor stimulus. The most common effect can be seen on endocrine and secretory glands, bringing about changes in the physiological process based on the substance secreted. Salivary IL-6 is a considerably easy marker in terms of sample collection and analysis. Saliva collection is a non – invasive method and an alternative to stressful serum sample collection.[5] The study aims to find the association of salivary IL-6 with stress perceived by medical students. The study also aims to determine the coping strategies used for different categories of perceived stress among medical students.

Methods

An institution-based descriptive study was conducted from February 2021- January 2022 in the Department of Physiology, Father Muller Medical College, Mangalore- India, after obtaining institutional ethical clearance. The ethical clearance was issued by Father Muller Institutional Ethics Committee (reference no – FMIEC/CCM/113/2021).

The sample size was estimated to be 75 which was determined using the *r* value (correlation coefficient of the reference study) with a confidence interval of 95%, using a reference study.[4] The study population consisted of medical students in their second year onwards to interns and were enlisted by snowball sampling technique. From the students who satisfied the inclusion and exclusion criteria, 76 were randomly chosen to participate in the study. Written informed consents of all the participants were taken with confidentiality assured. Students who smoked cigarettes, consumed alcohol, chronic drug users, and students taking antianxiety and anti-depressants medications were excluded. Students suffering from acute or chronic infections were also excluded.

The participants then underwent clinical examination to rule out any systemic illness which was then followed by answering the Cohen's perceived stress scale and BriefCOPE questionnaire on coping strategies provided to the participants as Google Forms. Unstimulated saliva was collected to assess the levels of IL-6.

Questionnaire

Cohen's Perceived Stress Scale (PSS) - a survey consisting of 10 questions that evaluates the feelings and thoughts in the previous month was used to assess the perceived stress in students, where the participants scored from 0 (never) to 4 (very often) for each question. For questions 4, 5, 7, and 8 reverse scoring was applied. The students were categorized as having mild (score 0-13), moderate (score 14-26), and severe perceived stress (score 27-40) based on the total score obtained.[6] BriefCOPE – a 28 item questionnaire - was used to assess the coping strategies of the students to handle stress. The participants indicated how frequently they used each coping strategy on a scale, ranging from 0 (*I haven't been doing this at all*) to 4 (*I have been doing this a lot*). The coping strategies were broadly categorized into avoidant and approach, where self-distraction, self-blame, denial, substance abuse, venting, and behavior were subcategories included in avoidant category and active, emotional, refrain, acceptance, planning, and information were subcategories included in approach category with each sub-category having 2 questions (score 2-8). The approach and avoidant categories were scored in the range of 12-48. This questionnaire has been pre-validated in the health-related research field.[7]

Salivary IL-6

Ten milliliters of unstimulated saliva were collected from each participant without spitting, a minimum of 1 hour after breakfast. The sample was centrifuged at 3400rpm for 7 minutes to get pure saliva in the supernatant. Hundred microliters of supernatant, along with control and diluent standard, and 50µl diluted biotinylated antibody were added into the ELISA wells and then incubated for 1 hour at room temperature. A Diaclone human IL-6 ELISA kit was used for the analysis. The sample was washed 3 times before the addition of 100µl of diluted streptavidin-HRP which was again incubated at room temperature for 30mins, producing blue colored complex. Hundred microliters of TMB substrate and 100µl of stop reagent were added after washing 3 times which arrests further color development, producing a final yellow color. The intensity of the color is proportional to IL-6 levels in the saliva sample. Absorbance was read at 450nm using a Biorad reader. The optical density obtained was used to calculate the levels of IL-6 in each sample. The results were expressed as picogram/milliliter (pg/ml) of saliva. The sensitivity/ minimum detectable dose of the IL-6 kit used was 2 pg/ml.[8]

Statistical Analysis

Data was collected using Excel and analyzed using SPSS software (IBM SPSS Statistics for Windows, Version 24.0. Armonk, New York, IBM Corp).

Mean ± SD for data following normal distribution and median/ interquartile range was used for skewed values. The PSS and BriefCOPE questionnaires were graded using Likert's Scales. The mean and standard deviation for each question was calculated. Using PSS, the students were categorized as mild (score 0-13), moderate (score 14-26), and severe perceived stress (score 27-40). In BriefCOPE, a score of 2-4 indicated that the coping strategy was least used by the student, a score of 4-6 indicated that the coping strategy was moderately used, and a score of 6-8 indicated the coping strategy was often used by the student to handle stressors. A Kruskal-Wallis test was used to explore the statistical significance of the questionnaire and demographic details. A p-value <0.05 was considered statistically significant.

Results

Table 1. **Demographic Characteristics with Lifestyle Data of the Participating Students.**

		Count	%	Kruskal-Wallis test p-value
Gender	Female	59	77.6%	0.268
	Male	17	22.4%	
Age	18 - 20 years	25	32.9%	<0.001
	21 - 23 years	51	67.1%	
Currently Studying In	Phase II	8	10.5%	0.001
	Phase III Part I	15	19.7%	
	Phase III Part II	40	52.6%	
	Interns	13	17.1%	
Sleep	1. Disturbed	7	9.2%	0.000
	2 Undisturbed	69	90.8%	
Bowel/Bladder Habits	Regular	69	90.8%	0.017
	Irregular	7	9.2%	
Lifestyle	Sedentary	37	48.7%	0.433
	Active	39	51.3%	
Exercise	Regular	24	31.6%	0.082
	Irregular	52	68.4%	
Are You Aware of The Benefits of Yoga And Breathing Exercises?	Yes	68	89.5%	0.906
	No	2	2.6%	
	Maybe	6	7.9%	
Do You Practice Yoga Or Breathing Exercises?	Yes	13	17.1%	0.264
	No	47	61.8%	
	Maybe	16	21.1%	

A total of 76 medical undergraduate students in their second year to intern year participated in the study. ***Table 1*** shows the demographic details of the participating students. The majority of the participants were females (77.6%) while only 22.4% of students were males.

Based on the response to the Cohen Perceived Stress Scale, students were categorized into mild, moderate, and severe stress as depicted in ***Figure 1***. Nine students perceived mild stress, 53 moderate, and 14 perceived severe stress.

Figure 1. **Performance of Respondents on the Cohen's Perceived Stress Scale (PSS).**

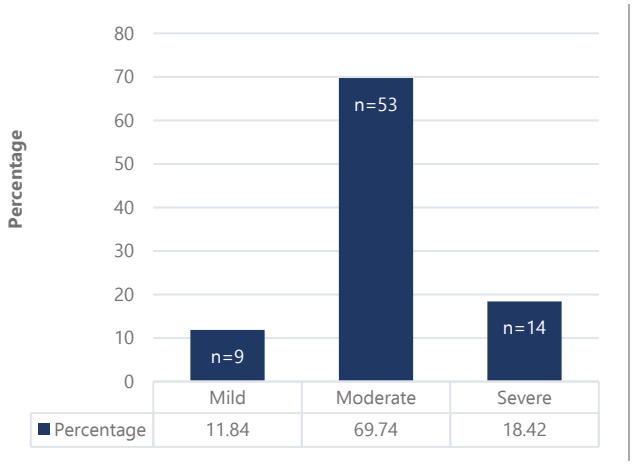


Table 2. **Awareness and Practice of Yoga Among the Three Perceived Stress Categories.**

		Mild Stress Count (Percentage)	Moderate Stress Count (Percentage)	Severe Stress Count (Percentage)
Are you aware of the benefits of yoga and breathing exercises?	Yes	8(11.8%)	47(69.1%)	13(19.1%)
	No	0(0.0%)	2(100.0%)	0(0.0%)
	Maybe	1(16.7%)	4(66.7%)	1(16.7%)
Do you practice yoga or breathing exercises?	Yes	2(15.4%)	10(76.9%)	1(7.7%)
	No	6(12.8%)	29(61.7%)	12(25.5%)
	Occasionally	1(6.3%)	14(87.5%)	1(6.3%)

Table 2 compares the awareness and practice of yoga among the three perceived stress categories. Most of the students were aware of the benefits of yoga (89.5%) but only a few actually practiced it (17.1%). Yoga can be used to manage stress; if the students use yoga as a method of coping, we can incorporate yoga into their curriculum. The p-value obtained by the Kruskal-Wallis test were 0.906 and 0.264, hence statistically not significant.

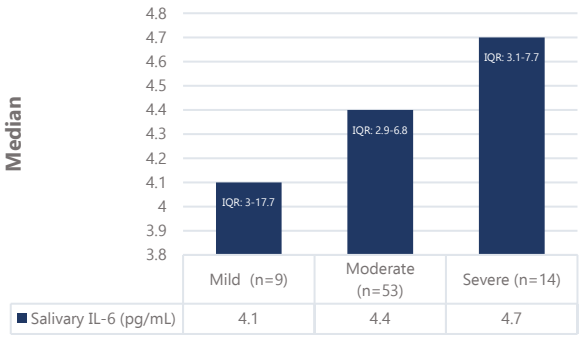
Table 3. **Responses to BriefCOPE Questionnaire.**

	Mild stress (n=9) mean± SD	Moderate stress (n=53) Mean± SD	Severe stress (n=14) Mean± SD	Kruskal-Wallis test p value
Avoidant	**21.11±5.09**	**23.98±4.57**	**30.50±4.67**	**<0.001**
a. Denial	4.11±1.05	4.04±0.88	4.79±0.89	0.026
b. Substance abuse	2.67±1.32	2.45±0.91	2.64±1.45	0.759
c. Venting	3.00±1.12	4.26±1.42	5.57±1.50	<0.001
d. Behavior disengagement	3.00±1.41	3.53±1.35	4.86±1.70	0.004
e. Self-distraction	4.89 ± 2.15	5.21±1.41	6.36±1.50	0.029
f. Self-blame	3.44±1.67	4.49±1.59	6.29±2.20	<0.001
Approach	**30.22±5.36**	**30.30±6.01**	**34.93±5.85**	**0.035**
a. Positive refrain	5.67±1.12	5.70±1.64	5.86±2.03	0.945
b. Planning	5.56±1.51	5.51±1.55	6.50±1.51	0.104
c. Acceptance	6.11±1.54	5.51±1.65	6.21±1.67	0.272
d. Emotional support	4.44±1.01	4.81±1.73	5.07±1.94	0.693
e. Use of instrumental support	4.33±1.50	4.49±1.44	6.07±1.49	0.002
f. Active	4.11±1.36	4.28±1.28	5.21±0.80	0.032
Humor	4.11±1.90	4.51±1.93	6.21±1.76	0.008
Religion	5.11±1.27	4.89±1.87	5.36±2.10	0.689

The responses to the BriefCOPE questionnaire are presented in ***Table 3***. The data has been compared against mild, moderate, and severe stress. Kruskal-Wallis test reveals approach coping strategies to be highly significant with a majority of students using it in all the categories of perceived stress.

Despite of perceived stress, there was no significant difference seen in the salivary IL-6 levels of the students among the three categories. The median salivary IL-6 in mild category (n=9) was 4.1 pg/ml (interquartile range = 3-17.7 pg/ml); 4.4 pg/ml (interquartile range = 2.9-6.8 pg/ml) in moderate category (n=53); and was 4.7 pg/ml (interquartile range = 3.1-7.7 pg/ml) in severe category (n=9) which was not statistically significant (p value=0.823).

***Figure 2*. Median Salivary IL-6 Levels with an Interquartile Range of Three Perceived Stress Categories.**



Discussion

This study aimed to investigate the stress levels and coping strategies in undergraduate medical students and their association with salivary IL-6. A total of 76 students participated in our study, of which 22.4% were males and 77.6% were females. Although stress in medical students has been studied previously, we aimed to assess the stress levels in the COVID era. The various coping strategies used by the students have also been tabulated. Based on Cohen's Perceived Stress Scale, we found that the majority of the students (69.7%) were moderately stressed, 18.4% were severely stressed, and 11.8% were found to be mildly stressed. The lowest score obtained was 5 and the maximum score obtained was 36. This indicates that all students were experiencing some degree of stress. Our study findings are comparable to the study done by Bhavani Nivetha M.et al, who found the prevalence of mild, moderate, and severe stress was 20%, 74%, and 6% respectively.[9] Another study, reported the stress levels to be 51.7% among medical students.[10]

We did not find a significant difference between gender and stress levels. A study by Amr et al also showed similar results, where the level of perceived stress and number of stressors were similar between males and females.[11] A study conducted by Das *et al* had concluded that gender influenced the level of depression rather than the level of stress.[12]

In our study, second-year students reported a higher degree of stress as compared to other years, but as the first-year students were excluded due to ethical considerations, it could be a limitation of the study. A previous study showed that stress was substantially greater in second and third-year students than in first-year students ($p < 0.05$).[13] This shift in the stress category could indicate effective coping strategies employed by the students. It could also be due to adaptation to the stress of medical education as the students pass out each year evincing their preparedness for the future. This is contrary to findings by Supe, Sherin, and Shaikh et al who have reported a higher level of perceived stress among third and fourth-phase students.[14,15,16]

Mental and physical adverse effects have been well-documented side effects of stress.[17] Cognitive decline and learning difficulties are associated with high levels of stress.[18] It is hypothesized that stress activates the hypothalamic-pituitary axis which causes changes in neurotransmitters serotonin, dopamine, and norepinephrine, which have serious mental effects like anxiety and depression.[2] Thus, there is a need to find ways to manage stress effectively.

The median weight of the students in the mild category was 69 kg (interquartile range 58-82) mean±SD=72.94±19.42, the moderate category was 60 kg (53.5-70) mean±SD=61.66±11.38 and the severe category was 54.5 kg (46.5-64.3) mean±SD=55.39±9.28, which was statistically significant (p value=0.005). This may be due to unhealthy eating habits that was used as a stress buster, a coping strategy adopted, leading to the students perceiving mild stress but at the same time gaining more weight than their peers.[19]

Although 89.5% of participants were aware of the benefits of yoga, only 10 students in the moderate category were actually practicing it. This result is consistent with the study done by Kathapillai where 89.26% of medical students knew the benefits of yoga but only 30.87% were practicing it.[20] Although students were aware of the benefits of yoga, they did not practice it. Thereby, the incorporation of yoga into the curriculum can be planned for the future.

Using the Brief Cope questionnaire, we studied the coping methods of the students. We found that in all grades of stress, the 'approach' method was the preferred coping strategy amongst respondents. The most commonly used coping strategies in students with mild stress were found to be acceptance, positive refrain, and planning. Students with moderate stress adopted positive refrain more commonly. Whereas in students with severe stress planning, self-distraction, and self-blame were adopted.[3] Previous work has shown coping strategies such as use of the alcohol, tobacco, and drugs were commonly used by medical students in the United Kingdom.[21] In our study, these were reported to be least commonly used. However, under-reporting cannot be definitively ruled out.[22-25] Among the 'avoidant' coping mechanisms, self-distraction, self-blame, and venting had higher scores and there was also a statistical significance between the groups in its usage. The use of avoidant coping mechanisms like denial and behavioral disengagement were also statistically different between the three groups, with the students in the high-stress group scoring higher. "Denial" is an attempt to reject the reality of a stressful event. "Behavioral disengagement" means giving up or withdrawing efforts to attain a goal. These coping strategies help in tackling stress but they are more likely to worsen the stress inclining them to psychological morbidity. Similar results of anger, distraction, and avoidance being the coping strategies of choice for highly stressed students were reported in other studies. [26-28]

Humor was also commonly reported to be used as a coping mechanism, especially by the high-stress group in our study. Humor is considered to be one of the mature defense mechanisms which contributes to one's resilience and well-being.[29] Among 'approach' strategies, active coping and the use of instrumental support were significantly used by the high-stress

group of students. "Active coping" means taking action or exerting efforts to remove or circumvent the stressor.[28,30] Students have cognitively refashioned stress as a daily challenge. They have embraced it and are coming up with ways to positively and effectively handle the stress experienced during medical school to achieve a socially and financially stable life in the future.[31]

In the present study, there was no significant association between stress levels and salivary IL-6 levels which is consistent with a study done by Edan.[32] But in a study done by Vernaza assessing the relationship between perceived stress and serum IL-6 levels, there was a significant association between the two: with an increase in stress levels, there was a statistically significant rise in serum IL-6 levels.[33] This could be due to various factors like genetics and others that affect salivary IL-6 levels more than serum IL-6 levels.[32,33] In a study done by Izawa et al, they found a significant rise in salivary IL-6 levels following acute psychological stress that was created among the young participants following an arithmetic task, which was attributed to sympathetic activity with cortisol secretion stimulated by the acute stress event.[34]

In conclusion, the common coping strategy employed by the students to handle stress was the approach, which is associated with better outcomes and more stable emotional responses. Despite using the approach strategy, a vast number of students have reported to experience stress. Thus, there exists a need to teach more effective coping strategies to efficiently handle the stress and demands of their profession without compromising their service and health. Incorporation of appropriate interventions and support groups in the curriculum and its impact on the stress levels could be a prospective study. At the same time, the salivary IL-6 levels did not show any association with stress levels with no causation proved, which could be attributed to the smaller sample size, providing room for studies addressing larger population.

Limitations of the study – The study involved self-reporting of stress, thus under-reporting or over-reporting cannot be ruled out. The majority of the participants were females and thus external generalizability to the population will be limited. Equal distribution of genders would have enabled better comparison between the groups. A larger sample size across states will help to better generalize the results. The study has used snowball sampling technique which could lead to sample and anchoring bias with lack of insight for accuracy regarding representativeness of the target population.

Summary – Accelerating Translation

Stress Levels and Coping Strategies in Medical Students and its Association with Salivary IL-6 Levels

The medical students experience stress from the time they enter the medical course. Stress alters various physiological processes, including serum and salivary markers and is also linked to the development of various diseases like hypertension, diabetes mellitus, depression etc. Students have developed their own coping mechanism to handle this stress.

Aim: The present study was conducted to correlate the stress levels and coping strategies in medical students and the effect of stress on salivary IL-6 levels among medical students.

Methods: This descriptive study was conducted in Father Muller Medical College after obtaining institutional ethical clearance. A total of 76 undergraduate medical students participated in the study. After ruling out Systemic illness clinically Cohen's perceived stress scale and BriefCOPE questionnaire were distributed and collected. Unstimulated saliva was collected to assess salivary IL-6 levels. The data was entered into Excel sheet and analyzed.

Results: Out of the 76 participants 59(77.6%) were females and 17(22.4%) were males. Based on the Cohen's perceived stress scale score, students were categorized into having mild stress (9 students), 53 participants with moderate stress, and 14 with severe stress. We found that in all grades of stress, approach method of coping had a higher score indicating that this was the method most employed by the students to handle stress. Under the approach method of coping, the most commonly used coping strategies in students with mild stress were found to be acceptance, positive-refrain, and planning. Students with medium stress adopted positive-refrain whereas students with severe stress, adopted planning, self-distraction, and self-blame. Despite the perceived stress, there was no significant difference seen in the salivary IL-6 levels of students among the three categories.

Conclusion: The common coping strategies employed by the students to handle stress was approach, which was associated with better outcomes and a more stable emotional response. In spite of this, a vast number of students have reported to experience stress. Therefore, there is a need to teach more effective coping strategies to handle stress and demands of their profession without comprising their service and health.

References

1. Ghosal K, Behera A. Study on prevalence of stress in medical students. J Res Med Dent Sci. 2018; 6:182-186.
2. Awoke M, Mamo G, Abdu S, Terefe B. Perceived Stress and Coping Strategies Among undergraduate Health Science students of Jimma University Amid The COVID-19 Outbreak: Online Cross-Sectional Survey. Front Psychol. 2021;12:639955.
3. Canestrari C, Bongelli R, Fermani A, Riccioni I, Bertolazzi A, Muzi M et al. Coronavirus disease stress among Italian healthcare workers: The role of coping humor. Front Psychol. 2021;11:601574.
4. Maydych V, Claus M, Watzl C, Kleinsorge T. Attention to Emotional Information Is Associated With Cytokine Responses to Psychological Stress. Front Neurosci. 2018; 12:687
5. Fratta IL, Tatangelo R, Campagna G, Rizzuto A, Franceschelli S, Ferrone A et al. The plasmatic and salivary levels of IL-1β, IL-18 and IL-6 are associated to emotional difference during stress in young male. Sci Rep. 2018; 8:3031.
6. Chen JY, Chin WY, Tiwari A, Wong J, Wong ICK, Worsley A et al. Validation of perceived stress scale in medical and health sciences students in Hong Kong. Asia Pac Sch. 2021;6(2):31-37
7. Carver CS. You want to measure coping but your protocol's too long: consider the brief COPE. Int J Behav Med. 1997;4(1):92-100.

8. Dineshkumar T, Ashwini BK, Rameshkumar A, Rajashree P, Ramya R, Rajkumar K. Salivary and serum Interleukin – 6 levels in oral premalignant disorders and Squamous Cell Carcinoma: Diagnostic value and Clinicopathologic Correlations. Asia Pac J /cancer Prev. 2016;17(11):4899-4906
9. Nivetha BM, Ahmed M, PB. Perceived stress and source of stress among undergraduate medical students of Government Medical College, Mysore International Journal of Community Medicine and Public Health. Int J Community Med Public Health. 2018; 5(8):3513-3518.
10. Shadid A, Shadid A M, Shadid A, Almutairi FE, Almotairi KE, Aldarwish T et al. Stress, Burnout, and Associated Risk Factors in Medical Students. Cureus. 2020;12(1): e6633.
11. Amr M, Hady El Gilany A, El-Hawary A. Does gender predict medical students' stress in Mansoura, Egypt? Med Educ Online. 2008;13:12.
12. Das PPP, Sahoo R. Stress and depression among post graduate students. Int J Sci Res Public. 2012;2:1–5.
13. Saravanan C, Wilks R. Medical students' experience of and reaction to stress: the role of depression and anxiety. Sci World J. 2014;2014:737382.
14. Supe AN. A study of stress in medical students at Seth G.S. Medical College. J Postgrad Med. 1998;44(1):1-6.
15. Sherina MS, Rampal L, Kaneson N. Psychological stress among undergraduate medical students. Med J Malaysia. 2004;59(2):207-11.
16. Shaikh BT, Kahloon A, Kazmi M, Khalid H, Nawaz K, Khan N et al. Students, stress and coping strategies: a case of Pakistani medical school. Educ Health (Abingdon). 2004;17(3):346-53.
17. Yusoff MSB, Jie TY, Esa AR. Stress, stressors and coping strategies among house officers in a Malaysian Hospital. ASEAN J Psychiatr. 2011;12(1).
18. Abdulghani HM, Irshad M, Al Zunitan MA, Al Sulihem AA, Al Dehaim MA, Al Esefir WA et al. Prevalence of stress in junior doctors during their internship training: a cross-sectional study of three Saudi medical colleges' hospitals. Neuropsychiatr Dis Treat. 2014;10:1879–1886.
19. AlJaber MI, Alwehaibi AI, Algaeed HA, Arafah AM, Binsebayel OA. Effect of academic stressors on eating habits among medical students in Riyadh, Saudi Arabia. J Family Med Prim Care. 2019;8(2):390-400.
20. Kathapillai M. Awareness about yoga asana and its benefits among undergraduate medical students: A descriptive study. Int J Yoga Physiotherapy Physical Educ. 2019;4:2:20-23.
21. Ashton CH, Kamali F. Personality, lifestyles, alcohol and drug consumption in a sample of British medical students. Med Educ 1995; 29:187-92.
22. Guthrie E, Black D, Bagalkote H, Shaw C, Campbell M, Creed F: Psychological stress and burnout in medical students: a 5-year prospective longitudinal study. J Roy Soc Med 1998, 91(5):237-243.
23. Ragab EA, Dafallah MA, Salih MH, Osman WN, Osman M, Miskeen E et al. Stress and its correlates among medical students in six medical colleges: an attempt to understand the current situation. Middle East Curr Psychiatr 2021; 28:75.
24. Fadhel SB, Adawi, TR. Perceived stress and coping strategies among University students. Eur. J. Res. Med. Sci.2020; 8 :19–25
25. Yikealo, D., Tareke, W. Stress Coping Strategies among College Students: A Case in the College of Education, Eritrea Institute of Technology. Open Sci J. 2018; 3: 10.
26. Bamuhair SS, Farhan AA, Althubaiti A, Agha S, Rahman SU, Ibrahim NO. Sources of Stress and Coping Strategies among Undergraduate Medical Students Enrolled in a Problem based Learning Curriculum. J Biomed Educ. 2015; 1-8.
27. Dijkstra, M., and Homan, A. C. Engaging in rather than disengaging from stress: effective coping and perceived control. Front. Psychol. 2016; 7:1415.
28. Melaku L, Bulcha G. Evaluation and Comparison of Medical Students Stressors and Coping Strategies among Undergraduate Preclinical and Clinical Year Students Enrolled in Medical School of Arsi University, Southeast Ethiopia. Educ Res Int. 2021; 1-12.
29. Datar MC, Shetty JV, Naphade NM. Stress and Coping Styles in Postgraduate Medical Students: A Medical College – based study. Indian J Soc Psychiatry 2017;33:370-4.
30. Dodek PM, Culjak A, Cheung EO, Hubinette MM, Holmes C, Schrewe B et al. Active coping in medical students is associated with less burnout and higher resilience. Am. J. Respir. Crit. Care Med. 2019; 199:A4300
31. Abouammoh N, Irfan F, Alfaris E. Stress coping strategies among medical students and trainees in Saudi Arabia: a qualitative study. BMC Med Educ 2020;20(1):124
32. Mohammed SB, Edan BJ, Al-Sultani AJM, Kitab MA. Effect of exam stress on salivary IL-6 in healthy students. Medical J of Babylon 13; 4:786-790
33. Vernaza P, Chavarria J, Dueñas R, Niño V, Ávila G, Klínger J et al. Relationship between perceived academic stress and Interleukin 6 levels in health students. Ciencia e Innovación en Salud. 2020; 68:1-19
34. Izawa S, Sugaya N, Kimura K, Ogawa N, Yamada KC, Shirotsuki K, et al. An increase in salivary interleukin-6 level following acute psychosocial stress and its biological correlates in healthy young adults. Biol Psychol. 2013; 94(2):249-54.

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Conflict of Interest Statement & Funding

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Author Contributions

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Original Article

The Impact of the COVID-19 Lockdown on Cancer Referrals in Primary Care in the UK: Two Years On

Olivia Whittle,[1] Lucy Bushby,[2] Rebecca Chambers,[3] Jayden Gittens.[4]

Abstract

Background: Cancer is common, with most cancer patients presenting initially to a general practitioner. The COVID-19 pandemic led to changes in the delivery of primary care, which could have affected cancer referrals. This observational study looked at two-week cancer referrals (2WRs) made before, during and after the first UK COVID-19 lockdown in 2020, at a GP practice in the Wirral, England. **Methods:** A search was conducted to find the cancer referrals made between 23rd March 2020 - 1st July 2020, during the first lockdown. Using the same methodology, cancer referral data was collected for the corresponding time periods in 2019 and 2021. The number of 2WRs and positive diagnostic yields were then compared. **Results:** The number of cancer referrals decreased by 40.4% in 2020, compared to 2019. In 2021, the number of referrals then increased by 225%, compared to 2020. Overall, the number of cancer referrals increased between 2019-2021. The positive diagnostic yield for the 2020 2WRs increased by 251.4%, compared to that of 2019. The calculated yield for the 2021 data then decreased by 10.8% compared to 2020. Overall, the positive diagnostic yield increased between 2019-2021. **Conclusion:** The numbers and outcomes of cancer referrals at this Wirral GP practice have changed considerably following the first UK COVID-19 lockdown in 2020, and the influence of the pandemic was still affecting cancer referrals in 2021. A greater focus on early cancer detection in primary care could help overcome the ways in which the pandemic has affected primary care delivery.

Introduction

Around one in three people in the UK will develop cancer in their lifetime.[1] The detection of people who have a possible cancer mainly happens in primary care, because most patients present initially to a primary care clinician.[1]

UK cancer referral guidelines have been developed using a "risk threshold" – if there is a high enough risk that a symptom is being caused by a cancer, then a referral is justified.[1] For an urgent cancer referral in England, the patient should be investigated for cancer within two weeks of presenting to their GP with their symptom(s). Scotland, Wales and Northern Ireland have slightly different timeframe limits compared to England with regards to how soon cancer referral patients should be investigated for cancer. However, throughout the UK, patients referred down the urgent cancer referral pathway will be seen by a specialist as soon as possible.[2]

The beginning of the COVID-19 pandemic led to a decrease in the number of routine GP patient consultations.[3] Following the announcement of a UK national lockdown on 23rd March 2020,[4] the Royal College of General Practitioners published data showing that there had been a shift in primary care delivery - about 70% of patients were receiving remote GP care, rather than face-to-face.[3] This could have had substantial implications to many aspects of patient care, including cancer referrals.

The aim of this study is to look at the differences in two-week cancer referrals (2WRs) made before, during and after the first UK COVID-19 lockdown at a GP practice in Birkenhead, Wirral, England. Contrasting the number of 2WRs made, as well as the outcomes of patients' investigations following their referrals, should help demonstrate some of the consequences that this pandemic has had on patients' health outcomes.

Methods

Study Design and Data Collection

The design of this study was an observational study, looking at three separate data sets in 2019, 2020 and 2021, respectively. The data was collected by searching and reading through patient notes at a Wirral GP practice:

A search was carried out on 'EMIS' (Egton Medical Information Systems), which is a healthcare technology provider used in primary care in the UK.[5] The search was to find all the 2WRs that were made at the Wirral GP practice in question, during the time period between 23rd March 2020 - 1st July 2020 (at the time that the UK was in its first COVID-19 lockdown[6]).

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Each patient from this collected data set was individually searched on 'EMIS' to look at their 2WR in more detail. 'Docman', which is a clinical correspondence software,[7] was then used to read through the subsequent clinical letters sent regarding each patient, to follow the timeline of investigations resulting from their initial referral, to determine whether each 2WR patient ultimately was, or was not, diagnosed with cancer.

Inclusion / Exclusion Criteria

Every patient's two-week referral was reviewed and the following were excluded:

- Any 2WR patient whose records were not accessible (e.g. inactive patient record on 'EMIS'), as the outcome of their referral could not be determined.
- Any patient whose 2WR led to a positive cancer diagnosis, but who had already previously been diagnosed with this same cancer. The reason these 2WRs were excluded was because this paper is looking at new cancer diagnoses only. The effect of the pandemic cannot not be studied by looking at old cancer diagnoses, where the initial diagnosis was made before the first COVID-19 lockdown
- Any 2WR where the patient was lost to follow-up.
- Any 2WR that was rejected.
- Any 2WR where the patient was incorrectly referred i.e. if the patient being referred did not have a suspected cancer.

Data Analysis

After the application of this criteria, a positive diagnostic yield was calculated to determine the proportion of 2WRs that led to a positive cancer diagnosis. The positive diagnostic yield was calculated by dividing the number of positive cancer diagnoses by the total number of 2WRs. The result of this calculation was multiplied by 100, to give a percentage.

The same methods were then used to collect data for the 2WRs for the same time periods, but in 2019 and 2021, in order to make comparisons.

The 2WR data collected for this study was scrutinized in terms of its validity, before conclusions were made. During this process, it was considered whether bias could have had any effect on the results, or whether this had been avoided.

The aim of the specific exclusion criteria was to avoid any ambiguity with regards to which cancer referrals should be included in this data set. In this way, sampling bias should not have affected which referrals were used in this study. As well as this, the intention of the systematic approach in the methods of this study was to prevent observer bias affecting the data being collected. This study's methods involved specifying the quantitative data that needed to be collected for each patient (number of 2WRs; positive/negative cancer diagnosis). In this way, the data collection process did not involve interpreting any subjective information, avoiding observer bias from influencing the data collection process. Furthermore, the fact that this paper received no financial support can categorically rule out the possibility that funding bias could have skewed the results of this study.

Results

The diagnostic outcomes and reasons for excluding certain referrals in each data set are summarized in Tables 1 and 2, respectively.

Table 1 displays the total number of 2WRs, the number included after applying exclusion criteria, the number of positive cancer diagnoses, and the positive diagnostic yield for each year studied. For the 2019 data set, there were a total of 117 2WRs during the time period between 23rd March – 1st July. Once the exclusion criteria had been applied, 114 2WRs were included in the 2019 data set. Out of these 114 referrals, 8 of the patients were found to have received a positive cancer diagnosis, giving a positive diagnostic yield of 7%.

For the 2020 data set, there were a total of 75 2WRs during the time period between 23rd March – 1st July. Once the exclusion criteria had been applied, a total of 68 2WRs were included in the 2020 data set. Of these 68 referrals, 12 patients were found to have received a positive cancer diagnosis, giving a positive diagnostic yield of 17.6%.

For the 2021 data set, there were a total of 172 2WRs during the time period between 23rd March – 1st July. Once the exclusion criteria had been applied, a total of 153 2WRs were included in the 2021 data set. Of these 153 referrals, 24 patients were found to have received a positive cancer diagnosis, giving a positive diagnostic yield of 15.7%.

Table 1. **Diagnostic Outcomes for the 2WRs Made in the Time Period Between 23rd March 2019 – 1st July for the 2019, 2020 and 2021 Data Sets.**

	2019	2020	2021
Total referrals	117	75	172
Included referrals	114	68	153
Positive cancer diagnoses	8	12	24
Positive diagnostic yield (%)	7	17.6	15.7

Table 2 outlines the reasons for excluding certain 2WRs from each year's data set. The exclusions were due to inaccessible patient records, prior diagnosis of the same cancer, patients lost to follow-up, rejected referrals, or incorrect referrals where the patient was not suspected of having cancer. Notably, the number of patients lost to follow-up increased in 2021 compared to previous years.

Figure 1 illustrates the changes in the number of 2WRs over the three years studied. The number of 2WRs decreased by 40.4% in 2020, compared to 2019. In 2021, the number of 2WRs then increased by 225%, compared to 2020. Overall, the number of 2WRs increased by 34.2% between 2019-2021. Put simply, the

number of 2WRs made was higher after the lockdown, in 2021, than before the lockdown, in 2019.

Figure 2 depicts the positive diagnostic yields calculated for each year. The positive diagnostic yield for the 2020 2WRs increased by 251.4%, compared to that of 2019. The calculated yield for the 2021 data then decreased by 10.8% compared to 2020. Overall, the positive diagnostic yield increased by 224.3% between 2019-2021. The positive diagnostic yield was higher after the lockdown, compared to before.

***Table 2*. Justification for Each 2WR that was Excluded in the 2019, 2020 and 2021 Data Sets.**

	2019	2020	2021
Patient records were not accessible	0	3	2
Patient had already previously been diagnosed with the same cancer	0	3	4
Patient was lost to follow-up	2	1	12
2WR was rejected	1	0	0
Incorrect 2WR – patient was not referred for a suspected cancer	0	0	1

***Figure 1*. The Difference Between the Number of 2WRs Made in the 2019, 2020 and 2021 Data Sets.**

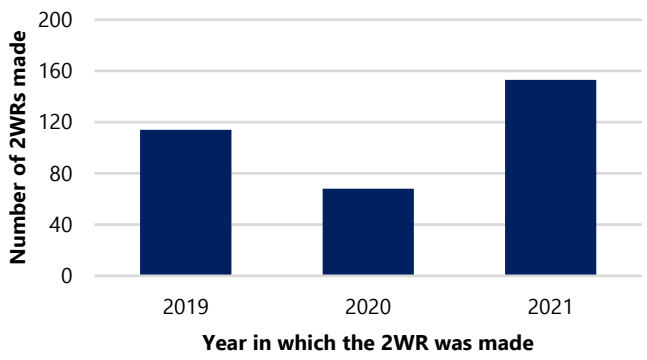
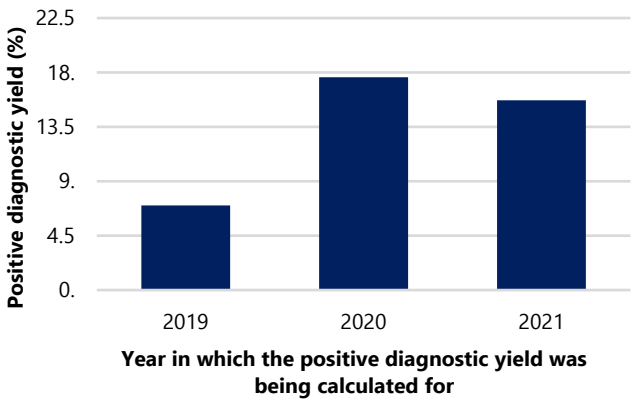


***Figure 2*. The Difference Between the Positive Diagnostic Yields Calculated for the 2019, 2020 and 2021 Data Sets.**



Discussion

The results of this study have demonstrated two key findings. Firstly, the number of 2WRs decreased from 2019 to 2020, before more than doubling from 2020 to 2021. As well as this, the positive diagnostic yield increased from 2019 to 2020, and then slightly reduced in 2021.

With regards to the decrease in the number of 2WRs made in the 2020 data set, compared to that of 2019 - there could be several reasons for this change.

The COVID-19 pandemic led to a "decline in routine patient consultations" in primary care.[3] Aside from the main purpose of their appointment, routine consultations provide patients with an opportunity to speak to their doctor about any other health concerns they may have. The decrease in these routine appointments during lockdown[3] could have reduced the number of opportunities for doctors to pick up on their patients' red flag symptoms (symptoms suggesting more serious pathology[8]), which could have decreased the number of 2WRs being made.

2020 also saw a shift to remote GP care with data from the Royal College of General Practitioners published in April 2020 showed that, at that time, the majority of consultations were being delivered remotely. This same publication showed how, in March/April 2019, the majority of GP care was face-to-face.[3] This transition to remote GP care could have changed the rapport between patients and their GPs - doctors weren't seeing their patients in person, so could have missed some patients' signs or symptoms that would warrant a 2WR.

For example, unexplained weight loss is considered a red flag for malignancies.[9] If a doctor is speaking to a patient over the phone, rather than face-to-face, they won't notice that the patient has lost weight, and may therefore be less inclined to ask the patient about any weight changes. In this way, over-the-phone consultations could have meant that opportunities were missed for patients' red flag symptoms to be noticed. It follows that this may have also contributed to the reduction in the number of 2WRs that were made in 2020, compared to 2019.

As well as changes in GP care delivery, there could also be patient factors that may have led to fewer 2WRs. For example, some patients may have feared leaving the house during the pandemic,[10] or may have falsely believed that GP surgeries were closed.[11] The reduction in the number of 2WRs seen in the 2020 data set could therefore be a result of a combination of doctor and patient factors associated with the lockdown.

This Wirral GP practice's data follows a national trend of a decrease in 2WRs during the first COVID-19 lockdown: a paper by Watt et al. demonstrated that, in England, "primary care consultations per person fell from an average of 4.1 before mid-March in 2020 to 3 consultations per person per year (around a 30% reduction) the week after the introduction of lockdown at the end of March." The same paper also found that, "from the middle of March to the end of June there were 43% fewer 2-week wait referrals than in the same weeks in 2019."[12] This Wirral study

therefore adds to a body of evidence that the COVID-19 lockdown affected cancer referrals.

A more recent study by Watt et al. looked at how deprivation influenced the reduction in the detection of new cancers since the beginning of this pandemic. The results showed that the poorest areas had the greatest reduction in the number of 2WRs.[13]

The relevance of Watt et al.'s findings to this Wirral observational study is that this study was done in a GP practice in Birkenhead, where there is a high index of multiple deprivation.[14] The GP practice is in an area which is in the second most deprived decile in the country.[15] Perhaps an area of further research to contextualise this study's findings would be to repeat the same study but in a more affluent area in the Wirral. There is considerable disparity in affluence across the different areas in the Wirral,[16] so this would be a good location to compare how deprivation affects health outcomes such as cancer referrals. Such research would give a better idea as to how the inverse care law[17] affected cancer detection during the pandemic.

Perhaps, during this pandemic, there have been particular factors in more deprived areas that are affecting cancer detection rates more so than in other areas. One suggestion could be to focus resources in such areas to hopefully tackle the barriers that these communities are facing where cancer detection is concerned.

With regards to the results from the 2021 data, there was a substantial increase in the number of 2WRs, compared to both the 2019 and 2020 data. The number of 2WRs more than doubled in the 2021 data compared to 2020 - there may have been influencing factors, following the easing of lockdown restrictions,[6] that contributed to this change.

The pandemic has led to a "growth in remote consultations" which "has allowed for a substantial increase in the number of overall consultations."[18] It therefore follows that, if GPs are having more patient consultations overall, the number of cancer referrals would proportionately increase, too. Perhaps this was a contributing factor to the increase in cancer referrals seen in this study in 2021 (following the easing of lockdown restrictions[6]), compared to 2020.

Another suggestion is that patients who feared leaving the house during the pandemic[10] felt more comfortable visiting their GP in 2021, compared to 2020. The cohort study by Williams et al. done during the pandemic suggested that there could be a "rebound in future workload" following the lifting of COVID restrictions.[19] Perhaps the increase in 2WRs in 2021 was as a result of this anticipated 'rebound,' therefore.

With regards to the positive diagnostic yields - various inferences could be made about the difference in percentages calculated. The National Institute for Health and Care Excellence (NICE)'s two-week referral guidelines use parameters that have a ≥3% positive predictive value,[1] which would mean that at least 3% of all patients referred (based on a particular parameter) would receive a confirmed cancer diagnosis. The positive diagnostic yield for both the 2019, 2020 and 2021 data sets from the above results are considerably higher than this 3% set out in the NICE guidelines. It could be argued that this demonstrates a successful implementation of the two-week referral pathway, where doctors were referring the right kind of patients down each two-week pathway accordingly. Alternatively, it could be the case that doctors were not referring enough patients who have red flag symptoms of a lower predictive value, whose 2WR would be less likely to lead to a cancer diagnosis.

However, the fact that the positive diagnostic yield in the 2020 data increased by more than two-fold compared to the same time period in 2019, suggests that there was a change in the type of patients that were being referred down the two-week referral pathways during the first COVID-19 lockdown.

A poll by NHS England revealed in April 2020 that "four in ten people" were "too concerned about being a burden on the NHS to seek help from their GP."[20] One hypothesis is that, during the COVID-19 lockdown, patients were more reluctant to go to their GP unless they had symptoms that they were very worried about, because patients were not wanting to bother the perceived busy NHS. Hence, perhaps the proportion of 2WR patients who received a negative cancer diagnosis in 2020, during lockdown, decreased because patients with more benign symptoms simply weren't going to their GP about it.

This increase in the positive diagnostic yield in the 2020 data set adds to the current evidence base,[12,13,19] by showing in more detail how the COVID pandemic has potentially affected cancer diagnoses, compared to another similar study in this field. A retrospective cohort study of general practices in Salford by Williams et al. showed that the gap between observed and expected cancer diagnoses between March 1 and May 31, 2020 was not statistically significant.[19] This study at the Wirral GP practice showed a considerable increase in the proportion of 2WRs that led to a positive cancer diagnosis in the 2020 referrals, compared to 2019. Furthermore, this study collected data over a three-year period, whereas Williams et al. collected data over a three-month period. This paper has therefore helped by allowing us to get a better idea of how the pandemic has affected cancer diagnoses, over a larger period of time, in a field where there is no clear relationship between COVID-19 and cancer referrals.

With regards to the positive diagnostic yield calculated in 2021, the results showed that it was 10.8% lower than that of 2020. However, the 2021 diagnostic yield was still more than double that of the 2019 positive diagnostic yield.

Perhaps it was the case that, those who were "too concerned about being a burden on the NHS to seek help from their GP"[20] in 2020, felt more comfortable booking a GP appointment in 2021, following the easing of lockdown restrictions.[6] It could be that, in 2021, patients were going to their GP about less worrying symptoms, whereas in 2020 patients were less likely to go to see their GP unless they had very worrying symptoms. This could be why the positive diagnostic yield decreased in 2021, compared to 2020, because the proportion 2WR patients having sinister pathology decreased.

The positive diagnostic yield in 2021 only decreased by 10.8%, however, compared to 2020, representing only a small change. The 2021 positive diagnostic yield still remained considerably higher than the pre-pandemic diagnostic yield for the 2019 data. This demonstrates how the proportion of 2WR patients in 2021 that resulted in cancer diagnoses was still much higher than that of 2019, and indeed the national average of 3%.[1]

This finding shows how fewer patients with benign pathology are being referred along the two-week referral pathways than before the pandemic, even after lockdown restrictions eased in 2021.[6] This could be associated with the "growth in remote consultations" since the pandemic.[18] The fact that a greater proportion of patients were being seen face-to-face in 2019, compared to 2021,[18] could be why there are still differences in the types of patients being referred down cancer pathways.

This increase in remote consultations seems to be a more permanent change following the pandemic, as the number of remote consultations has not decreased back to pre-pandemic levels following the lifting of lockdown restrictions.[6, 18] The ways in which red flag symptoms are identified during virtual consultations should be considered, therefore, moving forwards.

Future Applications

A future application of this study's finding could be to increase public awareness of red flag symptoms. Some vulnerable patients still feared COVID-19 in 2021, despite the shift to a 'new normal'[21] - hopefully, those that are still reluctant to visit their GP because of the current pandemic will be more likely to contact their doctor about potential cancer symptoms, if their awareness of red flag symptoms increased. It could be suggested, therefore, that GPs could increase their cancer detection rates during this pandemic by increasing their cancer health promotion.

It was mentioned earlier that the poorest areas had the greatest reduction in the number of 2WRs during lockdown.[13] Perhaps it was the case that, in more deprived communities, the awareness of red flag symptoms was lower. According to Public Health England, "people with limited financial and social resources are more likely to have limited health literacy."[22] It could be suggested that, having population-specific approaches to raising awareness of red flag symptoms in deprived communities could help bridge this gap. Such approaches could include "ensuring that health materials are clear and concise"[23-27] as well as "using trained community workers or health champions to relay health messages."[22]

It would be useful to carry out further studies following such future applications, to determine how effective these measures have been. For example, it would be interesting to see whether the positive diagnostic yield would decrease at all after increasing public awareness of red flag symptoms.

Strengths and Limitations

This paper's findings have enabled the aim of this study to be well-achieved, with regards to looking at numbers of 2WRs made, as well as investigation outcomes of the referrals (cancer diagnosis/no cancer diagnosis). By comparing the time period of the first COVID-19 lockdown to the exact same dates but different years, this study allowed the effect of the lockdown to be looked at more closely. If the 2WRs for different months were to be studied, for example, it might have been harder to determine whether the differences between the data sets were just due to variations during different times of the year, or whether it was the effect of lockdown.

However, the aim could have been better achieved if the investigation results of the cancer referrals had been looked at in closer detail. Perhaps further studies into e.g. what stage each cancer was at diagnosis in the different data sets, would allow us to look at the effect of the lockdown on cancer referrals in even closer detail, by comparing the prognosis of the patients that were diagnosed with cancer in the different data sets.

Another way of looking at the cancer referrals in more detail would be to look at whether certain referral pathways were affected more than others by the lockdown. It would be valuable to find out whether there were particular factors that led to the lockdown affecting some cancer referral pathways more so than others. This would help to give a better idea of what sort of future applications would be most effective, with regards to improving the detection of cancer in primary care. It would help to indicate which cancer referral pathways should perhaps be focused on, helping to determine which particular areas of the healthcare system to allocate extra resources to.

Since the positive diagnostic yields have been calculated as percentages, the potential inaccuracies of these calculated proportions should be considered. The data was collected by reading through the patients' notes - this study was therefore reliant on the patients' documents being correct and detailed enough, as well as being uploaded in a timely manner. The use of such qualitative data, rather than quantitative, in this study could be considered a weakness by some, however there was no alternative way of determining which patients' referrals led to a cancer diagnosis.

It is also important to consider the effect that excluding some of the referrals may have had on the results. The proportion of 2WRs that were excluded from each of the three data sets, respectively, was different. It could be argued that this may have skewed the results slightly.

The relatively large sample sizes used in this observational study should mean, however, that such factors would have less of an impact on the overall findings, compared to if smaller sample sizes had been used. This gives further confidence that the established differences found between the data sets are valid.

It therefore seems plausible to suggest that the considerable increase in the positive diagnostic yield of 2WRs in 2020, compared to 2019, was more likely to be related to the influence of the lockdown, rather than any limitations in the data.

Conclusion

Overall, this study's findings have shown a striking change in the numbers and outcomes of cancer referrals at this Wirral GP practice following the implementation of the first UK COVID-19 lockdown.[4] The 2021 data has demonstrated that the influence of the pandemic is still affecting cancer referrals, despite the easing of lockdown restrictions.[6] Although more such audits at other GP practices would validate this paper's findings further, it can be concluded from this study that it would be beneficial to put even more of a focus on early cancer detection in primary care, whilst GPs are still seeing a lower proportion of their patients face-to-face compared to before the pandemic.[18]

Summary – Accelerating Translation

Title: The Impact of the COVID-19 Lockdown on Cancer Referrals in Primary Care in the UK: Two Years On

Main Problem to Solve:

The COVID-19 pandemic led to a change in the delivery of primary care. This shift in primary care delivery could have had significant implications to many aspects of patient care, including cancer referrals. Understanding how cancer referrals have been affected could help us improve cancer detection moving forwards, as we adapt to a 'new normal.'

Aims of the Study:

To look at the differences in two-week cancer referrals (2WRs) made before, during and after the first UK COVID-19 lockdown at a GP practice in Birkenhead, Wirral, England. Contrasting the number of 2WRs made, as well as the outcomes of patients' investigations following their referrals, should help demonstrate some of the consequences that this pandemic has had on patients' health outcomes.

Methodology:

- A search was carried out to find all the 2WR's that were made between 23rd March 2020 - 1st July 2020.
- The subsequent clinical letters sent regarding each patient's 2WR were then read. This method was used to determine the outcome of every 2WR made between 23rd March 2020 – 1st July 2020 at the Wirral GP practice, to determine whether each 2WR patient ultimately was, or wasn't, diagnosed with cancer.
- Once every patient's 2WR had been reviewed in this way, it was decided which referrals from the initial data set should not be included in this audit, using exclusion criteria.
- After the application of the exclusion criteria, the remaining 2WR patients were included in the data set for further analysis. A positive diagnostic yield could then be calculated, to represent the proportion of 2WR's that led to a positive cancer diagnosis in the time period between 23rd March 2020 - 1st July 2020.
- The same method was used to study 2WR's made during the same time period, but in 2019 and 2021.

Results:

- The number of 2WRs decreased by 40.4% in 2020, compared to 2019. In 2021, the number of 2WRs then increased by 225%, compared to 2020.
- Overall, the number of 2WRs increased by 34.2% between 2019-2021. The number of 2WRs made was higher after the lockdown, in 2021, than before the lockdown, in 2019. Put simply, the number of 2WRs made was higher after the lockdown, in 2021, than before the lockdown, in 2019.
- The positive diagnostic yield for the 2020 2WRs increased by 251.4%, compared to that of 2019. The calculated yield for the 2021 data then decreased by 10.8% compared to 2020.
- Overall, the positive diagnostic yield increased by 224.3% between 2019-2021: the positive diagnostic yield was higher after the lockdown, compared to before.

Conclusion:

This study's findings show a striking change in the numbers and outcomes of 2WRs in primary care following the implementation of the first COVID-19 lockdown. Even more of a focus on early cancer detection in primary care would be beneficial, following the shift from face-to-face to virtual GP consultations since the beginning of the pandemic.

References

1. National Institute for Health and Care Excellence. Suspected cancer: recognition and referral. Available from: https://www.nice.org.uk/guidance/ng12. Last updated December 15, 2021; cited October 8, 2022.
2. Cancer Research UK. Cancer waiting times. Available from: https://www.cancerresearchuk.org/about-cancer/cancer-in-general/cancer-waiting-times. Last updated July 20, 2022; cited December 1, 2022.
3. Royal College of General Practitioners. Around 7 in 10 patients now receive GP care remotely in bid to keep patients safe during pandemic, says RCGP. Available from: https://www.rcgp.org.uk/News/Remote-care-rates. Last updated April 30, 2020; cited May 3, 2021.
4. GOV.UK. Prime Minister's statement on coronavirus (COVID-19): 23 March 2020. Available from: https://www.gov.uk/government/speeches/pm-address-to-the-nation-on-coronavirus-23-march-2020. Last updated March 23, 2020; cited May 3, 2021.
5. EMIS. About us. Available from: https://www.emishealth.com/about-us. Last updated: April, 2022; cited October 8, 2022.
6. Institute for government. Timeline of UK government coronavirus lockdowns and restrictions. Available from: https://www.instituteforgovernment.org.uk/charts/uk-government-coronavirus-lockdowns. Last updated December, 2021; cited October 11, 2022.
7. Docman. About Docman. Available from: https://www.docman.com/about-docman/. Last updated 2022; cited October 11, 2022.
8. GPonline. Red flag symptoms A-Z. Available from: https://www.gponline.com/education/medical-red-flags. Last updated September 21, 2022; cited October 11, 2022.
9. BMJ Best Practice. Assessment of unintentional weight loss. Available from: https://bestpractice.bmj.com/topics/en-gb/548. Last updated June 21, 2022; cited October 22, 2022.
10. Which? News. Coronavirus has left many older people too afraid to leave the house. Available from: https://www.which.co.uk/news/article/coronavirus-has-left-many-older-people-too-afraid-to-leave-the-house-akDgc6d2OKIF. Last updated October 22, 2020; cited May 3, 2021.
11. GPonline. Viewpoint: False claims about GP access must be challenged - or practices really will close. Available from: https://www.gponline.com/viewpoint-false-claims-gp-access-challenged-practices-really-will-close/article/1716101. Last updated May 18, 2021; cited October 11, 2022.

12. The Health Foundation. Use of primary care during the COVID-19 pandemic. Available from: https://www.health.org.uk/news-and-comment/charts-and-infographics/use-of-primary-care-during-the-covid-19-pandemic. Last updated September 17, 2020; cited May 3, 2021.
13. Watt T, Sullivan R, Aggarwal A. Primary care and cancer: an analysis of the impact and inequalities of the COVID-19 pandemic on patient pathways. BMJ Open. 2022;12(3):e059374.
14. Wirral Intelligence Service. Indices of Multiple Deprivation (IMD) 2019 | Deprivation by IMD Quintile and LSOA. Available from: https://app.powerbi.com/view?r=eyJrIjoiNzZmNTA5NTEtNDAxNy00YTAxLWIxOGItY2ExYjk1ZDM3NTN3IiwidCI6IjJjMjVlMGIwLWJkY2YtNDQ2MC1iOTgzLTE5MzczNWM3MTgzYiIsImMiOjh9. Last updated November, 2019; cited October 11, 2022.
15. Office for Health Improvement and Disparities. National General Practice Profiles. Available from: https://fingertips.phe.org.uk/profile/general-practice/data#page/12/gid/1938133086/pat/167/par/E38000208/ati/7/are/N85051/yrr/1/cid/4/tbm/1. Last updated 2022; cited October 15, 2022.
16. Public Health England. Health inequalities slides Wirral. Available from: https://www.wirralintelligenceservice.org/media/3120/inequalities-slides-wirral-jan-2020-1.pdf. Last updated January, 2020; cited October 11, 2022.
17. Tudor Hart J. The Inverse Care Law. The Lancet. 1971;297(7696):405-12
18. Green MA, McKee M, Katikireddi SV. Remote general practitioner consultations during COVID-19. The Lancet Digital Health. 2022;4(1):e7.
19. Williams R, Jenkins DA, Ashcroft DM, Brown B, Campbell S, Carr MJ, et al. Diagnosis of physical and mental health conditions in primary care during the COVID-19 pandemic: a retrospective cohort study. Lancet Public Health. 2020;5(10):e543-e50.
20. NHS England. Help us help you: NHS urges public to get care when they need it. Available from: https://www.england.nhs.uk/2020/04/help-us-help-you-nhs-urges-public-to-get-care-when-they-need-it/. Last updated April 25, 2020; cited May 3, 2021.
21. Şentürk S, Yıldırım Keskin A, Sarızayim Ş. The Relationship Between the Fear of COVID-19 in the Elderly Aged 65 Years and Over and Their Levels of Adaptation to the "New Normal": A Cross-Sectional Study. OMEGA - Journal of Death and Dying. 2021:00302228211054315.
22. Public Health England. Local action on health inequalities. Improving health literacy to reduce health inequalities. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/460710/4b_Health_Literacy-Briefing.pdf. Last updated September, 2015; cited October 11, 2022.
23. Paasche-Orlow MK, Riekert KA, Bilderback A, Chanmugam A, Hill P, Rand CS, et al. Tailored education may reduce health literacy disparities in asthma self-management. Am J Respir Crit Care Med. 2005;172(8):980-6.
24. Chang LC. [Health literacy: the new outcome indicator for evaluating a health education program]. Hu Li Za Zhi. 2008;55(1):81-6.
25. McCaffery KJ, Dixon A, Hayen A, Jansen J, Smith S, Simpson JM. The influence of graphic display format on the interpretations of quantitative risk information among adults with lower education and literacy: a randomized experimental study. Med Decis Making. 2012;32(4):532-44.
26. Bukman AJ, Teuscher D, Feskens EJM, van Baak MA, Meershoek A, Renes RJ. Perceptions on healthy eating, physical activity and lifestyle advice: opportunities for adapting lifestyle interventions to individuals with low socioeconomic status. BMC Public Health. 2014;14(1):1036.
27. World Health Organization. Physical activity promotion in socially disadvantaged groups: principles for action. Available from: https://www.euro.who.int/__data/assets/pdf_file/0006/193092/PHAN-brochure_ENG.pdf. Last updated 2013; cited October 15, 2022.

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Original Article

A Descriptive Analysis of the Use of Various Therapeutics in a Cohort of COVID-19 Patients and the Influence of Media Coverage

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Abstract

Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) impacted the healthcare system immensely throughout 2020-2022. Treatment practices varied in Texas, as guidelines were in flux. As a result, a variety of therapeutics were used. Many verified medications with scientific basis were trialed, while others were implemented despite a lack of scientific consensus. This study aimed to identify how practice patterns to treat and manage COVID-19 changed over time in a cohort of patients in the University of Texas Medical Branch hospital system. **Methods:** Ninety participants with a COVID-19 diagnosis were included in the analysis for this study. Data was collected by a retrospective chart review, and included medications administered before and during current admission. Medications were categorized as: antiviral, antibiotic, steroid, supplement, antibody, hydroxychloroquine, and others. **Results:** Differences in therapeutic use were identified based on hospitalization status (outpatient or inpatient) and month admitted. The largest difference in the antiviral remdesivir (78%), requiring intravenous administration for up to ten days. In the outpatient setting, antibiotics, primarily azithromycin, were quite common. Additionally, month-to-month variation in steroid use and antibiotic use was observed. **Conclusion:** This study shows that adapting medical guidelines and strong media coverage played a role in the clinical management of COVID-19 patients. At times, some ineffective medications were prescribed such as hydroxychloroquine. Medical leaders and news coverage should collaborate closely in future public health emergencies to prevent the prescription of ultimately ineffective and potentially hazardous treatments.

Introduction

In 2019, a novel coronavirus first identified in Wuhan, China, brought the world to a halt. Severe Acute Respiratory Syndrome (SARS) Coronavirus (CoV)-2 (SARS-COV-2) continues to be a focus of worldwide news as the world slowly emerges from the pandemic of 2020. The broad range of symptomatology of COVID-19, from mild upper respiratory symptoms to severe acute respiratory syndrome and death, added uncertainty and fear that fueled a desperate search for treatment. Clinicians in an overwhelmed healthcare system were pressured to offer therapeutic options without clinical data. While the race to vaccine development was underway, so were other therapies for both hospitalized and clinic outpatients, as poor health outcomes and death was a common occurrence at the pandemic's infancy. By April 2020, an estimated death toll of nearly 200,000 deaths was reported globally. In the interim of global research efforts, certain therapies were administered without proven efficacy. In response to the increasing demand for treatments, the Food and Drug Administration (FDA) issued Emergency Use Authorizations (EUA) to allow the initiation of unproven therapies.

Initially, various treatments were explored in both inpatient and outpatient settings based on anecdotal evidence or *in vitro* data. As clinical experience grew and results of clinical trials became available, acceptance of evidence-based therapies varied and was influenced by clinicians' access to clinical guidelines, popular perception, and patient expectations. As a result, standard of care rapidly changed as coronavirus research elucidated the mechanisms of the virus and the more effective treatment protocols developed over time. However, there was a gap in research as there was no way to track these changes in a methodical fashion, especially in the Texas healthcare system.

This project aimed to report how practice patterns changed over time in a cohort of hospitalized patients in an academic center on the Gulf Coast of Texas. We examined medication prescribing practices based on the type of clinical encounter: outpatient (represented as pre-admission) compared with inpatient (during admission). Finally, we discuss the media's role in influencing which therapies were used.

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Methods

Study Population

Participants were recruited from University of Texas Medical Branch (UTMB) hospitals in Galveston County from March 2020 to June 2021. Subjects consented to participate in either the Observational Protocol for Diseases and Exposures of Public Health Importance or the Clinical Characterization Protocol for Severe Emerging Infections and data was maintained in the UTMB Biorepository for Severe Emerging Infections (BSEI). Eligibility for participation in either protocol included confirmed or suspected infection with a pathogen of interest and English speaking. Consent was provided either by the subject or a legally authorized representative in writing. Only subjects with a confirmed SARS-CoV-2 infection were included in this analysis. No subjects were consented for enrollment for the study in April 2021; therefore, no data is available for this month.

Data Collection and Analysis

Data were collected by retrospective chart review and focused on patients admitted for treatment of COVID-19 infection. Each chart was reviewed by at least two researchers and compiled using REDCap. Medications reported by the patient as taken or prescribed for the current illness before admission were recorded, as well as medications administered during hospital admission based on chart review. Medications reported as outpatient may have been prescribed or recommended by providers outside of the UTMB Health system. Medications were categorized as: antiviral, antibiotic, steroid, supplement, antibody, hydroxychloroquine (HCQ), or other. Antibiotics were only included if administered within the first 48 hours of hospitalization as later treatment could indicate use for a hospital-acquired infection.[1, 2] UTMB participated in the Adaptive COVID-19 Treatment Trial (ACTT) which tested the efficacy of remdesivir.[3] Some study participants were enrolled in ACTT, and the use of remdesivir was counted as intention-to-treat. Disease severity was categorized by the highest oxygen therapy required: mild (no oxygen), moderate (nasal cannula), severe (high-flow nasal cannula, CPAP, BiPAP), and critical (mechanical ventilation, ECMO). The percentage of participants receiving each medication was calculated based on the month of admission to the hospital. Microsoft Excel was used for all calculations.

Results

Characteristics of Study Population

The cohort for this study mimics the population of the hospital catchment area for which patients presented, with a slightly higher proportion of non-Hispanic blacks and a lower proportion of non-Hispanic whites being represented. The cohort was 42% female, and consisted of 27% non-Hispanic blacks, 46% non-Hispanic whites, and 26% Hispanic whites ***Table 1.*** The average age was 56 years with a range of 22-91 years, and the median duration of hospital stay was 7 days (range of 2-56 days). Disease severity from mild to critical were represented in this cohort and one patient was included who was later determined to be in the convalescent stage of disease ***Table 1.***

Table 1. **Characteristics of the Study Population.**

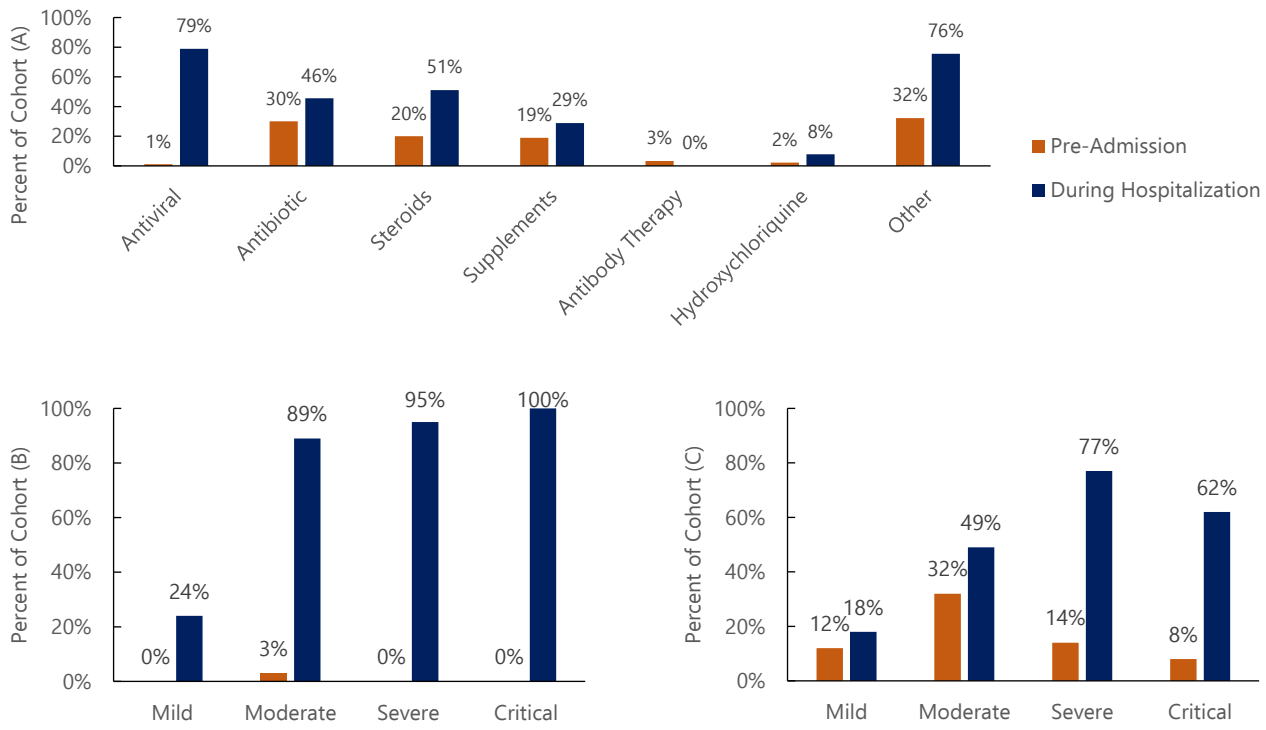
Characteristic	Value
Age (years), mean (range)	56 (22-91)
Total Population (n)	90
Female, n (%)	38 (42)
Race/Ethnicity, n (%)	
Non-Hispanic Black	24 (27)
Non-Hispanic White	41 (46)
Hispanic White	23 (26)
Native Hawaiian/Pacific Islander	1 (1)
Length of Hospitalization (days)	
Median	7
Range	2 - 56
Severity, n (%)	
Mild (no need for Oxygen)	17 (19)
Moderate (NC)	37 (41)
Severe (HFNC, CPAP, BiPAP)	22 (24)
Critical (MV, ECMO)	13 (14)
Convalescent	1 (1)

Legend: The severity of the disease was determined based on the highest oxygen needs during hospitalization. O2 – Oxygen; NC – nasal cannula; HFNC – high flow nasal cannula; CPAP – continuous positive airway pressure ventilation; BiPAP – bilevel positive airway pressure ventilation; MV – mechanical ventilation; ECMO – extracorporeal membrane oxygenation.

Summary of Therapeutic Use in Different Patient Care Settings

There were differences in the therapeutics used to treat COVID-19 infections based on the setting of treatment ***Figure 1A***. All therapeutics examined could be given in either setting, except for remdesivir. Seventy-one (79%) patients in this cohort received or were intended to receive the antiviral remdesivir during their hospitalization. In contrast, the one patient that received an antiviral in the outpatient setting received a neuraminidase inhibitor. Antibiotic, steroid, and supplement use were given in both settings but at a greater rate during hospitalization. Antibiotics were used to treat 41 (46%) participants during hospitalization, compared to 27 (30%) receiving antibiotics pre-admission. Forty-six (51%) of participants received steroids in the inpatient setting, while 18 (20%) received steroids pre-admission. remdesivir was given during hospitalization to all patients categorized with critical disease, and most of those categorized as having moderate or severe disease ***Figure 1B***. Only a quarter of those categorized as having mild disease received remdesivir. Those receiving steroids prior to hospital admission were typically categorized as having moderate disease ***Figure 1C***. Treatment guidelines were followed for those receiving steroids during hospitalization, being given to a large majority of those categorized as having severe or critical disease ***Figure 1C***. Supplements such as vitamin C, vitamin D, and Zinc were given to 17 (19%) and 26 (29%) patients in the outpatient and inpatient setting, respectively. No patients in this cohort received antibody therapy during hospitalization; only 3 received antibody therapy in the outpatient setting. HCQ use was infrequent, 2 patients in an outpatient setting and 7 during inpatient stay. Across all categories, patients in this cohort were more likely to receive treatment when hospitalized than in an outpatient setting.

Figure 1 (A, B, C). **Percentage of Cohort Using Specified Therapeutics Pre-admission (Outpatient) versus During Hospitalization (Inpatient)**



Legend: (A) Use of each therapeutic across entire cohort. (B) Use of antiviral therapy separated by disease severity. (C) Use of steroid therapy separated by disease severity.

Therapeutic Use Over Time in the Outpatient Setting

In March 2020, antibiotics were favored in the outpatient setting ***Figure 2A***. Antibiotic use declined over time and remained low throughout the rest of 2020. Usage increased during January, February, and June 2021, with minimal use the rest of 2021.

Initially, corticosteroid use for treating COVID-19 was debated due to previous concerns after use to treat SARS in 2003. The NIH issued specific guidelines recommending against the use of corticosteroids in non-hospitalized COVID-19 patients. Steroids were used minimally in the outpatient setting from March 2020 to January 2021 ***Figure 2B***. In February and March 2021, there was an increase to 60% of those hospitalized treated with steroids. After this brief increase, few participants received steroids in the outpatient setting. The trend of high steroid use does not correlate with the release of the Randomized Evaluation of COVID-19 (RECOVERY) trial or NIH and IDSA.[4] The results of the RECOVERY trial and inclusion of steroid use in NIH and IDSA guidelines were limited to the inpatient setting. Steroid use was not recommended for outpatient use. The increase in steroid use in early 2021 may have been due to a misunderstanding of guidelines.

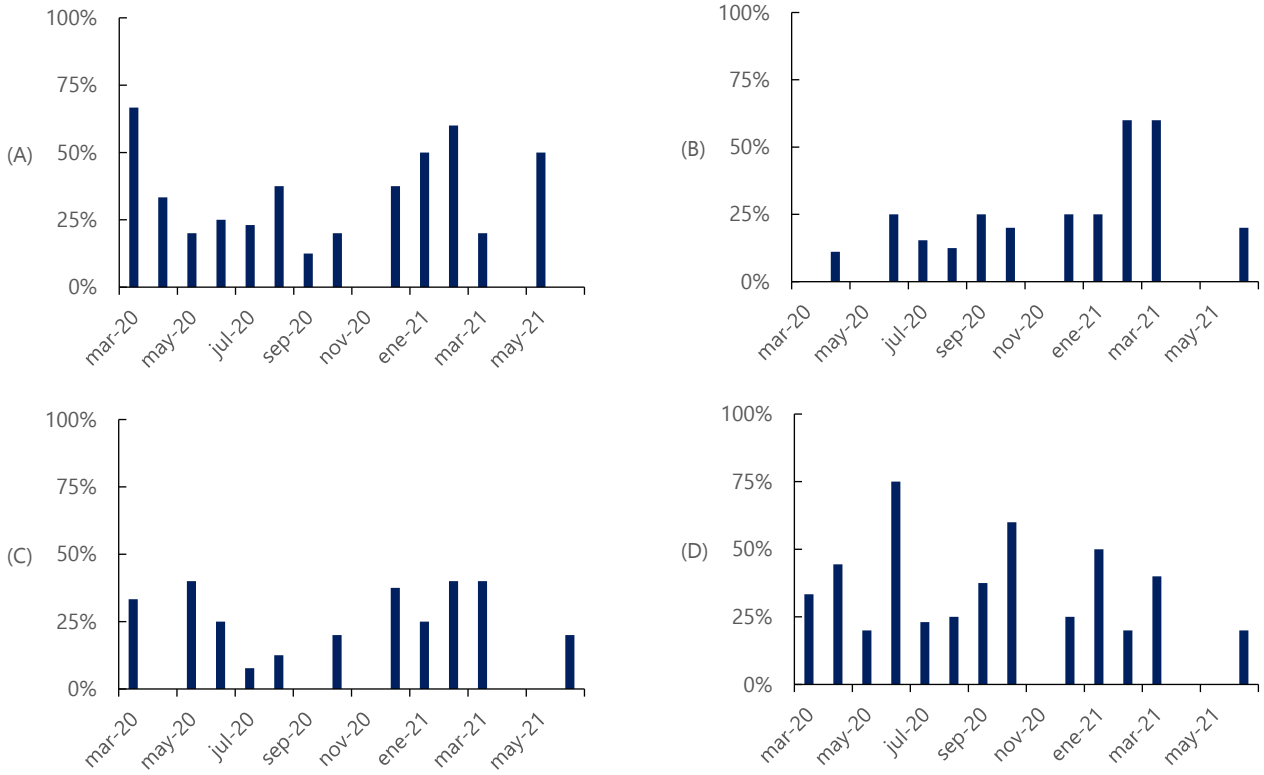
The use of supplements and other therapeutics (e.g., pain reliever, expectorant, cough suppressant, bronchodilator) in the outpatient setting did not show a distinct trend with respect to time ***Figure 2C-D***. Many of these medications are available without a prescription, and it was not determined if they were taken on the recommendation of a provider or at the patient's discretion. Antibody therapy and HCQ were used infrequently in the outpatient setting. Twenty percent of participants admitted in March 2021 and 40% in June 2021 received outpatient antibody therapy; 13% in December 2020 and 20% in March 2021 received HCQ (data not shown).

Therapeutic Use Over Time in the Inpatient Setting

Therapeutic use during hospitalization for COVID-19 followed a more predictable trend than in the outpatient setting. UTMB circulated institutional recommendations for treatment which typically followed NIH guidelines. remdesivir was given to most patients after the FDA granted an EUA on May 1, 2020 ***Figure 3A***. Before the issuance of the EUA, 83% and 44% of patients from this cohort in March and April 2020, respectively, were counted as receiving remdesivir in an intention to treat analysis as they were enrolled in ACTT-1.[3] Even after the EUA was issued for Remdesivir, universal use of this medication was not routine until December 2020.

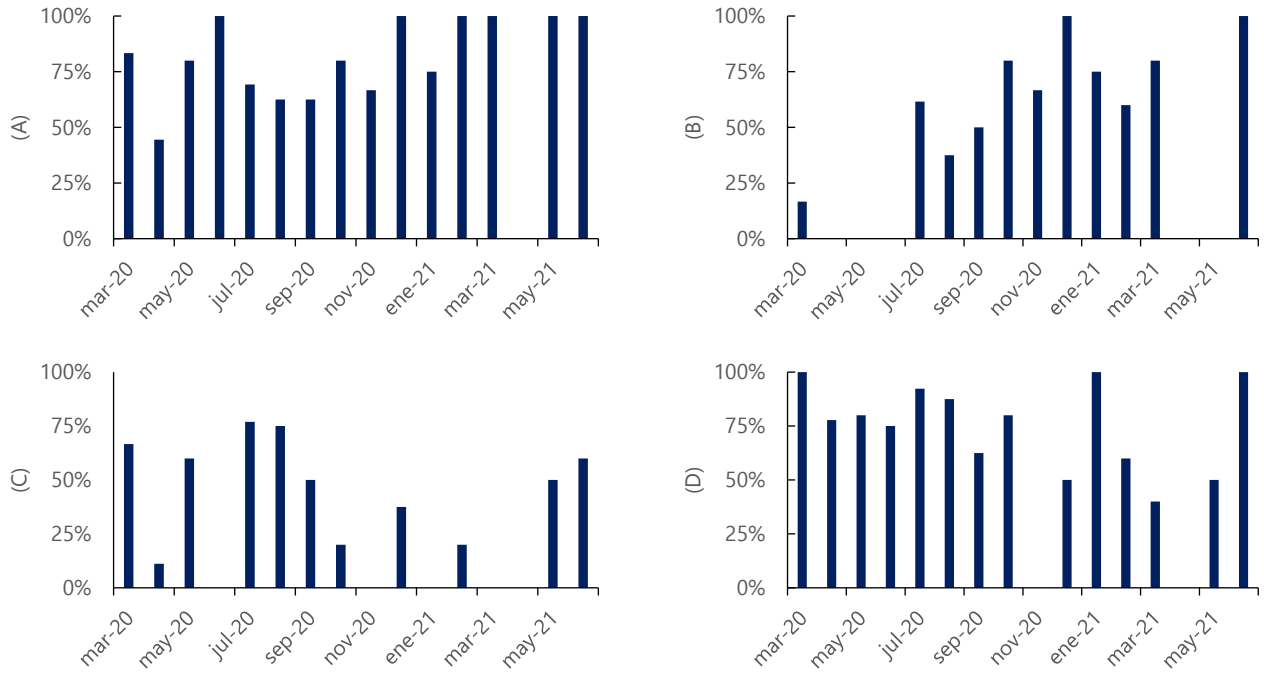
Steroid use, specifically dexamethasone, in hospitalized patients was rarely utilized until after the publication of the RECOVERY trial at the end of June 2020, showing benefits in hospitalized patients receiving oxygen therapy ***Figure 3B***.[4] There was a clear increase in dexamethasone use in August 2020. Dexamethasone use was given to most hospitalized participants for May 2021.

Figure 2 (A, B, C, D). **Percentage of Cohort Using Specified Therapeutics Before Admission (outpatient) Based on Month of Admission.**



Legend: (A) Antibiotics, (B) Steroids, (C) Supplements, (D) Other (e.g., Pain Relievers, Expectorants, Cough Suppressants, and Bronchodilators).

Figure 3 (A, B, C). **Percentage of Cohort Using Specified Therapeutics During Hospitalization (Inpatient) Based on Month of Admission**



Legend: (A) Antivirals, (B) Steroids, (C) Antibiotics, (D) Other (e.g., Pain Relievers, Expectorants, Cough Suppressants, and Bronchodilators).

Antibiotic use in hospitalized patients fluctuated ***Figure 3C***. Therapeutics categorized as "other" were used consistently from March to October 2020 ***Figure 3D***. Except for January and June 2021, the use of these medications was lower in 2021 compared to 2020. HCQ use was low in the inpatient setting, with only 7 patients receiving this therapy across the period analyzed (data not shown). Only one patient from this cohort received HCQ in 2021. Also categorized as "other" were anticoagulants. Use of anticoagulants, either prophylactically or therapeutically in hospitalized patients was low in this cohort. Prophylactic use was more common in patients categorized as having mild or moderate disease (10% and 13%, respectively) than those with severe or critical disease (4% and 1%, respectively). Therapeutic doses were only given to eight patients, one each for mild or moderate disease and three each for severe and critical disease.

Discussion

In three years, robust research centered on COVID-19 quickly resulted in guidelines based on clinical trial results for hospitalized and ambulatory patients. A retrospective look of these efforts to find an effective treatment is worth the discourse. The FDA issued several EUAs for the treatment of COVID-19 based on available data at the time, indicating these therapeutics could provide some benefit to patients. The cohort examined in this study offers insight into the therapeutics used to treat hospitalized COVID-19 patients at UTMB over the first 15 months of the pandemic. We reviewed several treatment types, including therapies that received an EUA and those touted as beneficial in mainstream media.

Our study found that antiviral, antibiotic, steroid, and supplement therapies saw greater use in the inpatient setting from March 2020 to June 2021. Antiviral therapy with remdesivir was more common in the inpatient setting since it was only available in this setting at the time of the study. Treatment with remdesivir is now available for non-hospitalized patients but requires access to a clinic capable of giving infusions over multiple days. Our study noted a greater use of antibiotics in outpatient settings, particularly azithromycin (AZM). Macrolides and HCQ were two frequently used antimicrobials in countries such as France and China. This is a surprising reality given the lack of data for their use in treating viral infections.[5] Although macrolides are commonly used to target a variety of bacterial infections, there is little reason to believe such a treatment would benefit a viral infection such as COVID-19. Similarly, HCQ is commonly used to treat autoimmune disorders and infections involving intracellular bacteria. One reason these therapeutics were considered could have been due to strong media coverage when COVID-19 treatments were unknown. The knowledge that certain micronutrients boost immunity likely influenced the use of supplements categorized as 'other' in our study such as vitamin C and Zinc. However, a third of patients reported having initiated these therapies before admission. Our data did not ascertain whether these medications used before hospital admission were initiated by a provider or at the patient's discretion.

When examining trends over time, clear patterns emerged in both settings. The data support the idea that the presentation date may influence the extent of use of any therapy. For example, in early 2020, when testing for COVID-19 was limited and community spread was presumed low, antibiotics were prescribed more heavily in the outpatient setting. Antibiotic use slowly declined as the year progressed but increased again starting in December 2020. This increase coincides with the second major wave of cases reported in the county from which this cohort resided. The use of steroids in the outpatient setting was not prominent throughout the period examined. Still a brief increase in use was seen during the first few months of 2021, when nearly 60% of patients received outpatient steroid therapy. Finally, supplements had no discernable pattern, with usage oscillating from month to month.

The EUA for remdesivir monotherapy, released on May 1, 2020, coincides with the greatest use in this cohort of patients.[6] In a large, randomized, placebo-controlled double-blinded trial, a statistically significant decrease in recovery time was found for the group receiving remdesivir.[3] The study thereby supported remdesivir's effectiveness in reducing recovery time in hospitalized patients infected with SARS-CoV-2. This led to the issuance of an EUA and eventual FDA approval with the addition of data from other trials. Another notable benefit of remdesivir was seen in patients receiving low-flow oxygen therapy, suggesting the antiviral prevented disease progression, as there was a lower frequency of patients needing higher-level oxygen therapy and other respiratory support.[3]

In the open-label Randomized Evaluation of COVID-19 Therapy (RECOVERY) trial that analyzed multiple therapies in hospitalized patients with COVID-19, the use of dexamethasone was compared to usual care alone, with 28-day mortality as the primary outcome.[4] The study found that significantly fewer patients died within 28 days in the dexamethasone treatment arm than those receiving standard of care. Results from this trial led to the recommendation of dexamethasone for all hospitalized adults requiring supplemental oxygen.

Overall, the use of antivirals and steroids from July 2020 to March 2021 in this cohort coincided with data releases for both remdesivir and dexamethasone and treatment guidelines, such as those published by the Infectious Diseases Society of America (IDSA), the National Institutes of Health (NIH), and the World Health Organization (WHO).[7-9] In the outpatient setting, dexamethasone and other corticosteroids were widely used as it was thought that their use would limit systemic inflammation.[10] Increased use continued even after the results of the RECOVERY trial were released and NIH guidelines were updated.

Another early consideration for COVID-19 treatment was the hydroxyl derivative of chloroquine, HCQ, due to its potential immunologic benefits, such as *in vitro* inhibition of toll-like receptor signaling and alteration of cellular pH.[11] An EUA was issued on March 28, 2020, for using HCQ to treat COVID-19;[12] however, several studies revealed its limited clinical benefit. One retrospective analysis of a large data set from over 96,000 patients found that HCQ did not offer any therapeutic benefit and could reduce survival by potentiating ventricular arrythmia, thus

increasing the risk of invasive ventilation or death. Given these safety concerns, the WHO removed HCQ as a treatment arm in the Solidarity trial. Its EUA was subsequently revoked three months after its release.[13]

Although primarily a respiratory virus, COVID-19 often showed coagulopathy. It is thought that during severe disease caused by the virus, dysregulated thrombosis cascade within the alveoli and pulmonary vessels resulted in an initial local hypercoagulability that then metastases.[14] COVID-19 was also found to result in cellular abnormalities such as lymphopenia, the degree of which correlated to disease severity.[14] One theory proposed that the mismatch in neutrophil to lymphocytes ratio triggered venous thrombosis and was a reliable predictor of mortality. Only a small percentage of the cohort examined in this study was given anticoagulation medication, either at prophylactic or therapeutic doses.

Monoclonal antibodies were not heavily used in this cohort, despite EUA. This is likely because the EUA letters were released later in 2020 and early 2021. In this study, bamlanivimab and etesevimab, which had EUAs released in February 2021, were used more frequently pre-admission than during, which follows one of the use limitations proposed by the FDA as neither had been studied in hospitalized patients.[15]

Among the treatments that had not received indications for use in COVID-19 infection, antibiotics had a fair amount of use in our cohort that notably varied over time. Benefits from AZM may be attributed to its mechanism of reducing the production of intercellular adhesion molecule synthesis (e.g., ICAM-1), a component crucial for viral adhesion.[16] However, this effect has not been well studied for use in SARS-CoV-2 infection. The studied effects of AZM came mainly from its adjunctive use with HCQ, as it was found that both together showed some ability to interfere with viral replication, as evidenced by a small clinical trial in France.[16] Among a few randomized trials that investigated the therapeutic benefits of AZM as monotherapy, one in 2021 conducted on 263 COVID-positive patients found that on day 14, no improvement or absence of symptoms was reported after a single dose of AZM.[17]

In our study, participants also had a considerable use of supplements. Several studies support the benefit of Zinc for its anti-inflammatory properties, aiding in the production of cytokines and improving the integrity of cellular tight junctions.[18] Similarly, vitamin C is a notable antioxidant that influences immune cell migration and function.[19] Thus, the frequent use seen in outpatient and inpatient settings was well supported *in vitro*.

Currently, several well-researched therapies are now accepted for COVID-19 therapy. Among these are intravenous remdesivir for hospitalized patients and baricitinib, an immune modulator. Although not heavily utilized in this cohort, convalescent plasma (CP) appeared to be a promising COVID-19 therapeutic early in the pandemic. CP received an EUA in August of 2020.[20] Given its variable therapeutic efficacy, in February 2021, the EUA for CP was revised to restrict its use only to hospitalized patients with poor humoral immunity and those in the early stage of infection.[21] Presently, the NIH advises against its use in immunocompetent hospitalized patients and CP collected before the omicron variant surge and its use in immunocompetent hospitalized patients.[8, 22] In the outpatient setting, the NIH led the Clinical Trial of COVID-19 Convalescent Plasma in Outpatients (C3PO) showed that CP offered little in the way of disease prevention when given in early disease. In February 2021, the trial was discontinued as little efficacy was found.[23] The RECOVERY trial also showed minimal benefit of high-titer CP.[24]

Throughout 2020 to 2021, adjusting guidelines, media, and other factors increased or decreased the use of certain therapeutics to treat COVID-19. Changes in the IDSA guidelines show how therapeutic recommendations have been adjusted over time.[7] As the pandemic progressed, additional research provided further guidance, contributing to updated treatment guidelines and an improved standard of care.[25] Furthermore, in the cohort examined here, there was a minimal delay in implementing guidelines and the corresponding changes in clinical practice. For example, the IDSA guidelines provided a strong recommendation for the use of dexamethasone on September 25, 2020. This change was evident in ***Figure 3B***, with inpatient steroid use increasing from September to October 2022.

When looking retrospectively at the progression of COVID-19 therapeutics, one cannot ignore the media's role, as unproven treatments were marketed through both mainstream and online media. One example was seen on October 1, 2020, when former President Donald Trump tested positive for COVID-19 and was treated with the antibody cocktail REGEN-COV (Casirivimab and Imdevimab), remdesivir, and steroids, in addition to vitamin D and Zinc.[26] This could correlate to several spikes in medication usage seen in October 2020 and the months immediately after, due to heavy media coverage. After Donald Trump was treated with remdesivir monotherapy, inpatient antiviral usage increased and remained high for this group ***Figure 3A***. While this does not indicate causation, the positive media coverage potentially increased patient willingness towards this treatment. Although not observed in this cohort, the media may have influenced changes in the use of HCQ and AZM, especially early in the pandemic. President Trump made statements regarding his use of HCQ and AZM to prevent illness from COVID-19 and publicly pressured the FDA to release an EUA for HCQ.[27, 28] This sentiment was further publicized by the group America's Frontier Doctors, whose own press conference went viral on social media. This struggle between media figures and scientists led to the public questioning what was true, prompting some to demand specific treatments when receiving care.

Overall medication use in the inpatient setting in this cohort mimicked what would be expected based on changing clinical guidelines. The outpatient use of medications showed a limited knowledge of disease etiology early in the pandemic, with antibiotics, unproven supplements, and "other" therapeutics regularly being used. The outpatient use of HCQ, AZM, Vitamin D, and Zinc for the treatment of Donald Trump showed a correlated increase in October 2020. Similar increases were seen after other notable press events and when NIH guidelines were

adjusted to include or exclude certain medications, possibly pointing to the effect that media coverage may have on medication use. In the face of a new disease, it is important to provide treatments based on scientific and clinical data rather than anecdotal evidence, and to communicate these findings with patients to ensure safe and productive treatment.

Our study reveals that the evolution of COVID-19 treatment guidelines has been significantly influenced by emerging clinical trial data, regional healthcare practices, and the varying interpretations of these data by medical experts. This observation aligns with previous findings which also note rapid guideline updates in response to major clinical trial outcomes.[29] For instance, the swift incorporation of findings from the RECOVERY trial into treatment guidelines reflects a broader trend of integrating high-quality evidence into clinical practice. Moreover, our analysis highlights regional variations in the adoption and implementation of treatment guidelines, which corroborates the work of Lee et al.[30] They emphasized the challenges of aligning global recommendations with local healthcare infrastructures and patient demographics. These variations underscore the necessity for flexible and adaptive guideline frameworks that can accommodate regional differences while maintaining a foundation in robust scientific evidence.

Limitations

Our study was limited to patients hospitalized at UTMB in Galveston County and may not represent the larger population. Further studies could benefit from a multi-center approach to encompass a broader demographic and geographic pool and add generalizability to the study. Additionally, patients who chose to participate in this research study may have been more open to receiving other therapeutic interventions, including medications undergoing clinical trials, even if they were not authorized or proven, potentially resulting in bias. Lastly, the data were collected retrospectively, and may be subject to recall bias. These limitations could be addressed through further patient outreach and using a broader cohort in future research.

Summary – Accelerating Translation

In this article titled "A Descriptive Analysis of the Use of Various Therapeutics in a Cohort of COVID-19 Patients," the authors investigated how a novel disease such as COVID-19 was clinically treated when national guidelines constantly changed. By understanding how hospital systems such as UTMB treat novel illnesses with mixed guidelines, future new diseases can be more effectively and efficiently managed. Being adaptable and implementing guidelines is an important aspect of medicine, as new diseases will likely emerge. The authors followed 90 patients with a positive COVID-19 diagnosis from March 2020 to June 2021. They collected a detailed accounting of what medications each patient took before admission, after admission, and if the patient was hospitalized. This data showed large differences were seen in patients who were managed in outpatient clinics versus in the hospital. Antibiotics such as AZM were given much more commonly in the outpatient setting despite a lack of guidelines for administering antibiotic treatment for COVID-19. When analyzing the data month to month, it was clear that guidelines and news coverage played a significant role in how physicians treated COVID-19 through 2020. Medications that received strong media coverage such as hydroxychloroquine, were prescribed noticeably in the months shortly after news coverage. This is despite no recommendation from national and local guidelines at the time, which would be later updated to recommend against the use of hydroxychloroquine. This descriptive analysis encourages policymakers in the United States to work closely with physicians when communicating the best treatment recommendations for a novel disease. A unified message to the medical community, media, and public would strengthen strong clinical treatment practices and prevent the use of ineffective medications.

References

1. Monegro AF, Muppidi V, Regunath H. Hospital-Acquired Infections. StatPearls. Treasure Island (FL)2023.
2. Revelas A. Healthcare - associated infections: A public health problem. Niger Med J. 2012;53(2):59-64.
3. Beigel JH, Tomashek KM, Dodd LE, Mehta AK, Zingman BS, Kalil AC, et al. Remdesivir for the Treatment of Covid-19 - Final Report. N Engl J Med. 2020;383(19):1813-26.
4. Recovery Collaborative Group, Horby P, Lim WS, Emberson JR, Mafham M, Bell JL, et al. Dexamethasone in Hospitalized Patients with Covid-19. N Engl J Med. 2021;384(8):693-704.
5. Recovery Collaborative Group, Horby P, Mafham M, Linsell L, Bell JL, Staplin N, et al. Effect of Hydroxychloroquine in Hospitalized Patients with Covid-19. N Engl J Med. 2020;383(21):2030-40.
6. Coronavirus (COVID-19) Update: FDA Issues Emergency Use Authorization for Potential COVID-19 Treatment [press release]. 05/01/2020 2020.
7. Infectious Diseases Society of America. IDSA Guidelines on the Treatment and Management of Patients with COVID-19. Available from: https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/. Last updated Aug 12, 2024; cited May 27, 2021.
8. National Institutes of Health. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. Available from: https://www.ncbi.nlm.nih.gov/books/NBK570371/. Last updated Mar 1, 2024; cited Apr 21, 2021.
9. World Health Organization. Therapeutics and COVID-19: Living guideline. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2023.2. Last updated Nov. 10, 2023; cited Sept. 2, 2020.
10. Bradley MC, Perez-Vilar S, Chillarige Y, Dong D, Martinez AI, Weckstein AR, et al. Systemic Corticosteroid Use for COVID-19 in US Outpatient Settings From April 2020 to August 2021. JAMA. 2022;327(20):2015-8.
11. Zhao M. Cytokine storm and immunomodulatory therapy in COVID-19: Role of chloroquine and anti-IL-6 monoclonal antibodies. Int J Antimicrob Agents. 2020;55(6):105982.
12. Coronavirus (COVID-19) Update: Daily Roundup March 30, 2020 [press release]. 03/30/2020 2020.
13. Coronavirus (COVID-19) Update: FDA Revokes Emergency Use Authorization for Chloroquine and Hydroxychloroquine [press release]. 06/15/2020 2020.
14. Abou-Ismail MY, Diamond A, Kapoor S, Arafah Y, Nayak L. The hypercoagulable state in COVID-19: Incidence, pathophysiology, and management. Thromb Res. 2020;194:101-15.
15. Coronavirus (COVID-19) Update: FDA Authorizes Monoclonal Antibodies for Treatment of COVID-19 [press release]. 02/09/2021 2021.

16. Parra-Lara LG, Martinez-Arboleda JJ, Rosso F. Azithromycin and SARS-CoV-2 infection: Where we are now and where we are going. J Glob Antimicrob Resist. 2020;22:680-4.
17. Oldenburg CE, Pinsky BA, Brogdon J, Chen C, Ruder K, Zhong L, et al. Effect of Oral Azithromycin vs Placebo on COVID-19 Symptoms in Outpatients With SARS-CoV-2 Infection: A Randomized Clinical Trial. JAMA. 2021;326(6):490-8.
18. Diyya ASM, Thomas NV. Multiple Micronutrient Supplementation: As a Supportive Therapy in the Treatment of COVID-19. Biomed Res Int. 2022;2022:3323825.
19. Holford P, Carr AC, Jovic TH, Ali SR, Whitaker IS, Marik PE, et al. Vitamin C-An Adjunctive Therapy for Respiratory Infection, Sepsis and COVID-19. Nutrients. 2020;12(12).
20. FDA Issues Emergency Use Authorization for Convalescent Plasma as Potential Promising COVID–19 Treatment, Another Achievement in Administration's Fight Against Pandemic [press release]. 08/23/2020 2020.
21. FDA In Brief: FDA Updates Emergency Use Authorization for COVID-19 Convalescent Plasma to Reflect New Data [press release]. 02/04/2021 2021.
22. Gavriatopoulou M, Ntanasis-Stathopoulos I, Korompoki E, Fotiou D, Migkou M, Tzanninis IG, et al. Emerging treatment strategies for COVID-19 infection. Clin Exp Med. 2021;21(2):167-79.
23. Korley FK, Durkalski-Mauldin V, Yeatts SD, Schulman K, Davenport RD, Dumont LJ, et al. Early Convalescent Plasma for High-Risk Outpatients with Covid-19. N Engl J Med. 2021;385(21):1951-60.
24. Recovery Collaborative Group. Convalescent plasma in patients admitted to hospital with COVID-19 (RECOVERY): a randomised controlled, open-label, platform trial. Lancet. 2021;397(10289):2049-59.
25. Potter GE, Bonnett T, Rubenstein K, Lindholm DA, Rapaka RR, Doernberg SB, et al. Temporal Improvements in COVID-19 Outcomes for Hospitalized Adults: A Post Hoc Observational Study of Remdesivir Group Participants in the Adaptive COVID-19 Treatment Trial. Ann Intern Med. 2022;175(12):1716-27.
26. Cohen J. Update: Here's what is known about Trump's COVID-19 treatment. 2020 10/05/2020.
27. abcnews. Timeline: Tracking Trump alongside scientific developments on hydroxychloroquine. Available from: https://abcnews.go.com/Health/timeline-tracking-trump-alongside-scientific-developments-hydroxychloroquine/story?id=72170553. Last updated Aug 8,2020; cited Aug 8,2020..
28. theguardian. Trump is taking hydroxychloroquine, White House confirms. Available from: https://www.theguardian.com/us-news/2020/may/19/trump-hydroxychloroquine-covid-19-white-house. Last updated May 19, 2020; cited May 19, 2020..
29. Li G, Hilgenfeld R, Whitley R, De Clercq E. Therapeutic strategies for COVID-19: progress and lessons learned. Nat Rev Drug Discov. 2023;22(6):449-75.
30. Cokljat M, Cruz CV, Carrara VI, Puttaraksa K, Capriglioni C, Insaurralde SM, et al. Comparison of WHO versus national COVID-19 therapeutic guidelines across the world: not exactly a perfect match. BMJ Glob Health. 2024;9(4).

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Conflict of Interest Statement & Funding

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Author Contributions

Conceptualization: AM, BM, SM, and CL. Investigation: AM, BM, JC, DM, RD, TG, SO, and CL. Supervision: SM and CL. Writing – Original Draft: AM, BM, and CL. Writing – Review & Editing: JC, DM, RD, TG, SO, and SM.

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Original Article

Assessment of Antimicrobial Resistance and Susceptibility Pattern of UTI-causing Microorganisms in Southern Punjab, Pakistan

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Abstract

Background: Bacterial resistance against antibiotics has become a global challenge and measures are needed to stop this. The aim of this study is to highlight this problem and to determine the antibiotic susceptibility pattern of organisms in Southern Punjab, Pakistan. **Method**: This descriptive cross-sectional study was conducted in Sheikh Zayed Medical Hospital, Rahim Yar Khan. The urine samples obtained from 4 different wards were sent for culture and sensitivity analysis. 9 antibiotics (Nitrofurantoin, Fosfomycin, Ciprofloxacin, Ceftriaxone, Trimethoprim-Sulfamethoxazole, Norfloxacin, Linezolid, Amoxicillin, and Imipenem) were tested against 5 isolated strains of uropathogens using Kirby Bauer disk diffusion test. The sensitivity reports were obtained, and data points were entered into a spreadsheet and analysed using SPSS. **Results**: Out of 101 samples of uropathogens that showed positive growths (42.08%), 53 (52.4%) were from male patients and 48 (47.5%) positive growths were from females. *Escherichia Coli* had the highest positive growths (58%) followed by *Pseudomonas* (19%) *Klebsiella* (13%), *Staphylococcus Aureus* (7%) and *Coagulase-negative staphylococci* (3%). Imipenem was the most sensitive drug whereas the highest resistance by organisms was developed against TMP-SMX. No significant association($p>0.05$) was found between any of the anti-microbial drugs and *Escherichia coli*, gram-positive uropathogens, and gram negative uropathogens. **Conclusion**: The high increasing rate of broad-spectrum antibiotics resistance suggests that diagnostic and culture tests should be encouraged in hospitals. Based on these test results, appropriate antibiotics should be prescribed. The limitations include the inability to distinguish between nosocomial and community-acquired urinary tract infections and also did not consider other demographic factors like age.

Introduction

Antibiotics play a vital role in the treatment of infectious diseases by bacterial stasis or lysis. However, the increased and improper use of antibiotics has led to the development of antibiotic resistance, where bacteria acquire the ability to survive antibiotic treatment.[1] Bacteria employ various mechanisms to develop resistance, including enzyme production, reduced drug sensitivity, and possession of numerous mobilizable genes within bacterial populations. Additionally, patient self-medication, over-prescribing, and incomplete dosing significantly contribute to bacterial resistance.[2]

In the context of antibiotic resistance, Pakistan, as a developing nation, faces the challenge of multiple drug-resistant and extensively drug-resistant bacteria.[3] An example of this issue is the synergistic action of Azithromycin and fluoroquinolones in treating co-infections alongside COVID-19, which has led to the associated overuse of antibiotics and the potential for antimicrobial resistance.[4] Given the prevalent misuse and overuse of antibiotics in Pakistan, understanding susceptibility patterns and developing effective strategies are imperative, especially since there has been no research of this kind conducted in the lower Punjab region, necessitating immediate action to establish efficient measures.

Urinary tract infections (UTIs) are prevalent infectious diseases, particularly in developing countries. The emergence of drug resistance among bacterial uropathogens has further complicated the problem, giving rise to antibiotic-resistant species.[5] The 2017-2018 GLASS (Global Antimicrobial Resistance and Use Surveillance System) report indicated over 70% resistance to ceftriaxone and ciprofloxacin in Escherichia coli in Pakistan. To tackle this issue effectively, it is crucial to determine the susceptibility patterns of uropathogens to specific antibiotics to minimize exacerbation of resistance. Moreover, the implementation of antibiotic stewardship programs is essential to enhance healthcare quality and ensure appropriate antibiotic use.[6] These collective measures will enable healthcare professionals to manage urinary tract infections more effectively, employing a targeted approach that reduces recurrence rates and achieves higher cure rates within shorter durations.

The primary objective of our study is to identify UTI causing pathogens and their antimicrobial susceptibility patterns based on gender, gram-staining, and hospital ward. This research aims to improve treatment efficacy and reduce recurrence rates. Additionally, our study seeks to promote culture testing and the practice of appropriate prescription of antibiotics based on culture and susceptibility patterns. By addressing these

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objectives, we aim to contribute valuable insights that will aid in the development of more effective treatment strategies for UTIs, while also improving appropriate antibiotic prescribing practices.

Methods

Study Design and Setting

The study was a descriptive cross-sectional study conducted at Sheikh Zayed Medical Hospital in Rahim Yar Khan, Punjab, Pakistan from May to July 2022. The purpose of the study was to investigate the prevalence of urinary tract infections (UTIs) in patients admitted to the medicine, gynecology, surgery, and nephrology wards. These departments were chosen due to the high burden of UTI patients in them, as observed by the researchers during their hospital rotations. The study was evaluated using the STROBE checklist for cross sectional studies. Ethical clearance was obtained from the Institutional Research Board Sheikh Zayed Medical College/Hospital, with the reference No: 479/IRB/SZMC/SZH, and written permission was obtained from the head of each department. The researchers had no potential conflicts of interest, and no external funding for the study.

Participants

Patients presenting with uncomplicated UTI symptoms (abdominal pain, burning micturition, cloudy or foul-smelling urine) were included in the study, while those at high risk of complications or in critical condition were excluded. Immunocompromised, septic, and patients with other comorbidities like diabetes and those who had taken antibiotics in the last 24 hours were also excluded. This was done as such patients may require different management approaches that may confound the results. This exclusion criterion resulted in a higher proportion of female patients in the study, as the gynecology ward primarily admitted female patients. Simple random sampling was employed.

Data Collection

Patients included in the study provided informed consent and their data was collected using a self-developed questionnaire which included variables such as name, age, gender, and ward name. The questionnaire was pre-tested through trial interviews to improve question-asking methods and variables. Based on previous studies and hospital records, a study sample size of more than 200 was expected between the period of study from May to July 2022.

Confirmation of Diagnosis

Early morning mid-stream urine samples were collected from the patients and stored in sterile urine collection containers. The urine culture samples were sent to the microbiological culture sensitivity laboratory for analysis. Positive results were determined when significant bacterial growth > 10^5 CFU/ml was observed. Colony study and biochemical tests were performed to identify the microorganisms. Some of the disks didn't show positive bacterial growth, which could be due to other microorganisms like fungi, however only UTI causing bacteria were studied in this study.

Antibiotic Sensitivity Testing

MacConkey agar was used to subculture the colonies and obtain pure growth of the microorganisms. The Kirby Bauer disk diffusion test was conducted to assess the sensitivity of the isolates to ten different antibiotics. The ten antibiotics used in the procedure were furnished separately as discs to the laboratory by the researchers, exclusively for use on these urine samples. The measurement of the zone of inhibition of bacterial growth was performed, and the results were compared with the guidelines of the Clinical and Laboratory Standards Institute (CLSI). All intermediate results were considered as sensitive too.

Antibiotics and Sensitivity Reports

The organisms were subjected to various groups of antibiotic discs from Oxoid, including Nitrofurantoin (300µg), Fosfomycin (50µg), Ciprofloxacin (5µg), Ceftriaxone (30µg), Trimethoprim/ Sulfamethoxazole (1:19 and 25µg), Norfloxacin (5µg), Linezolid (30µg), Amoxicillin (30µg), and Imipenem (10µg). The sensitivity reports of all patients were individually studied. Then the data points were entered into a spreadsheet.

Statistical Analysis

The data was analyzed using IBM's Statistical Package for Social Sciences (SPSS version 26). Descriptive statistics, including numbers, frequencies, and percentages, were used to describe the data. There was no missing data. Age was the only quantitative variable. Tables and charts were utilized to display the data, and the association between categorical variables was assessed using the Chi-square test. A standard p-value of <0.05 was considered statistically significant. The chi-square test was also conducted to assess the significance of antimicrobial drugs against gram-positive cocci (GPC) and gram-negative bacteria separately. No sensitivity analysis was applicable.

Results

The study analyzed 240 urine samples from suspected urinary tract infection cases admitted to the departments of medicine, gynecology, surgery, and nephrology. There was no attrition and no missing data or loss of patients to follow-up between admission and diagnosis and arrival of antimicrobial culture and sensitivity report. Among the 101 positive growths for uropathogens, 53 were male patients, and 48 were female patients. The most common organism was *Escherichia Coli (E. coli)* with a growth rate of 58%, followed by *Pseudomonas* (19%), *Klebsiella* (13%), *Staphylococcus Aureus (S. Aureus)* (7%), and *Coagulase-negative staphylococci (CoNS)* (3%). ***Table 1*** presents the growth rate of uropathogens and the drugs to which they are sensitive. ***Figure 1*** illustrates the distribution of microorganisms by gender of patients. The medicine ward had the highest growth rate (45%), followed by gynecology (41.86%), surgery (41.17%), and nephrology (38.75%). The uropathogens were further tested for antimicrobial susceptibility patterns. The results of urine culture analysis from the samples collected in these wards are summarized in ***Figure 2***, presenting the growth rates and distribution of these organisms.

Table 1. **Microorganisms and their Sensitivity in Percentage to Various Antibiotics.**

Microorganism	Total Growth	Antibiotic Used								
		NF [a]	CIP [b]	FOS [c]	CRO [d]	SXT [e]	NOR [f]	LNZ [g]	AMC [h]	IMP [i]
Escherichia Coli	59	45.76	42.37	50.84	55.93	27.11	37.28	45.76	50.84	77.96
Pseudomonas	19	36.84	31.57	42.10	42.10	21.05	26.31	63.15	31.57	68.42
Klebsiella	13	38.46	30.76	30.76	46.15	30.76	38.46	53.8	46.15	76.92
S. Aureus	7	42.85	28.57	57.14	57.14	28.57	28.57	42.85	57.14	71.42
CoNS [j]	3	33.33	33.33	66.66	66.66	0	33.33	33.33	66.66	100
	101									

Legend: [a] Nitrofurantoin, [b] Ciprofloxacin, [c] Fosfomycin, [d] Ceftriaxone, [e] Trimethoprim-Sulfamethoxazole, [f] Norfloxacin, [g] Linezolid, [h] Amoxicillin, [i] Imipenem, [j] Coagulase-negative staphylococci (CoNS). The numbers indicate in percentage the sensitivity of that uropathogen to the antibiotic used. For instance, in E. Coli 45.76% percentage of the positive growth cultures were sensitive to Nitrofurantoin and so on.

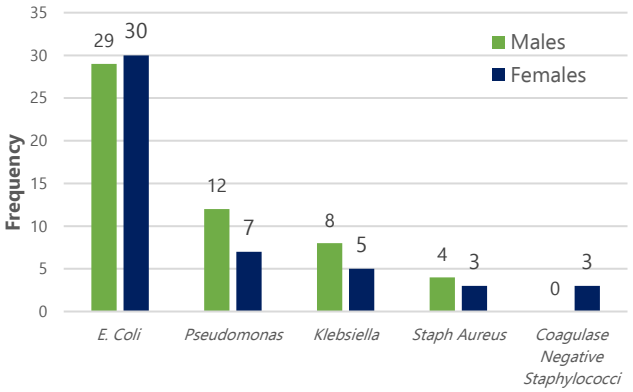
In this study, a total of 9 antibiotics, including Nitrofurantoin (NF), Ciprofloxacin (CIP), Fosfomycin (FOS), Ceftriaxone (CRO), Trimethoprim-Sulfamethoxazole (SXT), Norfloxacin (NOR), Linezolid (LNZ), Amoxicillin (AMC), and Imipenem (IMP), were checked for their sensitivity and resistance against the 5 organisms: *E. coli, Pseudomonas, Klebsiella, S. Aureus, and CoNS*.

Among gram-negative organisms, Imipenem showed the highest sensitivity (76%), while the highest resistance was observed against TMP-SMX (74%). The findings of resistance and sensitivity to these antibiotics by all uropathogens in general are summarized in ***Figure 3***. Gram-positive cocci demonstrated the highest sensitivity to Imipenem (80%) and the highest resistance to TMP-SMX (80%). Their sensitivity and resistance to other antibiotics is depicted in ***Figure 4***. Notably, there was a difference in sensitivity between gram-positive cocci and gram-negative uropathogens, particularly in relation to linezolid, as well as quantitative differences among Amoxicillin, Fosfomycin, and Ceftriaxone.

Regarding specific organisms, *E. coli* exhibited the highest sensitivity to IMP (78%) and the highest resistance against SXT (73%). *Pseudomonas* displayed the highest resistance against SXT (79%), while it showed high sensitivity to both LNZ (63%) and IMP (68%). *S. Aureus* isolates exhibited the highest resistance against CIP, SXT, and NOR (71%), while its sensitivity was highest against IMP (71%), followed by FOS and CRO (50%). *Klebsiella* showed the highest sensitivity to IMP (76.92%), followed by LNZ (53.8%), CRO, AMC (46.15%), and NF (38.46%). It displayed the highest resistance against SXT, CIP, and FOS (69.24%).

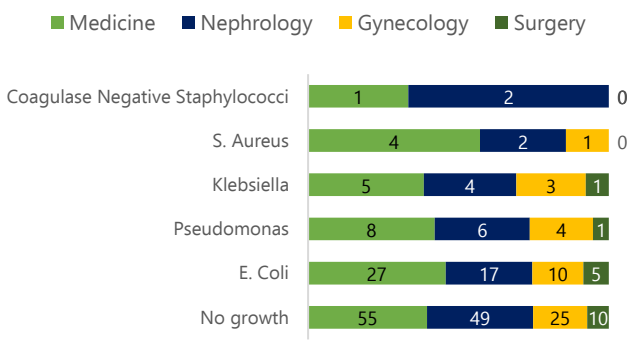
CoNS showed maximum sensitivity to IMP (100%) and maximum resistance to SXT (100%) among the few samples that showed its growth. The antimicrobial sensitivity pattern of *E. coli* based on the tissue culture sensitivity report is depicted in ***Figure 5***, while ***Figure 6*** presents the antimicrobial sensitivity pattern for *Pseudomonas*, and ***Figure 7*** reports the susceptibility pattern of *S. aureus*.

Figure 1. **Distribution of the Grown Microorganisms by Sex.**



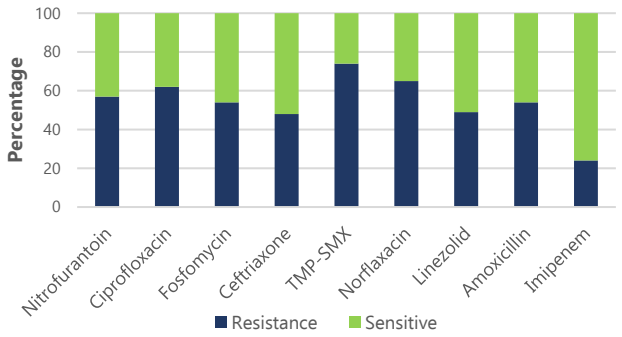
Legend: The distribution of microorganisms by patient sex includes 59 patients with *Escherichia coli* (29 males, 30 females), 19 with *Pseudomonas* (12 males, 7 females), 13 with *Klebsiella* (8 males, 5 females), 7 with *Staphylococcus aureus* (4 males, 3 females), and 3 with coagulase-negative staphylococci (0 males, 3 females).

Figure 2. **Growth Results by Ward of Sample Origin.**



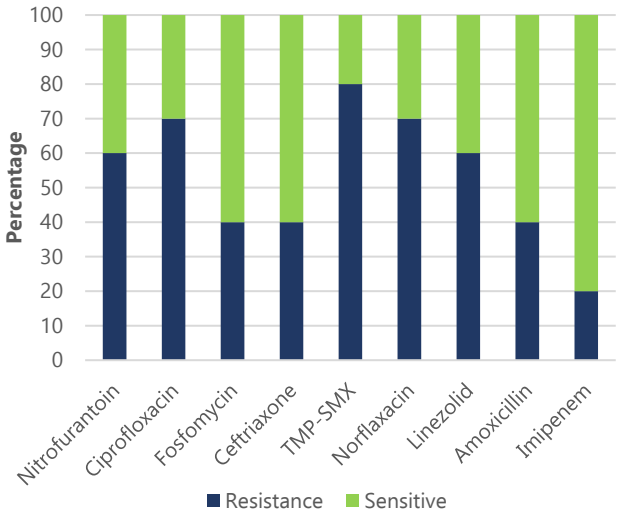
Legend: Uropathogens isolated from urine cultures by ward: Medicine ward had 45 positive growths—27 *E. coli*, 8 *Pseudomonas*, 5 *Klebsiella*, 4 *Staphylococcus aureus*, and 1 coagulase-negative staphylococci. There were no coagulase-negative staphylococci in the Gynecology or Surgery wards, and no *Staphylococcus aureus* causing UTIs in the Surgery ward.

***Figure 3*. Effectiveness of Various Antimicrobial Drugs Against Common Gram-Negative Pathogens.**



Legend: Resistance (R) and sensitivity (S) rates: Nitrofurantoin (57% R, 43% S), Ciprofloxacin (62% R, 38% S), Fosfomycin (54% R, 46% S), Ceftriaxone (48% R, 52% S), TMP-SMX (74% R, 26% S), Norfloxacin (65% R, 35% S), Linezolid (49% R, 51% S), Amoxicillin (54% R, 46% S), and Imipenem (24% R, 76% S).

***Figure 4*. Effectiveness of Various Antimicrobial Drugs Against Common Gram Positive Uropathogens.**



Legend: Resistance (R) and sensitivity (S) rates: Nitrofurantoin (60% R, 40% S), Ciprofloxacin (70% R, 30% S), Fosfomycin (40% R, 60% S), Ceftriaxone (40% R, 60% S), TMP-SMX (80% R, 20% S), Norfloxacin (70% R, 30% S), Linezolid (60% R, 40% S), Amoxicillin (40% R, 60% S), and Imipenem (20% R, 80% S).

With the Chi-square test, no significant association was found between any of the antimicrobial drugs and *E. coli* growth or sensitivity to Imipenem. No statistically significant findings were also observed in the efficacy of antimicrobial drugs against Gram-positive cocci (GPC) and Gram-negative bacteria separately.

Discussion

In the present study, we observed an increasing trend of resistance to commonly used antibiotics among uropathogens. The culture of bacteria revealed a positivity ratio of approximately 42%, with multiple isolated strains exhibiting resistance to the tested drugs. The susceptibility pattern differed between gram-positive and gram-negative organisms. Gram-negative organisms showed increasing resistance to traditional urinary tract infection antibiotics such as trimethoprim-sulfamethoxazole, norfloxacin, and ciprofloxacin, while most of them remained susceptible to ceftriaxone, linezolid, and imipenem. Gram-positive organisms demonstrated moderate susceptibility to ceftriaxone, fosfomycin, and amoxicillin, with imipenem being the most effective. Fluoroquinolones and other antibiotics had reduced effectiveness against most gram-positive strains. Coagulase-negative staphylococci were only found in women, and the medicine ward exhibited a higher incidence of urinary tract infections compared to other wards. *E. coli* affected more females than males, indicating a higher risk for females.[7] Amoxicillin and fosfomycin showed relatively better efficacy against *E. coli* compared to other gram-negative bacteria, while linezolid was less effective. These findings are consistent with previous research conducted in Europe.[8] *Pseudomonas* displayed high resistance to all antibiotics except imipenem and linezolid. The resistance observed can be attributed to various factors, including self-medication, overprescription, insufficient doses, and inappropriate antibiotic usage.

Limitations of this study should be acknowledged. Firstly, the study was unable to differentiate between nosocomial (hospital-acquired) urinary tract infections and those caused through other colonization routes. As the urine cultures were obtained from hospital patients, the identified microbes could represent multi-drug resistant strains present in the hospital environment, acquired by the patients due to stress, immunocompromise states, or other hospital-related factors.[9] This could give rise to selection bias as the selected population was from hospital settings and did not include patients treated in community settings. Additionally, the male-to-female patient ratio is not truly representative due to some data being primarily collected from the gynecology ward, which predominantly caters to women patients. The study also did not consider factors such as age, patient awareness, and habits related to self-medication, immune status, socio-economic status, hospital stay and other co morbidities. These variables can act as confounding factors and may create a bias. Human errors during antimicrobial disc sensitivity testing are also possible. Although the chi-square test showed no significance between the usage of any drug and the bacteria's sensitivity or resistance, further analysis with a larger sample size is warranted to confirm these findings. Additional studies should also be undertaken of patients with UTI with comorbidities, to study the disease trends in them.

Although the study was well-designed and conducted with ethical considerations, there is a chance of error in the procedures used, such as the disc sensitivity test and the delay between disc application and incubation while measuring the reading zone, creating a risk of measurement bias. This could be reduced by proper placing of the disk and timely measurements of the reading zone.

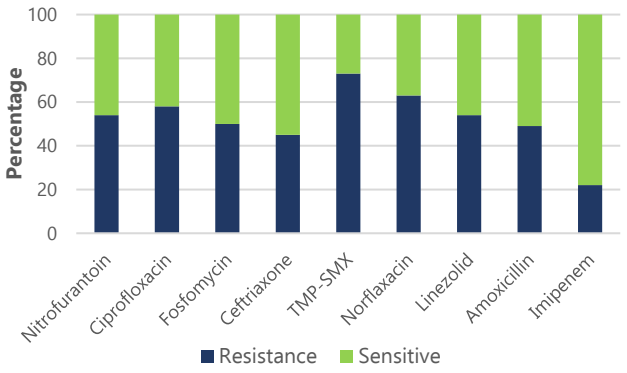
The growth positivity rate observed in the study is within a reasonable range, indicating the proficiency of the antimicrobial laboratory technique with minimal chances of missing potential

organism growth in the culture. *E. coli* and other gram-negative bacteria are commonly associated with UTIs due to their virulence factors that facilitate colonization and ascending infection in the urinary tract. *E. coli*, in particular, possesses specific Type I fimbriae and P pili containing hemolysin and other toxins, contributing to its pathogenicity in causing urinary tract infections. On the other hand, fewer gram-positive organisms were isolated in urine cultures of UTIs. It is important to note that UTIs can occur in patients within hospitals, even if they were not part of the initial presenting complaint.[10] For instance, post-operative patients in surgery or gynecology wards, particularly those who underwent caesarean section, were screened for urine culture, and some were found to have infections.

The reduced resistance to Imipenem across all bacteria indicates appropriate prescription practices for this drug and suggests a lower prevalence of carbapenemase-producing bacteria, especially among *E. coli* and *Klebsiella*, in the region. However, this also suggests a higher occurrence of extended-spectrum beta-lactamase (ESBL)-producing bacteria, rendering commonly used antibiotics for other infectious diseases less effective. Previous in-vitro studies have also shown increased effectiveness of Imipenem,[11] but it is worth noting that research from India indicates resistance to multiple carbapenems.[12] It is important to reconsider the use of Trimethoprim-sulfamethoxazole (TMP-SMX) as an antibiotic choice due to the high rate of resistance against it, despite its supposed activity against *Methicillin Resistant Staphylococcus Aureus* (MRSA) and gram-negative bacteria causing UTIs. Fluoroquinolones, especially the newer generations, were previously considered first-line therapy for complicated UTIs and pyelonephritis. However, a considerable amount of literature now refutes their use in UTIs for various reasons.[13] This overprescription of fluoroquinolones may have led to the development of resistance not only against these drugs but also against nitrofurantoin, which was commonly used in cystitis. Commonly used drugs like ceftriaxone and amoxicillin show average rates of sensitivity and resistance, indicating that these drugs could become ineffective if they continue to be self-medicated and prescribed without appropriate history and microbial culture. Fosfomycin, on the other hand, still retains some effectiveness against gram-positive strains, possibly due to its lesser usage and lower prevalence.[14] The increasing resistance to linezolid may be attributed to the high prevalence of MRSAand the drug being the first-line treatment for multi-drug resistant organisms, leading to its overuse.

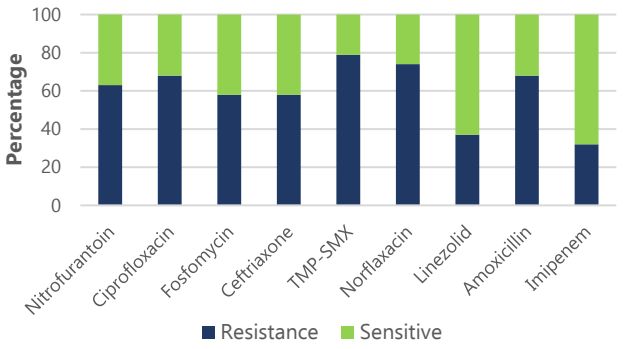
The findings from this study have significant implications and can be generalized, particularly among hospital populations worldwide. By looking at the susceptibility pattern of UTI causing pathogens various hospitals in the region should monitor their prescribed antibiotics and reassess their usage. A need for more culture and sensitivity-based practice would also be felt to reinforce the better prescription of antibiotics. Such practices will be particularly useful in low-income areas or in populations struggling with hygiene, both of which will have significant overlap with the area where the study was conducted as well. *E. coli, Klebsiella, and Pseudomonas*, which were studied for their

Figure 5. **Antimicrobial Drug Sensitivity and Resistance Pattern for *E. Coli*.**



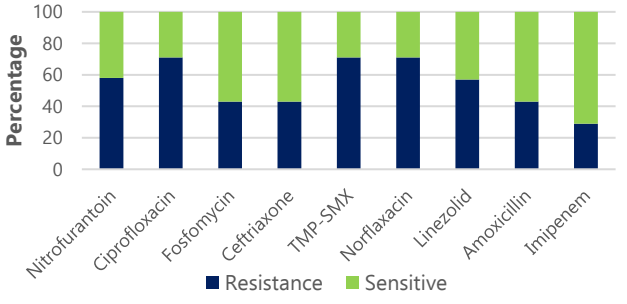
Legend: Resistance (R) and sensitivity (S) rates: Nitrofurantoin (54% R, 46% S), Ciprofloxacin (58% R, 42% S), Fosfomycin (50% R, 50% S), Ceftriaxone (45% R, 55% S), TMP-SMX (73% R, 27% S), Norfloxacin (63% R, 37% S), Linezolid (54% R, 46% S), Amoxicillin (49% R, 51% S), and Imipenem (22% R, 78% S).

Figure 6. **Antimicrobial Drug Sensitivity and Resistance Pattern for Pseudomonas.**



Legend: Resistance (R) and sensitivity (S) rates: Nitrofurantoin (63% R, 37% S), Ciprofloxacin (68% R, 32% S), Fosfomycin (58% R, 42% S), Ceftriaxone (58% R, 42% S), TMP-SMX (79% R, 21% S), Norfloxacin (74% R, 26% S), Linezolid (37% R, 63% S), Amoxicillin (68% R, 32% S), and Imipenem (32% R, 68% S).

Figure 7. **Antimicrobial Drug Sensitivity and Resistance Pattern for S. Aureus.**



Legend: Resistance (R) and sensitivity (S) rates: Nitrofurantoin (58% R, 42% S), Ciprofloxacin (71% R, 29% S), Fosfomycin (43% R, 57% S), Ceftriaxone (43% R, 57% S), TMP-SMX (71% R, 29% S), Norfloxacin (71% R, 29% S), Linezolid (57% R, 43% S), Amoxicillin (43% R, 57% S), and Imipenem (29% R, 71% S).

antimicrobial susceptibility patterns in urine cultures, are causative agents of both community- and hospital-acquired infections.[15] The increasing resistance to most antibiotics observed in these pathogens not only affects patients with UTIs but also those with other infectious diseases such as pneumonia, diarrhea, and sepsis, who may be prescribed commonly used antibiotics like ceftriaxone, amoxicillin, and linezolid without experiencing improvement due to resistance against them. To further explore these correlations and trends, future studies can investigate the antimicrobial susceptibility patterns of other frequently encountered infectious diseases. It would be valuable to isolate and identify specific strains of microorganisms with these resistance patterns and conduct genomic studies to explore the underlying mechanisms of resistance. Antimicrobial stewardship programs in hospitals should be promoted and implemented, along with systematic reviews of antibiotic prescriptions across all hospital wards.[16] It is crucial to increase awareness among healthcare professionals regarding the importance of microbial culture and sensitivity evaluation and to educate the general population about the risks of self-medication and microbial resistance.[17] Additionally, there is a need for the development of improved diagnostic features and testing methods that can differentiate not only between bacterial and viral infections but also among different bacterial infections. Global collaboration is essential to establish effective management plans based on accurate diagnosis.

Summary – Accelerating Translation

Title: Assessment of Antimicrobial Resistance and Susceptibility Pattern of UTI-causing microorganisms in Southern Punjab, Pakistan.

Main Problem to Solve: As use of antibiotics becomes commonplace without complete adherence or protocol, bacteria have started to emerge that are resistant to traditionally prescribed antibiotics. This study determines how some urinary tract infection causing organisms have become resistant to some common antibiotics.

Aim of Study: The aim of the study is to enhance treatment approaches, improve prescription practices, encourage microorganism culture and antibiotic sensitivity testing in hospital settings as well as encouraging antibiotic stewardships. Our goal is to provide valuable statistics regarding resistance patterns of UTI-causing microorganisms in the region as well as raise awareness and encourage health professionals to exercise caution in their prescription decisions and self-prescription among patients.

Methodology: Early morning mid-stream urine samples were collected from different wards of Sheikh Zayed Hospital, Rahim yar Khan. Informed consent and data like age, and ward name was collected through a self-developed questionnaire. Among those with positive growths were sent to microbiological culture sensitivity laboratory for analysis against 5 common antibiotics: Nitrofurantoin, Ciprofloxacin, Norfloxacin, TMP-SMX, Imipenem, Amoxicillin, Ceftriaxone, Fosfomycin, Linezolid. Kirby Bauer disk diffusion test was conducted to assess the sensitivity of the isolates. Data was analyzed using SPSS and the association between categorical variables was assessed using the Chi-square test. Descriptive statistics, including numbers, frequencies, and percentages, were used to describe the results obtained from culture and sensitivity tests.

Results: Out of the 101 urine samples tested, 42.08% showed positive growth of bacteria causing urinary tract infections. The most common bacteria found was *Escherichia coli (E. coli)*, which accounted for 58% of the positive growths followed by *Pseudomonas* (19%) and *Klebsiella* (13%), *Staphylococcus aureus (S. aureus)* (7%), and *coagulase-negative staphylococci (CoNS)* (3%)

Imipenem was found to be the most effective drug, with the highest sensitivity against bacteria causing urinary tract infections. It showed a sensitivity rate of 80% against gram-positive uropathogens, 78% against *E. coli*, and 76% against gram negative uropathogens. On the other hand, the bacteria showed the highest resistance to TMP-SMX, with resistance rates of 80% in gram-positive uropathogens, 74% in gram-negative uropathogens, and 73% in *E. coli*.

No significant association of sensitivity or resistance was found between any of the antimicrobial drugs and *E. Coli* or gram-positive uropathogens or gram negative uropathogens

Conclusion: The study concluded that urinary tract organisms displayed escalating resistance to commonly used antibiotics and antimicrobial stewardship programs are needed in hospitals along with development of improved diagnostic features and testing methods to differentiate among bacterial infections and eventually prescription of antibiotics accordingly.

References

1. Sulis G, Adam P, Nafade V, Gore G, Daniels B, Daftary A, et al. Antibiotic prescription practices in primary care in low- and middle-income countries: A systematic review and meta-analysis. PLoS Med. 2020;17(6):e1003139.
2. Abdelrazik E, El-Hadidi M. Tracking Antibiotic Resistance from the Environment to Human Health. Methods Mol Biol. 2023;2649:289–301.
3. Bilal H, Khan MN, Rehman T, Hameed MF, Yang X. Antibiotic resistance in Pakistan: a systematic review of past decade. BMC Infect Dis. 2021;21(1):244.
4. Ul Mustafa Z, Salman M, Aldeyab M, Kow CS, Hasan SS. Antimicrobial consumption among hospitalized patients with COVID-19 in Pakistan. SN Compr Clin Med. 2021;3(8):1691–5.
5. Muzammil M, Adnan M, Sikandar SM, Waheed MU, Javed N, Ur Rehman MF. Study of culture and sensitivity patterns of urinary tract infections in patients presenting with urinary symptoms in a tertiary care hospital. Cureus. 2020;12(2):e7013.
6. Alemkere G, Tenna A, Engidawork E. Antibiotic use practice and predictors of hospital outcome among patients with systemic bacterial infection: Identifying targets for antibiotic and health care resource stewardship. PLoS One. 2019;14(2):e0212661.
7. Tamadonfar KO, Omattage NS, Spaulding CN, Hultgren SJ. Reaching the end of the line: Urinary tract infections. Microbiol Spectr. 2019;7(3).
8. Kot B. Antibiotic Resistance Among Uropathogenic Escherichia coli. Pol J Microbiol. 2019;68(4):403–15.
9. Sante L, Lecuona M, Jaime-Aguirre A, Arias A. Risk factors to secondary nosocomial bacteremia to UTI in a tertiary hospital. Rev Esp Quimioter. 2019;32(4):311–6.
10. Kranz J, Schmidt S, Wagenlehner Florian and Schneidewind L. Catheter-associated urinary tract infections in adult patients. Dtsch Arztebl Int. 2020;117(6):83–8.

11. Karlowsky JA, Lob SH, Kazmierczak KM, Young K, Motyl MR, Sahm DF. In vitro activity of imipenem/relebactam against Enterobacteriaceae and Pseudomonas aeruginosa isolated from intraabdominal and urinary tract infection samples: SMART Surveillance United States 2015-2017. J Glob Antimicrob Resist. 2020;21:223–8.
12. Ravishankar U, P S, Thayanidhi P. Antimicrobial resistance among uropathogens: Surveillance report from south India. Cureus. 2021;13(1):e12913.
13. Chao YS, Farrah K. Fluoroquinolones for the Treatment of Urinary Tract Infection: A Review of Clinical Effectiveness, Cost-Effectiveness, and Guidelines. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2019.
14. Ten Doesschate T, Kuiper S, van Nieuwkoop Cees and Hassing RJ, Ketels T, van Mens Suzan P and van den Bijllaardt W, van der Bij AK, et al. Fosfomycin vs ciprofloxacin as oral step-down treatment for Escherichia coli febrile urinary tract infections in women: A randomized, placebo-controlled, double-blind, multicenter trial. Clin Infect Dis. 2022;75(2):221–9.
15. Miyoshi-Akiyama T, Tada T, Ohmagari N, Viet Hung N, Tharavichitkul P, Pokhrel BM, et al. Emergence and Spread of Epidemic Multidrug-Resistant Pseudomonas aeruginosa. Genome Biol Evol. 2017;9(12):3238–45.
16. Majumder MAA, Rahman S, Cohall Damian and Bharatha A, Singh K, Haque M, Gittens-St Hilaire M. Antimicrobial stewardship: Fighting antimicrobial resistance and protecting global public health. Infect Drug Resist. 2020;13:4713–38.
17. Redfern J, Bowater L, Coulthwaite L, Verran J. Raising awareness of antimicrobial resistance among the general public in the UK: the role of public engagement activities. JAC Antimicrob Resist. 2020;2(1):dlaa012.

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Original Article

Improving Access to Syphilis Screening Among Unhoused People in Yolo County, USA

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Abstract

Background: This study aimed to increase syphilis screening rates amongst unhoused residents of Yolo County, California, through the implementation of plan-do-study-act (PDSA) cycles. Yolo County has a strategic goal to eliminate congenital syphilis cases. Homelessness is a known risk factor for syphilis. **Methods:** The primary researcher was embedded in a street medicine team. Using quality improvement tools like stakeholder interviews, workflow diagrams, and best practices from literature, we outlined the team's workflow for syphilis screening and developed ideas to improve uptake and expand capacity. The most effective cycle implemented gift card incentives for syphilis screening. During the patient intake we offered the option to receive a syphilis test, informing the patient of the gift card incentive. **Results:** Prior to gift card incentives, the team screened 1.6 patients on average per clinic for a total of 30 patients screened in April to June of 2022. After the gift card incentive was implemented, the team screened 3.0 patients on average per clinic, screening a total of 223 patients from July 2022 to May 2023. The intervention produced an 87.5% increase in screening rates (P=0.0094). The data showed a significant increase in syphilis testing upon implementing the gift card incentive program. **Conclusion:** These findings contribute to evidence supporting the use of patient incentives for public health prevention measures. This model could be applied to other populations to increase health screening participation. More research is needed on the effect of gift card incentives on confirmatory testing and treatment rates for syphilis.

Introduction

Syphilis is a systemic, sexually transmitted infection (STI) caused by the spirochete bacterium. Treponema pallidum. Syphilis infections in the United States increased by 17.3% from 2021 to 2022 and, notably, congenital syphilis cases rose 30.6% during that time.[1] One in 1300 live births are affected by congenital syphilis.[2] If left untreated, syphilis can cause irreversible neurological damage, including cognitive impairment, paralysis and deafness. In neonates, the infection can cause seizures, vision problems and cranial nerve palsy.[2,3] Worse still, 2 of every 5 infants born with congenital syphilis will die from the infection soon after birth.[4] Most surviving infants face lifelong neurological deficits. Individuals with remote exposures and asymptomatic infections can still spread the disease, making screening a critical approach to controlling transmission.[5] Screening is particularly important in groups that account for disproportionate rates of syphilis and congenital syphilis cases, such as people experiencing homelessness.[6] Unfortunately, obtaining medical care, including screening and treatment for syphilis, is challenging for this vulnerable patient population.[7] People experiencing homelessness face unique barriers in accessing public services. For example, a trip to the clinic involves arranging help to guard belongings and watch over pets, coordinating timing to align with distribution of food and other essential needs and ensuring one's phone is charged, paid for, and has reception. Once these logistical barriers are overcome, the patient may face abuse from clinic staff. People experiencing homelessness delay or avoid medical care because of prior negative experiences with the health care system.[8] Homelessness also increases the risk of syphilis transmission because people are more likely to engage in transactional sex for survival and safety.[9] In addition, lack of transportation often impedes testing and treatments that require multiple clinic visits. Thus, people experiencing homelessness need a tailored approach for syphilis screening that is immediate, flexible, and overcomes trust barriers. Street medicine is a way to provide low-barrier care to unhoused patients. Our team sought to leverage the unique role of a street medicine team to increase syphilis screening for unhoused patients in Yolo County, California.

Yolo County, California is seated north of the Bay Area and west of the state capitol, Sacramento. Yolo has three major towns:

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Davis, Woodland, and West Sacramento. It has about a quarter of a million residents, half of whom are white and one third of whom are Hispanic.[10] About one in five residents live in poverty.[11] The county is geographically diverse with over 250,000 acres of farmland, a large state university (University of California at Davis) and an urban center, West Sacramento. The street medicine team we partnered with serves patients throughout the county in both rural and urban settings. Locations of service include farm worker housing, encampments, homeless shelters, day programs and temporary supportive housing units. The team also partnered with county public health officials and a homeless outreach team. Additionally, the county holds regular stakeholder meetings to monitor progress towards its strategic goal of congenital syphilis elimination. We attended these stakeholder meetings with the street medicine team to understand the challenges facing service providers.

The street medicine team we partnered with consists of a nurse, medical assistant, health coach, peer advocate, and prescriber. Services provided by the team include management of chronic and acute conditions, substance use treatment, and wound care. Listening to the street medicine team and county stakeholders, we realized that the street medicine team could increase capacity and uptake of its existing syphilis screening. We used the "Quality Improvement Essentials Toolkit" to identify targets for improvement and make systematic adjustments in workflows.[12] By working closely with stakeholders, and though a generous grant for incentives, we were able to increase syphilis screening by 87.5% per clinic day.

Methods

Our quality improvement project consisted of conducting interviews with stakeholders, characterizing the current workflow, and executing a series of Plan-Do-Study-Act (PDSA) cycles. Our stakeholders had hypothesized many reasons for why the team had low syphilis screening rates. These reasons included patient hesitancy, staffing and supply variables and environmental challenges. PDSA cycles allowed us to assess the impact of a particular change on screening update and capacity.

We conducted informal interviews with a variety of stakeholders including clinic managers, front-line staff, public health officers and patients, asking how to improve uptake of syphilis screening. We used their input to develop a cause and effect diagram and workflow. We drew on these documents to develop interventions for each PDSA cycle. For each PDSA cycle, the team decided on an intervention aimed at increasing the rates of syphilis screening, implemented it for 1-3 weeks, and observed whether it impacted the screening rate. Interventions included: altering patient flow, adjusting how the STI tests were offered (verbally vs nonverbally), developing a script for staff and using a rolling cart to transport testing materials to make them more accessible. However, none of these workflow adjustments significantly increased screening rates.

In our last and most successful PDSA cycle, we implemented an incentive system which provided patients with gift cards upon receiving STI testing for syphilis, human immunodeficiency virus (HIV), and hepatitis C. Patients were also offered chlamydia and gonorrhea testing, however these tests were not associated with the gift card incentive. This approach was inspired by the health teams' improved uptake of COVID-19 vaccines with gift card incentives. Furthermore, literature shows that incentivizing HIV/STI testing increases screening rates, especially when tailored to the specific population being screened.[13-16] Patients were offered a choice between a $25 Target or Walmart gift card. Funding for a 30-day pilot was provided by Partnership Healthplan of California, the primary Medicaid insurer for Yolo County. We described the intervention to each patient before asking if they would like to participate. Patient confidentiality was maintained according to standard healthcare privacy rules. For analysis, data was disaggregated from identifying information. We communicated with the patient that their decision to receive a gift card for screening would not affect their care in any manner.

Additional parameters around the gift cards were developed over fine-tuning PDSA cycles. Patients were eligible for the gift card if they had no prior syphilis infection and if their last screening test was over 90 days prior. The screening test used cannot detect new infections for patients with a history of treated syphilis. Patients with a history of syphilis were advised to get a blood test for antigen titers to assess for new infections. However, these patients could still receive the gift card incentive if they opted-in for HIV or HCV screening (if they were eligible, i.e. had no known infection and had not been tested in the prior 90 days).

Syphilis naive patients could receive testing more frequently than every three months but would not receive a gift card for those additional tests. Patients who opted in to the syphilis screening were encouraged to also get testing for HIV, HCV, gonorrhea and chlamydia. However, this additional testing was not required to receive a gift card. These parameters were developed to optimize limited resources, to limit complexity around the incentive and support equity for patients with a history of syphilis.

Table 1. **Participant Characteristics.**

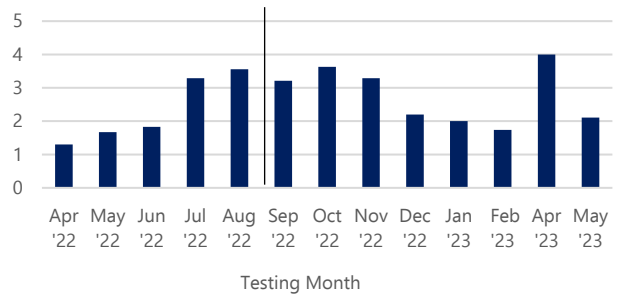
Race/ethnicity of participants	Number of participants (n)	Percentage of participants (%)
Hispanic/ Latino	86	34.1%
White / Caucasian	88	34.9%
Black/ African American	13	5.2%
American Indian / Alaska Native	9	3.6%
Multiracial	8	3.2%
Not reported	49	19.4%

Legend*:* This table describes the self-reported race/ethnicity of the study participants. The number of participants (n) of each race/ethnicity is reported in the second column and the percentage of total participants of that race/ethnicity is reported in the third column

Results

Slightly less than half (42.9%) of the patients tested identified as male. The racial/ethnic breakdown of the patients was: 34.1% Hispanic/Latino, 34.9% White, 5.2% Black/African American and 3.6% American Indian, with 19.4% declining to report ***Table 1***. This racial breakdown reflects known inequities in California housing.[17] In particular, Black Californians are four times more likely to be unhoused as compared to white Californians.[18]

***Figure 1*. Average Participants Tested per Clinic Day by Month**



Legend: The figure demonstrates the average number of participants tested per clinic day per month. The month of March 2023 was removed due to patient registration changes which resulted in the loss of data. Initiation of the gift card intervention is indicated by the black vertical line after June 2022. The vertical axis represents average number of patients tested per clinic day per month and the horizontal axis shows each month of the study.

Throughout the study, the average number of patients screened each month was determined by the sum of the patients screened each day divided by the total clinic days a health coach was present and offering screening. Prior to gift card incentives, the mean number of patients screened per clinic day was 1.6 (SD = 0.27) for a total of 30 patients screened from April to June of 2022. After the gift card incentive was implemented, the mean patients screened per clinic day was 3.0 (SD = 0.74) for a total of 223 patients seen from July 2022 to May 2023. The data revealed an 87.5% increase in screening rates after the gift card incentive program was implemented, the t-test revealing a significant increase, with $P = 0.0094$ (***Figure 1***). In an effort to prevent losing patients to follow up, the team initiated same day syphilis treatment. The initiative is ongoing.

Discussion

Challenges faced by the team included difficulties in the field-based venipuncture for confirmatory testing, gift card inclusion criteria, developing a workflow for people with a known syphilis diagnosis, and wording choice (infectious disease screening vs STI test). The biggest logistical challenge was weather. The test parameters require test storage at an ambient temperature of less than 86F. However, the team's workflow required seeing patients outdoors to reduce the risk of COVID-19 transmission. In July, as temperatures reached above 100F, the tests yielded false positives. The team donned additional personal protective equipment and moved services into air-conditioned spaces when possible. Staff turnover and scheduling barriers also affected results. High staff turnover resulted in inconsistencies when describing the intervention to the patients. Furthermore, fewer tests were performed in December through February because of holiday schedules. We also had to exclude data from March 2023 due to a change in the clinic's patient registration methods which resulted in missing and unaccounted-for data.

Overall, in this small study, the gift card intervention provided to be a highly effective method for increasing rates of syphilis testing among unhoused patients. The intervention period ended in July of 2023. We are now tracking testing uptake after withdrawal of gift card incentives. Furthermore, including pre-intervention data from December, January and February could reveal whether the low testing rates in those months were random or due to external factors as those mentioned previously. These findings show that gift card incentives can be a health equity tool. For patients who have unreliable sources of food, clothing, shelter, or hygiene supplies, a gift card incentive can provide the additional benefit needed to encourage engagement in services. The incentives may also provide a positive association with health care services, perhaps ameliorating some of the mistrust that has built up. Patient interactions should be conducted with respect, humility and reliability to reinforce the positive impact of the gift card incentive. This study contributes to evidence supporting the use of patient incentives for public health prevention measures, particularly for vulnerable populations. More research is needed on the effect of gift card incentives on treatment rates for syphilis and prevention of congenital syphilis.

Bias And Limitations.

The study's generalizability is limited by influences such as seasonal variations, holidays, small sample size and individual bias. For example, during the summer, seasonal agriculture workers make up half of the patients seen. This may produce fluctuations in testing rates. The patient population was also affected by seasonal variations as people experiencing homelessness may change their location based on weather. This may partially explain the drop in testing seen in the coldest winter months. Holidays in the winter months also resulted in more clinics missed and reduced patient population size, likely also contributing to the drop in testing seen during these months. The relatively small sample size weakens the generalizability of the study and should be addressed by future studies which implement the intervention to more patients, across different geographic regions. Despite standardized training in how to offer and conduct the STI testing, individuals involved in the intervention were also subject to bias. Language barriers and use of translators with Spanish-speaking patients may have created additional limitations in standardizing the interventions protocols. Because unhoused people often are in unstable financial situations, the gift card incentive may be more effective in this group compared to other groups. Further studies should examine if this incentive program is effective when applied to other groups.

References

1. Centers Centers for Disease Control and Prevention. Available online: https://www.cdc.gov/std/statistics/2022/overview.htm#Syphilis (accessed on 30 January 2024)
2. Stafford, I. A., Workowski, K. A., & Bachmann, L. H. (2024). Syphilis complicating pregnancy and congenital syphilis. New England Journal of Medicine, 390(13). https://doi.org/10.1056/nejmc2401932
3. Medoro AK, Sánchez PJ. Syphilis in Neonates and Infants. Clin Perinatol. 2021;48(2):293-309.
4. Leslie SW, Vaidya R. Congenital and Maternal Syphilis. [Updated 2024 Aug 17]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK537087/
5. Bourchier, L., Goller, J., & Bittleston, H. (2023). Detecting asymptomatic syphilis. The Lancet Regional Health - Western Pacific, 40, 100901.
6. Liu CY, Chai SJ, Watt JP. Communicable disease among people experiencing homelessness in California. Epidemiol Infect. 2020;148:e85.
7. Fazel S, Geddes JR and Kushel M. The health of homeless people in high-income countries: descriptive epidemiology, health consequences, and clinical and policy recommendations. The Lancet 2014;384(9953):1529–1540.
8. Thorndike AL, Yetman HE, Thorndike AN, Jeffrys M, Rowe M. Unmet health needs and barriers to health care among people experiencing homelessness in San Francisco's Mission District: a qualitative study. BMC Public Health. 2022;22(1):1071.
9. Weiser SD et al. (2006) Gender-specific correlates of sex trade among homeless and marginally housed individuals in San Francisco. Journal of Urban Health 83, 736–740.
10. Demographic indicators | Yolo County. (n.d.). https://www.yolocounty.gov/government/general-government-departments/county-administrator/yolo-county-community-indicator-dashboard-3347
11. New infographic summarizing preliminary results from the UC davis research team that is evaluating the Yolo County Basic Income. Center for Poverty and Inequality Research. (n.d.). https://poverty.ucdavis.edu/post/new-infographic-summarizing-preliminary-results-uc-davis-research-team-evaluating-yolo-county
12. Quality Improvement Essentials Toolkit. Boston: Institute for Healthcare Improvement; 2017. (Available at ihi.org)
13. Lambert T, Finlay J, Krahn J, Meyer G, Singh AE, Kennedy M, Caine V. Incentive-Based Sexually Transmitted and Blood-Borne Infections Screening in High-Income Countries: A Systematic Review. Sex Transm Dis. 2022;49(6):398-402.
14. Rapid Response Service. Effectiveness of and best practices for using contingency management and incentives for health care issues related to HIV, sexually transmitted infections (STIs), and pre-exposure prophylaxis (PrEP). Toronto, ON: The Ontario HIV Treatment Network; June 2021.
15. Gambone GF, Feldman MB, Thomas-Ferraioli AY, Shubert V, Ghose T. Integrating Financial Incentives for Viral Load Suppression into HIV Care Coordination Programs: Considerations for Development and Implementation. J Public Health Manag Pract. 2020;26(5):471-480.
16. Montoy JCC, Dow WH, Kaplan BC. Cash incentives versus defaults for HIV testing: A randomized clinical trial. PLoS One. 2018;13(7):e0199833.
17. Willison C, Unwala N, Singer PM, Creedon TB, Mullin B, Cook BL. Persistent Disparities: Trends in Rates of Sheltered Homelessness Across Demographic Subgroups in the USA. J Racial Ethn Health Disparities. 2024;11(1):326-338.
18. California statewide study of people experiencing homelessness. Benioff Homelessness and Housing Initiative. (2023, June). https://homelessness.ucsf.edu/our-impact/studies/california-statewide-study-people-experiencing-homelessness

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Short Communication

Evolving Patterns in Inpatient Pediatric Consultations to Allergy/Immunology at an Academic Medical Center

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Abstract

Background: Consultations to pediatric allergy/immunology are of benefit to many hospitalized inpatients, but there is limited current information about how T-cell receptor excision circles (TREC) screening may have changed these patterns for pediatric populations. We aimed to determine the types of consults being requested and their relative frequencies for primary pediatric allergy/immunology consults under an academic fellowship program since the start of TREC screening in 2016. Information gained could help identify focal concepts for pediatric allergy inpatient training curricula for fellowship and graduate medical education programs. **Methods**: Under an IRB approved study of an academic allergy fellowship consultation log, we retrospectively reviewed electronic medical records of pediatric allergy and immunology consults and categorized consultations by their primary indication. **Results**: Three-hundred and eighty-three pediatric allergy/immunology consultations were seen between September 4, 2016 to November 24, 2022. In terms of frequency, the most common consultation was for immunodeficiency evaluation or treatment, n=205 (53.5%), followed by drug allergy n=55 (14.4%), general allergy concerns n=43 (11.2%), skin allergy n=35 (9.1%), and less commonly inflammatory syndromes, n=26 (6.8%) and food allergy, n=19 (5.0%). Questions related to TREC screening comprised 21% of all immunodeficiency consults, at n=43. **Conclusion**: At an academic allergy center where all allergy/immunology service lines are currently provided, the most common reason for pediatric consultations were for help with immunodeficiency evaluation/treatment and drug allergy. TREC screening is a new key indication for consultation. Fellowship programs may benefit from focusing on these content areas for the pediatric inpatient setting.

Introduction

Allergy and Immunology are increasingly important disciplines as the rates of pediatric and adult allergies continue to rise and treatments for immunodeficiency improve. According to the CDC in 2021, over 1 in 4 children in the United States report having seasonal, food, or skin allergy.[1] Allergist/Immunologists within both the pediatric and adult patient population care for a wide variety of isolated or systemic disorders, ranging from autoimmune, inflammatory, and allergic conditions to diseases relating to immunodeficiency. Within the field of pediatric allergy/immunology, some commonly followed conditions include allergic rhinitis, allergic conjunctivitis, drug allergy, food allergy, anaphylaxis, atopic dermatitis, urticaria, angioedema, asthma, common variable immunodeficiency, congenital immunodeficiencies, etc. Training clinically and in the field of research allows of these clinicians to see and treat a wide variety of allergic and immunologic disorders both in the inpatient and outpatient setting.

Consultations to Pediatric Allergy/Immunology are of benefit to many hospitalized inpatients, but there is limited information about the scenarios under which allergists are currently consulted in pediatric inpatient care. Such information might help Allergy/Immunology fellowship training programs and graduate medical education programs develop their Pediatric Allergy/Immunology curricula. Therefore, we sought to retrospectively determine the types and frequencies of Pediatric Allergy/Immunology consults being requested from an academic fellowship program within the Vanderbilt Monroe Carell Children's Hospital System.

Severe combined immunodeficiency disorder (SCID) refers to many disorders that culminate in a deficient functional T cell phenotype and represents the most severe form of immunodeficiency in the pediatric patient population. Previously, clinical suspicion to further explore and identify SCID was based off recurrent and often fatal infectious complications. T-cell receptor excision circles (TRECs) are stable circular DNA molecules generated during the development of T cell receptor diversification in the thymus. By recombining genes in the anticipation of any foreign antigen presented to the body, TRECs are a subsequent byproduct formed and can serve as an indicator for recently produced naïve T cells. Integrating TREC measurement as a part of newborn screening (NBS) guidelines has allowed for the initiation of life-saving treatment and reinstatement of a functional immune system in an infant otherwise susceptible to life-threatening infection.[2,3]

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Importantly, we sought to investigate the current information about how new practices of TREC screening in newborns may have changed patterns in Allergy/Immunology consultation for pediatric populations.

Methods

Design and Study Population

This was a cross-sectional descriptive study. The patient population consisted of 383 pediatric allergy/immunology patients whose records of consultation were collected retrospectively in a HIPAA compliant REDCap[4] consultation log between September 4, 2016 to November 24, 2022. This time period allowed for the capture of a comprehensive dataset pertinent to the introduction of TREC as part of newborn screening in the state of Tennessee starting January 2016. Inclusion criteria included pediatric patients consulted to allergy/immunology within this time frame with an age range from 0 days up to, but not exceeding, 18 years of age. Exclusion criteria included patients greater than the age of 18 years and consultations falling outside the study's defined time frame. Convenience sampling was employed to include all relevant consultations within the specified time frame and accurately assess their relative frequencies. A retrospective review approach was employed to collect consultation records under an IRB approved study (#211354), to review the log and electronic medical records from these pediatric allergy and immunology consults, and subsequently categorize these consultations by their primary indication.

Statistical Methodology

Categorization of primary reason for consult was based on broadly observed categories of immunodeficiency evaluation, inflammatory syndromes, drug allergy, food allergy, skin allergy, and general allergy (which included asthma, idiopathic anaphylaxis, urticaria/angioedema, rhinitis). Each primary reason was then subcategorized to create a deeper understanding of the reason for consultation and identify any large groupings. In cases where patients had multiple reasons for consultation, only the primary reason for consultation counted toward the patient's finalized categorization and subcategorization. For instance, a patient could be consulted for severe eczema and amoxicillin allergy. Through further chart review, it could be discovered the primary focus of the consultation was for severe eczema. Drug allergy may have remained part of the clinical question for consultation; however, after further investigation it was not clinically relevant to their current need for impatient consultation service nor had impact on their current hospital stay. Such complex cases often required chart review to discover true etiology of consultation need and help clarify proper and primary category and subcategory placement.

Categorical statistical calculation was employed by comparing the number of patients assigned to each category to the overall study population (n=383). Subcategorical statistical calculation was employed by comparing the number of patients assigned to each subcategory to the number of patients assigned to the broader category (e.g., FPIES n=6 (31.6%) where food allergy n=19). Percentages of respective categorical and subcategorical groupings were utilized for gross comparison of frequency of consultation.

Results

Patient Characteristic and Categorization Results

The age distribution of the cohort of Pediatric Allergy/ Immunology consults at Vanderbilt ranged from 0 days to 18 years (Mean, 6.06 years, SD = 6.71 years). The gender distribution included n=203 (53.3%) males and n=178 (46.7%) females. During years for which we had complete calendar data (2017-2021), we observed 47 consultations performed in 2017, 79 in 2018, 58 in 2019, 55 in 2020, and 74 in 2021 (***Table 1***). In terms of frequency, the most common consultation was for immunodeficiency evaluation or treatment, n=205 (53.5%), followed by drug allergy n=55 (14.4%), general allergy concerns n=43 (11.2%), skin allergy n=35 (9.1%), and less commonly inflammatory syndromes, n=26 (6.8%) and food allergy, n=19 (5.0%). Questions related to TREC screening comprised 11% of all consults, at n=43 (21% of all immunodeficiency consults) as shown in ***Table 2***.

Table 1. **Patient Characteristics of 383 Pediatric Allergy and Immunology Consultations During the Study Period.**

Patient Characteristic	Frequency (n)	%
Age at Time of Consultation **(n = 379)	6.06 years (±6.71)*	
Reported Sex (n = 381) **		
Males	203	53.3
Females	178	46.7
Year of Consultation (n=382)**		
Sep 4th '16-Dec 31st '16	16	4.2
2017	47	12.3
2018	79	20.7
2019	58	15.2
2020	55	14.4

Legend: *mean ± SD. ** small numbers of patients with missing age, sex, and year of consultation data.

Patient Subcategorization Results

One hundred and four (51%) of 205 consultations for immunodeficiency were either requests to evaluate immune function or related to TREC screening results. Additional immune evaluation subcategories included secondary immunodeficiency in undiagnosed patients, such as lymphopenia, hypoplastic left heart syndrome (HLHS), etc. Other reasons for pediatric immunodeficiency consult included frequent, recurrent or disseminated infections, n=35 (17.1%), IVIG management, n=32 (15.6%), congenital syndromes, n=22 (10.7%), fever, n=7 (3.4%), management of diagnosed immunodeficiency, n=3 (1.5%), and immunodeficiency associated with transplant, n=2 (1.0%), as shown in ***Table 2***.

Table 2. **Patient Categories and Subcategories of 383 Pediatric Allergy and Immunology Consultations During the Study Period.**

Consults Received	Category Consultation (n)	Overall Consultation (%)
Immune Evaluation	*205*	*53.5*
TREC screening	43	21.0
Infection	35	17.1
IVIG management	32	15.6
Congenital Syndrome	22	10.7
Fever	7	3.4
Diagnosed Immunodeficiency	3	1.5
Transplant	2	1.0
Drug Allergy	*55*	*14.4*
Antimicrobial	32	58.2
Other Drug	11	20.0
DRESS/SJS	6	10.9
Contrast Media	4	7.3
Reaction During Catheterization	2	3.6
General Allergy	*43*	*11.2*
Angioedema (± anaphylaxis)	20	46.5
Anaphylaxis only	18	41.9
Asthma (± anaphylaxis)	3	7.0
Nasal Secretions	1	2.3
Vocal Cord Dysfunction	1	2.3
Skin Allergy (n = 35)	*35*	*9.1*
Urticaria (± angioedema)	15	42.9
Eczema	13	37.1
Rash	3	8.6
Contact Dermatitis	2	5.7
Erythema	1	2.9
Skin Care	1	2.9
Inflammatory Syndromes (n = 26)	*26*	*6.8*
IBD/Colitis	10	38.5
Mastocytosis/Hypereosinophilia/ Hyper IgE	9	34.6
Recurrent Fever	3	11.5
HLH	2	7.7
Cytokine Storm	1	3.9
Food Allergy	*19*	*5.0*

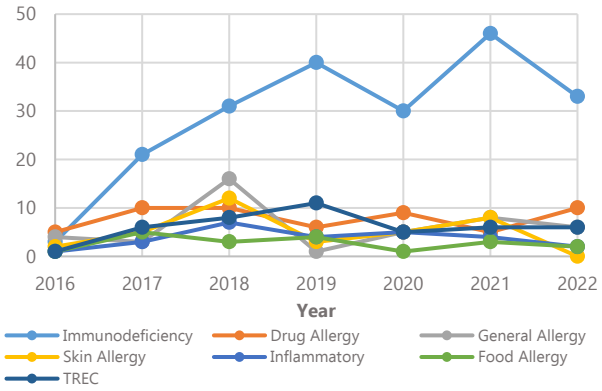
Legend: *mean ± Standard deviation. ** small numbers of patients with missing age, sex, and year of consultation data. Immunodeficiency subcategories include infections requiring workup, IVIG therapy management, congenital syndromes, fever indicating immunodeficiency, prior diagnoses needing care, and transplant-related complications. Drug allergy subcategories cover non-antimicrobial allergies and severe reactions (DRESS/SJS). General allergy includes angioedema and anaphylaxis consultations, while skin allergy covers urticaria and eczema cases.

Drug allergy comprised 14.4% of consultation requests, for which 58% of drugs were antimicrobials, consistent with their prominent therapeutic role.[5] Drug challenges were performed in 3 patients and desensitization for 1 patient, together comprising 12.5% of the antimicrobial subcategory. Reasons for pediatric drug allergy consults also included other drugs specified, n=11 (20.0%), Drug Rash with Eosinophilia and Systemic Symptoms and Stevens-Johnson syndrome (DRESS/SJS), n=6 (10.9%), contrast media reaction, n=4 (7.3%), and reaction during a catheterization, n=2 (3.6%), as shown in ***Table 2***.

Angioedema and idiopathic anaphylaxis comprised 88% of the primary reasons for general allergy consults. Other general allergy subcategories included asthma, n=3 (7.0%), nasal secretions/rhinitis, n=1 (2.3%), and vocal cord dysfunction, n=1 (2.3%) as shown in ***Table 2***.

Urticaria and eczema/atopic dermatitis comprised 80% of the primary reasons for skin allergy consult. Other subcategories for skin allergy consult included rash, n=3 (8.6%), contact dermatitis, n=2 (5.7%), erythema, n=1 (2.9%), and questions about how to perform skin care, n=1 (2.9%) as shown in ***Table 2***.

Figure 1. **Number of Category and T-cell receptor excision circles (TREC) Consults per Year.**



Legend: The Mann-Kendall test was used to determine Kendall's tau correlations for the number of consults in each category from 2017-2021, excluding 2016 and 2022 due to incomplete data. For immunodeficiency, the correlation was 0.600 (p = 0.142); for drug allergy, -0.738 (p = 0.077); for general allergy, 0.200 (p = 0.624); for skin allergy, 0.200 (p = 0.624); for inflammatory, 0.316 (p = 0.448); for food allergy, -0.527 (p = 0.207); and for TREC, -0.105 (p = 0.801).

Inflammatory syndromes and food allergy together comprised 12% of the overall consultations, comprising the least common reason for Allergy/Immunology consults. Inflammatory bowel disease/colitis, n=10 (38.5%), and mastocytosis/ hypereosinophilia/hyper IgE syndromes, n=9 (34.6%), comprised the largest subcategories for inflammatory syndrome consult. Other subcategories for inflammatory syndrome consult included recurrent fever, n=3 (11.5%), hemophagocytic lymphohistiocytosis (HLH), n=2 (7.7%), cytokine storm, n=1 (3.8%), and hypersensitivity pneumonitis, n=1 (3.8%). General food allergy, n=11 (57.9%), comprised the largest subcategory of food allergy, with other subcategories including food protein-induced enterocolitis syndrome (FPIES), n=6 (31.6%), and alpha-gal syndrome, n=2 (10.5%) as shown in ***Table 2***.

Mann-Kendall test was utilized to identify Kendall's tau correlation between number of consults in each category as well as TREC subcategorization over time, including only years 2017-2021 due to incomplete yearly data from 2016 and 2022. Overall, there was not a significant trend of change of category or TREC consultations over the study period as shown in **Figure 1**.

Discussion

Key Findings

Overall, the highest area for consultation was immunodeficiency, followed by drug allergy, general allergy, skin allergy, inflammatory syndromes, and food allergy. Of interest, the highest subcategorization of immunodeficiency consultations was to evaluate immune function and second highest relating to TREC screening results. There was no significant trend in category or TREC consultation change over time, which may be seen due to limited amount of consultations made to inpatient pediatric allergy/immunology as a field to the inpatient setting. A multicenter study with larger study population may be employed in the future to rectify a potential type 2 error. Within this greater context, immunodeficiency is clearly a key, prominent area for inpatient pediatric consultation at our center, followed by drug allergy consultations. Conversely, at our medical center, anaphylaxis, food allergy, and asthma exacerbations requiring hospitalization are typically managed by the inpatient general pediatric team with outpatient follow up in allergy/immunology, without the need for allergy consultation, which may differ at other institutions.

Investigation of Relevant Literature

The results of this study are interesting when contrasted with a few earlier studies that are available. In contrast to a previous study reviewing pediatric inpatient consults to Allergy/Immunology from 1995 to 1999, where immunodeficiency evaluations accounted for only 9.7% of cases, our dataset revealed a notably increased shift, comprising 53.5% of our dataset. This stark difference underscores the evolving landscape of pediatric healthcare, with asthma remaining the primary consultation category at 58% in the earlier study.[6] This earlier study also found that ruling out DiGeorge syndrome was the leading reason for immunodeficiency evaluation.[6] In contrast, congenital syndromes accounted for only 11% of reason for immunodeficiency consults in our patient population. Compared to a study by Kim et al. from 1999-2013, we found that asthma was not our predominant reason for pediatric consultation, but the order of common indications was similar thereafter.[7] Our findings are similar to those of Kempe et al, who reported on consultations at a pediatric academic center with immunodeficiency services between 2009-2014. However, the addition of newborn TRECs screen has added a new high-volume indication for consults.[8] Compared to studies from other centers, the frequency of consultations for food allergy, inflammatory syndromes and skin allergy in this study are similar, suggesting that allergy/immunology is not the primary service involved in acute management of most of these events. Future research may be necessary to elucidate the reasoning behind the overall increase in immunodeficiency consultations compared to studies from previous time periods.

Impact of TREC in Newborn Screening

Tennessee initiated TREC screening in newborns in the year 2016, which likely corresponds with the high rates of TREC consults reasons seen within the timeframe of this study.[9] SCID is considered a pediatric emergency with a high mortality within the first 1 to 2 years of life if left untreated. Bone marrow transplant of patients <3.5 months of age and without infection has been shown to improve their overall survival.[10] Furthermore, patients diagnosed earlier through NBS were less likely to develop infection before bone marrow transplantation.[11] Similar success has been found in long-term outcome follow-up.[12] Our study demonstrates real change in the wake of TREC becoming part of newborn screening in 2016, with a high volume of relevant consultations.

Impact of Physician Education

It has been shown that implementing educational opportunities increases physician knowledge of immunodeficiency.[13] This can thereby increase early detection and subsequently initiate lifesaving treatment in a time sensitive manner for relevant populations. This is especially relevant in the wake of increasing immunodeficiency related consultations as seen in this study. Most allergy/immunology programs are relatively small and therefore place a significant burden on program faculty to prepare content for learners in areas they may only rarely encounter themselves. Therefore, educational gaps may be in place when trying to teach the next generation of physicians the knowledge base that is necessary for continuity of this field.[14] Alongside the increase of telemedicine utilization in medical practice there is an additional increase in online educational opportunities and support for physicians practicing in the field of immunodeficiency. Medical education programs and listserves utilizing these growing resources and closing these educational gaps remains imperative to further proper patient care while there continue to be rapid gains of knowledge and evolution in the allergy/immunology field.

Limitations

Our study may have limitations in generalizability due to being conducted at a single, academic, tertiary medical center. However, the breadth of consulting services and relevant expertise in different aspects of allergy/immunology at a tertiary center may also identify the range of consults it is possible to receive. Limitations of this study may also include inability to rule out occasional missing data on consultations performed during this time period.

Conclusion

In conclusion, at an academic allergy center where all pediatric Allergy/Immunology service lines are currently provided, the most common reasons for pediatric consultation were for immunodeficiency evaluation/treatment and drug allergy, suggesting that these two areas may have a higher rate of needs specific to the inpatient setting. With recent rapid changes occurring in both of these content areas, fellowship programs may benefit from a training focus in immunology, pediatric immunodeficiency, and drug allergy relevant to the pediatric inpatient setting. Our findings suggest that formal training on the implications and evaluation of TREC screening results and common drug allergy scenarios should be a part of the core pediatric allergy/immunology curriculum at every fellowship. In particular, the inclusion of TREC testing in neonatal screens has resulted in a prominent subcategory of consultations that will likely need a specific focus when educating future clinicians.

Summary – Accelerating Translation

Understanding the Patterns of in Pediatric Inpatient Allergy and Immunology Consultations

Main Problem to Solve: Pediatric allergies and immunological issues continue to be on the rise and even require intervention in the hospital; however, there is still limited information out there as to the key reasons for consulting such specialists. This study aimed to investigate reasons behind consultation to Allergy/Immunology services in the inpatient setting as new technology and screening practices continue to evolve. In 2016, TREC was introduced as part of the newborn screen, which checks for serious and rare treatable health conditions at birth. This implementation was especially important for the early diagnosis and treatment of severe combined immunodeficiency disease (SCID), a group of rare and life-threatening diseases that can severely impact the ability of a child to fight infection. As such, we sought to investigate the current information about how new practices of TREC screening in newborns may have changed these patterns of consultation for pediatric populations.

Aim of the Study: The goal of this study was to uncover the types and frequencies of pediatric allergy and immunology consultations within the Vanderbilt Monroe Carrel Children's Hospital System. Identifying patterns in consultations and assessing how new practices, such as the introduction of TREC as part of Newborn Screening, would influence key reasons for seeking specialized care. This could provide valuable information for medical training programs to help tailor their curricula to meet the evolving needs of patients and physicians.

Methodology: This study included 383 hospitalized pediatric patients who sought allergy/immunology consultations between September 2016 and November 2022. All records collected ensured the legal right to medical privacy was maintained. Following review of the consultation logs and electronic medical records, consultations were categorized based on primary reasons for allergy/immunology subspecialty involvement. Top primary reasons for consult included of immunodeficiency evaluation, inflammatory syndromes, drug allergy, food allergy, skin allergy, and general allergy. These reasons were then further subdivided to gain a deeper understanding of the specific issues prompting consultation.

Results: The age range of pediatric patients seeking allergy/immunology consultations in the hospitalized setting at Vanderbilt ranged from 0 days to 18 years. The gender distribution was relatively balanced, with slightly more males (53.3%) than females (46.7%). In terms of frequency, the most common primary reasons for consultation included immunodeficiency evaluation or treatment (53.5%), followed by drug allergy (14.4%), general allergy (11.2%), skin allergy (9.1%), inflammatory syndromes (6.8%), and less commonly food allergy (5.0%).

The study identified specific subcategories within each primary reason to offer a more detailed look into consultation reasoning. Importantly, from this it was found that questions related to TREC screening comprised 21% of all immunodeficiency consults and 11% of all total consults.

Conclusion: The results of this study show the diverse reasons for Allergist and Immunologist need within the pediatric inpatient setting. Immunodeficiency and drug allergy related consultations emerged as the most common reasons for seeking specialized care. Notably, the inclusion of TREC screening as part of Newborn Screening practices across the nation starting in 2016 has impacted consultation patterns as compared to earlier scientific studies on this topic. This shows how dynamic the field of pediatric allergy and immunology care are as medical and technological advances continue to progress. This is especially important in the cases of life-threatening disease where early intervention is imperative towards child survival, such as in SCID.
In conclusion, this study suggests that for allergy and immunology experts, there is a higher rate of need for immunodeficiency evaluation/treatment and drug allergy intervention in the inpatient setting. The findings underscore the importance of adapting education to address evolving trends and incorporating new screening practices into training programs. In particular, the inclusion of TREC testing in neonatal screens has resulted in a prominent subcategory of consultations that will likely need a specific focus when educating future clinicians. By doing so, medical professionals can stay well-equipped to handle the changing landscape of pediatric allergy and immunology and ensure optimal care.

References

1. Centers for Disease Control and Prevention. Diagnosed Allergic Conditions in Children Aged 0-17 Years: United States, 2021. Available from: https://stacks.cdc.gov/view/cdc/123250. Last updated Jan 23, 2023; cited Jul 16, 2024.
2. Quinn J, Orange JS, Modell V, Modell F. The case for severe combined immunodeficiency (SCID) and T cell lymphopenia newborn screening: saving lives… one at a time. Immunol Res. 2020;68(1):48-53.
3. Puck JM. Newborn screening for severe combined immunodeficiency and T-cell lymphopenia. Immunol Rev. 2019;287(1):241-52.
4. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform. 2009;42(2):377-81.
5. Blumenthal KG, Peter JG, Trubiano JA, Phillips EJ. Antibiotic allergy. Lancet. 2019;393(10167):183-98.
6. Quinn JM. Pediatric inpatient consultation of allergy/immunology. Pediatr Asthma Allergy Immunol. 2000;14(4):293-9.
7. Kim SJ, Sheikh J, Kaplan MS, Goldberg BJ. Trends in allergy/immunology inpatient consultations, 1991–2013. Ann Allergy Asthma Immunol. 2014;113(5):577-8.
8. Kempe E, Stukus DR, Strothman K, Scherzer R. Allergy and immunology inpatient and emergency department consultations at a pediatric academic medical center. Ann Allergy Asthma Immunol. 2016;116(4):373-4.
9. Krantz MS, Stone CA, Jr., Connelly JA, Norton AE, Khan YW. The effect of delayed and early diagnosis in siblings, and importance of newborn screening for SCID. Ann Allergy Asthma Immunol. 2019;122(2):211-3.
10. Pai S-Y, Logan BR, Griffith LM, Buckley RH, Parrott RE, Dvorak CC, et al. Transplantation outcomes for severe combined immunodeficiency, 2000–2009. N Engl J Med. 2014;371(5):434-46.
11. Heimall J, Logan BR, Cowan MJ, Notarangelo LD, Griffith LM, Puck JM, et al. Immune reconstitution and survival of 100 SCID patients post–hematopoietic cell transplant: a PIDTC natural history study. Blood. 2017;130(25):2718-27.
12. Buckley RH. Transplantation of hematopoietic stem cells in human severe combined immunodeficiency: longterm outcomes. Immunol Res. 2011;49:25-43.
13. Hariyan T, Kinash M, Kovalenko R, Boyarchuk O. Evaluation of awareness about primary immunodeficiencies among physicians before and after implementation of the educational program: A longitudinal study. PLoS One. 2020;15(5):e0233342.

14. Pien LC, Colbert CY. Time to develop more clinician-educators in allergy and immunology. J Allergy Clin Immunol. 2020;145(2):456-62.

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Review

Vascular Anomalies Review of the Head and Neck for Physicians in Training

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Abstract

A basic understanding of vascular anomalies will aid physicians-in-training as they seek to properly diagnose and determine interventions for these patient presentations. The aim of this review is to create a resource for physicians in training that encompasses the most important clinical aspects of vascular anomalies. Vascular anomalies of the head and neck are divided into two categories: vascular tumors and vascular malformations. This review will first describe vascular tumors followed by vascular malformations and discuss major pathology found in both categories of vascular anomaly. The MEDLINE/PubMed database was searched for primary research and reviews discussing various vascular anomalies which include infantile hemangioma, congenital hemangioma, pyogenic granuloma, tufted angioma, kaposiform hemangioendothelioma, capillary malformations, lymphatic malformations, venous malformations, and arteriovenous malformations. We conducted the search from July 5, 2023, to March 21, 2024. Vascular anomalies are frequently found in pediatric populations and can persist into adulthood, making it important for trainees to identify them on physical exam. This developing field seeks to improve form, function, and quality of life for patients with vascular anomalies and often requires a multidisciplinary approach (i.e., otolaryngology, dermatology, genetics, plastic surgery, interventional radiology). Various medical and surgical treatment options are available. A basic knowledge of these anomalies will allow for accurate, early diagnosis and appropriate intervention which can ultimately improve patient outcomes.

Introduction

Vascular anomalies are diseases that involve abnormal development of blood vessels. Further understanding of their development and behavior have helped us differentiate these diagnoses into vascular tumors and vascular malformations.[3] Proper categorization of these diagnoses informs treatment, helps to identify potential complications, and aids patients' families to understand the natural course of these conditions. One of the most common vascular anomalies, infantile hemangioma, has been found to have an incidence as high as 4.5%,[1] making it crucial for physicians-in-training to recognize and understand the management of its pathology. While various articles and textbooks[2] intended for physicians are available to study vascular anomalies, a review of the common pathologies, their diagnosis and treatment targeted toward trainees does not yet exist. The purpose of this review is to provide a resource for physicians-in-training seeking to aid their patients in diagnosis and treatment decision-making. To achieve an appropriate diagnosis, trainees should recognize various pitfalls that may present. For example, vascular tumors can be mistaken for other tumors or infections. Additionally, different imaging modalities may show varying degrees of malformation that can be misinterpreted by radiologists. Therefore, an adequate history and physical exam should be performed to ensure a comprehensive understanding of the malformation.

Vascular Tumors

Vascular tumors are neoplasms originating from vessels that impact vessel organization and development. They are classified based on their malignant or local destruction potentials.[4] The following is a description of the epidemiology, pathophysiology, diagnosis, and management of some of the common vascular tumors.

Infantile Hemangioma

Epidemiology

Infantile hemangioma (IH) is the most commonly diagnosed soft tissue tumor and is present in 4-10% of children.[5] Though not typically present at birth, they generally become clinically apparent within the first month of life and continue to proliferate until 3-4 months of age.[5] Growth of IH ultimately plateaus, followed by an involution phase. Generally, 50% involution occurs by age 5 and 70% by age 7. Involution is often incomplete and can cause permanent skin changes or disfigurement.[5–7] The most common risk factors for IH include preterm birth, placental abnormalities, female gender, low birth weight, being a product of multiple gestations, and family history.[8]

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Figure 1. **Infantile Hemangiomas.**

Legend: A. Segmental upper extremity IH. B. Superficial hemangioma of the forehead. C. Deep hemangioma of the back. D. Segmental facial hemangioma, concerning for PHACES.[2] E. Hemangiomatosis. Multiple infantile hemangiomas (≥5) place patients at increased risk of hepatic hemangioma.

Pathophysiology

Although the pathophysiology of IH is unclear, growing evidence suggests a placental origin due to multiple similarities including growth pattern (9 months of rapid growth) and presence of similar molecular markers (GLUT1, transcriptome, microRNA profiles).[2,9–11]

Diagnosis

The most common location for IH to present is the head and neck, potentially impacting aesthetics, and functionality.[12] Clinical appearance varies broadly depending on location, depth, extent, and stage of evolution.[5] IH are classified by depth: superficial, mixed, or deep. Superficial IH present as bright red plaques, nodules, or masses. Deep IH appear as skin-colored masses with a bluish tint (***Figure 1, A-C***). Mixed IH are a combination of bright plaques and skin-colored masses.[13] An alternative classification is employed based on extent: IH arising from a single growth focus are categorized as localized/focal, while segmental IH presents in a linear or geographic cutaneous area.[13,14] IH is primarily diagnosed via history and physical exam. Imaging is used when uncertainties arise (i.e., distinguishing among vascular anomalies from more aggressive neoplasia, to delineate the extent of the tumor).[115] Generally, ultrasonography with doppler is the first modality of choice. An IH in the proliferative phase appears as a well-defined mass with non-homogeneous echostructure that demonstrates high-flow uniform vessel distribution.[16] While the mass is involuting, it will appear more hyperechoic due to the increased fat deposition and present with less vascular density.[16] MRI is helpful when determining depth of involvement or in cases of visceral involvement. IH are well-circumscribed masses that are isointense on T1-weighted sequences, hyperintense on T2-weighted sequences, and show avid post-contrast enhancement without arteriovenous shunting (as seen in arteriovenous malformations).[17]

Management and Prevention

It is important to keep in mind that the most common treatment for hemangiomas is observation, as they commonly undergo involution. Treatment is reserved for complicated and high risk IH cases. Complications are typically seen during the proliferative phase for large IH located on the face including bleeding, airway compromise, visual compromise, ulceration, pain, difficulty feeding or risk permanent disfigurement.[18] See ***Table 1*** for special clinical considerations.

First line therapy for IH is oral propranolol, a nonselective beta-adrenergic blocker.[19] Contraindications to propranolol treatment should be considered including cardiogenic shock, sinus bradycardia, heart failure, bronchial asthma, allergy, and history of hypoglycemia. However, these conditions are all uncommon in infants. Dosing of the propranolol for IH is between 1 and 3 mg/kg/day separated into 2-3 doses with 6 hours between doses. Cardiac consult should be obtained before therapy initiation if there is concern for cardiac disease. Patients should be monitored for side effects including bradycardia, hypoglycemia, hypotension, and bronchospasm. These are not common and typically not life threatening.[19,20] Historically, corticosteroids were the first-line medical therapy for IH. Intralesional corticosteroids can still be used to decrease the size of small IH, but propranolol is preferred.[21] Another treatment option is pulsed dye laser (PDL). This technique can be used for ulcerated IH or residual visible vascularity after IH involution. Finally, surgical excision may be performed for patients who cannot undergo systemic therapy. Additionally, surgery may be performed if propranolol is ineffective, for cosmetic deformity, or caregiver preference.[2] See ***Table 2*** for a summary of indications for treatment of IH.

Segmental IH and Syndromes

PHACES Syndrome

PHACES syndrome stands for *p*osterior fossa intracranial abnormalities, *h*emangiomas, *a*rterial abnormalities, *c*ardiac defects and coarctation of the aorta, *e*ye abnormalities, and *s*ternal clefting.[22] This syndrome is associated with cervicofacial IH (***Figure 1C***). Patients with PHACES are more likely to have an airway IH and abnormal cerebral vasculature, a risk factor for stroke.[23]

SACRAL and PELVIS Syndromes

PELVIS is another syndrome associated with hemangiomas that stands for *p*erineal hemangiomas, *e*xternal genital malformations, *l*ipomyelomeningocele, *v*esicorenal abnormalities, *i*mperforate anus, or *s*kin tags.[24] Furthermore, SACRAL syndrome is associated with angiomas in the lumbosacral region and stands for *s*pinal dysraphism with *a*nogenital, *c*utaneous, *r*enal, and urologic anomalies, associated with *a*ngiomas in the *l*umbosacral region.[25]

Hemangiomatosis

Infants with five or more cutaneous IH (***Figure 1E***) have an increased risk of hepatic IH which prompts screening imaging via abdominal ultrasound.[26] Though often clinically benign, hepatic IH can be complicated by bleeding, congestive cardiac failure, hypothyroidism, and abdominal compartment syndrome.[27] Hepatic IH generally undergo involution similar to cutaneous IH.[27]

Table 1. **Special Considerations for Infantile Hemangiomas.**

Clinical Presentation	Concern	Workup
Hemangiomatosis (>5)	Screen for intrahepatic/visceral hemangiomas	Abdominal ultrasound.[82] Consider thyroid function tests in multifocal and diffuse hepatic hemangiomas.[7]
Segmental facial hemangioma	Rule out PHACES syndrome [posterior fossa brain malformations, segmental cervicofacial hemangioma, arterial abnormalities (vessel abnormalities in the head or neck), cardiac abnormalities or aortic coarctation, eye abnormalities, sternal clefting].[83]	Ophthalmology referral. Echocardiogram, cardiology referral. MRI/MRA of head, neck, and arch.[84]
Midline lumbosacral hemangiomas	Rule out SACRAL syndrome (spinal dysraphism, anogenital anomalies, urogenital anomalies).	Referral to dermatology urology, nephrology, neurology, and/or neurosurgery based on clinical needs.
Large hemangiomas, particularly in the liver	Risk of high-output cardiac failure and hypothyroidism.	Cardiology evaluation and TFT if concern.
Beard distribution segmental hemangioma (facial lower third and neck) or central neck	Rule out airway hemangiomas.[85]	Otolaryngology evaluation to consider airway evaluation.
Ulceration and bleeding		
Perineal, axilla, neck	Risk of ulceration related to friction.	Monitor clinically and treat as needed. Treatment can include topical antibiotic ointment, wound care, and on occasions culture and oral antibiotics.
Compromise vital functions		
Periorbital	Can cause astigmatism, strabismus, or amblyopia.	Ophthalmology referral.
Perioral, lip	Feeding difficulties.	Otolaryngology evaluation and feeding therapy consultation if appropriate.
Airway	Becoming symptomatic (stridor, feeding difficulties, etc.) and can become life-threatening if airway obstruction progresses.	Otolaryngology evaluation for airway assessment.
Nasal	Nasal obstruction.	Otolaryngology evaluation for airway assessment.
Slow Involution or Deformity		
Parotid	Can be deep and without cutaneous manifestations.	Ultrasound can aid in diagnosis.[86] Risk to the facial nerve during surgery. Recommend facial nerve monitoring ±mapping.[87]
Cosmetic Concern		
Nasal tip, ear, large facial	Social impact from facial disfigurement.	Lower threshold to treat.

Congenital Hemangioma

In contrast to IH, congenital hemangiomas are present at birth (***Figure 2A***) and are GLUT-1 negative despite having similar histology.[28] Congenital hemangiomas are divided into two subtypes: rapidly involuting congenital hemangioma (RICH) and non-involuting congenital hemangioma (NICH). RICH will resolve over the first year of life while NICH do not generally resolve spontaneously.[29] Thus, NICH can treated with surgery or laser.

Pyogenic Granuloma

This benign vascular tumor, also known as lobular capillary hemangioma, can arise in both children and adults (***Figure 2B***). Children will generally develop pyogenic granuloma in the head and neck region while adults often develop lesions on the trunk.[30,31] Mucosal pyogenic granulomas also occur in about 2% of pregnancies between the second and fifth months.[32] These tumors are rapidly growing, exophytic, red-colored papules that bleed commonly. Similar to congenital hemangioma, they are GLUT-1 negative on histopathology. The treatment is surgical, either by complete excision or punch excision with curettage or electrodesiccation of the feeding vascular stalk.[33]

Kaposiform Hemangioendothelioma And Tufted Angioma

Both tufted angioma (TA) and kaposiform hemangioendothelioma (KHE) are vascular tumors with a lymphatic component. TA is localized and noninvasive, however KHE invades nearby tissue.[34] KHE presents clinically as violaceous nodules and demonstrates tissue invasion on imaging (***Figure 2C***). TA present similarly, may or may not involve skin, and do not invade local tissue. Both of these conditions are associated with the Kasabach-Meritt phenomenon (KMP), a consumptive coagulopathy characterized by thrombocytopenia, hypofibrinogenemia, and anemia.[35] Surgery and medical therapy (e.g., sirolimus, vincristine) can be employed for treatment of both conditions.[36]

Vascular Malformations

Vascular malformations occur due to errors in the initial development of blood and lymph vessels and tend to be present at birth and grow with the child.[37] Vascular malformations can present with complex clinical presentations and management.[37] See ***Table 3*** for a summary of vascular malformations by common complications and treatment.

Capillary Malformations

The most common vascular malformations involve capillaries. Capillary malformations (CM) (***Figure 3A***) encompass a wide range of cutaneous malformations linked by their abnormal capillary morphology on histology.

Nevus simplex

This CM, commonly found in Caucasian infants,[38] has a wide range of names including salmon patch, angel's kiss (when located on the glabella), and stork bite (when located on the nape of the neck). These blanching erythematous macules present with indistinct borders and typically resolve over months to years. They are occasionally linked with Beckwith-Wiedmann syndrome, Nova syndrome, and macrocephaly-capillary malformation syndrome (MCAP).[2]

Figure 2. **Vascular Tumors.**

Legend: A. Congenital hemangioma. Blue-purple deep mass with surrounding pale halo. B. Pyogenic granuloma.[2] Pedunculated, erythematous growth that commonly ulcerates and presents with bleeding. C. Kaposiform hemangioendothelioma. Violaceous skin discoloration with palpable mass underlying.

Table 2. **Indications for Treatment of Infantile Hemangiomas.**

Indication	Locations to consider	Special considerations
Compromise vital functions	Periorbital	Can cause astigmatism, strabismus, or deprivation amblyopia. Consider ophthalmology referral.
	Perioral, lip	Can result in feeding difficulties. Consider feeding therapy and/or otolaryngology evaluation.
	Airway	Can present with stridor or feeding difficulties and may become life threatening. Recommend otolaryngology evaluation.
	Nasal	Can disrupt nasal airflow in obligate nasal breathers. Consider otolaryngology evaluation.
Slow Involution or Deformity	Parotid	Can be deep and without cutaneous manifestations so ultrasound aids in diagnosis. [80] Risk to the facial nerve during surgery. Recommend facial nerve monitoring +/- mapping. [81]
Cosmetic Concern	Nasal tip, ear, large facial	Can result in permanent disfigurement.

Port Wine Stain and Sturge Weber Syndrome

One CM that does not resolve is the port wine stain (PWS), also known as nevus flammeus. PWS will grow in conjunction with the child and present as pink to dark red patches with well-demarcated borders (***Figure 3B***). Also, it may thicken or become darker over time and is associated with soft tissue and bone hypertrophy, gingival hyperplasia, and dental anomalies.[39] Around 10% of patients with facial PWS have Sturge-Weber syndrome (SWS).[40] SWS is the association of facial CM with leptomeningeal angiomatosis and glaucoma. Some patients with SWS may develop epilepsy. MRI with contrast is the gold standard for diagnosis.[41]

Telangiectasias and hereditary hemorrhagic telangiectasia

Telangiectasias are small, dilated capillary vessels that present as red macules with stellate shape and a pale halo. Isolated, they are nonsyndromic; however, multiple telangiectasias together may indicate hereditary hemorrhagic telangiectasia (HHT). This autosomal dominant disorder presents with telangiectasias affecting multiple systems, arteriovenous malformations (AVM), and vascular dysplasia. This disorder most commonly presents at age 12 and its severity increases with age. HHT can lead to life-threatening bleeding.[42]

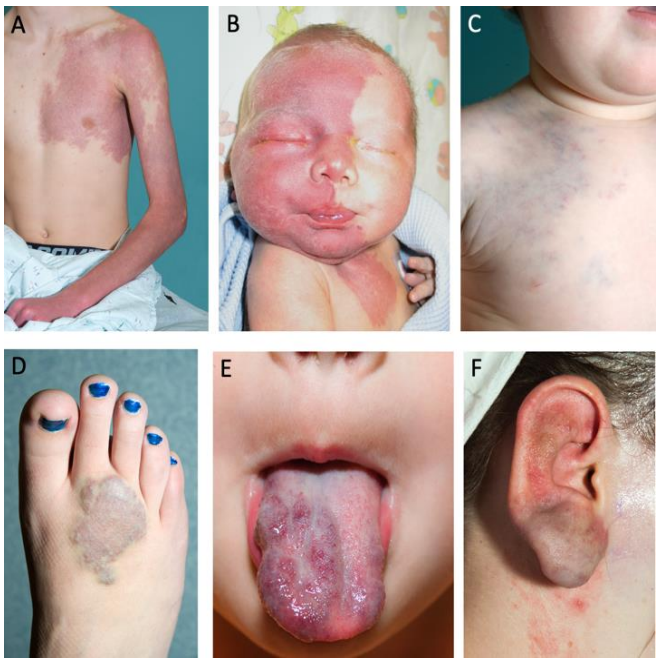
Treatment

CM treatment is tailored to each individual presentation and the needs of the patient. Generally, a balance is sought between intervening before the lesion thickens and becomes nodular, while minimizing risks of anesthetics (generally after 6 months of age).[2] First-line treatment for CM is pulsed dye laser with or without topical sirolimus.[43,44]

Lymphatic Malformations

Lymphatic malformations (LM) are a subset of vascular malformations that present with abnormal lymphatic vessel morphology. LM occur in approximately 1 in 4000 live births. Prior nomenclature used to describe LM included cystic hygroma and lymphangioma, however these terms imply a watery tumor rather than a collection of ill-formed lymphatic vessels and are no longer in use. Some LM such as posterior cervical LM or extensive cervicofacial LM can be diagnosed prenatally. Posterior cervical LM are sometimes associated with syndromic conditions and regress by birth.[45] Ventral, isolated LM can also be diagnosed prenatally or shortly after birth and commonly present in the neck and face. In utero, LM may be associated with polyhydramnios if swallowing function is impaired and/or may have airway compromise at birth. A LM with airway obstruction requires delivery planning and a possible EXIT (ex-utero intrapartum treatment) procedure.[46,47]

***Figure 3*. Vascular Malformations.**



Legend: A. Capillary malformation of the left upper extremity and chest. B. Segmental facial port wine stain (PWS) associated with Sturge Weber syndrome (SWS).[2] Venous malformations. C-E: cutaneous presentation of venous malformations of the chest (C) and foot (D) seen as violaceous discoloration of the skin. E: mucosal venous malformation of the tongue. F. Arteriovenous malformations of the ear.

Diagnosis and classification

LM are diagnosed via a combination of history, physical exam, and imaging. Depending on the extent of the malformation, MRI and CT are commonly used modalities that can aid in the diagnosis of LM and selection is based on preference. The authors prefer MRI given the better soft tissue delineation and avoidance of radiation in children. If radiographic cystic spaces in the LM are >2cm in diameter they are classified as macrocystic. Those less than 2cm in diameter are classified as microcystic. LM that presents in the head and neck are classified using de Serres stages, which is based on laterality and location relative to the hyoid.[48] More than 80% of LM are stage I-III with unilateral involvement.

***Table 3*. Complications and Treatment for Vascular Malformation Categories.**

Vascular malformation	Complications	Treatment
Capillary malformations	Generally cosmetic (see ***Figure 3A***), can be associated with Beckwith-Wiedemann, Nova, macrocephaly-capillary malformation, and Sturge Weber syndromes.[9, 36]	Pulsed dye laser and topical sirolimus.[9]
Lymphatic malformations	Impaired swallowing function, airway compromise, cosmetic.[42, 43] Can be associated with CLOVES and KTS syndromes.[48]	Many resolve spontaneously.[45] Sclerotherapy, surgical excision, medications (sirolimus; aspirin and PI3K inhibitors under investigation).[51]
Venous malformations	Pain and localized intravascular coagulopathy which may predispose to disseminated intravascular coagulopathy. Associated with Klippel-Trenaunay syndrome.[54]	Perioperative treatment with low molecular weight heparin (LMWH) and surgery. Medical treatments include aspirin and sirolimus. Compression may be helpful with extremity presentations.[62]
Arteriovenous malformations	Deformity, bleeding, and high output cardiac failure. Other complications include infiltration of surrounding tissues and increased size during pregnancy, puberty, and trauma.[9, 65]	Medical management with doxycycline, sirolimus, and trametinib for severe cases. Intralesional bleomycin has shown variable results. Other options include ablation of draining veins with flashlamp-pumped pulsed dye laser (FPDL) and Nd:YAG laser. Surgical resection for focal AVM.[9, 72, 73]

Generally, unilateral LM do not cause functional compromise and can resolve spontaneously.[49] Large, bilateral LM typically cause functional compromise and do not resolve spontaneously.[49] LM are not hereditary, rather, they are associated with somatic mutations in *PIK3CA*, an oncogene associated with cancer and other overgrowth disorders.[50,51]

Associated syndromes: CLOVES and KTS

LM are not generally associated with a syndrome and present in isolation but may be associated with other *PIK3CA*-related overgrowth syndromes (PROS). PROS associated with LM include CLOVES syndrome (congenital lipomatosis, overgrowth, vascular malformations, epidermal nevi, and skeletal anomalies) and Klippel-Trenaunay syndrome (KTS) (port wine stains, venous malformations, LM, and overgrowth).[52] Overgrowth in CLOVES syndrome can be very severe and generally involves multiple limbs and possibly trunk. Klippel-Trenaunay syndrome generally only has overgrowth of a single extremity.[53]

Management and Prevention

Treatment of LM is typically pursued in response to functional or aesthetic compromise. Many resolve spontaneously, especially unilateral macrocystic LM.[49] If infected, it typically responds well to systemic antibiotics and corticosteroids. Another treatment that may be pursued for macrocystic LM is sclerotherapy, a procedure in which interventional radiology drains the associated fluid and injects a sclerosing agent.[54] This procedure is often required multiple times to achieve a sustained result. Surgical excision is also an option. The most commonly used medication for LM is sirolimus, an MTOR inhibitor. Aspirin and targeted PI3K inhibitors (alpelisib) are undergoing investigation as potential treatments for LM.[55]

Venous Malformations

Epidemiology

Around 1-4% of individuals have a venous malformation (VeM). VeM commonly present in the head and neck, generally on mucosal surfaces or within muscles.[56] The next most common area for a VeM to arise is the upper and lower extremities. VeM often clinically present at puberty, but most are present even at birth and grow proportionately with the child.[57] VeM are visualized as a mass with a bluish hue overlying the skin but may also present without the blue hue (***Figure 3C-E***). Mucosal VeM typically presents with blue-purple discoloration.

Diagnosis

A combination of clinical history, physical exam, and imaging is used for diagnosis. Choosing the imaging modality depends on the location, patient age, and ability to receive contrast. Ultrasound, CT, and MRI may all provide valuable information. Many VeM present with pain and there may also be localized intravascular coagulopathy (LIC) which can occasionally predispose to disseminated intravascular coagulopathy (DIC). LIC is most commonly seen in large lesions (>10 mL), when phleboliths are present, in multifocal disease, and when associated with Klippel-Trenaunay syndrome.[58] Elevated D-dimer levels in a patient with VeM has a high specificity (>97%) for LIC.[59]

Etiology and associated syndromes

VeM can arise sporadically or hereditarily. Various mutations are linked with VeM: sporadic venous malformations are associated with somatic mutations in *TIE2/TEK* and *PIK3CA*,[60,61] some familial VeM are associated with mutations in *RASA1*,[62] and hereditary venous malformations, also known as familial venous malformation cutaneo-mucosal (VMCM), are associated with inherited mutations in *TIE2/TEK*.[63] Glomuvenous malformation is a hereditary disease associated with inherited mutations in *GLMN* (glomulin) with a distinct pathologic phenotype that involves glomus cells, a type of immature vascular smooth muscle cell.[64] Blue rubber bleb nevus syndrome is a form of VeM that presents with compressible mucocutaneous VeM and involves the visceral organs, most commonly in the gastrointestinal tract.[65]

Management and Prevention

Patients with bothersome VeM or who present with LIC are candidates for treatment. A patient with VeM and elevated D dimer should be treated perioperatively with LMWH for any sedated procedure as well as 14 days pre and post procedure.[66] Medical therapies include aspirin and sirolimus. For patients with VeM on the extremity, compression can help to relieve symptoms though it is not known whether it helps to prevent LIC.

VeM often requires invasive therapy such as laser therapy, sclerotherapy, and surgery. Laser therapy can include PDL or Nd:YAG for superficial lesions. Sclerotherapy is also available but often requires multiple procedures to achieve an effect.[67] Surgical excision can be performed, often with glue embolization in which interventional radiology injects the VeM with n-BCA glue immediately prior to resection to decrease the risk of bleeding and allow for more thorough resection.[68]

Arteriovenous Malformations

Epidemiology

Arteriovenous malformations (AVM) involve atypical connections between arteries and veins (Figure 3F). AVM have a central nidus, one or more arteries that feed the nidus, and one or more veins that drain it. AVM can be intracranial or extracranial. When extracranial they are most likely to occur in the head and neck. AVM are present at birth but commonly increase in size during pregnancy, puberty, or trauma.[2,69] Contrary to other vascular malformations, AVM commonly infiltrate adjacent tissue. Common complications include deformity, bleeding, and high output cardiac failure if large in size. If extracranial, the Schobinger classification can categorize AVM based on presentation and exam. Intracranial AVM are classified based on size and morphology with the Spetzler-Martin scale.[70] Imaging is helpful for diagnosis and requires arteriography or MR-angiogram. Smaller AVM with a single feeding artery may be treatable, but effective therapeutic treatments for diffuse AVM are more challenging.

Etiology and associated syndromes

AVM are generally sporadic and can be associated with somatic mutations in *KRAS*, *BRAF* and *MAP2K1*.[71–73] Some forms of AVM can be inherited. For example, CM-AVM is an autosomal dominant disorder, commonly associated with mutations in RASA1, that presents with multiple round to oval vascular stains with a vasoconstrictive halo.[62] Around one third of individuals with a CM-AVM also have an AVM in the brain, spine, bone, skin, or soft tissue.[74] One subtype of CM-AVM is Parkes-Weber syndrome which can present with arteriovenous fistula (AVF) and lower extremity limb overgrowth. Hereditary hemorrhagic telangiectasia (HHT), a syndrome associated with mutations in the TGF-beta pathway, is most commonly associated with pulmonary AVM, but may also present with gastrointestinal tract, liver, spine, or brain AVM.[75]

Treatment

AVM differ from VeM and LM in that they should not be observed. They warrant aggressive therapy given their propensity to infiltrate surrounding tissue. However, functional and aesthetic outcomes associated with treatment must be taken into consideration. Medical management has seen some response with doxycycline (matrix metalloproteinase inhibitor), sirolimus (MTOR inhibitor), and trametinib (MAP2K1 inhibitor) for severe AVM.[76,77] Intralesional bleomycin has also been trialed with variable results. Other options include flashlamp-pumped pulsed dye laser (FPDL) and Nd:YAG laser to ablate superficial draining veins.[2]The primary treatment of AVM is embolization and surgical resection. Embolization can be done with various agents including onyx, ethanol, and n-BCA (glue). Onyx and n-BCA embolization are generally used as an adjunct to surgery in both intracranial and extracranial AVM.[78] Surgical resection is most successful in focal AVM and is generally performed after or in conjunction with embolization.[79]

Discussion

This review of vascular anomalies has discussed the pathogenesis, diagnosis, and management of the two main categories: vascular tumors and vascular malformations. Vascular anomalies are prevelant[5] and recognizing them clinically and understanding management will aid trainees in their clinical efforts. Various reviews of vascular anomalies have previously been published. For example, a brief review by Cox et. al[80] organized vascular anomalies by subtype to help clinicians develop a clear understanding of the clinical aspects, diagnostic tools, imaging modalities, and options for interventions available. More extensive reviews, such as Perkins and Balakrishnan,[2] have been developed to provide a comprehensive resource of current evidence-based management of head and neck vascular anomalies for providers. The purpose of this review was to provide an educational tool for physicians-in-training seeking to gain an understanding and assist in the recognition of these pathologies, as well as to offer an insight into the various treatment methods.

This review has several strengths, including a concise delineation of common vascular anomalyies, visual images to support recognition, and its originality as the first vascular anomalies review with physicians-in-training as the target audience. Limitations, however, do exist. Our understanding of the epidemiology of vascular anomalies continues to develop and studies evaluating the effectiveness of treatment options continue to be published. Thus, our understanding and explanations of certain vascular anomalies is extensive, while less is known about more recently identified pathologies. This understanding will continue to develop as future research will likely focus on the refinement of genetic and molecular therapies, improved diagnostic techniques, and the development of personalized treatment protocols.[3,19,81]Future reviews of vascular anomalies should continue to be published in an effort to provide up-to-date resources for this developing field.

Conclusion

This review seeks to describe the epidemiology, diagnosis, and treatment of the most common vascular anomalies. It is intended for physicians-in-training seeking an up-to-date resource for understanding and managing vascular anomalies that is appropriate to their training level. As medical school curricula vary in the depth of coverage of vascular anomalies, this review will allow students to have a comprehensive, trainee-level guide. As studies continue to further our knowledge of these pathologies, updated reviews should continue to be published to provide up-to-date resources for trainees and clinicians.

Summary – Accelerating Translation

Title: Vascular Anomalies Review of the Head and Neck for Physicians in Training

The main problem to solve: Limited training on vascular anomalies of the head and neck is given to medical students. However, a basic understanding of vascular anomalies can aid physicians-in-training as they seek to properly diagnose and determine interventions for these patient presentations.

Aim of this review: To create a resource for physicians in training that encompasses the most important clinical aspects of vascular anomalies.

Methodology: Current evaluation, diagnosis, and treatment for vascular tumors and vascular malformations were compiled into a trainee-level resource through literature review.

Results: Current evaluation, diagnosis, and treatment guidelines were described for infantile hemangioma, segmental IH and syndromes, pyogenic granuloma, kaposiform hemangioendothelioma and tufted angioma, capillary malformations, lymphatic malformations, venous malformations, and arteriovenous malformations.

Conclusion: A basic knowledge of these anomalies will allow students to assist in accurate, early diagnosis and appropriate intervention of vascular anomalies. This can ultimately improve patient outcomes.

References

1. Munden A, Butschek R, Tom WL, Marshal JS, Poeltler DM, Krohne SE, et al. Prospective study of infantile haemangiomas: incidence, clinical characteristics and association with placental anomalies. Br J Dermatol. 2014;170(4):907-913.
2. Perkins JA, Balakrishnan K. Evidence-Based Management of Head and Neck Vascular Anomalies. (Springer International Publishing, ed.).; 2018.
3. Wassef M, Blei F, Adams D, Alomari A, Baselga E, Berenstein A, et al. Vascular Anomalies Classification: Recommendations From the International Society for the Study of Vascular Anomalies. Pediatrics. 2015;136(1):e203-14.
4. Mansfield SA, Williams RF, Iacobas I. Vascular tumors. Semin Pediatr Surg. 2020;29(5):150975.
5. Drolet BA, Esterly NB, Frieden IJ. Hemangiomas in children. N Engl J Med. 1999;341(3):173-181. 10.1056/NEJM199907153410307
6. Leung AKC, Lam JM, Leong KF, Hon KL. Infantile Hemangioma: An Updated Review. Curr Pediatr Rev. 2021;17(1):55-69.
7. DeHart A, Richter G. Hemangioma: Recent Advances. F1000Res. 2019;8.
8. Smith CJF, Friedlander SF, Guma M, Kavanaugh A, Chambers CD. Infantile Hemangiomas: An Updated Review on Risk Factors, Pathogenesis, and Treatment. Birth Defects Res. 2017;109(11):809-815.
9. North PE, Waner M, Mizeracki A, Mihm MC. GLUT1: a newly discovered immunohistochemical marker for juvenile hemangiomas. Hum Pathol. 2000;31(1):11-22.
10. Barnés CM, Huang S, Kaipainen A, Sanoudou D, Chen E, Eichler, G, et al. Evidence by molecular profiling for a placental origin of infantile hemangioma. Proc Natl Acad Sci U S A. 2005;102(52):19097-19102.
11. Strub GM, Kirsh AL, Whipple ME, Kuo W, Keller R, Kapur R, et al. Endothelial and circulating C19MC microRNAs are biomarkers of infantile hemangioma. JCI Insight. 2016;1(14):e88856.
12. Huoh KC, Rosbe KW. Infantile hemangiomas of the head and neck. Pediatr Clin North Am. 2013;60(4):937-949.
13. Chiller KG, Passaro D, Frieden IJ. Hemangiomas of infancy: clinical characteristics, morphologic subtypes, and their relationship to race, ethnicity, and sex. Arch Dermatol. 2002;138(12):1567-1576.
14. Haggstrom AN, Lammer EJ, Schneider RA, Marcucio R, Frieden IJ. Patterns of infantile hemangiomas: new clues to hemangioma pathogenesis and embryonic facial development. Pediatrics. 2006;117(3):698-703.
15. Darrow DH, Greene AK, Mancini AJ, Nopper AJ, SECTION ON DERMATOLOGY SOOANS and SOPS. Diagnosis and Management of Infantile Hemangioma. Pediatrics. 2015;136(4):e1060-104.
16. Esposito F, Ferrara D, Di Serafino M, Severino M, Nosari R, Galdieri M, et al. Classification and ultrasound findings of vascular anomalies in pediatric age: the essential. J Ultrasound. 2019;22(1):13-25.
17. Moukaddam H, Pollak J, Haims AH. MRI characteristics and classification of peripheral vascular malformations and tumors. Skeletal Radiol. 2009;38(6):535-547.
18. Haggstrom AN, Drolet BA, Baselga E, Chamlin S, Garzon M, Horii K, et al. Prospective study of infantile hemangiomas: clinical characteristics predicting complications and treatment. Pediatrics. 2006;118(3):882-887.
19. Drolet BA, Frommelt PC, Chamlin SL, Haggstrom A, Bauman N, Chiu R, et al. Initiation and use of propranolol for infantile hemangioma: report of a consensus conference. Pediatrics. 2013;131(1):128-140.
20. Hoeger PH, Harper JI, Baselga E, Bonnet D, Boon LM, Atti MCD, et al. Treatment of infantile haemangiomas: recommendations of a European expert group. Eur J Pediatr. 2015;174(7):855-865.
21. Barrio VR, Drolet BA. Treatment of hemangiomas of infancy. Dermatol Ther. 2005;18(2):151-159.
22. Frieden IJ, Reese V, Cohen D. PHACE syndrome. The association of posterior fossa brain malformations, hemangiomas, arterial anomalies, coarctation of the aorta and cardiac defects, and eye abnormalities. Arch Dermatol. 1996;132(3):307-311.
23. Hess CP, Fullerton HJ, Metry DW, Drolet B, Siegel D, Auguste KI, et al. Cervical and intracranial arterial anomalies in 70 patients with PHACE syndrome. AJNR Am J Neuroradiol. 2010;31(10):1980-1986.
24. Girard C, Bigorre M, Guillot B, Bessis D. PELVIS Syndrome. Arch Dermatol. 2006;142(7):884-888.
25. Stockman A, Boralevi F, Taïeb A, Léauté-Labrèze C. SACRAL syndrome: spinal dysraphism, anogenital, cutaneous, renal and urologic anomalies, associated with an angioma of lumbosacral localization. Dermatology. 2007;214(1):40-45.
26. Glick ZR, Frieden IJ, Garzon MC, Mully TW, Drolet BA. Diffuse neonatal hemangiomatosis: an evidence-based review of case reports in the literature. J Am Acad Dermatol. 2012;67(5):898-903.
27. Yeh I, Bruckner AL, Sanchez R, Jeng MR, Newell BD, Frieden IJ. Diffuse infantile hepatic hemangiomas: a report of four cases successfully managed with medical therapy. Pediatr Dermatol. 2011;28(3):267-275.
28. Berenguer B, Mulliken JB, Enjolras O, Bellini C, Burrows PE, Sundel RP, et al. Rapidly involuting congenital hemangioma: clinical and histopathologic features. Pediatr Dev Pathol. 2003;6(6):495-510.
29. Mulliken JB, Enjolras O. Congenital hemangiomas and infantile hemangioma: missing links. J Am Acad Dermatol. 2004;50(6):875-882.
30. Patrice SJ, Wiss K, Mulliken JB. Pyogenic granuloma (lobular capillary hemangioma): a clinicopathologic study of 178 cases. Pediatr Dermatol. 1991;8(4):267-276.
31. Harris MN, Desai R, Chuang TY, Hood AF, Mirowski GW. Lobular capillary hemangiomas: An epidemiologic report, with emphasis on cutaneous lesions. J Am Acad Dermatol. 2000;42(6):1012-1016.
32. Kroumpouzos G, Cohen LM. Dermatoses of pregnancy. J Am Acad Dermatol. 2001;45(1):1-19; quiz 19-22.
33. Eshkevari S, Kabir S, Alizadeh N, Nickhaha N. Curettage and punch excision of the vascular base: an effective method for treatment of pyogenic granuloma with excellent results. Iran J Dermatol. 2014;17(69):91-5.
34. Croteau SE, Gupta D. The clinical spectrum of kaposiform hemangioendothelioma and tufted angioma. Semin Cutan Med Surg. 2016;35(3):147-152.
35. Kelly M. Kasabach-Merritt phenomenon. Pediatr Clin North Am. 2010;57(5):1085-1089.
36. McDaniel CG, Adams DM, Steele KE, Hammill AM, Merrow AC, Crane JL, et al. Kaposiform lymphangiomatosis: Diagnosis, pathogenesis, and treatment. Pediatr Blood Cancer. 2023;70(4):e30219.
37. Carqueja IM, Sousa J, Mansilha A. Vascular malformations: classification, diagnosis and treatment. Int Angiol. 2018;37(2):127-142.
38. Kanada KN, Merin MR, Munden A, Friedlander SF. A prospective study of cutaneous findings in newborns in the United States: correlation with race, ethnicity, and gestational status using updated classification and nomenclature. J Pediatr. 2012;161(2):240-245.
39. Dutkiewicz AS, Ezzedine K, Mazereeuw-Hautier J, Lacour JP, Barbarot S, Vabres P, et al. A prospective study of risk for Sturge-Weber syndrome in children with upper facial port-wine stain. J Am Acad Dermatol. 2015;72(3):473-480.
40. Roach ES. Neurocutaneous syndromes. Pediatr Clin North Am. 1992;39(4):591-620.
41. Adams ME, Aylett SE, Squier W, Chong W. A spectrum of unusual neuroimaging findings in patients with suspected Sturge-Weber syndrome. AJNR Am J Neuroradiol. 2009;30(2):276-281.
42. Gonzalez CD, Mcdonald J, Stevenson DA, Whitehead KJ, Petersen MG, Presson AP, et al. Epistaxis in children and adolescents with hereditary hemorrhagic telangiectasia. Laryngoscope. 2018;128(7):1714-1719.
43. Faurschou A, Olesen AB, Leonardi-Bee J, Haedersdal M. Lasers or light sources for treating port-wine stains. Cochrane Database Syst Rev. 2011;(11):CD007152.
44. Marqués L, Núñez-Córdoba JM, Aguado L, Pretel M, Boixeda P, Nagore E, et al. Topical rapamycin combined with pulsed dye laser in the treatment of capillary vascular malformations in Sturge-Weber syndrome: phase II,

randomized, double-blind, intraindividual placebo-controlled clinical trial. J Am Acad Dermatol. 2015;72(1):151-8.e1.

45. Longstreet B, Balakrishnan K, Saltzman B, Perkins JA, Dighe M. Prognostic value of a simplified anatomically based nomenclature for fetal nuchal lymphatic anomalies. Otolaryngol Head Neck Surg. 2015;152(2):342-347.
46. Cash H, Bly R, Masco V, Shwayhat EU, Lutz DR, Van Tine LP, et al. Prenatal Imaging Findings Predict Obstructive Fetal Airways Requiring EXIT. Laryngoscope. 2021;131(4):E1357-E1362.
47. Dighe MK, Peterson SE, Dubinsky TJ, Perkins J, Cheng E. EXIT procedure: technique and indications with prenatal imaging parameters for assessment of airway patency. Radiographics. 2011;31(2):511-526.
48. de Serres LM, Sie KC, Richardson MA. Lymphatic malformations of the head and neck. A proposal for staging. Arch Otolaryngol Head Neck Surg. 1995;121(5):577-582.
49. Bonilla-Velez J, Whitlock KB, Ganti S, Theeuwen HA, Manning S, Bly R, et al. Active Observation as an Alternative to Invasive Treatments for Pediatric Head and Neck Lymphatic Malformations. Laryngoscope. 2021;131(6):1392-1397.
50. Luks VL, Kamitaki N, Vivero MP, Wang K, Ameen N, Bader A, et al. Lymphatic and other vascular malformative/overgrowth disorders are caused by somatic mutations in PIK3CA. J Pediatr. 2015;166(4):1048-54.e1-5.
51. Zenner K, Cheng CV, Jensen DM, Timms A, Shivaram G, Bly R, et al. Genotype correlates with clinical severity in PIK3CA-associated lymphatic malformations. JCI Insight. 2019;4(21).
52. Keppler-Noreuil KM, Rios JJ, Parker VER, Semple RK, Lindhurst MJ, Sapp JC, et al. PIK3CA-related overgrowth spectrum (PROS): diagnostic and testing eligibility criteria, differential diagnosis, and evaluation. Am J Med Genet A. 2015;167A(2):287-295.
53. Kurek KC, Luks VL, Ayturk UM, Alomari AI, Fishman SJ, Spencer SA, et al. Somatic mosaic activating mutations in PIK3CA cause CLOVES syndrome. Am J Hum Genet. 2012;90(6):1108-1115.
54. Balakrishnan K, Menezes MD, Chen BS, Magit AE, Perkins JA. Primary surgery vs primary sclerotherapy for head and neck lymphatic malformations. JAMA Otolaryngol Head Neck Surg. 2014;140(1):41-45.
55. Bonilla-Velez J, Whitlock KB, Ganti S, Theeuwen HA, Manning SC, Bly RA, et al. Acetylsalicylic acid suppression of the PI3K pathway as a novel medical therapy for head and neck lymphatic malformations. Int J Pediatr Otorhinolaryngol. 2021;151:110869.
56. Fraulin FO, Flannigan RK, Sharma VK, McPhalen DF, Harrop RA. The epidemiological profile of the Vascular Birthmark Clinic at the Alberta Children's Hospital. Can J Plast Surg. 2012;20(2):67-70.
57. Hung JWS, Leung MWY, Liu CSW, Choi CHT, Wong KW, Kwan HN. Venous Malformation and Localized Intravascular Coagulopathy in Children. Eur J Pediatr Surg. 2017;27(2):181-184.
58. Koo KSH, Dowd CF, Mathes EF, Sidhu K, Fuchs HE, Peters SM, et al. MRI phenotypes of localized intravascular coagulopathy in venous malformations. Pediatr Radiol. 2015;45(11):1690-1695.
59. Dompmartin A, Ballieux F, Thibon P, Veyrac C, Verlaine M, Lacour JP, et al. Elevated D-dimer level in the differential diagnosis of venous malformations. Arch Dermatol. 2009;145(11):1239-1244.
60. Soblet J, Limaye N, Uebelhoer M, Boon LM, Vikkula M. Variable Somatic TIE2 Mutations in Half of Sporadic Venous Malformations. Mol Syndromol. 2013;4(4):179-183.
61. Limaye N, Wouters V, Uebelhoer M, Pappas P, Mahoney W, Van Agtmael T, et al. Somatic mutations in angiopoietin receptor gene TEK cause solitary and multiple sporadic venous malformations. Nat Genet. 2009;41(1):118-124.
62. Eerola I, Boon LM, Mulliken JB, Aylett A, Dompmartin A, Lemaire A, et al. Capillary malformation-arteriovenous malformation, a new clinical and genetic disorder caused by RASA1 mutations. Am J Hum Genet. 2003;73(6):1240-1249.
63. Wouters V, Limaye N, Uebelhoer M, Ghosh S, Kim D, D'Amore PA, et al. Hereditary cutaneomucosal venous malformations are caused by TIE2 mutations with widely variable hyper-phosphorylating effects. Eur J Hum Genet. 2010;18(4):414-420.
64. Brouillard P, Boon LM, Revencu N, McCuaig C, Vikkula M, Pannett A, et al. Genotypes and phenotypes of 162 families with a glomulin mutation. Mol Syndromol. 2013;4(4):157-164.
65. Soblet J, Kangas J, Nätynki M, Järvinen P, Eerola I, Vikkula M, et al. Blue Rubber Bleb Nevus (BRBN) Syndrome Is Caused by Somatic TEK (TIE2) Mutations. J Invest Dermatol. 2017;137(1):207-216.
66. Seront E, Boon LM, Vikkula M. TEK-Related Venous Malformations. In: Adam MP, Feldman J, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1967/. Last updated Mar 2, 2023; cited Oct 16, 2024.
67. Heit JJ, Do HM, Prestigiacomo CJ, McCuaig C, Wu Y, Kuo A, et al. Guidelines and parameters: percutaneous sclerotherapy for the treatment of head and neck venous and lymphatic malformations. J Neurointerv Surg. 2017;9(6):611-617.
68. Tieu DD, Ghodke B V, Vo NJ, Perkins JA. Single-stage excision of localized head and neck venous malformations using preoperative glue embolization. Otolaryngol Head Neck Surg. 2013;148(4):678-684.
69. Liu AS, Mulliken JB, Zurakowski D, Fishman SJ, Greene AK. Extracranial arteriovenous malformations: natural progression and recurrence after treatment. Plast Reconstr Surg. 2010;125(4):1185-1194.
70. Spetzler RF, Martin NA. A proposed grading system for arteriovenous malformations. J Neurosurg. 1986;65(4):476-483.
71. Al-Olabi L, Polubothu S, Dowsett K, Kwan H, Larkin J, Lee D, et al. Mosaic RAS/MAPK variants cause sporadic vascular malformations which respond to targeted therapy. J Clin Invest. 2018;128(4):1496-1508.
72. Nikolaev SI, Vetiska S, Bonilla X, Pannett A, Tsang R, Smith A, et al. Somatic Activating KRAS Mutations in Arteriovenous Malformations of the Brain. N Engl J Med. 2018;378(3):250-261.
73. Couto JA, Huang AY, Konczyk DJ, DiGuglielmo C, Chang K, Wang C, et al. Somatic MAP2K1 Mutations Are Associated with Extracranial Arteriovenous Malformation. Am J Hum Genet. 2017;100(3):546-554.
74. Revencu N, Boon LM, Mendola A, MacKenzie R, Ghosh S, Vikkula M, et al. RASA1 mutations and associated phenotypes in 68 families with capillary malformation-arteriovenous malformation. Hum Mutat. 2013;34(12):1632-1641.
75. Parambil JG. Hereditary Hemorrhagic Telangiectasia. Clin Chest Med. 2016;37(3):513-521.
76. Lekwuttikarn R, Lim YH, Admani S, Choate KA, Teng JMC. Genotype-Guided Medical Treatment of an Arteriovenous Malformation in a Child. JAMA Dermatol. 2019;155(2):256-257.
77. Hashimoto T, Matsumoto MM, Li JF, Lawton MT, Young WL, University of California SFBSG. Suppression of MMP-9 by doxycycline in brain arteriovenous malformations. BMC Neurol. 2005;5(1):1.
78. Elsenousi A, Aletich VA, Alaraj A. Neurological outcomes and cure rates of embolization of brain arteriovenous malformations with n-butyl cyanoacrylate or Onyx: a meta-analysis. J Neurointerv Surg. 2016;8(3):265-272.
79. Kim JY, Kim DI, Do YS, Lee DY, Kim JH, Cho YP, et al. Surgical treatment for congenital arteriovenous malformation: 10 years' experience. Eur J Vasc Endovasc Surg. 2006;32(1):101-106.
80. Cox JA, Bartlett E, Lee EI. Vascular malformations: a review. Semin Plast Surg. 2014;28(2):58-63.
81. Ng AT, Tower RL, Drolet BA. Targeted treatment of vascular anomalies. Int J Womens Dermatol. 2021;7(5Part A):636-639.
82. Horii KA, Drolet BA, Frieden IJ, Munden A, Blei F, McCuaig C, et al. Prospective study of the frequency of hepatic hemangiomas in infants with multiple cutaneous infantile hemangiomas. Pediatr Dermatol. 2011;28(3):245-253.
83. Metry DW, Haggstrom AN, Drolet BA, Frieden IJ, Lammer EJ, Schaffer R, et al. A prospective study of PHACE syndrome in infantile hemangiomas: demographic features, clinical findings, and complications. Am J Med Genet A. 2006;140(9):975-986.

84. Garzon MC, Epstein LG, Heyer GL, Grieden IJ, Haggstrom AN, Drolet BA, et al. PHACE Syndrome: Consensus-Derived Diagnosis and Care Recommendations. J Pediatr. 2016;178:24-33.e2.

85. Orlow SJ, Isakoff MS, Blei F. Increased risk of symptomatic hemangiomas of the airway in association with cutaneous hemangiomas in a "beard" distribution. J Pediatr. 1997;131(4):643-646.

86. Weber FC, Greene AK, Adams DM, Blei F, Drolet BA, Leach JL, et al. Role of imaging in the diagnosis of parotid infantile hemangiomas. Int J Pediatr Otorhinolaryngol. 2017;102:61-66.

87. Bly RA, Holdefer RN, Slimp J, Kelly S, Craig J, Stal S, et al. Preoperative Facial Nerve Mapping to Plan and Guide Pediatric Facial Vascular Anomaly Resection. JAMA Otolaryngol Head Neck Surg. 2018;144(5):418-426.

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Review

A Scoping Review on the Utility of Ultrasound to Visualize Bursae in Anatomical Dissection Courses

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Abstract

Bursitis is a common condition in clinical practice, often causing pain in the shoulder and buttock areas due to inflamed bursae. Proper diagnosis and treatment depend on knowing the presence and exact location of these bursae. Anatomy classes typically provide limited instruction on bursae because they are difficult to demonstrate during dissection courses. High-resolution ultrasound is an essential and versatile technique for detecting bursitis, and it could also serve as a valuable tool for students to better understand bursae. Relevant studies were screened in the following databases: CENTRAL, MEDLINE, BIOSIS Previews, EMBASE, and Web of Science Core Collection. Grey literature was also considered. Literature was screened on January 3, 2023. Only ultrasound investigations in human cadaver bursae were included, specifically using B-Mode ultrasound. The general characteristics of the included studies and the ultrasound-guided approaches for labeling the bursae were analyzed and examined. T The search found 8,899 matches, but only 15 met the criteria. Fifteen different bursae were studied, and 12 studies were included in the analysis. Both the marking substrate and the injected volume varied. Despite a high overall accuracy of 99% achieved using ultrasound-guided labeling approaches in the included studies, caution is advised due to the small sample size (1 to 24). The current study serves as a review to examine ultrasound studies on bursae in human cadavers. Ultrasound-guided labeling techniques achieve high accuracy and could be a valuable teaching tool in dissection courses. These techniques help visualize difficult-to-dissect structures and provide students with an understanding of sonoanatomy.

Introduction

The first complete description of the bursae was published by Alexander Monro in 1788.[1] Like sesamoid bones and tendon sheaths, bursae or bursas for the plural form, are extra-articular components. They present as thin, fluid-filled sacs that can sometimes communicate with the joint cavity[2] or other nearby bursae[3]. There are two categories of bursae; native and non-native. Usually, the communicating bursae are a part of the native bursae. Native bursae are present from birth and are lined with a synovial membrane, therefore they are also called synovial bursae. Most commonly, they exist near large joints, and if they communicate with these joints, the synovial membranes (of the bursa and the joint) are continuous. Histologically, this synovial membrane consists of two layers[4]; one deep or outer layer and one superficial or inner layer. The inner lying cell layer produces a capillary film of synovial fluid on the inner surface of the sac, which acts as a lubricant. The deep vascularized layer is responsible for blood supply. Non-native bursae, which are also referred to as adventitious bursae, differ histologically from anatomical bursae (native bursae) because the synovial layer is absent[5] and permeability is greater. As a result, hyaluronan and serum proteins can diffuse more easily.[6]

Depending on the position of both types of bursae, they are classified as subcutaneous, subtendinous, submuscular, or subfascial bursae and can be further named according to the location within the human body (e.g., subacromial, subscapular, ischiogluteal, trochanteric bursa).[7] Bursae are classified as superficial (e.g., olecranon bursa) when they lie between bones, tendons or skin, and deep when they are between bones and muscles.[7] Subcutaneous bursae are part of the superficial bursae and are often adventitious. They are created as a fusion of the superficial and deep fasciae, so they are a specialized form of fascia rather than a separate entity.[8] The synovial fluid here is produced by specialized fibroblast-like cells, called fasciacytes, which also produce hyaluronan.[9]

All types of bursae have the function to reduce the friction that occurs during translation of the different tissues. Therefore, they are useful components in reducing tension and the negative effects of wear-and-tear at points of friction and provide resistance-free movement by the human body.[10]

In anatomy classes, bursae are taught in a limited fashion. This is because in the dissection course, bursae can rarely be shown, if at all in some cases. For bursae like the iliopectineal or the Pes

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Anserinus bursae, visualization can be successful with a careful approach. Students are often surprised at how much fluid leaks out which is a good indicator for a bursa when dissecting the area. Often, the iliopectineal bursa – which is connected to the hip joint - in particular shows a cartilaginous change as an expression of the pressure present in this area. Macroscopically, the surface of the bursa is shiny, highlighting its gliding ability. Other bursae such as the subdeltoid-subacromial or the bursae in the area of the greater trochanter are hardly visible. However, studies show that ultrasound-guided marking of the bursa on cadavers can be successful and thus, theoretically, may be useful in the visualization of bursae that are difficult for students to macroscopically observe during dissection courses.[11] Technological advancements have led to significant developments. With the capacity for equipment to easily connect to tablets via Wi-Fi or Bluetooth, integrating ultrasound into medical student education has never been simpler. Consequently, students benefit doubly from early integration, as it enhances their anatomical knowledge and familiarizes them with ultrasound technology. Its benefit for clinical understanding is additionally enhanced.

Using modern ultrasound equipment with high resolution probes, superficial but also deep-seated bursae can be easily visualized. Many bursae are only visible when a pathology is present (e.g., bursitis iliopectinea), others are physiologically filled with fluid (e.g., bursa infrapatellaris profunda). We most frequently see clinically relevant bursitis in the shoulder and the greater trochanter[12], where more than a dozen bursae exist.[13] In the context of inflammatory bursitis, pain at rest and at night may occur (e.g., in the context of polymyalgia rheumatica of the hip or shoulders). In mechanically-induced bursitis, pain often occurs during movement. Some bursitis may also occur without pain (bursitis olecrani, bursitis prepatellaris). The etiology of bursitis varies. Causes can be systemic diseases such as rheumatoid arthritis, after vaccinations (shoulder injury related to vaccine administration = SIRVA), in the context of septic or infectious bursitis, in crystal arthritis, in the context of hydroxylapatite-associated bursitis, in large-vessel vasculitis (for example, in polymyalgia rheumatica), in the case of mechanical overload, after trauma or as accompanying symptoms of capsulitis.

The aim of the current paper is to provide an overview of the existing ultrasonographic observations and visualization methods on bursae of human cadavers found in the literature. The three specific objectives of this scoping review were to conduct a systematic search of the published and grey literature for ultrasonographic investigations on bursae of human cadavers, map out the key features and ultrasound-guided labeling techniques of the identified articles, and identify new research avenues with potential to advance the field.

Methods

The methodology followed the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews) guidelines.[14] The review included the following five key stages: (1) identifying the research question, (2) identifying relevant studies, (3) study selection, (4) charting the data and (5) collating, summarizing, and reporting the results.

Research Question

This review was guided by the question, "Is there evidence that ultrasound guided labeling techniques of bursae can be beneficial for learning anatomy in dissection courses?". Therefore, a protocol was registered on November 28, 2022, on OSF Registries (osf.io/mx468).

Search Strategy

The following databases were screened for relevant studies: CENTRAL, MEDLINE, BIOSIS Previews, EMBASE and Web of Science Core Collection. Grey literature was also considered in two different ways. (1) the grey literature database National Grey Literature Collection was regarded, (2) for PhD theses and dissertations, the databases EThOS and Open Access Theses and Dissertations were screened for relevant studies by combining the keywords used in the search strategy.

Backward and forward citation tracking was also performed. Search process was conducted on the 3rd of January 2023. The search strategy is attached below ***Supplementary Material 1***. A librarian was contacted to develop the search strategy and reviewed the final version prior to use.

Citation Management

Following the search, all identified citations were collated using Endnote.[15] Duplicates were removed by Endnote following Bramer, Giustini [16] and manually with further duplicates removed when found later in the review process. Title and abstract screening were also performed using Endnote.

Eligibility Criteria

Only ultrasound investigations in human cadavers were included. Since animal anatomy differs from human anatomy and Ultrasound in animals is still under-researched, these studies were excluded. Studies on phantoms were excluded due to the lower quality of ultrasound imaging.[17] Other imaging techniques (MRI, CT) were not considered, primarily because ultrasound is distinguished as a low-radiation and resource-saving diagnostic instrument. It is portable, inexpensive and allows bedside examination. The article was included, if the investigated subject was a bursa. For the analysis of the ultrasound approaches only B-Mode ultrasound was included. Sonoeleastography was not used because actively perfused "living" tissue and tissue under a certain tension would be necessary (e.g. tense or relaxed tendon). At the present time, sonoelastography is not yet standardized and depends on the technique and the particular device. Doppler sonography makes little sense in cadavers. Since this work focuses on bursae, intravascular, intraosseous, intraarticular ultrasound was deliberately omitted. Only studies in English and German were included. In order to understand the exclusion criteria of the individual studies a PRISMA flowchart was created.

All types of relevant information including articles, PhD theses, dissertations and chapters in textbooks were considered. No restriction was placed on the year of publication.

Title and Abstract Screening

First, title and abstract screening was performed for reviewing minimum inclusion criteria by one reviewer. References were added for full text screening if neither the title nor the abstract provided sufficient information. If uncertainties appeared, a second reviewer checked the references. Full text screening was performed by two reviewers. At each stage, disagreements were resolved by discussion or involvement of a third author. Anatomical structures were used to order the references. A critical appraisal of the included sources and a risk of bias assessment of the included studies were not performed. But for the publication bias, we checked whether the included studies registered a protocol.

Data Characterization

Data were extracted from the papers included in the scoping review by one reviewer manually. General characteristics extracted included author, year of publication, title, investigated bursa and journal. The characteristics of ultrasound-guided labeling techniques that were extracted from the data comprised the marking substrate, injected volume, needle and sample size.

Data Summary and Synthesis of Results

The data were further categorized in the citation manager Endnote and a spreadsheet was created and imported into Microsoft Excel 2019. Tables were created for the general characteristics and the ultrasound-guided labeling techniques. The articles were categorized by investigation approaches and presented in a narrative way.

Ultrasound-Guided Injection of Iliopectineal Bursa in a Human Cadaver

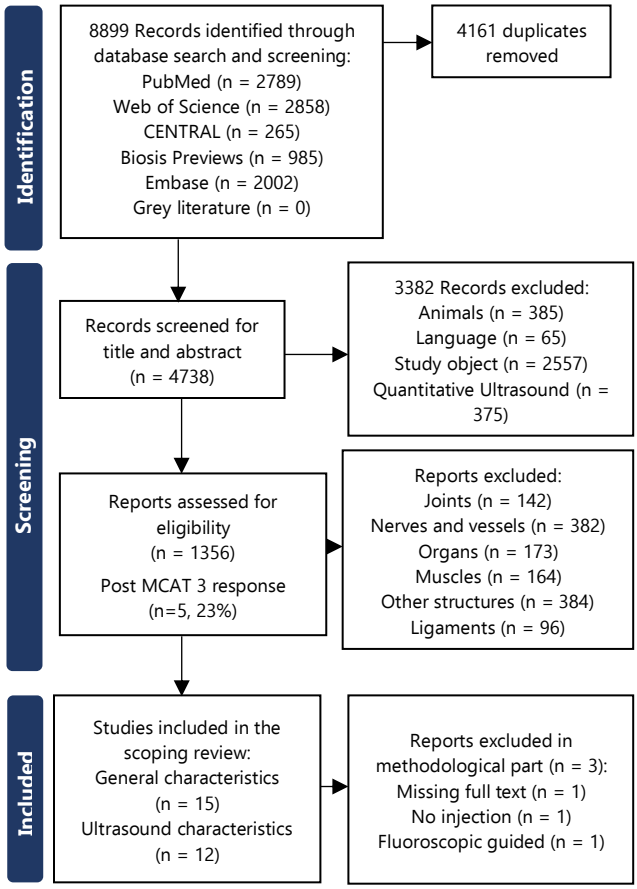
One female 68-year-old formalin-fixed human specimen lying in supine position was used for the labeling of the iliopectineal bursa on the right side. Before injection a CT scan of the cadaver was performed and evaluated by a radiologist. No relevant pathologies were present. A sonographer with EULAR *(https://www.eular.org/musculoskeletal-imaging-network-centres-list)* certificate performed the ultrasound-guided injection with a linear probe (M12L, General Electric, model LOGIQ 9) using a standard in-plane technique.

Results

Search and Selection of Included Studies

The search yielded 8899 results, of which 15 met the eligibility criteria. The authors agreed on all eligibility decisions upon discussion without the need for a third party to be involved. Forward and backward citation tracking of the 15 included publications did not yield any additional publications. The PRISMA flowchart is presented in ***Figure 1***.

Figure 1. **PRISMA Flowchart.**



General Characteristics of Included Studies

The general characteristics of the 15 studies are presented in ***Supplementary Material 2.***

Seven of the included studies were published before 2015 and eight were from 2016 or earlier. Leading journals were AJR Am J Roentgenol and PM&R (both n = 3). All of the included studies were published in English. Only the subacromial bursa was investigated by two different studies.[11, 18] The following bursae were studied: the radial and ulnar bursae [19], the prepatellar bursa [20], the Pes Anserinus bursa [21], the Gruberi bursa [22], the subgluteus maximus and medius bursae [23], the trochanteric bursa [24], the medial collateral ligament bursa [25], the subdeltoid bursa [26], the semimembranosus bursa [27], the retrocalcaneal bursa [28], the subacromial bursa [11], the obturator internus bursa [29], the subacromial-subdeltoid bursa[18], the infrapatellar bursa [30], and the ischial bursa[31].

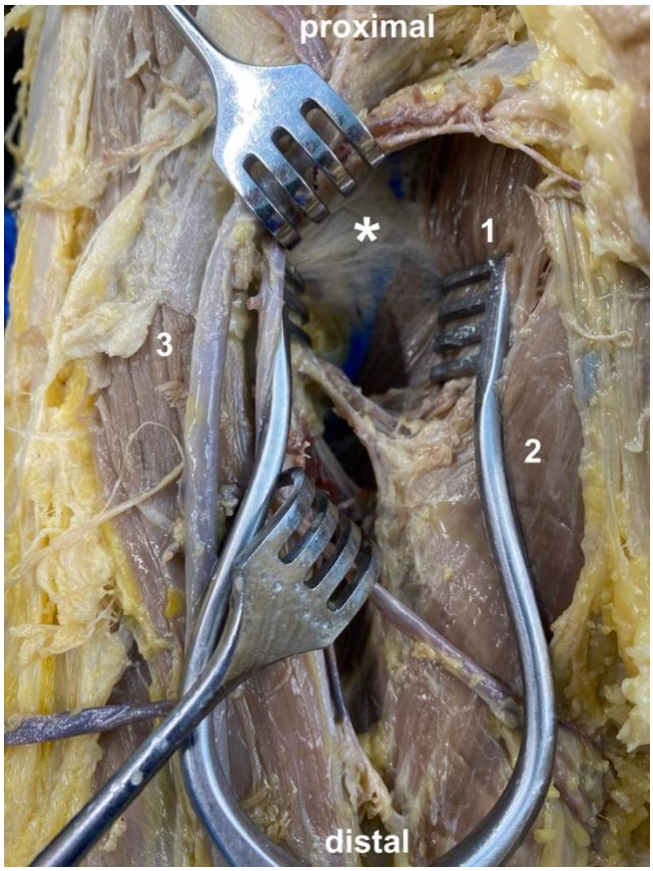
Ultrasound-Guided Labeling Techniques

In the methodological analysis, 12 studies were included ***Table 1***. Missing full text [23], no injection performed [26] and fluoroscopic guided bursography [18] were the main reasons why the three other studies were excluded. The sample sizes ranged from 1 to 24. Only in one study were some of the specimens formalin-embalmed [24], in all the other studies they were left non-embalmed. A latex solution had been applied in 6 investigations

Table 1. **Summary of Ultrasound (US) Injection Characteristics of Included Studies (n = 12).**

Author (Year)	Structure	Sample characteristics	Substrate	Injection volume	Needle
Aguiar, Gasparetto [19]	Radial and ulnar bursae	Ten hands from nine fresh cadavers (five men and four women, mean age: 83.8 years), arms transected and immediately deep-frozen at -40 C; thaw for 24 hours at room temperature before Ultrasound	Solution consisting of 1 ml of gadopentate dimeglumine, diluted in 250 ml of saline solution and mixed with 0.5 ml of iohexol and 0.5 ml of a mixture of gelatin and different colors	5-15 mL	25-gauge needle
Aguiar, Viegas [20]	Prepatellar bursa	Nine knees from eight unembalmed cadavers (five women, four men, mean age: 76 years), transected and immediately deep-frozen at -40 C; thaw for 30 hours at room temperature before Ultrasound	Dilute gadolinium solution, two parts of 4 mmol/L gadopentate dimeglumine, one part of iodinated contrast material and one part of 15% concentrated solution of gelatin	1-3 mL	n/c
Finnoff, Nutz [21]	Pes anserinus bursa	24 unembalmed adult cadaveric lower extremity specimens; thawed at room temperature	Colored latex solution diluted by 50% with tap water	2 mL	25-gauge needle, 38-mm stainless steel needle
Gaetke-Udager, Jacobson [22]	Gruberi bursa	A single unembalmed cadaveric anklefoot specimen	Diluted blue latex (50% latex and 50% water)	2 mL	22-gauge needle
Mu, Peng [24]	Trochanteric bursa (Deep gluteus maximus bursa)	24 hip specimens (10 male/14 female) from 12 cadavers (9 formalin-embalmed/3 fresh) with mean age of 79.5 years	Methylene blue	1 mL	22-gauge, 3.5-inch Quincke spinal needle
Nakase, Yoshimizu [25]	Medial collateral ligament bursa	Three fresh-frozen cadaver knees	Green ink	1 mL	n/c
Onishi, Sellon [27]	Semimembranosus bursa	10 unembalmed cadaveric knee specimens	Diluted blue-colored latex	3 mL	22-gauge, 63-mm, stainless steel needle
Pekala, Henry [28]	Retrocalcaneal bursa	10 fresh-frozen specimens injected with ink 10 fresh-frozen specimens injected with iopromide All male, mean age 49.7 years, thawed for eight hours at room temperature prior to investigation	• India ink • Iopromide	2 mL	n/c
Pujalte, Hudspeth [11]	Subacromial bursa	12 unembalmed cadaveric shoulder and complete upper extremity specimens (all males, with ages at death ranging from 40 to 50)	Combination of colored latex injection medium and uncompounded latex injection solution	2-3 mL	25-gauge, 38-mm stainless steel needle
Smith, Wisniewski [29]	Obturator internus bursa	5 unembalmed cadaveric pelvis specimens, fresh-frozen, thawed at room temperature immediately before the study, mean age 78 years	• Saline • diluted yellow latex (50% water and 50% latex)	First small amount of saline than 1.5 mL diluted yellow latex	22-gauge, 87.5-mm stainless steel needle
Viegas, Aguiar [30]	Deep and superficial infrapatellar bursae	Nine knee specimens from eight non-embalmed cadavers (five women, three men; mean age 76 years); immediately deep-frozen at – 40 C; thaw for 30 h at room temperature	Dilute gadolinium solution (two parts of 4 mmol/l of gadopentate dimeglumine, one part iodinated contrast material, one part 15% concentrated solution of gelatin)	0.5-1.5 mL	n/c
Wisniewski, Hurdle [31]	Ischial bursa	One unembalmed cadaveric pelvis	Diluted blue liquid latex (diluted by 50% with tap water	3 mL	22-gauge, 9-cm stainless-steel needle

***Figure 2*. Staining of the Iliopectineal Bursa.**



Legend: Anatomical dissection of the right femoral triangle of a 68-year-old female formalin-fixed specimen. The iliopectineal bursa (asterisk) is located deep to the psoas tendon and ventral to the pectineus muscle (1). The femoral triangle is flanked by the adductor longus (2) and sartorius muscles (3). The proximal border (inguinal ligament) is not shown. An ultrasound-guided right iliopectineal bursa injection with 3 mL of blue latex was performed before dissection as shown.

to label the bursae. The volumes of the latex solution ranged from 1.5 mL to 3 mL. ***Figure 2*** shows an example staining of the iliopectineal bursa. Three studies performed a bursography via magnetic resonance imaging and therefore used a solution of gadopentate dimeglumine and other ingredients like iohexol or gelatin. They used volumes between 0.5 mL and 15 mL. One study injected, before the labeling substrate, a little amount of saline to spread the bursa.[29] There were either 22-gauge or 25-gauge needles. The needle size was not addressed in four studies.[19,25,28,30]

Cadaveric Investigation of Regional Anatomy Using Magnetic Resonance Imaging (MRI) After Ultrasound-Guided Bursography

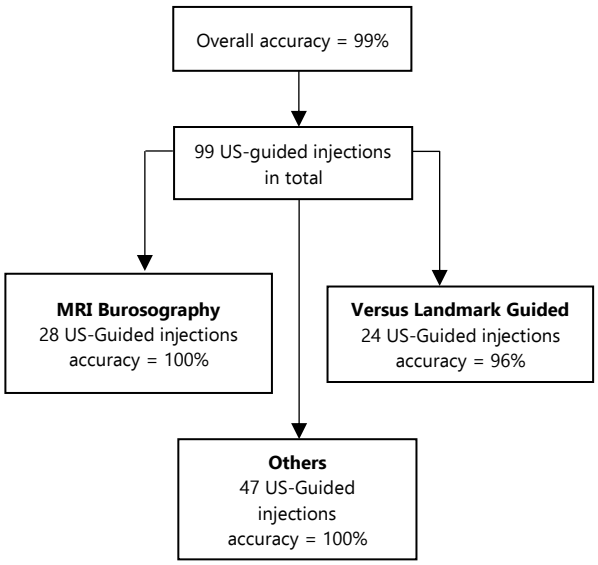
All three studies using MRI after bursography were able to successfully inject contrast agent into the investigated bursae with ultrasound guidance.[19, 20, 30] With the help of the subsequent MRI, the extent of the bursae could be analyzed in detail. In the study by Aguiar, Gasparetto [19] for example, a communication between the radial and ulnar bursae could be found in every case. Furthermore, an "hourglass" or "figure of eight" shape with the constricting portion at the level of the carpal tunnel could be visualized. Aguiar, Viegas [20] saw a most frequently trilaminar (78%), followed by bilaminar (22%), anteriorly to the patella placed (= prepatellar) bursa. The average expansions were 3.2 mm (anteroposterior), 40.5 mm (lateromedial), and 39.7 mm (craniocaudal). Also, in the study by Viegas, Aguiar [30] the size and expansion of the deep and superficial infrapatellar bursae could be investigated. The average dimensions of deep infrapatellar bursa were as followed: craniocaudal 25 mm, mediolateral 28.7 mm and anteroposterior 6 mm. In 89% of the cases, it was subdivided into an anterior and posterior compartment. Lateral extension beyond the edge of the patellar tendon was observed in all specimens. Communication into the superficial bursa was observed once, but none communicated with the joint cavity of the knee. The edges of the superficial infrapatellar bursa could be defined in five specimens showing an average smaller size (craniocaudal 19.5 mm, mediolateral 21.2 mm and anteroposterior 2.2. mm).

Accuracy of Ultrasound-Guided Injection Techniques Confirmed by Dissection

Two studies compared ultrasound-guided versus landmark-guided approaches for bursae injection. Mu, Peng [24] injected methylene blue 12 times with ultrasound guidance and 12 times using landmark guidance into the subgluteus maximus bursa. The ultrasound-guided approach achieved 84% accuracy, the landmark-guided 60%. Finnoff, Nutz [21] also performed 12 ultrasound-guided and landmark-guided injection approaches into the Pes Anserinus bursa. Accuracies were 92% for ultrasound-guided and 17% for LM-guided injection. Three studies achieved an accuracy of 100% without overflow for the ultrasound-guided injection of the bursa which they investigated: Nakase, Yoshimizu [25] successfully targeted the medial collateral ligament bursa, Wisniewski, Hurdle [31] the ischial bursa on both sides, and Gaetke-Udager, Jacobson [22] the Gruberi bursa. Onishi, Sellon [27] injected latex with an accuracy of 100% by an overflow rate outside of the bursa of 80%. Pujalte, Hudspeth [11] injected the long head of the biceps tendon sheath successfully 12 times with concomitant subacromial bursa injection via the same needle. In two specimens (17%), the surrounding areas were penetrated by injectate. Smith, Wisniewski [29] included two different ultrasound-guided approaches into the obturator internus bursa. The two injections through the short-axis achieved an accuracy of 100% without overflow. One of the trans-tendinous injections was also completely effective, whereas the other achieved 80% of the injection with the remaining 20% in the obturator internus. Also the study by Pekala, Henry [28] had a high accuracy rate. In 10 fresh frozen Achilles tendon specimens, ink was injected into the retrocalcaneal bursa via ultrasound guidance. A similar pattern of ink spread could be found when comparing the radiographs that were made with contrast injections.

In total 99 ultrasound-guided injections into bursae were performed with an overall accuracy of 99%. ***Figure 3*** summarizes the key findings.

***Figure 3*. Summary of the key findings.**



Discussion

This article represents a comprehensive review screening ultrasound investigations on bursae of cadavers. Reviews of ultrasound investigations on bursae of living objects are numerous. [32, 33] Our study demonstrates the feasibility and viability of using ultrasound to conduct examinations on cadaveric bursae in multiple body regions. In this setting, bursae injections guided by ultrasound in cadavers are also distinguished by their great precision.[11, 21, 27]

In our view, and following a thorough exchange with the largest Universities in Switzerland - Zurich, Basel and Bern - learning about bursae tends to be less emphasized in anatomical educational institutions, particularly during the dissection course. This is not due to the anatomist's level of skill, but rather because the spaces are difficult to visualize macroscopically and thus difficult for students to understand. However, since bursae encompass a common etiology of pain syndromes, the present work could serve as an impetus to place more emphasis on teaching students about the importance of bursae. In this regard, the ultrasound-guided labeling technique may be an appropriate option. With the help of this method, bursae can be successfully labelled, and therefore students can better locate and observe them through this process. Learning with the help of colors seems to facilitate the memory consolidation process[34] and implementing this does not require a lot of material. Even small amounts of a labelling substance (e.g., latex, methylene blue or ink; which are all equal); usually 1-3 mL are sufficient to label the bursa successfully with ultrasound-guidance.[21, 24, 25] Furthermore, the use of ultrasound as a teaching tool allows for medical students to gain practical skills [35] and their clinical anatomical knowledge will be also be improved. We believe that this should be taught intensively in medical school and not after the end of training. The survey from O'Keeffe, Davy [36] to radiologists proves the assumption that this clinical-anatomical knowledge should be taught only as a combination. Ultrasound is flexible, inexpensive, and versatile. There are now portable probes with high resolution that can be easily connected to tablets or even smartphones via Bluetooth or WLAN. Protective covers for the tablets and ultrasound devices ensure cleanliness, even if the dissection is already at an advanced stage. Assuming approximately 8-10 students per dissection table, the practical application of ultrasound by the students themselves is also conceivable. Students could visualize difficult-to-dissect structures with the assistance of instructors trained in ultrasound. By using this tool already in the dissection course will set the students up for diagnostic and therapeutic skills and prove that the ultrasound is the next new pocket-sized stethoscope.[37]

The question that arises, however, is whether the injection techniques, which have been performed primarily on fresh-frozen body donations, can be transferred to the dissection course which commonly uses formalin-fixed body donations. Fresh frozen cadavers pose numerous challenges, including the requirement of freezers for storage and limited work time (a few weeks at the most) because of rapid decomposition following thawing. [38] Therefore, they are not suitable for a dissection course that typically spans several months. Formalin on the other hand hardens the tissues, thus its use is generally associated with extreme rigidity and has been found to severely affect the quality of cadaveric tissue, particularly soft tissues. [39] Only the study of Mu, Peng [24] included formalin fixed cadavers in addition to fresh frozen cadavers. Differences in the accuracy rate for ultrasound-guided trochanteric bursa injections between the two cadaver types was not reported. Further studies should be performed on formalin-fixed body donors to provide clarity. Thiel fixation could be an alternative. Eisma, Lamb [40] argue that Thiel-embalmed cadavers are advantageous, especially for teaching of the musculoskeletal system. However, they are more expensive than formalin-fixed cadavers, and the embalming procedure is more complex. [41] None of the included studies used Thiel preserved cadavers so it is unclear whether Thiel-fixed cadavers can better represent the bursae and whether they may be beneficial for teaching bursae anatomy. Bursae are among the most difficult structures to visualize in the dissection course, belong according to Stecco's work on the fasciae and are therefore largely influenced by the fixation method similar to fascial tissue. [42]

Strengths and Limitations

In the current text, all processes were conducted with rigor and transparency. It followed a protocol that was listed in the OSF Registries. To provide a complete search of the literature, five digital bibliographical databases and a grey literature search were incorporated in the course of the investigation. Since the initial goal was to examine all ultrasound tests conducted on body donors, the search terms were purposefully broad. As a result, there were many studies returned by the search, which made the title and abstract screening process time-consuming and perhaps mistake-prone.

As mentioned above, most studies were conducted on fresh frozen cadavers. Therefore, the transferability of these results to formalin-fixed cadavers should be considered cautiously, as studies indicate that ultrasound quality and visibility of structures

varies significantly between preservation methods.[43] Further research is needed on formalin-fixed cadavers. Although high accuracy was achieved, some studies were conducted on only one cadaver with fewer than five injections performed. [22, 31]

Scoping reviews do not adhere to the same strict standards that systematic reviews do, and there is no risk of bias assessment, which leaves space for biases like selection bias. Publication bias is strong since none of the included studies registered a visible protocol prior to their investigation. Generally, caution should be taken when drawing conclusions from scoping reviews because they frequently summarize the findings without fully synthesizing the results.

Conclusions

The present study evaluates the current literature on the bursae and acts as a comprehensive review to screen ultrasound studies of human cadaveric bursae. The ultrasound-guided labeling procedures produced bursae labels with a high degree of accuracy. Therefore, ultrasound as a versatile and portable instrument could be a potential teaching tool to visualize difficult-to-dissect structures such as bursae during the dissection course and provide students with an understanding of sonoanatomy. But, caution is advised in drawing general conclusions because of the small number of identified studies, small sample sizes and different methodologies in the studies. Future larger-scale research on different fixation methods (Formalin, Thiel) are necessary.

Summary – Accelerating Translation

Ziel unserer Arbeit «Schleimbeutel im Präparationskurs – der Wert von Ultraschallbildgebungsverfahren zur Verbesserung der anatomischen Visualisierung und des Verständnisses der Studierenden» war es eine Übersicht von Ultraschalluntersuchungen an Schleimbeuteln von menschlichen Körperspendern zu generieren. Die Anatomie und klinische Bedeutung von Schleimbeuteln wird im Medizinstudium gelehrt, jedoch können Schleimbeutel im Präparationskurs, unter anderem aufgrund der Fixiationsmethode, nur schwer dargestellt und somit nur schwer von Studierenden nachvollzogen werden. Ultraschall ist in der Lage Schleimbeutel und deren Erkrankungen sicher am Lebenden nachzuweisen. Allerdings gibt es wenig Daten ob dies an Körperspendern auch möglich ist. Die weiterführende Idee dieser Arbeit war es die Daten zu Ultaschalluntersuchungen an Körperspendern systematisch zusammenzufassen, um Schlussfolgerungen für die Verbesserung der Lehre schliessen zu können. Die Leitfrage dabei war: Ist die frühe Integration des Ultraschalls in die medizinische Lehre für Medizinstudierende vorteilhaft?

Eine systematische Literaturrecherche wurde streng nach den PRISMA Vorgaben durchgeführt. 8899 Referenzen wurde gefunden, wovon sich 15 mit dem Thema Schleimbeutel befassten. Es zeigten sich unterschiedliche Ultraschallexperimente: Ultraschall gestützte Injektionen von Schleimbeuteln mit Kontrastmittel oder Latex wurden durchgeführt. Anschliessende Magnetresonanztomographie- oder Röntgen-Aufnahmen wurden erstellt. In den meisten Studien wurde eine Dissektion der Region durchgeführt. Eine hohe Präzision der Injektionen konnte in allen Studien gezeigt werden. Während der Dissektion konnten die Schleimbeutel durch die Anfärbung (bspw. mit Latex) sicher lokalisiert und nachvollzogen werden. Die Ergebnisse zeigen, dass der Ultraschall und Ultraschall gestützte Injektionen Schleimbeutel auch an Körperspendern sicher lokalisieren und darstellen können. Studierende würden von einer frühen Implementierung des Ultraschalls in den Präparationskurs zweifach profitieren: Sie würden einerseits den frühen Umgang mit Ultraschall erlernen und andererseits Ihr anatomisches Wissen vertiefen. Daher sprechen wir uns für eine frühe Integration des Ultraschalls während des Medizinstudiums aus.

References

1. Monro A. A description of all the bursae mucosae of the human body; their structure explained, and compared with that of the capsular ligaments of the joints, and of those sacs which line the cavities of the thorax and abdomen; with remarks on the accidents and diseases which affect those several sacs, and on the operations necessary for their cure. Edinburgh: Printed for C. Elliot, T. Kay ..., London; and for Charles Elliot, Edinburgh; 1788.
2. Koudela K, Jr., Koudelová J, Koudela K, Sr., Kunesová M. Bursitis iliopectinea. Acta Chir Orthop Traumatol Cech. 2008;75(5):347-54.
3. Dihlmann W, Peters A, Tillmann B. The bursa iliopectinea--a morphologic-computed tomographic study. Rofo. 1989;150(3):274-9.
4. Resnick DLK, H. S.; Pretterklieber, M. L. Internal derangements of joints. 2nd ed. Philadelphia: Saunders; 2007.
5. Canoso JJ, Stack MT, Brandt KD. Hyaluronic acid content of deep and subcutaneous bursae of man. Ann Rheum Dis. 1983;42(2):171-5.
6. Van Mieghem IM, Boets A, Sciot R, Van Breuseghem I. Ischiogluteal bursitis: an uncommon type of bursitis. Skeletal Radiol. 2004;33(7):413-6.
7. Sawyer E, Varacallo M. Anatomy, shoulder and upper limb, hand ulnar bursa. StatPearls. Treasure Island (FL): StatPearls Publishing, Copyright © 2023, StatPearls Publishing LLC.; 2023.
8. Stecco C. Atlas des menschlichen fasziensystems: Elsevier Health Sciences; 2016.
9. Stecco C, Fede C, Macchi V, Porzionato A, Petrelli L, Biz C, et al. The fasciacytes: A new cell devoted to fascial gliding regulation. Clin Anat. 2018;31(5):667-76.
10. De Oliveira-Lagôa S, Cruz FB, Azócar DLM, Lavilla EO, Abdala V. Anuran forelimb muscle tendinous structures and their relationship with locomotor modes and habitat use. Curr Zool. 2019;65(5):599-608.
11. Pujalte G, Hudspeth LJ, Troyer WD, Shapiro SA. Ultrasound-guided injection of the long head of the biceps tendon sheath with concomitant subacromial bursa injection through the same needlestick. Clin Anat. 2022.
12. Tamborrini G, Marx C. Cme-rheumatology 7: trochanter major pain syndrome. Praxis (Bern 1994). 2016;105(3):172-4.
13. Tamborrini G, Müller-Gerbl M, Müller SA. Cme-sonography 106: subacromial bursa - a myth. Praxis (Bern 1994). 2022;111(15):833-46.
14. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. Ann Intern Med. 2018;169(7):467-73.
15. Gotschall T. EndNote 20 desktop version. J Med Libr Assoc. 2021;109(3):520-2.
16. Bramer WM, Giustini D, de Jonge GB, Holland L, Bekhuis T. De-duplication of database search results for systematic reviews in EndNote. J Med Libr Assoc. 2016;104(3):240-3.
17. Dang D, Kamal M, Kumar M, Paliwal B, Nayyar A, Bhatia P, et al. Comparison of human cadaver and blue phantom for teaching ultrasound-guided regional anesthesia to novice postgraduate students of anesthesiology: a randomized controlled trial. J Anaesthesiol Clin Pharmacol. 2024;40(2):276-82.
18. Stallenberg B, Destate N, Feipel V, Gevenois PA. Involvement of the anterior portion of the subacromial-subdeltoid bursa in the painful shoulder. AJR Am J Roentgenol. 2006;187(4):894-900.

19. Aguiar RO, Gasparetto EL, Escuissato DL, Marchiori E, Trudell DJ, Haghighi P, et al. Radial and ulnar bursae of the wrist: cadaveric investigation of regional anatomy with ultrasonographic-guided tenography and MR imaging. Skeletal Radiol. 2006;35(11):828-32.
20. Aguiar RO, Viegas FC, Fernandez RY, Trudell D, Haghighi P, Resnick D. The prepatellar bursa: cadaveric investigation of regional anatomy with mri after sonographically guided bursography. AJR Am J Roentgenol. 2007;188(4):W355-8.
21. Finnoff JT, Nutz DJ, Henning PT, Hollman JH, Smith J. Accuracy of ultrasound-guided versus unguided pes anserinus bursa injections. PM&R. 2010;2(8):732-9.
22. Gaetke-Udager K, Jacobson JA, Bhatti ZS, Smith J, Parameswaran A, Fessell DP. Ultrasound of the gruberi bursa with cadaveric and mri correlation. AJR Am J Roentgenol. 2016;207(2):386-91.
23. Moore BJ, Johnson W, Finnoff JT, Smith J, Sellon JL. Distribution of sonographically guided injections of the subgluteus minimus and medius bursae in cadaveric model. Med Sci Sports Exerc. 2019;51(6, Suppl. S):592.
24. Mu A, Peng P, Agur A. Landmark-guided and ultrasound-guided approaches for trochanteric bursa injection: a cadaveric study. Anesth Analg. 2017;124(3):966-71.
25. Nakase J, Yoshimizu R, Kimura M, Kanayama T, Yanatori Y, Tsuchiya H. Anatomical description and short-term follow up clinical results for ultrasound-guided injection of medial collateral ligament bursa: New conservative treatment option for symptomatic degenerative medial meniscus tear. Knee. 2022;38:1-8.
26. Norbury JW, Karr NC, Sindhi V, Rathbun KM, Charles SC, McIver MB, et al. Improving the performance time and accuracy of ultrasound-guided interventions: a randomized controlled double-blind trial of the line-of-sight approach and the „apples" mnemonic. J Ultrasound Med. 2018;37(12):2909-14.
27. Onishi K, Sellon JL, Smith J. Sonographically guided semimembranosus bursa injection: technique and validation. PM&R. 2016;8(1):51-7.
28. Pekala PA, Henry BM, Pekala JR, Piska K, Tomaszewski KA. The Achilles tendon and the retrocalcaneal bursa an anatomical and radiological study. Bone Jt Res. 2017;6(7):446-51.
29. Smith J, Wisniewski SJ, Wempe MK, Landry BW, Sellon JL. Sonographically guided obturator internus injections: techniques and validation. J Ultrasound Med. 2012;31(10):1597-608.
30. Viegas FC, Aguiar RO, Gasparetto E, Marchiori E, Trudell DJ, Haghighi P, et al. Deep and superficial infrapatellar bursae: cadaveric investigation of regional anatomy using magnetic resonance after ultrasound-guided bursography. Skeletal Radiol. 2007;36(1):41-6.
31. Wisniewski SJ, Hurdle M, Erickson JM, Finnoff JT, Smith J. Ultrasound-guided ischial bursa injection: technique and positioning considerations. PM&R. 2014;6(1):56-60.
32. Wu T, Song HX, Dong Y, Li JH. Ultrasound-guided versus blind subacromial-subdeltoid bursa injection in adults with shoulder pain: a systematic review and meta-analysis. Semin Arthritis Rheum. 2015;45(3):374-8.
33. McGill KC, Patel R, Chen D, Okwelogu N. Ultrasound-guided bursal injections. Skeletal Radiol. 2023;52(5):967-78.
34. Dzulkifli MA, Mustafar MF. The influence of colour on memory performance: a review. Malays J Med Sci. 2013;20(2):3-9.
35. Hamza A, Radosa J, Meyberg-Solomayer G, Solomayer EF, Takacs Z, Juhasz-Boess I, et al. Trial integration of combined ultrasound and laparoscopy tuition in an undergraduate anatomy class with volunteer participation - a pilot study. Ann Anat. 2019;221:101-7.
36. O'Keeffe GW, Davy S, Barry DS. Radiologist's views on anatomical knowledge amongst junior doctors and the teaching of anatomy in medical curricula. Ann Anat. 2019;223:70-6.
37. Bledsoe A, Zimmerman J. Ultrasound: the new stethoscope (point-of-care ultrasound). Anesthesiol Clin. 2021;39(3):537-53.
38. Hayashi S, Naito M, Kawata S, Qu N, Hatayama N, Hirai S, et al. History and future of human cadaver preservation for surgical training: from formalin to saturated salt solution method. Anat Sci Int. 2016;91(1):1-7.
39. Wilke HJ, Werner K, Häussler K, Reinehr M, Böckers TM. Thiel-fixation preserves the non-linear load-deformation characteristic of spinal motion segments, but increases their flexibility. J Mech Behav Biomed Mater. 2011;4(8):2133-7.
40. Eisma R, Lamb C, Soames RW. From formalin to thiel embalming: what changes? One anatomy department's experiences. Clin Anat. 2013;26(5):564-71.
41. Wolff KD, Kesting M, Mücke T, Rau A, Hölzle F. Thiel embalming technique: a valuable method for microvascular exercise and teaching of flap raising. Microsurgery. 2008;28(4):273-8.
42. Stecco C, Fantoni I, Macchi V, Del Borrello M, Porzionato A, Biz C, et al. The role of fasciae in civinini-morton's syndrome. J Anat. 2015;227(5):654-64.
43. Sawhney C, Lalwani S, Ray BR, Sinha S, Kumar A. Benefits and Pitfalls of Cadavers as Learning Tool for Ultrasound-guided Regional Anesthesia. Anesth Essays Res. 2017;11(1):3-6.

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Author Contributions

Conceptualization: FM, and AZ. Methodology: FM, and AZ. Investigation: FM, and GT. Resources: MM. Writing – Original Draft: FM. Writing – Review & Editing: AZ, GT, JP, MN, and AP. Visualization: FM, AZ, and AP. Supervision: MM. Project Administration: MM.

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Supplementary Material

Appendix 1. **Search Strategy.**

Database	**Search term** (translated with the aid of https://sr-accelerator.com/#/polyglot)
PubMed	(ultrasonography[mesh] OR ultrasonography[tiab] OR ultraso*[tiab]) AND (cadaver[mesh] OR cadaver*[tiab] OR corpse*[tiab] OR dead bod*[tiab] OR donated bod*[tiab] OR body donation*[tiab] OR deceased*[tiab] OR lifeless[tiab]) NOT (animals[mesh] NOT humans[mesh]) NOT (animal*[tiab] NOT human*[tiab]) NOT (transplantation[mesh]) NOT (transplantation[tiab])
CENTRAL	(ultrasonography OR ultrasonography OR ultraso*) AND (cadaver OR cadaver* OR corpse* OR dead bod* OR donated bod* OR body donation* OR deceased* OR lifeless) NOT (animals NOT humans) NOT (animal* NOT human*) NOT (transplantation)
Embase	('ultrasonography'/exp OR ultrasonography:ti,ab) AND ('cadaver'/exp OR cadaver*:ti,ab) NOT ('animals'/exp NOT 'humans'/exp) NOT (animal*:ti,ab NOT human*:ti,ab) NOT ('transplantation'/exp) NOT (transplantation:ti,ab)
Web of Science	(ultrasonography OR ultrasonography OR ultraso*) AND (cadaver OR cadaver* OR corpse* OR "dead bod*" OR "donated bod*" OR "body donation*" OR deceased* OR lifeless) NOT (animals NOT humans) NOT (animal* NOT human*) NOT (transplantation)
Biosis Previews	(ultrasonography OR ultrasonography OR ultraso*) AND (cadaver OR cadaver* OR corpse* OR "dead bod*" OR "donated bod*" OR "body donation*" OR deceased* OR lifeless) NOT (animals NOT humans) NOT (animal* NOT human*) NOT (transplantation)

Appendix 2. **Summary of General Characteristics of Included Studies (n = 15).**

Author/Year	**Title**	**Bursa/e**	**Journal**
Aguiar, Gasparetto [19]	*Radial and ulnar bursae of the wrist: cadaveric investigation of regional anatomy with ultrasonographic-guided tenography and MR imaging*	Radial and ulnar bursae	Skeletal Radiol
Aguiar, Viegas [20]	*The prepatellar bursa: cadaveric investigation of regional anatomy with MRI after sonographically guided bursography*	Prepatellar bursa	AJR Am J Roentgenol
Finnoff, Nutz [21]	*Accuracy of Ultrasound-Guided versus Unguided Pes Anserinus Bursa Injections*	Pes anserinus bursa	PM&R
Gaetke-Udager, Jacobson [22]	*Ultrasound of the Gruberi Bursa With Cadaveric and MRI Correlation*	Gruberi bursa	AJR Am J Roentgenol
Moore, Johnson [23]	*Distribution of Sonographically Guided Injections of the Subgluteus Minimus and Medius Bursae in Cadaveric Model*	Subgluteus and medius bursae	Med Sci Sports Exerc
Mu, Peng [24]	*Landmark-Guided and Ultrasound-Guided Approaches for Trochanteric Bursa Injection: A Cadaveric Study*	Trochanteric bursa	Anesth Analg
Nakase, Yoshimizu [25]	*Anatomical description and short-term follow up clinical results for ultrasound-guided injection of medial collateral ligament bursa: New conservative treatment option for symptomatic degenerative medial meniscus tear*	Medial collateral ligament bursa	Knee
Norbury, Karr [26]	*Improving the Performance Time and Accuracy of Ultrasound-Guided Interventions: A Randomized Controlled Double-Blind Trial of the Line-of-Sight Approach and the "APPLES" Mnemonic*	Subdeltoid bursa	J Ultrasound Med
Onishi, Sellon [27]	*Sonographically Guided Semimembranosus Bursa Injection: Technique and Validation*	Semimembranosus bursa	PM&R
Pekala, Henry [28]	*The Achilles tendon and the retrocalcaneal bursa: an anatomical and radiological study*	Retrocalcaneal bursa	Bone Jt Res
Pujalte, Hudspeth [11]	*Ultrasound-guided injection of the long head of the biceps tendon sheath with concomitant subacromial bursa injection through the same needlestick*	Subacromial bursa	Clin Anat
Smith, Wisniewski [29]	*Sonographically guided obturator internus injections: techniques and validation*	Obturator internus bursa	J Ultrasound Med
Stallenberg, Destate [18]	*Involvement of the anterior portion of the subacromial-subdeltoid bursa in the painful shoulder*	Subacromial-subdeltoid bursa	AJR Am J Roentgenol
Viegas, Aguiar [30]	*Deep and superficial infrapatellar bursae: cadaveric investigation of regional anatomy using magnetic resonance after ultrasound-guided bursography*	Infrapatellar bursa	Skeletal Radiol
Wisniewski, Hurdle [31]	*Ultrasound-guided Ischial Bursa Injection: Technique and Positioning Considerations*	Ischial bursa	PM&R

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Review

Integrating Tendinous Pathophysiology Into Rotator Cuff Tears And Greater Trochanteric Pain Syndrome: A Narrative Review

Joshua R. Poole,[1] Erin Alaia,[2] Robert J. Meislin.[3]

Abstract

This narrative review aims to use the similarities between the shoulder and hip joints to better understand why rotator cuff (RC) tendinopathy and hip abductor tendinopathy occur and inform about diagnosis and treatment of both orthopedic complaints. A search of the literature was done using Google Scholar and Pubmed and initially followed a systematic review protocol, but the nature of the topic, current literature and data necessitated a narrative review. Reports that discussed pathomechanics of RC and gluteal tendinopathy individually, together and with other muscles groups were reviewed. It was found that the methods measuring and describing the processes of tendinopathy differ significantly, for each individual joint and between all joints. A review of a large body of quantifiable measures and theoretical ideas regarding tendinopathy was performed to address this lack of consensus in current literature. Initial literature yielded 74 articles. After review, only 43 articles were used from a broad range of approaches and methodologies. The review found a body of evidence suggesting that fibrocartilage overgrowth and compressive forces over bony structures cause tendonous pathology of the RC and hip abductor tendons. These findings support the idea that tendinopathy is often caused by intrinsic factors rather than the traditional view of external factors. Earlier treatment and improved outcomes without surgery are possible using current imaging technology to identify these intrinsic factors that affect tendinous properties.

Introduction

The similarities between the musculature of the shoulder joint and the hip joint have long been acknowledged. The tendons surrounding the hip joint are often referred to as the "rotator cuff of the hip".[1–4] This comparison is fitting because of how similar the joints are in anatomy, pathology, and treatment. The muscles that of the rotator cuff(RC) of the shoulder and hip abductors that have drawn the most comparison include the subscapularis, supraspinatus, infraspinatus, teres minor, gluteus medius and gluteus minimus. Current literature is replete with connections between these muscle groups.

The RC has been more thoroughly studied than the hip abductors primarily due to the prevalence of RC injury. Tears of the hip abductors are often discussed in terms of findings in RC literature. Treatments for hip abductor injury and lateral hip pain are even discussed in terms of effectiveness in the RC rather than the gluteus medius or minimus.[2] Lateral hip pain affects 1.8 out of 1000 patients annually in the United states[5]. For many years, pain of the lateral hip has been poorly understood resulting in a diagnosis of trochanteric bursitis without further clinical investigation.[2] Recent research suggests that the differential is far more broad. Greater trochanteric pain syndrome(GTPS) has gained traction as one of the newly considered diagnosis for lateral hip pain and in some studies is considered more prevalent than Trochanteric bursitis.[2,6,7] In one particular study, MRI was used to confirm diagnosis of trochanteric bursitis in 24 female patients. It found that 45.8% of patients had gluteus medius tears and 62.5% had isolated gluteus medius tendinopathy with no findings of trochanteric bursitis[8]. As a result of many studies like this, trochanteric bursitis is no longer accepted as the principal cause of lateral hip. It is now just a part of the broad differential of lateral hip pain[8,9]. Causes of lateral hip pain are often injuries that lead to hip abductor tears . Hip abductor tears are due to degenerative wear that occurs commonly in adults over 40 years old, more commonly in women, and rarely occur because of trauma.[5,10] In exploring the role of GTPS in hip abductor pathophysiology we can start to understand its similarity to RC tendinopathy.

In orthopedics, pain of the RC and limited shoulder range of motion are among the most common complaints and the more heavily studied conditions. It is currently considered the third most common musculoskeletal complaints in the united states.[11,12] RC cuff based complaints have a lifetime prevalence of 67% in the Unites States and are also highly age dependent with a global prevalence between 5-10% in patients 20 years old or younger and above 60% in those older than 80 years old (77). Despite its prevalence its pathophysiology is still not well defined.

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Dr. Charles Neer first described impingement of the supraspinatus muscles in 1972. He proposed that extrinsic acromial impingement was the principal cause of the symptoms experienced so commonly and recommended acromioplasty and coracoacromial ligament release as treatment.[13,14] At the time, his idea was well accepted and followed but has since been challenged. In fact, many recent studies suggest that rotator cuff tendinopathy and eventual tears have very little to do with acromial impingement but rather due to intrinsic impingement and apoptosis.[13–18] Extrinsic acromial impingement as the cause of RC tendinopathy is further questioned by a 2012 report from the American Academy of Orthopedic Surgeons that declared "routine acromioplasty is not required at the time of rotator cuff repair".[19]

Describing RC injury or gluteus medius/minimus tear in terms of impingement or trochanteric bursitis limits the thinking of researchers and physicians alike.[14] Arguments and evidence in support of the prevalence of acromial impingement and trochanteric bursitis are still present but the frequency and impact of these arguments has since diminished. The original insights have led to new theories and ideas surrounding tendinopathy and tears of the hip abductors and RC. Researching these gaps in current literature is important to providing the highest quality of care based upon the most accurate understanding of these complaints. The aim of this paper is to review current literature on the anatomy, pathology, and biomechanics of each muscle group to understand the cause of both sets of symptoms more fully. Elaborating on the causes of these orthopedic complains can lead to better treatment and as a result better patient outcomes.

Methods

A comprehensive search was conducted using two electronic databases, Google Scholar and PubMed, to identify articles related to the pathomechanics of RC and gluteal tendinopathy. The search terms included keywords such as "Rotator Cuff," "Gluteal Tendinopathy," "Greater Trochanteric Pain Syndrome," and "Hip Abductor Tendons." Articles that discussed the pathomechanics of RC and gluteal tendinopathy individually, together, and with other muscle groups were included in the review. The initial search results were screened by title and abstract for relevance and yielded 74 articles by two authors. These articles were then reviewed in detail with a focus on identifying the causes of tendonous pathology in the RC and hip abductor tendons. After a thorough screening process, 43 articles were used to provide the insights found in this review. These articles were from a broad range of approaches, methodologies and demographics, including biomechanical studies, clinical trials, and case reports. When necessary, articles were critically evaluated to determine the quality of evidence presented and to extract relevant data. Not all papers were used for statistical reasons but rather for insight and theories in order to collect a broad range of ideas to consider in this narrative review. The nature of the topic demanded this approach given its limited current research. Scale for the Assessment of Narrative Review Articles (SANRA) was used to guide this review.

Results

Anatomical Comparison of the Hip and Shoulder Joint Musculature

The supraspinatus originates from the supraspinous fossa. It crosses underneath the acromion, passes over the glenoid and bicipital groove to attach to the greater tuberosity on the anterior lateral side of the humerus deep to the deltoid. It is a primary initiator of abduction of the shoulder. Gluteus minimus originates from the area of the ilium between the anterior and inferior gluteal lines. Gluteus medius originates from the area of the ilium between the anterior and inferior gluteal lines. The gluteus medius inserts into the lateral and superior aspect of the greater trochanter. Gluteus minimus inserts onto the anterolateral aspect of the greater trochanter located deep to the Iliotibial band band/tensor fascia lata. Both muscles function to abduct and medially rotate the hip are the primary muscles of concern for tendinous degeneration. Both tendons course posterior medially to inferior lateral and attach just millimeters after taking a sharp turn over bony prominence. This is one of the major contributors to the pathology of these muscles ***Table 1***.

Infraspinatus and teres minor attach proximally to the infraspinous fossa. The infraspinatus courses superior to medial and the teres minor courses laterally. The infraspinatus inserts on the greater tuberosity inferior and posterior to the supraspinatus insertion. It shares fibrous insertion with the supraspinatus. For this reason, the infraspinatus tendon is also of concern for RC based injury. The teres minor inserts on the greater tubercle just inferior to the infraspinatus insertion. The piriformis originates from the pelvic surface of the sacrum and inserts on the superior border of the greater trochanter. All three of these muscles function to externally rotate their respective joints.

The subscapularis originates at the subscapular fossa and inserts onto the lesser tuberosity of the humerus. The Iliopsoas is composed of the psoas and the iliacus which originate at the

Table 1. **Comparing Function of Shoulder and Hip Joint Musculature.**

Hip	Rotator Cuff	Function
Gluteus medius / Gluteus minimius	Supraspinatus	Abduction / Stabilizer
Iliopsoas*	Subscapularis	Internal rotator
Piriformis*	Infraspinatus / Teres minor	External rotator
Rectus femoris	Long head of biceps brachii	Crosses over the anterior portion of both joint of the limb**
Iliotibial band / Tensor fascia lata	deltoid	Overlies the bony prominance

Legend: Shoulder and hip joints have muscles that are identical in function, directionality, and contribution to pathology of the joint. *One of many, **In the lower extremity this includes the knee and the hip, in the upper extremity this includes the elbow and shoulder.

transverse process and vertebral bodies of T12-L5 and the iliac crest respectively. These muscles join as a common tendon that attaches onto the lesser trochanter. Both muscles originate posterior from their insertion. All these muscles function to internally rotate the joint.

The long head of the biceps brachii originates at the supraglenoid tubercle and inserts at the radial tuberosity. Its proximal tendon courses through the bicipital groove as it crosses the glenohumeral joint. It most prominently flexes the arm but also functions to flex the shoulder. The rectus femoris originates at the anterior inferior iliac spine and inserts onto the tibial tuberosity via the patellar tendon. This muscle primarily flexes the hip and extends the knee. Both muscles are unique because they course anteriorly across two joints and influence motion of both.

The deltoid originates from the distal third of the clavicle, the acromion and the spine of the scapula. All three parts of the muscle converge to form the deltoid tendon and insert on the deltoid tuberosity of the humerus. The tensor fascia lata originates at the anterior superior iliac spine and anterior one third of the outer lip of the iliac crest. Parts of the gluteus maximus fuse with the tensor fascia lata to form the iliotibial band wphich inserts on the lateral aspect of the tibia via the iliotibial tract. These muscles are the most superficial and lateral of their respective joints and serve as a means of compression over the RC and hip abductors respectively. This results in higher compressive forces over the tendons.

Biomechanics

Tendons are naturally developed to withstand large tensile loads but there is little known about their ability to withstand compressive forces. Tendons are so strong in resisting tears from tensile loads that tears occur at the muscle tendon junction before the bony insertion under extreme testing conditions.[20] The supraspinatus and the gluteus medius tendons are wrapped over the greater tuberosity and the greater trochanter respectively until attaching to their insertions. To contract, both muscles must transmit forces nonlinearly from attachment to insertion and exert force onto the joint. This vector relationship is not uncommon anatomically but what sets these tendons apart is the extreme change in direction that occurs just before insertion and the large forces exerted through muscles. Compressive forces alone do not result in pathology. This is because of the bursa that is between the bone and tendon. Rather, compressive forces can be a catalyst when combined with excessive tensile forces.

The nature of the gluteus medius tendon differs based upon insertion location. The anterolateral insertion is identified as the thinnest portion and the most prone to injury and tendinopathy.[1,9,21–24] Gluteus medius tears are mostly degenerative in nature, starting as undersurface tears at the anterior border of the lateral facet footprint and progressing posteriorly to become full-thickness tears.[25] The supraspinatus tendon is also split into anterior and posterior portions. The anterior portion has a higher modulus of elasticity and still more prone to pathology.[26] Tears at both joints primarily occur on the undersurface of the tendons.[6] The tendinous tissue along the bony prominence is stretched less compared to the more superficial side during contraction and therefore experiences less tensile load but experiences a greater compressive force along the bony prominence. Differences in tensile load along cross-sectional areas of the tendon is often referred to as stress shielding.[10,27,28] This is further intensified by increased iltiotibial band tightness exerting that exerts pressure onto the greater trochanter over the gluteal tendons. The same scenario is seen with acromial pressure on the tendon of the RC. Hyperadducted positions are implicated in the pathology of both joints because of the increased force down onto bone when abduction is performed exiting hyperadducted positions. Abducting from an acute angle of the tendon over the bone produces more downward force than in a larger angle over the bone.[10,29–31] Due to these differences in the nature of the forces exerted on the tissue they take on different morphology within the tendon. This is the main thought as the leading cause for these tendinopathies.[20,27,30–34] One of the major issues in current literature is whether these challenges are pathological or adaptive to these tendons.

Metaplastic Changes in Fibrocartilage

According to a review done by Cook et al. and findings in Benjamin et al., tendinous tissue that inserts onto the bony prominences are considered fibrocartilage.[27,33] Tendons under influence of compressive forces undergo metaplasia consisting of a transition from type I collagen to type II collagen, large proteoglycan aggregates, and neurovascular infiltration. All of these changes lead to tissue with increased capacity to withstand compressive forces. These metaplastic changes present new questions such as whether these changes are natural to all tendons in response to compression or are they specific to certain tendons and do they ultimately have a negative impact.

The review presented by Cook et al. reports these changes as native to the tissue. Rather than being a pathological response, fibrocartilage is just a subset of tendons specific to areas under compression. The principal theory proffered by Cook et al. to explain the damage that leads to tendinopathy is that compressive forces lead to reduced water content of the tendon which is essential to its ability to withstand compressive forces.[27] Grigg et al. shared research showing decreased tendon thickness in tendinopathy of the Achilles tendon that supports this idea.[35] This research is a good foundation for supporting this theory but will need further application to the gluteus medius and rotator cuff.

Benjamin et al. support the idea that this form of tissue is native to "wrap around tendons".[33] This suggests that these metaplastic changes occur strictly in wrap around tendons. Regardless of this, they still question whether this process is pathological or adaptive in nature.[33,34] Another important observation made by Cook et al. is that the bony prominence that the Achilles tendon rubs on is in close proximity to the tendinous attachment to the calcaneus.[27] This is of concern because the tendon is undergoing a transition from normal tendon to that which attaches to the bone with fundamentally different types of tissue. They briefly describe how the proximity of these two zones and increased fibrocartilage metaplasia causes instability and tearing of the tendon. This expansion of fibrocartilage outside of its normal zone is

supported more previous reports because tears occur primarily in the tendon in proximity to the enthesis, this insight will be elaborated on later in this review.[20,36]

Continuum of Tendinous Pathology

Cellular and extracellular intratendonal differences have been investigated since 1978 when Gillard et al. found that tendons adapt to compressive and tensile loads.[37] To prove this they surgically detached tendon from over a bony prominence to an insertion with a direct course and observed a gradual loss of the fibrocartilage tissue. Afterwards they reattached the tissue and saw an increase in fibrocartilage. This is evidence of an adaptive measure by tendons to compensate for compressive forces but is very outdated and may need reevaluation. Even the model of tendon morphology between normal, fibrocartilage and pathology used by Cook et al. is from a paper written in 1996.[27]

As in most physiological processes, tendinopathy is considered a process that fluctuates along a continuum of presentations based upon more recent models.[36,38] Cook et al. presents tendinopathy in three stages and the initial stage of reactive tendinopathy fits those pathological stages elaborated on already.[38] Namely, compression leading to a change in composition of the tissue with higher type II collagen and increased proteoglycans. The second stage is tendon disrepair which is characterized by greater matrix breakdown and hyperplasia with chondrocytes and myofibroblasts resulting in increased protein production including proteoglycan and collagen deposition causing decreased organization in the matrix. The last stage is degenerative tendinopathy. This stage includes areas of cell death due to apoptosis and trauma or tenocyte exhaustion. There is little capacity for reversibility of pathology at this stage.

In comparison, Macdonald et al. argue that the first stage of tendinopathy is not a characteristic of adaptation but rather a pathological reaction to acute overload or stress.[15] Cook et al. describe this process as acute and easily reversible which implies it to be a normal response to new stimuli within the tendon. They even call it a response to compression but do not consider it in the context of wrap around tendons like the RC of the gluteus medius.[38]

In a follow up report, Cook et al. suggest that all models of tendinopathy can be divided into three categories.[34] The category most in line with pathology of the RC and gluteus medius is the "tendon cell response" model. It views tendinopathy as a direct result of tenocyte activation in response to compression. It displays the exact morphology of those mentioned in development of fibrocartilage in wrap around tendons. The problem they find is knowing when these changes go from healthy adaptation to damaging pathology. They cite a study using the Achilles tendon in Australian football players that shows this adaptation as a healthy part of increased tendon load and use but the study also showed 3 of the 18 of the participants progressed to a painful tendinopathy which complicated their conclusion of normal adaptation.[39]

Tendon Cell Response Model in the RC and Gluteus Medius

Direct evidence of the tendon cell response model in the RC and gluteus tendons is minimal. Almekinders et al. share evidence about the gluteal tendon being thinner in pathological states but does not comment on its compositional makeup.[20] Allison et al. elaborates on muscle atrophy and weakening in gluteal tendons but they are unsure if the atrophy is a result of the tendinopathy or if the atrophy comes before the tendinopathy.[31] Another model mentioned by Cook at al. explains tendinopathy as part of a lack of electrical stimulation from chronic damage that is correlated with atrophy of muscle. This model is not investigated in a particular muscle, but it is broadly applied to all muscle tendinopathy, so knowing how this may apply to the RC or gluteal tendons is conjectural. This draws into question whether the tendinopathy indirectly results in reduced muscle function. Allison et al. also consider disuse atrophy from patients involuntarily reducing use of the muscle plays a role in causing the atrophy of muscle.[31]

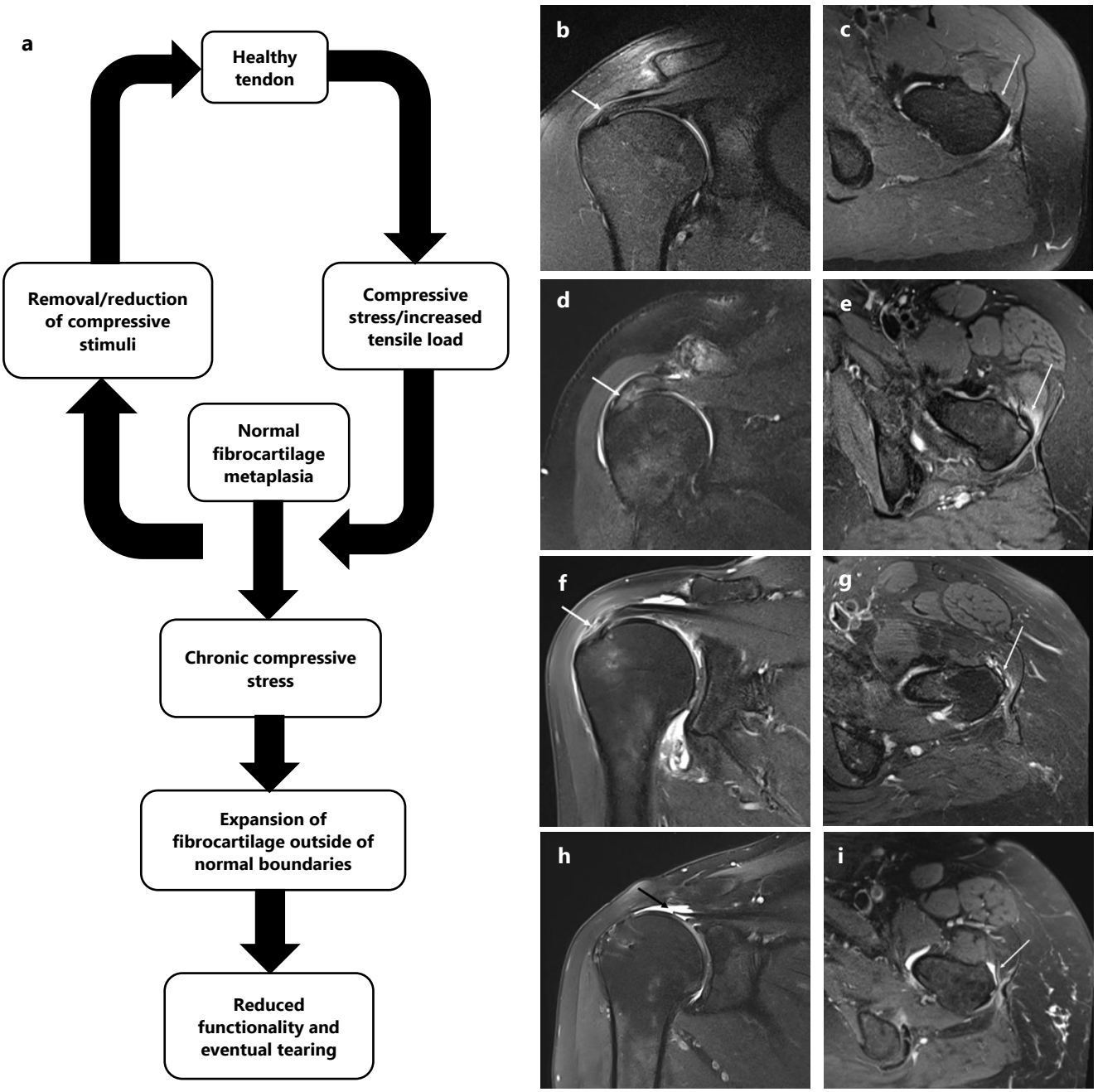
Strong evidence for compressive forces being the principal cause of gluteal tendinopathy is supported by the findings of a study investigating why females experience a much higher degree of gluteus medius tears.[29] They found that on average females have a much lower femoral neck shaft angle, giving them a slight coxa vara compared to males. This causes a more acute angle over which the gluteus medius passes over the greater trochanter which translates to greater compressive forces over the bony prominence.[10,29–31] Evidence suggests that this is the cause of higher rates of gluteus medius tears in adult females. In addition, repetitive movements into and out of hyper adduction are implicated in worse outcomes and symptoms for gluteal pathology. Contraction of the gluteal muscles in hyperadducted positions would maximize the force of the tendon onto the bone due to a lower angle of contraction between insertion and attachment as stated earlier in this review.[20,30,32,33]

In a study done by Soslowsky et al. tensile and modulus testing was performed on rat supraspinatus where they compared repetitive tensile loads used to simulate acromion impingement and overuse stress on the tendon.[40] They found that acromial impingement alone was not enough to induce tendinopathy but required both tensile overuse and impingement to replicate rotator cuff pathology. They also found that the thickness of the tendon and diameter of the tendon was significantly lower and the modulus was significantly lower. This supports the theory regarding dehydration of the tendon and is in line with lower modulus being a likely effect of these combined forces. They did not consider the impact of compressive forces intrinsic to the tendons as they considered them to be a non-physiological component of the supraspinatus.

Perhaps the greatest insight as to why these tendons ultimately fail has been shown from fibrocartilage metaplasia as expressed by Cook et al..[27] They demonstrated that tenocyte overactivity extends outside of the margins of fibrocartilage to zones of the tendon that are essential to sustaining tensile load and the transition into enthesis. This type of change requires destruction of existing tissue and deposition of new matrix and cellular metaplasia. The expansion of these zones is detrimental to other essential functions of the tendons. Just as the expansion of the fibrocartilage is necessary, the expansion of normal tendinous

tissue becomes a demand of the tendon as less normal tendon is present. These two essential tissue types and functions compete and ultimately decrease the overall functionality of the tendon leading to damage. The tendon is stuck between repair, metaplasia and proper function. Tissue consisting of proteoglycan and type II collagen along the bony surface and normal tendinous tissue proximal to the bony surface coexist within a microscopic section of tendon. This continuum of change and adaption with a single tendon ultimately limits the tendon's ability to function and repair as needed. Impaired function and repair leads to the damage that is seen in the RC and hip abductors and eventual tears (*Figure 1*).

Figure 1. **Progression of Rotator Cuff and Hip Abductor Tendinopathy.**



Legend: Side by side progression of tendinopathy of the RC and gluteus medius and minimus. Injuries to both tendons occur on spectrum that is reversable at early stages but may lead to chronic complications. (a) Healthy tendons that are exposed to compressive and tensile stress compensate with fibrocartilaginous metaplasia. Metaplasia may be sufficient to avoid damage and tearing. Alternatively, removal of the stimuli will allow continued healthy function. Under chronic over exposure to compression and tensile load, metaplasia disrupts proper function of the tendon and leads to pain and tearing. (b) Coronal T2 fat suppressed image showing a normal supraspinatus tendon. (c) Axial T2 fat suppressed image showing a normal gluteus minimus tendon. (d) Coronal T2 fat suppressed image showing a supraspinatus tendinosis. (e) Axial T2 fat suppressed image showing tendinosis of the gluteus minimus tendon. (f) Coronal T2 fat suppressed image showing a severe supraspinatus tendinosis with a high-grade partial-thickness bursal surface tear. (g) Axial T2 fat suppressed image showing tendinosis and high-grade partial-thickness tearing of the glutes minimus tendon. (h) Coronal T2 fat suppressed image showing a fill- thickness retracted re-tear of the supraspinatus tendon. (i) Axial T2 fat suppressed image showing a complete tear of the gluteus minimus tendon and underlying subgluteus minimums bursal fluid.

Discussion

This collection of evidence supports the idea that the source of damage to the tendons is due to intrinsic adaptation. It is likely that these changes are both pathological and adaptive. Fibrocartilage is an essential adaptation to compressional forces on the tendon but can become pathological as demonstrated in ***Figure 1***. In situations that decrease the muscle angle in females, over abducting or in overstressing the tendon, fibrocartilage overgrows and ultimately leads to decreased functionality. The need to investigate these findings is especially important to the RC and gluteal tendon because these two tendons experience the greatest compressive forces, have no definitive explanation for the cause of their pathology and are common complaints among orthopedic patients. The gluteal tendon and RC are not a point of focus in the research that defined these insights. This leaves a gap in the knowledge of these two prevalent medical issues.

Clinical Implications

Patients who manifest an overgrowth of fibrocartilage could be treated at early stages to reduce overgrowth and the damage that occurs in chronic stages of this pathology. In detecting early morphological overgrowth, we can advise and treat the patient non-invasively before the tendon is damaged enough to necessitate surgical intervention. Treatments such as lifestyle and work modifications, physical therapy and pain management can slow progression in chronic stages. The limiting factor is the ability to determine the current morphological state of a tendon in vivo. The invasion of fibrocartilage into adjacent zones would be a matter of micrometers in difference and is not currently within the capabilities of modern imaging see ***Figure 1***.

One alternative to this would be to measure the tensile modulus, compressive modulus and thickness of the tendon over time. This relates to the idea of how the morphology changes the water content and ability of the tendon to withstand certain forces.[20,27,34–36,38,40] Tendon thickness would be indicative of certain stages of pathology. Early fibrocartilage induces water retention and tendon thickening. Later tendinous damage would manifest as a thinner tendon as water is poorly retained from over compression and damage. Ability to withstand tensile load would decrease as normal tendon is broken down in favor of fibrocartilage. This would manifest as a reduced tensile modulus.

Shear-wave elastography (SWE) and other ultrasonographic techniques are used currently to measure these very parameters in tendons.[41–45] SWE is widely available but rarely used in clinical practice. These methods of imaging enable physicians to avoid invasive and expensive imaging in favor of measures that tell us about the morphological state of the tissue. The principal measure that is relevant to tendinopathy is tendon shear elastic modulus otherwise known as stiffness. The higher stiffness in the tendon, the less metaplastic change has occurred in the tendon. Dirrichs et al. used intraindividual and interindividual comparisons of tendinopathies to compare SWE, ultrasound and power doppler.[41] This study showed that SWE significantly improved the identification of painful tendinopathy across a wide age group 20-71years old and different tendons including Achilles, patellar and humeral epicondylar tendons.

Zhang et al. compared the patellar tendon stiffness and cross-sectional area of sedentary and active 18-35 year old men.[45] They found a significant decrease in stiffness and increase in cross-sectional area in those who were more active and putting increased stress on their tendons. The authors showed that the evaluated tendon demonstrated a normal response to tensile load. Taking this in light of findings in the healthy active population we can correlate this with a healthy metaplastic change in the tendons. The findings of Dirrichs et al.[41] and Zhang et al.[45] in some ways contradict each other but also support each other. The next step for this diagnostic tool is to use cross sectional area, stiffness and patient presentation can be used to create diagnostic criteria.

The next logical question to be addressed is whether these cross-sectional area and stiffness parameters lead to tendinopathy impacting RC and gluteal tendinopathy treatment. Performing experiments to correlate the tendon morphology to physical parameters and matching them to stages of pathology within patients could potentially change the patient experience and reduce the need for surgery in patients in the long term.

Limitations

This review is limited due to the nature of the topics and current literature available for comparison and analysis that necessitated a narrative review. It relies primarily on a collection of theories, ideas and anatomical understanding to build its argument. This can be a foundation for a discussion that can lead to many other research opportunities to test these theories spark innovation in orthopedic care of Hip tendinopathy and shoulder tendinopathy.

Conclusion

Theories on the root cause of RC and hip abductor tendinous degeneration have evolved over time. The anatomy, biomechanics and pathophysiology of these tendons is so similar that we can use them to further our understanding. In doing so is it apparent that increased tensile load and compression over bony prominences lead to metaplastic changes within the tendon. These changes are natural adaptive responses that become pathological with chronic overload of the tendon. The metaplastic changes decrease the capabilities of the joints to function normally and lead to tearing of the tendon. This process points to intrinsic factors of the tendons as being the principal cause of these complaints as opposed to extrinsic factors. These intrinsic factors can be measured using modern SWE techniques. In understanding and identifying early signs of degeneration that are intrinsic to RC and hip abductor tendons that were previously unknown it may be possible to slow or even stop the progression of tendon degeneration before a tear becomes evident.

Summary – Accelerating Translation

This study explores the similarities between the muscles in the shoulder and hip joints, and how this can provide a better understanding of the cellular and mechanical problems associated with Greater Trochanteric Pain Syndrome and Rotator Cuff Tendinopathy. This is a literature review and analysis of relevant insights and connections that were found applicable to the aims of this project. By comparing these two conditions along with current theories regarding of tendinopathy it is suspected that factors within the tendons themselves, rather than external factors, lead to pain and tearing. Shear Wave Elastography, a non-invasive ultrasound technique, can measure these intrinsic factors and can be used to test these theories. The study suggests that earlier and more affordable diagnosis and treatment of tendinopathy could be achieved by testing the insights of this review.

References

1. Lequesne M. From "periarthritis" to hip "rotator cuff" tears. Trochanteric tendinobursitis. Joint Bone Spine. 2006;73(4):344–348.
2. Ho GWK, Howard TM. Greater trochanteric pain syndrome: more than bursitis and iliotibial tract friction. Curr Sports Med Rep. 2012;11(5):232–238.
3. Zhu MF, Musson DS, Cornish J, Young SW, Munro JT. Hip abductor tendon tears: where are we now? Hip Int. 2020;30(5):500–512.
4. Bunker TD, Esler CN, Leach WJ. Rotator-cuff tear of the hip. J Bone Joint Surg Br. 1997;79(4):618–620.
5. Varacallo M, El Bitar Y, Mair SD. Rotator Cuff Tendonitis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023.
6. Domb BG, Nasser RM, Botser IB. Partial-thickness tears of the gluteus medius: rationale and technique for trans-tendinous endoscopic repair. Arthroscopy. 2010;26(12):1697–1705.
7. Dwek JR, Pfirrmann CW, Stanley AJ, Pathria MN, Chung CB. MR imaging of the hip abductors: normal anatomy and commonly encountered pathology at the greater trochanter. Magn Reson Imaging Clin N Am. 2005;13(4):691–704.
8. Bird PA, Oakley SP, Shnier R, Kirkham BW. Prospective evaluation of magnetic resonance imaging and physical examination findings in patients with greater trochanteric pain syndrome. Arthritis Rheum. 2001;44(9):2138–2145.
9. Connell DA, Bass C, Sykes CA, Young D, Edwards E. Sonographic evaluation of gluteus medius and minimus tendinopathy. Eur Radiol. 2003;13(6):1339–1347.
10. Grimaldi A, Fearon A. Gluteal tendinopathy: integrating pathomechanics and clinical features in its management. J Orthop Sports Phys Ther. 2015;45(11):910–922.
11. Syed MA, Azim SR, Baig M. Frequency of orthopedic problems among patients attending an orthopedic outpatient department: a retrospective analysis of 23,495 cases. Ann Saudi Med. 2019;39(3):172–177.
12. Seidman A, Taqi M, Varacallo M. Trochanteric Bursitis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023.
13. Neer CS II. Anterior acromioplasty for the chronic impingement syndrome in the shoulder: a preliminary report. J Bone Joint Surg Am. 1972;54(1):41–50.
14. McFarland EG, Maffulli N, Del Buono A, Murrell GA, Garzon-Muvdi J, Petersen SA. Impingement is not impingement: the case for calling it "rotator cuff disease." Muscles Ligaments Tendons J. 2013;3(3):196–200.
15. MacDonald P, McRae S, Leiter J, Mascarenhas R, Lapner P. Arthroscopic rotator cuff repair with and without acromioplasty in the treatment of full-thickness rotator cuff tears: a multicenter, randomized controlled trial. J Bone Joint Surg Am. 2011;93(21):1953–1960.
16. Milano G, Grasso A, Salvatore M, Zarelli D, Deriu L, Fabbriciani C. Arthroscopic rotator cuff repair with and without subacromial decompression: a prospective randomized study. Arthroscopy. 2007;23(1):81–88.
17. Henkus HE, de Witte PB, Nelissen RG, Brand R, van Arkel ER. Bursectomy compared with acromioplasty in the management of subacromial impingement syndrome: a prospective randomized study. J Bone Joint Surg Br. 2009;91(4):504–510.
18. Shin SJ, Oh JH, Chung SW, Song MK. The efficacy of acromioplasty in the arthroscopic repair of small to medium-sized rotator cuff tears without acromial spur: prospective comparative study. Arthroscopy. 2012;28(5):628–635.
19. Pedowitz RA, Yamaguchi K, Ahmad CS, Burks RT, Flatow EL, et al. Optimizing the management of rotator cuff problems. J Am Acad Orthop Surg. 2011;19(6):368–379.
20. Almekinders LC, Weinhold PS, Maffulli N. Compression etiology in tendinopathy. Clin Sports Med. 2003;22(4):703–710.
21. Tsutsumi M, Nimura A, Akita K. The gluteus medius tendon and its insertion sites: an anatomical study with possible implications for gluteus medius tears. J Bone Joint Surg Am. 2019;101(2):177–184.
22. Walsh MJ, Walton JR, Walsh NA. Surgical repair of the gluteal tendons. J Arthroplasty. 2011;26(8):1514–1519.
23. Cvitanic O, Henzie G, Skezas N, Lyons J, Minter J. MRI diagnosis of tears of the hip abductor tendons (gluteus medius and gluteus minimus). AJR Am J Roentgenol. 2004;182(1):137–143.
24. Makridis KG, Lequesne M, Bard H, Dijan P. Clinical and MRI results in 67 patients operated for gluteus medius and minimus tendon tears with a median follow-up of 4.6 years. Orthop Traumatol Surg Res. 2014;100(8):849–853.
25. Robertson WJ, Gardner MJ, Barker JU, Boraiah S, Lorich DG, Kelly BT. Anatomy and dimensions of the gluteus medius tendon insertion. Arthroscopy. 2008;24(2):130–136.
26. Huegel J, Williams AA, Soslowsky LJ. Rotator cuff biology and biomechanics: a review of normal and pathological conditions. Curr Rheumatol Rep. 2015;17(1):476.
27. Cook JL, Purdam CR. Is compressive load a factor in the development of tendinopathy? Br J Sports Med. 2012;46(3):163–168.
28. Orchard J, Cook JL, Halpin N. Stress-shielding as a cause of insertional tendinopathy: the operative technique of limited adductor tenotomy supports this theory. J Sci Med Sport. 2004;7(4):424–428.
29. Woyski D, Olinger A, Wright B. Smaller insertion area and inefficient mechanics of the gluteus medius in females. Surg Radiol Anat. 2013;35(8):713–719.
30. Birnbaum K, Siebert CH, Pandorf T, Schwenker C, Prescher A, Niethard FU. Anatomical and biomechanical investigations of the iliotibial tract. Surg Radiol Anat. 2004;26(6):433–446.
31. Allison K, Vicenzino B, Wrigley TV, Grimaldi A, Hodges PW, Bennell KL. Hip abductor muscle weakness in individuals with gluteal tendinopathy. Med Sci Sports Exerc. 2016;48(3):346–352.
32. Birnbaum K, Schwenker C, Hohmann D, Schrempf A, Prescher A, Bullmann V. Finite element model of the proximal femur under consideration of the hip centralizing forces of the iliotibial tract. Clin Biomech (Bristol, Avon). 2011;26(1):58–64.
33. Benjamin M, Ralphs JR. Fibrocartilage in tendons and ligaments—an adaptation to compressive load. J Anat. 1998;193(Pt 4):481–494.
34. Cook JL, Rio E, Purdam CR, Docking SI. Revisiting the continuum model of tendon pathology: what is its merit in clinical practice and research? Br J Sports Med. 2016;50(19):1187–1191.
35. Grigg NL, Wearing SC, Smeathers JE. Eccentric calf muscle exercise produces a greater acute reduction in Achilles tendon thickness than concentric exercise. Br J Sports Med. 2009;43(4):280–283.
36. Scott A, Cook JL, Hart DA, Walker DC, Duronio V, Khan KM. Tenocyte responses to mechanical loading in vivo: a role for local insulin-like

growth factor 1 signaling in early tendinosis in rats. Arthritis Rheum. 2007;56(3):871–881.

37. Gillard GC, Reilly HC, Bell-Booth PG, Flint MH. The influence of mechanical forces on the glycosaminoglycan content of the rabbit flexor digitorum profundus tendon. Connect Tissue Res. 1979;7(1):37–46.
38. Cook JL, Purdam CR. Is tendon pathology a continuum? A pathology model to explain the clinical presentation of load-induced tendinopathy. Br J Sports Med. 2009;43(6):409–416.
39. van Schie HT, de Vos RJ, de Jonge S, Bakker EM, Heijboer MP, Verhaar JA, Tol JL. Ultrasonographic tissue characterisation of human Achilles tendons: quantification of tendon structure through a novel non-invasive approach. Br J Sports Med. 2010;44(16):1153–1159.
40. Soslowsky LJ, Thomopoulos S, Esmail A, Flanagan CL, Iannotti JP, Williamson JD, Carpenter JE. Rotator cuff tendinosis in an animal model: role of extrinsic and overuse factors. Ann Biomed Eng. 2002;30(8):1057–1063.
41. Dirrichs T, Quack V, Gatz M, Tingart M, Kuhl C, Schrading S. Shear wave elastography (SWE) for the evaluation of patients with tendinopathies. Acad Radiol. 2016;23(10):1204–1213.
42. Taljanovic MS, Gimber LH, Becker GW, Latt LD, Klauser AS, Melville DM, Gao L, Witte RS. Shear-wave elastography: basic physics and musculoskeletal applications. Radiographics. 2017;37(3):855–870.
43. Feng YN, Li YP, Liu CL, Zhang ZJ. Assessing the elastic properties of skeletal muscle and tendon using shearwave ultrasound elastography and MyotonPRO. Sci Rep. 2018;8(1):17064.
44. Garra BS. Imaging and estimation of tissue elasticity by ultrasound. Ultrasound Q. 2007;23(4):255–268.
45. Zhang ZJ, Ng GY, Fu SN. Effects of habitual loading on patellar tendon mechanical and morphological properties in basketball and volleyball players. Eur J Appl Physiol. 2015;115(11):2263–2269.

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Review

Effects of the COVID-19 Pandemic on Physical Activity in Children: A Systematic Review

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Abstract

Background: Extended lockdowns established to minimize the spread of COVID-19, may have affected physical activity (PA). The objective of this systematic review is to report how PA of children was impacted by the COVID-19 pandemic. **Methods:** A database search of CINAHOL, Embase, MEDLINE, PsycInfo, and Web of Science was conducted on 03/29/2021 in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines. Studies were included if they reported a measure of PA for children ≤18 years and were published in English in a peer-reviewed journal. The search generated 673 unique citations. After applying the criteria above, 69 articles were included. The quality of the included articles was assessed using the NIH NHLBI Study Quality Assessment Toolbox. **Results:** Unstructured play, walking, and virtual PA (e.g., YouTube, online classes) were the most frequently reported modes of PA during the COVID-19 pandemic. The PA of children decreased among 89% of articles that reported changes in PA (e.g., frequency, intensity, duration, or the percentage of children who met PA recommendations) of children during the COVID-19 pandemic. Increased PA was reported more often among younger children, boys, children who lived with other children, and children with more outdoor space. **Conclusion:** Globally, PA of children decreased during the COVID-19 pandemic. Further work is needed to develop policies to support global PA increases. Limitations of this review include the use of online surveys which are limited by participants ability to recall PA behaviors and access to online resources.

Introduction

The COVID-19 pandemic (the pandemic) and its effects rapidly permeated the globe with over 100 million cases by February 1st, 2020.[1] By March 2020, many governments issued stay-at home orders, shelter-in-place orders, lockdowns, and various social-distancing guidelines to mitigate the spread of COVID-19.[2] These restrictions, including the closure of schools, parks, and organized sports, may have altered movement behaviors, including physical activity (PA).[3,4] PA in children encompasses a variety of modes (e.g., exercise, sports, and active play).[5] It has been defined as any body movement that increases energy expenditure and can be characterized by the components of the FITT principle: frequency, intensity, time (e.g., duration), and type.[6] The WHO recommends children (ages 5-17) engage in ≥60 min/day of moderate-to-vigorous (MVPA) intensity PA[7] where 3 days/week include vigorous-intensity aerobic activities, muscle-strengthening and bone-strengthening activities.[8] As a critical component of child development, PA has substantial long-term health benefits including the prevention of chronic health conditions.[9,10] Conversely, insufficient PA in children can increase the risk of developing cancer, heart disease, obesity, and type 2 diabetes.[11] Despite the known benefits of PA on health, global levels of PA were insufficient in 4 out of 5 children prior to the pandemic.[12] Thus, the prolonged stay-at-home orders brought on by the pandemic may have exacerbated the proportion of children with insufficient PA, as previous studies have shown that children have less PA when they are outside of school (e.g., holidays, summer, weekends).[13,14] Although children seem to have a lower risk of contracting COVID-19,[15,16] the physical health burden of the pandemic and the resulting restrictions are of increasing interest.[1,17,18]

Previous studies have demonstrated that childhood health behaviors, including PA, are likely to persist through adulthood and can impact lifetime health.[19,20] It is important to monitor PA changes in children to reduce the risk of developing long-term health consequences associated with inadequate PA (e.g., cardiovascular disease, type 2 diabetes, obesity).[21,22] Not only can PA prevent many chronic diseases,[23] but it can also have acute health benefits such as boosting the immune system.[24,25] A recent study in adults infected with COVID-19 found reduced risk of critical outcomes in individuals who routinely adhered to PA recommendations.[26] Although this relationship has not yet been established in children, several studies have found obesity to be the most prevalent characteristic in children infected with COVID-19.[27,28] The disruption of PA in children may increase the prevalence of childhood obesity and other comorbidities which could, in turn, increase the risk of infection and subsequent severity in outcomes from COVID-19.[15,29]

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As childhood is a critical period of development, understanding the implications of the pandemic on health behaviors is important and there is a need to highlight potential adverse effects that may need to be actively monitored and remediated as COVID-19 restrictions lift and vaccines are distributed. Identifying changes in PA (FITT principle) of children is important for understanding the extent to which the pandemic impacted the already low levels of global PA among children. In addition, recognizing the biological, social, and environmental factors that affected changes in PA is critical for the development of effective programs to prevent short- and long-term health consequences. To the authors' knowledge, this is the first review to synthesize the literature at the time of the data search regarding the global impact of the pandemic on the duration and types of PA children participated in and what biological, social, and environmental factors contributed to those changes. The goal of this review was to synthesize the global impact of the pandemic on PA of children by addressing the following questions:

1) What types of PA did children participate?
2) To what extent did PA (e.g., duration of PA, percentage of children meeting PA recommendations) of children change?
3) What biological, social, and environmental factors affected changes in PA of children?

Methods

This review was conducted using the PRISMA guidelines.[30] The selection process for the included articles is summarized in ***Figure 1***.

Search Strategy

Two research librarians independently searched MEDLINE, Embase, PsycInfo, CINAHOL, and Web of Science on 03/29/2021. The searches were limited to the English language, COVID-19, and 2020-current (03/29/2021). The key words used in the search strategy included various combinations of terms such as: "physical activity," "exercise," "activity level," or "sports" AND "child," "adolescent," "girl," "boy," or "youth" AND "covid-19," "severe acute respiratory syndrome coronavirus 2" or "'sars-cov-2". Following their independent searches, the librarians compared results and removed duplicates.

Article Inclusion and Exclusion Criteria

Included studies were those that were published in English in a peer-reviewed journal, measured PA during the pandemic, and encompassed PA data for children ≤18 years. Articles were excluded if they did not present original empirical findings, if they described the development of a tool or measure, or if they were inaccessible to the authors (e.g., no free full-text download was available).

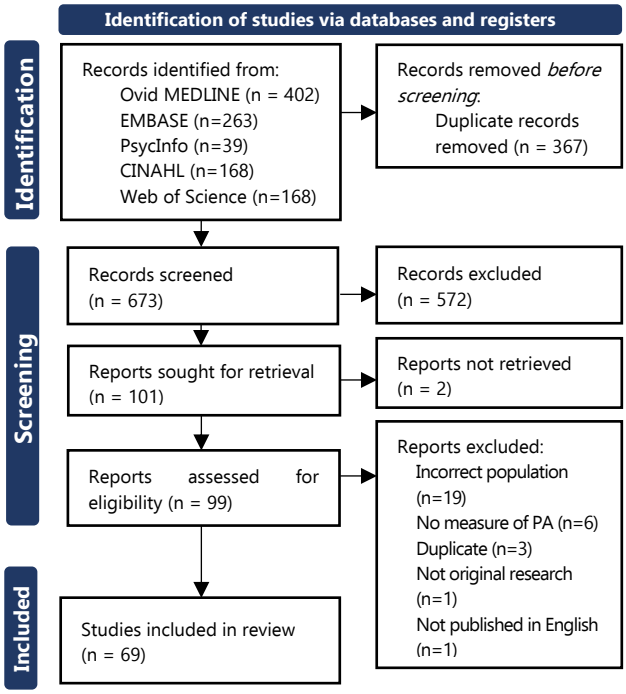
Article Selection

After the librarians eliminated duplicate articles, 673 articles remained. The following article selection process was conducted in 4 steps. First, 2 authors conducted an independent abstract review to determine whether each article should be included or not based on the inclusion and exclusion criteria. Second, the 2 authors discussed any articles they disagreed on until consensus. Following this discussion, 572 articles were excluded because they had a study population outside the context of the current review, meaning that PA data presented in the findings were not specified for participants ≤18 years old. Third, the full text of the remaining 101 articles was reviewed to ensure the articles were within the scope. The data extracted included authors, year of publication, sample source (e.g., the country the sample was gathered from), sample size, sample age range, PA measure, main findings, and factors (e.g., biological, social, and environment) related to PA and are outlined in ***Table 1***. Ultimately, 32 of these articles were excluded because they met ≥1 exclusion criteria. In the fourth step, all authors met to confirm the final 69 articles should be included. The data from the 69 articles was synthesized into a table adapted from a review paper of a similar topic ***Table 1***.[31]

Quality Assessment

The quality of the included articles was assessed using the NIH NHLBI Study Quality Assessment Toolbox.[32] This quality assessment tool describes a "good" study as one with a low risk of bias and a "fair" study as one with some bias.[32]

Figure 1. **Article Selection Diagram Using PRISMA.**



Results

General Characteristics

General characteristics of the included articles are shown in ***Table 2***. Most articles included participants in Europe (n=34),[33-66] North America (n=13),[67-79] or South America (n=6).[49,58,80-83] The distribution of countries represented by the articles in this review are depicted in a heat map in ***Figure 2***.

Table 1. **Characteristics of Included Articles (N=69) and Effects of the COVID-19 Pandemic on Physical Activity (PA) and Biological, Environmental, and Social Factors that Affected PA.**

No.	Author (Year)	PA Measure; PA Data Reported by[a]	Sample Source (Country)	Sample Size	Age Ranges	Findings	Biological, Environmental, and Social Factors that Affected PA	NIH NHLBI Quality Assessment
33	Alonso-Martinez (2021)	Wrist-worn GENEActiv tri-axial accelerometer	Spain	Pre-pandemic: 268 children. Pandemic (03-04/2020): 145 children, PA measured in 21	4-6	On average, preschoolers had 43.3 minutes less/day (95% confidence interval (CI) −68.1 to −18.5 (p=.002)) of total PA during the Pandemic. MVPA also decreased an average of 17 min/day (p<0.001).	Children who met PA recommendations had lower internalizing scores (i.e. social withdrawal, shyness, anxiety).	Good
34	Androutsos (2021)	Online survey; 2	Greece	397 children	2-18	During lockdown, 66.9% of parents reported their child's PA level decreased.	Decreased PA was associated with body weight increase (p<0.001).	Good
35	Cachon-Zagalaz (2021)	Online survey; 2	Spain	837 children	0-12	The highest percentage of participants (34%) spent 0 days/week on PA during lockdown, followed by 32.6% for 2-3 days/week, 19.6% for 4-5days/week, and 13% for 6-7 days/week.	Children with an established routine/schedule (M = 38.13; SD = 35.01) and children in the 6 to 12 years old age group (M = 38.95; SD = 30.25) reported higher levels of daily PA. 34.8% of the sample reported 0 days/week of PA during the Pandemic.	Good
36	Chambonniere (2021)	Online survey; 1,2	France	6491 children	6-17	During lockdown, PA decreased for 42% of children, stayed the same for 21.3% of children, and increased for 36.7% of children. Similarly, PA decreased for 58.7%, stayed the same for 21.8%, and increased for 19.6% of adolescents.	PA decreased among 35.2% of children in rural areas, 46.7% of children in suburban areas, and 47.9% of children in urban areas (PA was significantly associated with geographic location p<0.001). Living in an urban environment was associated with a decrease in PA (p<0.001). Among children without access to an outdoor area, 64.2% reported decreased PA, while among children with access to an outdoor area, only 37.8% reported decrease PA during the Pandemic (p<0.001). The proportion of participants who increased, decreased or did not change their PAL during the lockdown was significantly associated with gender in adolescents (p<0.001) but not in children (p=0.10). Children and adolescents who were more active prior to the Pandemic had greater reductions in PA compared to those who were initially less active (p>0.001).	Good
37	Delisle (2020)	Telephone questionnaire; 2	Sweden	100 children	3-5	PA (+53 min/day) and outdoor time on weekdays (+124 min/day) and weekends (+68 min/day) significantly increased (all p-values ≤ 0.001). PA guidelines were met by 90.3% (n = 65) of the children.	Boys had higher levels of PA (262.5 ± 60.3 vs. 220.4 ± 39.2 min, p = 0.002), MVPA (136.9 ± 43.8 vs. 107.8 ± 29.2 min, p = 0.004), and vigorous PA (39.0 ± 19.4 vs. 29.4 ± 15.7 min, p = 0.028) compared to girls. However, gender was not significantly associated with meeting PA recommendations.	Good
38	Gilic, B., et al. (2020).	PAQ-A; 1	Bosnia and Herzegovina	688 children	15-18	Compared to before the Pandemic, the PAL of the entire sample decreased (from 2.98 ± 0.71 to 2.31 ± 0.68; t-test: 11.88, p < 0.001), as well as among girls (2.69 ± 0.49 to 1.95 ± 0.56; t-test: 8.88, p<0.001) and boys (from 3.12±0.56 to 2.50±0.44; t-test: 10.01, p<0.01).	Boys were more likely to achieve a sufficient PAL during the Pandemic (OR: 2.41, 95%CI: 1.11–4.01). Higher paternal education was associated with a greater likelihood of achieving a sufficient PAL during the Pandemic (OR: 1.33, 95%CI: 1.19–2.01). In contrast, children with more parental/family conflict had a lower likelihood of achieving a sufficient PAL (OR: 0.77, 95%CI: 0.60–0.99).	Good

No.	Author (Year)	PA Measure; PA Data Reported by[a]	Sample Source (Country)	Sample Size	Age Ranges	Findings	Biological, Environmental, and Social Factors that Affected PA	NIH NHLBI Quality Assessment
39	Gilic, B., et al. (2021).	PAQ-A; 1	Bosnia and Herzegovina	661 children	15-18	67% of boys and 28% of girls (48% overall) had a sufficient PAL before the Pandemic, while 37% of boys and 9% of girls (24% overall) had a sufficient PAL during the Pandemic (April 2020).	Children with a sufficient PAL during the Pandemic had higher participation in individual and team sports prior to the Pandemic (MWZ: 6.65, 7.95, respectively, all $p < 0.01$).	Good
40	Sekulic, D., et al. (2020).	PAQ-A; 1	Croatia	388 children	15-18	There was a significant decrease in PAL of children from before to during the Pandemic (2.99 ± 0.70 and 2.67 ± 0.60 for PAL-BL and PAL-FU, respectively; t-test = 3.46, $p < 0.001$).	The decrease in PAL of boys (3.10 ± 0.78 and 2.79 ± 0.82 for PAL-BL and PAL-FU, respectively; t-test = 5.15, $p < 0.001$), but not girls (2.71 ± 0.66 and 2.59 ±0.90, respectively; t-test = 0.61, $p > 0.05$) was statistically significant. Boys had significantly higher PALs than girls during the Pandemic (t-test = 2.11, $p < 0.05$), with	Good
41	Zenic, N., et al. (2020).	PAQ-A; 1	Croatia	823 children	14-18	PAL decreased among the entire sample (from 2.97±0.61 to 2.63±0.68,$p<0.01$) as well as for urban adolescents (from 3.11±0.64 to 2.68±0.67,$p<0.001$).	Children who lived in urban areas had greater reductions in PA level.	Good
42	Francisco, R., et al. (2020).	Online survey; 2	Italy, Spain, and Portugal.	1480 children	3-18	During the Pandemic, most children experienced <30 min of PA daily (53%) compared to 30 to 60 minutes daily before the Pandemic (33.1%). The changes in PA from before to during quarantine were significant for the entire sample ($z = -25.56$, $p < 0.001$, $r = 0.66$) as well as for each country (Italy: $z = -16.08$, $p < 0.001$, $r = 0.60$; Spain: $z = -15.45$, $p < 0.001$, $r = 0.74$; Portugal: $z = -12.48$, $p < 0.001$, $r = 0.66$).	Not reported.	Good
43	Hommes, F., et al. (2021).	Questionnaire; 1	Germany	385 children	8-18	42.2% of primary school students (8 to 13 years old) reported decreased PA during the Pandemic.	A greater proportion of primary school students (8 to 13 years old) reported decreased PA than secondary school students (13 to 18 years old) during the Pandemic.	Good
44	Konstantinou, C., et al. (2021).	PAQ-C; 2	Greece	1509 children	5-14	Compared to before the Pandemic, children's PA decreased in school and out of school after schools were re-opened ($p<0.001$). The frequency of activities (i.e., sports, cycling, dance) children engaged with also decreased compared to before the Pandemic (post-Pandemic: median [Q1, Q3]: 1.38 [1.25, 1.62]) vs. pre-Pandemic: 1.5 [1.38, 1.75]).	Not reported.	Fair
45	Kovacs Va Md, P., et al. (2021).	PAQ-C; 1, 2	Russian Federation, Spain, Italy, Germany, France, Belgium, Portugal, Romania, Hungary, Poland, and Slovenia	8395 children	6-18	Among the entire sample, children met PA guidelines an average of 4 days/week and 19% of children met the 60 minutes of moderate-to-vigorous PA/day guideline during the Pandemic. However, most countries, individually, had < 20% of children able to meet PA recommendations (range of 7.5% to 26.7%). Slovenia and Romania had the greatest proportion of children able to meet PA recommendations (26.7% and 23.5%) as well as the greatest proportion of children playing outside for more than 2 hrs/day (56.1% and 66.3%). During the pandemic, 56.6% of children were active in online P.E..	In countries mildly affected by the Pandemic (Germany, Romania, Poland, Slovenia, and Hungary), children were more likely to meet PA recommendations if they had a structured daily routine (OR = 1.62 [95%CI, 1.24–2.13]). Children were also more likely to meet PA recommendations if they played outdoors for more than 2 hrs/day, however this relationship was more predominant among older children (OR = 2.56 [95%CI, 1.98–3.32]). Among older children in countries strongly affected by the Pandemic (Spain, Italy, France, Russia, Portugal), children who participated in online P.E. were more likely to have higher levels of PA (OR = 1.27 [95%CI, 1.12–1.44]).	Good

No.	Author (Year)	PA Measure; PA Data Reported by[a]	Sample Source (Country)	Sample Size	Age Ranges	Findings	Biological, Environmental, and Social Factors that Affected PA	NIH NHLBI Quality Assessment
46	Lopez-Bueno, R., et al. (2021).	VO2 (20m shuttle run)	Spain	89 children	12-14	The average VO2 max of the sample decreased 0.5 ml.kg−1.min−1 (SD 0.3) (p = 0.12) from before to after the Pandemic (before: 46.2 ml.kg−1.min−1 (SD 0.6), after: 45.7 ml.kg−1.min−1 (SD 0.7)). The greatest reduction in VO2 max was reported for 14-year-old girls, with a reduction of 1.5 ml.kg−1.min−1 (SD 0.6) (p=0.02).	Not reported.	Good
47	Lopez-Bueno, R., et al. (2020).	Online survey; 2	Spain	860 children	3-16	PA decreased for all gender and age groups from before to during the Pandemic, with an average of 96.1 minutes of PA/week during the Pandemic compared to 198.6 (SD 180.9) minutes of PA/week before (-102.5 minutes/week). The greatest reduction in PA was among 6- to 12-year-old children with a reduction of 120.4 (SD 159.0) min/week.	Boys and younger children participated in the most weekly minutes of PA (211.9 (SD 188.4) and 223.0 (SD198.0) min/wk).	Good
48	Medrano, M., et al. (2021).	"The Youth Activity Profile" questionnaire (YAP); 1	Spain	113 children	8-16	Children participated in PA an average of 63 (SD 39) min/day during the Pandemic, with an average decrease in PA of 91 ± 55 min/day (P < .001) compared to before the Pandemic. Decreased PA was reported among 95.2% of children during the Pandemic.	Children of mothers with a higher education level had smaller reductions in PA during the Pandemic (−1.3 ± 0.1 hour/day vs −1.7 ± 0.1 hour/day, P < .005). Children with access to an outdoor area at home or a large indoor space (i.e. attic or garage) also had lower reductions in PA compared to children without access. (−1.4 ± 0.1 h/d vs −1.7 ± 0.1 h/d, P < .01).	Good
49	Lopez-Gil, J. F., et al. (2021)	Online survey; 2	Spain and Brazil	1099 children	3-17	Compared to before the Pandemic, Spanish and Brazilian children engaged in less days of PA/week during the Pandemic (p<0.001, p<0.001). Before the Pandemic, 34.6% of Spanish children and 30.6% of Brazilian children met PA recommendations. During the Pandemic, 26.5% of Spanish children and 21.8% of Brazilian children met PA recommendations.	Not reported.	Good
50	Morgul, E., et al. (2020).	Online survey; 2	UK	927 caregivers	5-11	Daily PA of children significantly decreased during the Pandemic (x2 (15, n=927) = 121.26, p < .001). Before the Pandemic, 67.3% of children met PA recommendations (at least 60 min of PA/day), while 51.1% of children met PA recommendations during the pandemic.	Not reported.	Good
51	Poulain, T., et al. (2021).	Online questionnaire; 2	Germany	285 children	1-10	From before the during the Pandemic, there was a significant decrease in indoor sports (p=0.001) and an increase in the frequency of outdoor play (before 60%, during 71%).	Lower SES was associated with less frequent outdoor play, while more frequent outdoor play was significantly associated with more children at home (p<0.001).	Fair
52	Ng, K., et al. (2020).	PACE +; 1	Ireland	1214 children	12-18	During the Pandemic, 50% of children reported decreased PA, 30% reported no change in PA, and 20% reported increased PA compared to before the Pandemic. The most frequently reported barriers to PA included coronavirus and sports cancellation, while facilitators to PA included having nothing else to do, school cancellation, and going on walks.	Children with well-established PA habits before the Pandemic were less likely (OR=0.4, CI=0.2–0.6) to report decreased PA, while overweight (OR=1.8, CI=1.2–2.7) or obese (OR=2.2, CI=1.2–4.0) children were more likely to report decreased PA during the Pandemic. Furthermore, participation in strength-training exercises a minimum of three times in the past week was strongly associated with higher levels of PA (OR=1.7, CI=1.3–2.4).	Good

No.	Author (Year)	PA Measure; PA Data Reported by[a]	Sample Source (Country)	Sample Size	Age Ranges	Findings	Biological, Environmental, and Social Factors that Affected PA	NIH NHLBI Quality Assessment
53	Orgiles, M., et al. (2020).	Online survey; 2	Italy and Spain	1143 parents	3-18	During lockdown, the time children spent doing PA decreased (β = 0.04, SE = 0.07, Wald $\chi 2$ 95% CI [0.03, 0.04], p < 0.001). For example, the proportion of children who reported < 30 minutes of PA/day increased from 13.6% before the Pandemic to 55.6% during the Pandemic. Similarly, the proportion of children who met PA recommendations (at least 60 mins of PA/day) decreased from 54.1% to 14.8%.	Easier family coexistence was associated with a higher duration of exercise in children (ρ = 0.08; p = 0.004). In contrast, children of parents with high stress levels were more likely to have less PA (ρ = −0.10; p ≤ 0.001).	Good
54	Pietrobelli, A., et al. (2020).	Telephone questionnaire; 2	Italy	41 children	6-18	Among kids with obesity, sports activity decreased by 2.30±4.60 hours/week (p=0.003).	Not reported.	Good
55	Pombo, A., et al. (2020).	Online survey; 2	Portugal	2159 children	0-12	During the Pandemic, 0 to 2 year old children had the highest percentages of PA (%PA). (%PA: play with PA (tag, hide and seek, etc.) + PA (organized indoor and outdoor PA) / (intellectual activity + playful screen time + play w/o PA + play w/ PA + PA)).	Outdoor space (p<0.001), the presence of other children in the home (p=0.002), younger age (p<0.001), and having an adult at home not working were significantly associated with higher levels of %PA (P < .001). In contrast, lower levels of %PA in children were associated with families in which all adults worked from home (p=0.016). There was no significant effect of gender on differences in %PA.	Good
56	Predieri, B., et al. (2020).	Telephone questionnaire; 1	Italy	62 children	1-18	Among children with type 1 diabetes, time spent on exercise significantly decreased from before to during the Pandemic (3.27 ± 2.82 vs. 0.24 ± 0.59 h/week, respectively; p <0.0001).	Not reported.	Good
57	Roe, A., et al. (2020).	Online survey; 2, 3	Norway	5368; 4642 parents, 726 teachers	6-16	About one-third of all participants reported their child participated in more than 60 minutes of daily PA. Students in grades 1-4 (5 to 10 years) had the most PA, with more than 60 minutes of daily PA reported by 43% of parents. In contrast, only 18% of students in grades 8-10 (13 to 16 years) reported more than 60 minutes of daily PA.	Duration of daily PA increased with age of participants. Boys participated in more PA than girls in grades 1-7.	Good
58	Ruiz-Roso, M. B., et al. (2020).	IPAQ; 1	Italy, Spain, Brazil, Chile, and Colombia	726 children	10-19	Before the Pandemic, 27% of all participants were physically active compared to 20.5% during the Pandemic.	Boys were more active than girls [OR 2.22 (CI 95% 1.28–3.86)] before and during the Pandemic. Higher maternal education was associated with lower levels of PA during the pandemic [OR 0.40 (CI 95% 0.20–0.84)].	Good
59	Schmidt, S. C. E., et al. (2020).	MoMo PAQ; 1	Germany	1711 children	4-17	While the duration of organized and nonorganized sports decreased (10.8 min/day, p<0.01), there was an increase in habitual PA (i.e., playing outside, walking, cycling, gardening, housework) (36.2 min/day, p<0.01). The proportion of children who met PA recommendations increased by 11.1% (p<0.01) during the Pandemic. Among the entire sample, the number of active days also increased by 0.4 days/week (p<0.01).	Older children (ages 14 to 17) had greater increases in nonorganized sports than younger children (ages 4 to 5) (17.0 vs 11.8 min/day). Older children had greater reductions in total sports than younger children (15.6 vs 2.2 min/day). Younger children had higher levels of habitual PA overall, but also played outside more, while older children walked and cycled more. Boys reported more min/day playing outside, walking, and cycling than girls. The proportion of children who met PA recommendations increase among 14.7% of children aged 4 to 5 compared to only 4.8% of children aged 14 to 17.	Fair
60	Schmidt, T. and C. S.	Online survey; 1	Denmark	142 children	15-18	From before to during the Pandemic, the average minutes of PA/week decreased by 36.6% (p<0.001). Prior to the Pandemic, most children reported	Not reported.	Good

No.	Author (Year)	PA Measure; PA Data Reported by[a]	Sample Source (Country)	Sample Size	Age Ranges	Findings	Biological, Environmental, and Social Factors that Affected PA	NIH NHLBI Quality Assessment
	Pawlowski (2020).					being physically active 2 to 4 times per week (50.4%), while during the Pandemic most children reported being physically active 5 times or more per week (44.9%). The proportion of children who participated in PA 5 times or more per week increased by 19.1%, while the proportion of children who rarely or never did PA increased by 71.8%. Although outdoor activity was still a frequently reported form of PA, less children reported doing street activities and team ball games compared to before to Pandemic. 57.1% of children reported doing the most PA at home and 33.3% reported doing the most PA in public. Children were most physically active with family (40.8%) or alone (57.7%) in comparison to with friends (83.5%) before the pandemic.		
61	Salzano, G., et al. (2021).	Online survey; 1	Italy	1860 children	12-18	During the Pandemic, 84.5% of children participated in PA at home. PA at home was most often practiced for 1 to 3 hrs/week (30.1%), followed by < 1 hour per week (19.1%).	Not reported.	Fair
62	Ten Velde, G., et al. (2021).	Cohort A: BAECKE questionnaire, Cohort B: BAECKE questionnaire and ActiGraph GT3X accelerometer; 1	Netherlands	Cohort A: 102 children, Cohort B: 131 children	Cohort A: 4-18, Cohort B: 7-12	During the Pandemic, decreased PA was reported by 62% of children in cohort A and 54% of children in cohort B. In cohort A, school, sports, and leisure time PA significantly decreased ($p<0.01$) compared to before the Pandemic, whereas in cohort B, only sports PA significantly decreased ($p<0.01$). In cohort B, light PA (LPA) and MVPA decreased from 252 ± 34 and 65 ± 18 min/d before the Pandemic (May/June 2019) to 218 ± 39 and 48 ± 18 min/d during the Pandemic (June 2020) (-34 ± 42 min/d, $p<0.01$; -17 ± 19 min/d, $p<0.01$). Similarly, while 64% of children in cohort B met PA recommendations (60 minutes of MVPA/day) before the Pandemic, only 20% met recommendations during the Pandemic ($p<0.01$). Total PA in cohort B was decreased by 51 ± 52 min/d compared to before the pandemic.	While girls had larger decreases in light PA (LPA) and MVPA than boys, only the difference in reduction of LPA between boys and girls was significant (−18 ± 38 vs −44 ± 41 min/day, $p=0.02$). Children with more MVPA min/d before the Pandemic had larger reductions in MVPA compared to children with less MVPA before the Pandemic.	Good
63	Theis, N., et al. (2021). "	IPAQ-SF; 2	UK	125 parents	8-16	The frequency of vigorous and light/moderate intensity PA decreased from 2 and 5 to 0 and 3 days/week from before to during the Pandemic (median values; $z = -4.699$, $P < 0.001$; median values; $z = -3.979$, $P < 0.001$). However, the duration of vigorous and light/moderate intensity PA did not significantly change with most children achieving < 30 minutes of vigorous intensity PA ($z = -1.040$, $P = 0.073$) and between 30 to 60 minutes of light/moderate intensity PA ($z = -1.102$, $P = 0.070$). ($z = -1.040$, $P = 0.073$). The MET values of vigorous and light/moderate intensity PA decreased by 48% ($z = -4.334$, $P > 0.001$) and 38% ($z = -5.434$, $P > 0.001$) from before to during the Pandemic. Indoor play,	Not reported.	Fair

No.	Author (Year)	PA Measure; PA Data Reported by[a]	Sample Source (Country)	Sample Size	Age Ranges	Findings	Biological, Environmental, and Social Factors that Affected PA	NIH NHLBI Quality Assessment
						cycling, walking, and at home PA classes reported as types of PA children engaged in during the Pandemic.		
64	Tornaghi, M., et al. (2020).	IPAQ; 1	Italy	1568 children	15-18	Before the Pandemic, 6.8% of children met PA recommendations (60 min of MVPA/day) compared to 14.7% during the Pandemic. From before to during the Pandemic, the percentage of children with a inactive (<700 MET-min/week) (17.8% vs 25.8%) or intense (>2520 MET-min/week) PA level increased (15.8% vs. 19.8%), while the percentage of children with a moderate (700-2519 MET-min/week) PA level decreased (66.3% to 53.6%).	Not reported.	Good
65	Wunsch, K., et al. (2021).	MoMo-PAQ; 1, 2	Germany	1711 children	4-17	Before the Pandemic, male and female children (4-10) met PA recommendations (at least 60 minutes of PA) 4.74 and 4.62 days/week, while during the Pandemic boys and girls met PA recommendations 5.39 and 5.27 days/week. Similarly, the days/week that male and female adolescents (11-17) met PA recommendations increased from 3.90 and 3.55 days/week to 4.08 and 3.96 days/week.	Sedentary time before the Pandemic had a negative association with PA during the Pandemic, independent of age and gender. In contrast, among females and children < 10 years, health related quality of life before the Pandemic was positively associated with PA during the Pandemic.	Good
66	Zorcec, T., et al. (2020).	Questionnaire; 2	Republic of Macedonia	72 parents/caregivers	7.3±2.89	Among children with cystic fibrosis (CF), asthma, tuberculosis (TB) and allergic rhinitis, the percentage of children who participated in more than 2 hours of PA/day significantly decreased from before to during the pandemic (52.8% and 20.8%, p=0.0001). 11.4% of children before the Pandemic compared to 30.2% of children during the Pandemic participated in only a few hours of PA/week (p=0.0056).	Not reported.	Fair
67	Carroll (2020)	IPAQ; 2	Canada	310 children, 254 families	18 months - 5 years	During lockdown, decreased PA was reported for 52% of children, with an average time spent outdoors and in active play of one hr/day. Parents reported decreased intensity of PA among children during the pandemic.	Parents reported PA was limited during the Pandemic because of a lack of space and variety of tools/toys.	Good
68	Ellis, W. E., et al. (2020).	Godin Leisure-Time Exercise questionnaire; 1	Canada	1054 children	14-18	Many participants reported no strenuous (40%) or moderate (21.3%) physical activity over the past week. During the Pandemic, children participated in >5 minutes of mild PA 3.47 times, moderate PA 2.7 times, and strenuous PA 1.93 times.	Not reported.	Good
69	Guerrero, M. D., et al. (2020).	Online survey; 2	Canada	1472 parents	5-17	81.8% of children did not meet the PA recommendation.	Children were more likely to achieve PA recommendations if their parents were able to restrict screen time, had a higher income, or were younger than 43 years old. Furthermore, boys and children with increased outdoor PA and sport during the Pandemic were more likely to achieve PA recommendations.	Good
70	Hemphill, N. M., et al. (2020).	Fitbit (step count)	Canada	109 children	9-16	Children with congenital heart disease obtained 21%-24% less daily steps during early-COVID. Daily steps were consistently below the Canadian PA guidelines of 60	Daily step counts were higher among boys than girls.	Good

No.	Author (Year)	PA Measure; PA Data Reported by[a]	Sample Source (Country)	Sample Size	Age Ranges	Findings	Biological, Environmental, and Social Factors that Affected PA	NIH NHLBI Quality Assessment
						minutes of MVPA/day (approximately equivalent to 12,000 steps/day).		
71	McCormack, G. R., et al. (2020).	Online questionnaire; 2	Canada	328 parents	5-17	During the Pandemic, children met PA recommendations (≥60 min of MVPA) an average of 3.48 ± 2.41 days/week. Children played 4.52 ± 2.75 days in the past week and went to a park on 4.85 ± 6.39 days in the past month. Meanwhile, 18.3% of children reported 0 days of MVPA/week, 16.5% had 0 days of play per week, and 34.5% had no visits to a park in the past month. 48.8% of parents reported their child's PA at home increased and 32.9% of parents reported that their child's PA was the same compared to before the Pandemic. 38.7% of parents reported their child's PA outdoors increased, while 39% of parents reported their child's PA outdoors decreased. 52.7% of parents reported their child's play at a park decreased, while 15.5% of parents reported their child's play at a park increased. 53.7% of parents reported their child's play in public spaces decreased, while 9.5% of parents reported their child's play in public spaces increased.	Children of parents with high COVID-19 anxiety had fewer days at the park and less PA both in the home (14.2% vs. 25.6%, $p < .05$) and outdoors (33.2% vs. 49.6%) compared to children of parents with low COVID-19 anxiety (3.00 days vs. 5.42, $p < .05$).	Fair
72	Mitra, R., et al. (2020).	Online survey; 2	Canada	1472 parents	5-17	More youth than children experienced a decrease in physical activity-related movements during the pandemic, including walking/biking, outdoor or indoor physical exercise and outdoor play. The majority of children reported a decrease in walking or biking (53.2%), PA or sport outside (63.8%), and outdoor play (51.2%) during the Pandemic. In contrast, the majority of children reported PA or sport inside stayed the same (40.5%), while indoor play increased (53.1%).	Compared to children who reported decreased outdoor activity during the Pandemic, a greater proportion of children who reported increased outdoor activity met PA guidelines (11.6% vs 26.5%, $p<0.001$) (60 minutes of MVPA/day). Younger children, children with a higher household income, children living in houses (vs apartments), living in multi-child households, and living further from major roads were more likely to cluster into the increased outdoor activity group. Gender was not associated with changes in outdoor activity. While neighborhood density was negatively associated with clustering into the increased outdoor activity group, access to a park within 1 km increased the likelihood of children living in high density neighborhoods clustering into the increased outdoor activity group (OR = 1.19).	Good
73	Moore, S. A., et al. (2020).	Online survey; 2	Canada	1472 parents	5-17	During the Pandemic, 23.8% of children (5-13 years) and 13.2% of youth (14-17 years) met PA recommendations (60 minutes of MVPA/day). Children and youth attained 60 minutes of MVPA an average of 3.55 and 2.59 days/week, respectively. PA included activities such as walks or bikes in the neighborhood, PA or sport outside and inside, and outdoor play. Overall, children and youth had decreased PA and outside time during the Pandemic, with the greatest reduction in outdoor PA and sport. In contrast, children and youth reported increased indoor play. Among outdoor activities, biking (6.1%), walking/hiking (5.5%), and sports (3.5%) increased the most during the pandemic.	A greater proportion of children (23.8%) met PA recommendations than youth (13.2%). More boys (5-11 years) met PA recommendations than girls (27.9% boys, 19.0% girls). Younger parental age, parental encouragement, parental co-participation in PA, parental cohabitation, living in a detached house (vs. apartment) and having a dog were positively associated with PA.	Good

No.	Author (Year)	PA Measure; PA Data Reported by[a]	Sample Source (Country)	Sample Size	Age Ranges	Findings	Biological, Environmental, and Social Factors that Affected PA	NIH NHLBI Quality Assessment
74	Bazett-Jones (2020)	Online questionnaire; 1	US	287 children	9-19	During COVID-19 restrictions, runners reported shorter distance runs ($p < 0.001$), fewer runs ($p < 0.001$), and fewer intense runs ($p < 0.001$) per week.	Not reported.	Fair
75	Dunton, G. F., et al. (2020).	Online survey; 2	US	211 children	5-13	During the Pandemic, the most reported forms of PA were free play/unstructured activity (i.e. running around, tag) (90% of children) and walking (55% of children). Remote/streaming services were also used for PA programs (i.e. martial arts, dance, yoga classes) (28.9% of children), with older children (ages 9-13) five times more likely to participate in virtual team sports training sessions compared to younger children (ages 5-8)(OR = 5.40, 95% CI [1.70,17.15], Wald = 8.19, p = .004)Wald = .288, p = .633). Younger children (age 5–8) were more likely to participate in free play/unstructured physical activity, biking, and scootering/skateboarding/roller skating, while older children (ages 9–13) were more likely to participate in circuit training/conditioning. During the Pandemic, the likelihood of participating in PA at home (OR = 2.49, 95% CI[1.35, 4.60], Wald = 8.593, p = .003 and in the neighborhood (i.e. on sidewalks and roads)(OR = 1.92, 95% CI [1.04,4.60], Wald = 4.28, p = .038) increased compared to before the Pandemic. In contrast, the likelihood of participating in PA at parks and trails decreased (OR = 0.47, 95% CI [0.23, 0.97], Wald = 4.22, p = .040).	Parents perceived greater decreases in PA among older children (ages 9–13) compared to younger children (ages 5–8).	Good
76	Garcia, J. M., et al. (2020).	Online survey; 1	US	9 children	14-19	Prior to the pandemic, participants reported more days that they participated in 60 minutes or more of PA more frequently (4.17 days vs. 2.27 days; p = 0.0006) and participated in more activities (3.4 activities vs 2.11 activities; p = 0.007) than during the pandemic. 78% of the participants felt that their PA decreased.	The participants with decreased PA reported school PA program cancellations and fear of going outdoors as barriers to PA. The participant with increased PA reported it was because his family started riding bikes together.	Good
77	McGuine, T. A., et al. (2020).	Pediatric Functional Activity Brief Scale (PFABS); 1	US	13002 children	3-19	Among team sport athletes, lower levels of PA were reported compared to athletes involved in individual sports.	Lower levels of PA were reported among girls, athletes in the 12th grade, athletes who participated in team sports, and athletes from more impoverished areas.	Good
78	Pavlovic, A., et al. (2021).	Online questionnaire; 3	US	2440; 1789 PE teachers, 64 district administrators, 62 school administrators, and 3 nurses	not specified (grades 3-12)	During the Pandemic, 79% of participants reported students PA was "significantly less" or "somewhat less". Frequently reported online PA resources included YouTube (29%),virtual learning platforms (27.9%), and PE teacher-led virtual classes (25.6%). Among schools that closed due to the Pandemic, barriers to PA included student access to virtual learning and communication between teachers and students. Among schools that remained open, barriers to PA were social distancing guidelines and access to equipment and space for PA.	There were no significant differences in PA between children in different education levels (i.e., elementary, middle, or high schools) or regions of the U.S.	Good

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79	Tulchin-Francis, K., et al. (2021).	Weighted Leisure-Time Score Index (unvalidated modified Godin Leisure-Time Exercise Questionnaire (mGodin); 2	US	1083 parents	3-18	While light PA was unchanged, MVPA of children significantly decreased during the Pandemic (before: 46.7, during: 34.7, $p < 0.001$). For all ages, PA with friends, yard and neighborhood play (18.1%–39.8%, $p < 0.05$), and indoor child and parent-led play (6.8%–23.4%, $p < 0.05$) decreased. Preschool and elementary children reported decreased PA with family (8.3%–23.5%, $p < 0.05$) and a 7.1% to 20.1% increase in independent, virtual PA. Among preschool and elementary girls (20.3% and 5.7%, $p < 0.05$), as well as, elementary and middle school boys (5.1% and 13.8%, $p < 0.05$), increased yard play was reported. In contrast, there were no significant increases in outdoor PA among high school students. Before the Pandemic, 78.6% of children participated in organized sports, while during the Pandemic only 10.6% participated in organized sports.	The Pandemic had the lowest impact on PA (based on quantity, variety, and intensity of PA) of preschool students and the highest impact on PA of high school students. Boys had higher reductions in PA than girls.	Good
80	de Matos (2020)	IPAQ; 1	Brazil	69 children	8-18	Weekly energy expenditure was significantly reduced among children (male: ES: 3.02, CI95%: [1.93; 4.12], $p<0.0001$; female: ES: 3.26, CI95%: [1.82; 4.69], $p<0.0001$) and adolescents (male: ES: 4.25, CI 95%: [3.06; 5.44], $p<0.0001$; female: ES: 4.01, CI 95%: [3.02; 5.00]; $p<0.0001$) during the Pandemic.	Not reported.	Fair
81	Sa, C., et al. (2020).	Online survey; 2	Brazil	816 children	0-12	Most parents reported a decrease in PA during the Pandemic, with children doing either much less PA (46.1% of parents) or less PA than during a normal school year (37% of parents). Children participated in 0.4±0.6 to 0.7±1.0 hours of PA/day during the Pandemic.	Older children had lower levels of playing with PA than younger children. There were no significant relationships between age and sex and organized or outdoor PA.	Good
82	Siegle, C. B. H., et al. (2020).	Online questionnaire; 2	Brazil	816 children	0-12	During the Pandemic, the highest average percentage of daily PA was 10.3±16.2% among boys ages 0 to 2, while the lowest average percentage of daily PA was 3.9±5.7 among girls ages 6 to 9. (%PA = playtime w/ PA + PA (planned, inside/outside the house, dog walking) / (playtime w/ PA + PA + playtime w/o PA + playtime on screens + intellectual (school)).	Percentage of PA (%PA) was higher among children with large external spaces at home than children with small external space ($p=0.001$) or with no external space ($p<0.001$). Older children had lower %PA than younger children. There was no significant effect of gender on differences in %PA.	Good
83	Aguilar-Farias (2020)	Online survey; 2	Chile	3157 children	1-5	For all age groups, the average duration of PA decreased by 0.75 hrs/day (−0.75 [CI 95% −0.81, −0.70] h/day).	Greater reductions in PA were reported for children with a more educated main caregiver or who lived in an apartment. Smaller reductions in PA were reported for children living with more children or with five or more people, children in rural areas, and children with space at home to play. While there was no effect of gender on PA, older children had less PA.	Good
84	Reece, L. J., et al. (2020).	Online survey; 2	Australia	16177 parents	4-18	During the Pandemic, 31% of participants reported children's PA decreased a lot, while 39% reported children's PA decreased a little. For PA, 82% of children were active at home,	Not reported.	Fair

No.	Author (Year)	PA Measure; PA Data Reported by[a]	Sample Source (Country)	Sample Size	Age Ranges	Findings	Biological, Environmental, and Social Factors that Affected PA	NIH NHLBI Quality Assessment
						while 52% of children were active in public spaces.		
85	Cahal (2021)	Online questionnaire; 2	Israel	445 children	0-18	PA decreased in 53.9% of patients with chronic respiratory disorders (i.e. asthma, recurrent pneumonia).	Older patients (>5 years old) had decreased PA compared to younger patients (p<.001).	Fair
86	Chaturvedi (2021)	Online survey; 1	India	303 children	7-17	Children spent an average of 0.82 hrs/day on fitness during the Pandemic.	Not reported.	Good
87	Ghanamah, R. and H. Eghbaria-Ghanamah (2021).	Online survey; 2	Israel	382 parents	5-11	Children spent less time in physical activities during the Pandemic than before. (before: 2.88 hours/day during: 2.02 hours/day, p<0.001)	Children spent less time in PA when a family member was diagnosed with COVID-19.	Good
88	Masi, A., et al. (2021).	Online survey; 2	Australia	302 caregivers	2-17	68% of caregivers for children with neurodevelopmental disabilities reported a decrease in exercise.	Not reported.	Fair
89	Munasinghe, S., et al. (2020).	PACE +, smartphone sensors (pedometer, MBAR); 1	Australia	582 children	13-19	PA decreased from before to during the Pandemic (odds ratio [OR] = .53, 95% confidence interval [CI] = .34–.83), with a concurrent decrease in the average number of steps/day.	Not reported.	Fair
90	Nathan, A., et al. (2021).	Online survey; 2	Australia	157 children	5-9	Compared to before the Pandemic, the total minutes of PA/week did not significantly change during the Pandemic. However, there was a 65.7% and 65% reduction in the duration and frequency of organized PA (-124.6 min/week, p<0.001; -1.3 times/week, p<0.001). In contrast, the duration and frequency of total (23.1% or 146.3 min/week, p=0.005 and 30% or 1.8 times/week, p<0.001) and home-based (58.7% or 201 min/week, p<0.001) unstructured PA increased. Other activities that significantly increased from before to during the Pandemic included outdoor play (i.e., in the yard or street around the house, in a park or outdoor recreation area) and home indoor play. There was a 95% increase in the min/week reported for outdoor play in a park, playground, or outdoor recreation area.	Parents reported facilitators of PA during the Pandemic as increased time at home to support PA, more children outside playing together, more utilization of local PA resources (i.e., parks), more unstructured PA, and more parental encouragement.	Good
91	Parker, K., et al. (2021).	Online survey; 1	Australia	963 children	13-17	During the Pandemic, 7.2% of children met PA recommendations (60 min of MVPA/day). Among the 26.5% of children who used digital platforms for PA, streaming services were used by 40.0%, online classes were used by 30.2%, and subscriber fitness programs were used by 13.7% of those children. The median frequency and duration of digital platform use for PA were 4 (IQR 3-7) times per week and 120 (IQR 60-260) min/week.	Children who used digital platforms for PA during the Pandemic were over 2 times more likely to meet PA recommendations.	Good
92	Sciberras, E., et al. (2020).	Online survey; 2	Australia	213 children	5-17	Among kids with ADHD, there was decreased exercise (Odds Ratio (OR) = 0.4; 95% CI 0.3–0.6) and outdoor	Not reported.	Good

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						time (OR = 0.4; 95% 0.3–0.6) compared to pre-COVID.		
93	Zhao, Y., et al. (2020).	Online questionnaire; 1, 2	China	738 students, 1062 parents	11.0±1.7	During the Pandemic, 26% of children reported 0 hours, 18% reported <1 hour, 37.9% reported 1-2 hours, and 18% reported more than 2 hours of daily outdoor activity. In contrast, 43.7% of parents reported their child's daily outdoor activity was 0 hours. 42.9% of children in grades 7-9 reported 0 hours of daily outdoor activity compared to 24.1% of children in grades 1-3 and 23.8% of children in grades 4-6.	Not reported.	Fair
95	Wu, X., et al. (2021).	Telephone questionnaire; 2	China	43 children	0-18	Among children with type 1 diabetes, 44.1% reported PA decreased during the Pandemic. Before the Pandemic, outdoor activities (i.e., cycling, basketball) were predominant forms of exercise. However, during the Pandemic, the predominant form of exercise was indoor activities (i.e., pacing, skipping rope).	Not reported.	Fair
96	Zhang, X., et al. (2020).	IPAQ-SF; 1	China	9979 children	9-14	Students obtained an average of 23.19 minutes of moderate-to-vigorous PA (MVPA)/ day (1193.02 ± 1621.88 MET-min/week). Vigorous PA made up 42.74% (510.40 ± 934.18 MET-min/week) of total PA, while walking for PA made up 24.19% (288.60 ± 613.08 MET-min/week).	Girls participated in significantly more MVPA and moderate PA than boys during the Pandemic ($p<0.01$). Similarly, younger children in grade 4 participated in significantly less MVPA and moderate PA than older children in grades 5 and 6. ($p<0.01$)	Good
97	Abid (2021)	Ricci and Gagnon sedentary behavior questionnaire; 1	Tunisia	100 children	5-12	Compared to before the Pandemic, sports and recreational PA decreased by 35%, daily PA decreased by 16% for boys and 27% for girls, and total PA decreased by 7% for boys and 17% for girls during the Pandemic ($p<0.001$).	There was no significant effect of gender on PA.	Fair
98	Shinomiya, Y., et al. (2021).	Online survey; 2	Japan	2019: 2017 children, 2020: 295 children	18-30 months	The percentage of leisure time that consisted of outdoor play decreased from an average of 64.0 ± 26.0% before the Pandemic (March 2019) to 61.0±27.1% during the Pandemic (March 2020) ($p=0.058$).	Children who stayed at home had less outdoor play than children who received childcare at a nursery school ($p=0.019$).	Good
99	Xiang, M., et al. (2020).	Global Physical Activity questionnaire (GPAQ); 1	China	2426 children	6-17	Before the Pandemic, PA decreased from a median of 540 min/week to 105 min/week during the Pandemic (-435 min/week, $p<0.001$). The percentage of children who met PA recommendations (at least 60 min of PA/day) decreased from 60% to 17.7% during the Pandemic (-42.3%).	Not reported.	Fair
100	Yang, S., et al. (2020).	IPAQ-long form; 1	China	2824 children	17.5 ± 1.2	High school students reported their MVPA (80.4%), active transport for commuting and errands (77.4%), housework activity (50.1%), and walking for leisure (79.9%) stayed the same. The hrs/week that high school students participated in MVPA remained	Not reported.	Fair

No.	Author (Year)	PA Measure; PA Data Reported by[a]	Sample Source (Country)	Sample Size	Age Ranges	Findings	Biological, Environmental, and Social Factors that Affected PA	NIH NHLBI Quality Assessment
						unchanged at an average of 1.5 hrs/week.		
101	Elnaggar, R. K., et al. (2020).	PAQ-A; 1	Saudi Arabia	63 children	14-18	From baseline to follow-up, the PA level (PAL) of all participants was significantly reduced (BL-PAL: 3.05 ± 0.54; FL-PAL: 2.77 ± 0.47; P < .001).	While PAL decreased for both genders, only the PAL reduction was significant in boys (BL-PAL: 3.20 ± 0.57; FU-PAL: 2.76 ± 0.49; P < .001). At baseline, boys achieved significantly higher PAL than girls (P = .014), but at follow-up both genders had similar PAL (P = .86).	Fair
102	Jia, P., et al. (2021).	IPAQ-long form; 1	China	2824 children	16-18	Compared to before the Pandemic, the frequency of active transport (i.e., commuting and errands) among high school students decreased from 1.3 to 0.9 days/week (p<0.001), while leisure-time walking decreased from 1.0 to 0.7 days/week (p<0.001) during the Pandemic. Similarly, the frequency of moderate-to-vigorous housework decreased from 2.3 to 1.9 days/week (p < 0.05) and leisure-time moderate-to-vigorous PA decreased from 0.7 to 0.65 days/week (p < 0.001).	Not reported.	Good

Legend: [a] 1 = child reported measure; 2 = parent reported measure, 3 = other secondary subjective reported measure. Abbreviations: PA, physical activity; NIH NHLBI, National Institute of Health National Heart, Lung, and Blood Institute; CI, confidence interval; h/day, hrs/day; MVPA, moderate-to-vigorous physical activity; M, mean; SD, standard deviation; PAL, physical activity level; ES, effect size; min/d, min/day; OR, odds ratio; Wald, Wald test; BL, baseline; FU, follow up; P.E., physical education; min/wk, min/week; ml.kg−1.min−1, millimeters per kilogram per minute; h/d, hrs/day; km, kilometers; ADHD, attention-deficit/hyperactivity disorder; LPA, light physical activity; MET, metabolic equivalent task.

The sample sizes ranged from 9 children[76]-16177 parents.[84] Most articles (n=32) [33-35,38-41,43,47,48,50,51,58,60,62,63,67,70,71,74,75,81,82,85-93] had a sample size between 100-1000, but 2 articles had a sample size >10000.[77,84] As the present study is focused on children, most of the articles are inclusive of age groups between 0-18 years. However, 5 articles included participants ≤19 years because the articles specified their sample as either adolescents (n=4)[58,76,77,89] or school-aged youth (n=1).[74] Because adolescents are defined by the WHO as individuals 10-19 years old,[94] these articles were included despite the exclusion criteria of ≤18 years. One article did not specify the age of participants,[78] however, specified participants were in grades 3-12, and was ultimately included.

Most participants were children without chronic health conditions, but some articles focused on characterizing PA during the pandemic for children with various health conditions (e.g., autism spectrum disorder, congenital heart disease, chronic respiratory disorders, obesity, type 1 diabetes, attention-deficit/hyperactivity disorder; n=11).[52,54,56,63,66,70,76,85,88,92,95] Some articles examined PA during the pandemic only (n=13),[35,45,55,57,61,68,69,77,82,86,91,93,96] while others compared PA from before to during the pandemic (n=56).[33,34,36-44,46-54,56,58-60,62-67,70-76,78-81,83-85,87-90,92,95,97-102]

PA data was reported by either the child (n=28),[38-41,43,48,52,56,58-62,64,68,74,76,77,80,86,89,91,96,97,99-102] the parent or guardian (n=32),[34,35,37,42,44,47,49-51,53-55,63,66,67,69,71-73,75,79,81-85,87,88,90,92,95,98] a different secondary subjective individual such as a school administrator (n=1),[78] or a combination of these groups (n=5).[36,45,57,65,93] Based on the NIH NHLBI Study Quality Assessment Toolbox,[32] 50 articles received a rating of "good," while 19 articles received a rating of "fair" ***Table 1***.

PA Measures

PA measures used in the included articles are depicted in ***Table 2***. Online surveys were predominantly used to collect PA data. Common PA questionnaires included the International Physical Activity Questionnaire (IPAQ, short or long form; n=8)[58,63,64,67,80,96,100,102] and the Physical Activity Questionnaire for Adolescents (PAQ-A; n=5)[38-41,101] or for children (PAQ-C; n=2).[44,45] The PAQ-A designates a physical activity level (PAL) based off a scale of 1-5: 1 designating no activity or a low activity level and 5 designating a high activity level. A PAL score below 2.73 suggests an insufficient PAL and a score above 2.73 suggests a sufficient PAL. A few surveys took place in-person (n=2)[43,66] or over the phone (n=4).[37,54,56,95] Seven studies used objective measures to collect PA data, including the use of a Fitbit,[70] accelerometer,[33,37,48,62] smartphone sensors (e.g., pedometer),[89] or a 20-meter shuttle run test to measure VO2 max.[46] The most prevalent FITT principle collected to determine PA was time (e.g., duration of PA; n=46),[33,36,42,45,47,48,50,52-68,71-73,75,76,80-84,86,87,89-93,96-100] followed by frequency (n=30),[38,39,43-45,49,51,52,59,60,63-65,68,69,71,73,74,76,77,79-81,84,90-92,96,102]

type of exercise (n=30),[36,38,39,43-45,51,59,60,62,63,68,71-73,75,77-79,84,89-92,95-98,100,102] and intensity (n=25).[33,36,45,48,52,53,59,62-64,67,68,71-74,79,80,84,91,96,97,99,100,102]

Types of PA

Among the articles included, there were conflicting results concerning the effects of the pandemic on the types of PA in which children participated. Five articles reported that outdoor PA declined during the pandemic,[71-73,95,98] while 3 studies reported that outdoor PA increased.[37,51,90] The types of outdoor PA included activities such as walking, biking, outdoor play, playing at parks or other public spaces, and sports. Eight studies reported that many children (e.g., 82%)[84] were active at home.[60,61,63,71,75,84,90,95] Some studies reported the use of online platforms such as streaming services (e.g., YouTube), virtual classes (e.g., yoga),[45,75] or other virtual PA forms[79] to accumulate PA during the pandemic.[78,91] In a US study, the most common forms of PA during the pandemic were unstructured play (90%) and walking (55%).[75] In contrast, a Chinese study reported the most common form of PA changed from outdoor activities (e.g., cycling) to indoor activities (e.g., rope skipping).[95]

Extent to Which PA Changed During the Pandemic

Several studies (n=10) reported most children obtained <30 min/day or <3 hrs/week of PA,[33,35,42,47,56,61,66,68,96,99] with 2 reporting most children participated in PA 0 days/week.[35,68,99] Of the 12 articles [37,45,49,50,53,57,62,64,69,73,91,99] that reported the percentage of children meeting PA guidelines (i.e., 60 MVPA min/day), 1 article reported <10%,[91] 9 articles reported 10-30%,[45,49,53,57,62,64,69,73,99] and 2 articles reported >50% [37,50] of children met PA recommendations during the pandemic. All articles that utilized the PAQ-A to assess PA(n=5),[38-41,101] reported a significant decrease in PAL.

Of the articles that compared PA before the pandemic to during the pandemic (n=56),[33,34,36-44,46-54,56,58-60,62-67,70-76,78-81,83-85,87-90,92,95,97-102] 89% reported a decrease in PA (i.e., frequency, intensity, type/duration, type) of children. Among these articles, the proportion of participants that reported a decrease in PA behaviors during the pandemic ranged from 42%[43]- 95%.[48] One study reported that although the total minutes of PA/week did not significantly change, the duration and frequency of organized PA decreased, while unstructured PA and outdoor play increased.[90]

Similarly, another study found 80.4% of high school students reported their MVPA stayed the same at 1.5 hrs/week.[100] Two studies [37,59] reported an increase in PA (e.g., duration, frequency of meeting PA recommendations/week) of children (n=4), 1 of which reported a specific increase in outdoor time compared to before the pandemic.[37] One study reported 90.3% of preschoolers (3- 5 years old) met PA guidelines of ≤180 minutes of PA/day, with 60 minutes of MVPA/day.[37] The articles that reported PA (e.g., duration, frequency of meeting PA recommendations per week) increased during the pandemic had samples from Sweden,[37] Canada,[71] and Germany.[59,65]

Conversely, four studies from Canada,[67,70,72,73] four studies from Australia,[84,88,89,92] and one study from Germany[43] reported PA (e.g., frequency, intensity, daily steps, meeting PA recommendations) decreased. For studies that included children with pre-existing health conditions (n=11),[52,54,56,63,66,70,76,85,88,92,95] PA (e.g., daily steps, duration, frequency) decreased compared to before the pandemic. For example, among children with obesity in Italy, sports participation decreased by 2.30±4.60 hrs/week (p=0.003).[54]

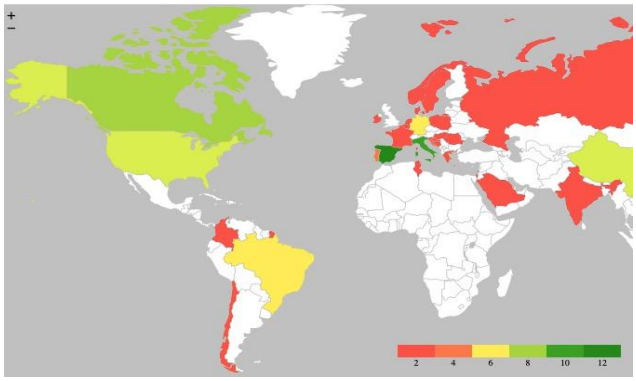
Biological, Environmental, and Social Factors Affecting PA

Common trends were evident among the studies of this review that related factors such as gender, age, and the environment outside as well as inside the home to the PA of children during the pandemic. In general, boys had higher levels of PA (e.g., more minutes of PA/day or more likely to meet PA recommendations) than girls. A study in Tunisia found that total PA (score from the Ricci and Gagnon sedentary behavior questionnaire based on duration and intensity of PA) decreased by 17% and 7% among girls and boys, respectively. [97] Older children tended to have greater reductions in time/duration of PA compared to younger children. For example, in 2 Spanish studies, PA decreased an average of 43.3 min/day among preschoolers aged 4- 6 years old,[33] while PA decreased an average of 91 ± 55 min/day among older children aged 8- 16 years old.[48]

There were mixed results for PA of children and parents' socioeconomic status (e.g., lower levels of PA were reported almost equally for both high and low parental income and education). Children who lived in a rural areas [83] or had more outdoor space to play [36,48,55,82] had lower reductions in PA (e.g., duration, less likely to report decreased PA, greater percentage of day spent participating in PA). For example, children with access to an outdoor area at home had a 1.4 ± 0.1 hrs/day reduction in PA compared to a 1.7 ± 0.1 hrs/day reduction in children without access (p<.01).[48] In contrast, children who lived in a high-density neighborhood [72] or urban area[36,41] had greater reductions in PA (e.g., more likely to report decreased PA, less likely to meet PA recommendations, greater reduction in PAL). Children who lived in an apartment had lower levels of PA (e.g., decrease in duration of PA or less likely to meet PA recommendations) compared to children who lived in a house.[72,83]

The environment inside the home also seemed to affect PA of children during the pandemic. One study reported that children who lived in a home with more people had greater reductions in duration of PA,[83] while 3 studies reported children who lived in multi-child households (e.g., with siblings) participated in more PA (e.g., greater duration or greater percentage of day spent participating in PA)[55,83] or more frequent outdoor play.[51,72] Children who had less family conflict, more parental support, and more family engagement in PA had greater durations of PA.[53,73,76] However, children who had more conflict with their parents or who had parents with higher stress levels had less PA (e.g., shorter duration of PA or less likely to achieve a sufficient PAL).[38,53]

***Figure 2*. Sample Source (Countries) of Included Articles.**



Discussion

The present study aimed to address the types of PA children participated in, the extent to which PA (e.g., frequency, intensity, duration, and type) changed, and factors affecting PA during the pandemic. Schools, active transportation (e.g., walking to and from school), afterschool programs, and sport programs were predominant sources of MVPA prior to the pandemic.[103,104] The stay-at-home orders and social distancing policies put in place to mitigate the spread of COVID-19 restricted the ability of children to obtain PA through these previously popular sources. While the studies in this review revealed walking, outdoor activity, and activity at home were types of PA children engaged in during the pandemic, a study before the pandemic found that children were less likely to participate in routine PA (e.g., going to the gym, walking) compared to unstructured play.[5] Social distancing restrictions could have contributed to shorter durations of PA and overall decreased participation, despite walking becoming a common source of PA during the pandemic.[75] In addition, some studies reported many children were active at home (e.g., indoors or not at a park/public space).[60,61,63,71,75,84,90,95] Studies conducted prior to the pandemic found that indoor PA (e.g., at home, at school) tends to be a greater source of lighter intensity PA,[103] which could help to explain the reduction in children able to meet MVPA recommendations during the pandemic.

The results of this review suggested that while there was heterogeneity in the extent to which the pandemic affected PA (e.g., frequency, intensity, duration, and type) in children, overall, there was a decrease in PA of children globally. Although the impact of the pandemic on PA of children is still evolving, trends before the pandemic have shown that children tend to have lower levels of PA when they are not in school.[13,14] Studies that investigated changes in MVPA during time out of school (e.g., weekends or a 3-week school break) found that MVPA decreased by 10-14 minutes compared to week days during the school year.[13,105] In contrast, the reductions in PA presented by the studies in this review ranged from 32-91 min/day.[33,48,54,83,99] These results revealed that the decreases in time/duration of PA during the pandemic may have been greater than those typically observed during days when children are not in school. Prior to the pandemic, global PA levels of children were already low, with 81% of children insufficiently physically active.[12] Of the studies that

***Table 2* Characteristics of the Physical Activity Data for the Included Articles (n=69).**

Study Characteristic	Total Articles	Articles
PA Data Reported by:		
Child	28	38-41, 43, 48, 52, 56, 58-62, 64, 68, 74, 76, 77, 80, 86, 89, 91, 96, 97, 99-102
Parent	32	34, 35, 37, 42, 44, 47, 49-51, 53-55, 63, 66, 67, 69, 71-73, 75, 79, 81-85, 87, 88, 90, 92, 95, 98
Child and Parent	5	36, 45, 57, 65, 93
Other (Fitbit, accelerometer, VO2, smartphone sensor)	7	33, 37, 46, 48, 62, 70, 89
Teacher and Parent	1	58
Teacher and School Administrator	1	78
PA Measure		
IPAQ (short or long form)	8	59, 64, 65, 68, 81, 97, 101, 103
PAQ-A	5	39-42, 102
PAQ-C	2	44, 45
PACE+	2	52, 89
Godin Leisure-Time Exercise Questionnaire (or modified version)	2	68, 79
Other online survey	39	34-36, 42, 47-51, 53, 55, 57, 60-62, 69, 71-78, 81-88, 90-93, 97-99
MoMo-PAQ	2	59, 65
Telephone interview	4	37, 54, 56, 95
In-person questionnaire	2	43, 66
Accelerometer (GENEActiv tri-axial, ActiGraph GT3X)	4	34, 38, 49, 63
FitBit	1	70
Smartphone sensors (pedometer, MBAR)	1	89
VO2 max (20 meter shuttle run test)	1	46
Physical Activity Time Frame		
During the COVID-19 pandemic	13	35, 45, 55, 57, 61, 68, 69, 77, 82, 86, 91, 93, 96
Compared PA before to during the COVID-19 pandemic	56	33, 34, 36-44, 46-54, 56, 58-60, 62-67, 70-76, 78-81, 83-85, 87-90, 92, 95, 97-102
Did PA increase or decrease?		
PA decreased	50	33, 34, 36, 38-44, 46-54, 56, 58, 60, 62-64, 66, 67, 70, 72-76, 78-81, 83-85, 87-89, 92, 95, 97-102
PA increased	4	37, 59, 65, 71
PA stayed the same	2	90, 100
FITT Principle reported		
Frequency	30	38, 39, 43-45, 49, 51, 52, 59, 60, 63-65, 68, 69, 71, 73, 74, 76, 77, 79-81, 84, 90-92, 96, 102
Intensity	25	34, 37, 46, 49, 53, 54, 60, 63-65, 68, 69, 72-75, 80, 81, 85, 92, 97, 98, 100, 101, 103
Time	46	33, 36, 42, 45, 47, 48, 50, 52-68, 71-73, 75, 76, 80-84, 86, 87, 89-93, 96-100
Type	30	37, 39, 40, 44-46, 52, 60, 61, 63, 64, 69, 72-74, 76, 78-80, 85, 90-93, 96-99, 101, 103

Legend: Abbreviations: PA, physical activity; IPAQ, International Physical Activity Questionnaire; PAQ-A, Physical Activity Questionnaire for Adolescents; PAQ-C, Physical Activity Questionnaire for Children; PACE+, Patient-centered Assessment and Counseling for Exercise plus Nutrition; MoMo-PAQ, Motorik-Modul Physical Activity Questionnaire.

reported a decrease in PA during the pandemic, the percentage of children who did not meet PA recommendations ranged from 80%- 99.7%.[45,49,62,69,73,91] This suggests that global levels of PA in children may have worsened during the pandemic.

The results of the current study indicate that during the pandemic, boys, and younger children tended to have higher levels of PA (e.g., more likely to meet PA recommendations), which is consistent with PA trends that existed prior to the pandemic.[104,106-109] Previous studies have found that self-efficacy is an important predictor of PA.[108,110] Not only are girls less likely to participate in PA,[111] but they also tend to have a lower perceived ability to overcome PA barriers.[112] The social cognitive theory suggests that self-efficacy moderates the relationship between the social and physical environment and changes in PA, such that individuals with a high self-efficacy for overcoming PA barriers should be more likely to participate PA despite changes in the environment.[113] With the changes in the social and physical environment surrounding children during the pandemic, self-efficacy for overcoming PA barriers may have played a role in the observed changes in PA. Similarly, lower levels of self-efficacy in girls may also be due to lower levels of social support to participate in PA compared to boys.[111]

The relationship between self-efficacy, social support, and PA may also apply to age-related changes in PA. Several studies prior to the pandemic reported that children and adolescents with higher levels of peer and family support had higher levels of PA (e.g., frequency, more likely to meet PA recommendations).[5,114-116] For example, one study found that adolescents with higher parental support were 40% more likely to achieve sufficient PA (60 minutes of MVPA/day).[115] While it has been established that PA (e.g., proportion of children meeting PA recommendations) decreases with age,[117-120] 1 such study reported that adolescents with greater self-efficacy had lower age-related reductions in PA.[118] The benefits of social support on child PA behaviors could have been especially critical in providing additional support to children navigating barriers to PA during the pandemic. In addition, a past study also found that older girls prefer to do PA at school or in a community setting than at home and participate in team sports.[121]

The changes in PA behaviors during the pandemic were likely due to the intersectionality of many social factors that resulted in decreased PA (e.g., frequency, intensity, duration), especially among girls and older children. Greater participation in PA among children with greater social support could also explain why children living in multi-child home had higher levels of PA (e.g., frequency, duration) during the pandemic. Studies before the pandemic have shown that children with siblings or other children to play with participated in more spontaneous and unstructured play.[122-124] More children inside the home may have been a protective factor for PA in children during the pandemic, as it could have offered greater opportunities and incitement to participate in PA.

The studies in this review suggested that during the pandemic, children in rural areas had lower reductions in PA (e.g., duration) compared to children in urban areas. While some studies before the pandemic have shown MVPA of children was higher in environments with less urbanization,[125,126] one study suggested that children in suburban or rural areas have less PA.[110] The inconclusive relationship between rurality and PA in children could be due to the lack of a global definition of rurality and different distributions of built environments that are conducive to PA in different countries. A study of low- and medium-income countries in Africa found that urban development led to changes in the environment that were less favorable for outdoor PA.[127] While outdoor time has been shown to be positively related to PA,[128-130] rural environments do not guarantee higher levels of outdoor time. Instead, rural environments may also create barriers to PA such as limited quantity of and access to resources that promote PA, such as playgrounds, parks, trails, and other recreational areas. Another study found that differences in MVPA between children in rural and non-rural areas of the U.S. were mediated by differences in neighborhood resources.[131] Rather than comparing PA levels by rurality, more general characteristics of the PA environment such as quantity of and accessibility to community recreational areas, neighborhood safety, traffic levels, and walkability may be more helpful in identifying global factors that affected PA in children during the pandemic.

In conclusion, the purpose of the present review was to synthesize the global impact of the pandemic on PA of children. This review adds to the current body of literature on the effects of the pandemic on PA by specifying changes in the frequency, intensity, duration, and type of PA performed by children, as well as the proportion of children who met PA recommendations. The greatest strength of this systematic review is the range of PA data presented for a wide geographic distribution. Information about different changes in PA (e.g., frequency, intensity, duration, type), as well as characterizations of PA during the pandemic may help to create a succinct picture of the impact of the pandemic on PA in children. A limitation of the systematic review process is some relevant studies may have been missed in the database search due to database selection and exclusion of studies not published in English. In addition, the use of online surveys, the most frequent data-collecting method used in the included studies, is an important limitation of this review, as surveys can only report subjective measures of PA. Furthermore, studies that asked participants to recall PA behaviors prior to the pandemic could be inaccurate. Moreover, online surveys may not have been accessible to individuals of low socioeconomic status who may not have access to the internet. Limited representation of individuals of low socioeconomic status could, therefore, affect the generalizability of the results of this review.

While many PA trends that existed prior to the pandemic persisted, the further reductions in already low global PA levels among children is worrisome. As the world reopens and vaccines are distributed, it is important to determine whether these PA trends will persist and for how long. Following a natural disaster in East Japan in 2011, significantly decreased child PA levels persisted more than 3 years later.[132] Consistently insufficient levels of PA in children around the world may have detrimental

effects on overall population health. The results of this review may be helpful in identifying barriers and facilitators to PA in children during the pandemic to determine what policies and programs would be most effective at increasing PA of children after the pandemic and beyond.

Summary – Accelerating Translation

The goal of "Effects of the COVID-19 Pandemic on Physical Activity in Children: A Systematic Review" was to synthesize the global impact of the COVID-19 pandemic on physical activity of children. Identifying changes in physical activity of children is important for understanding the extent to which the pandemic has affected already low levels of global physical activity among children. In addition, recognizing the biological, social, and environmental factors that affected changes in physical activity is critical for the development of effective programs to prevent short- and long-term health consequences. To the authors' knowledge, this is the first review to summarize the literature at the time of the data search regarding the global impact of the pandemic on the duration and types of physical activity children participated in and what biological, social, and environmental factors contributed to those changes. Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines were used to conduct a database search on 03/29/2021. Included studies were peer- reviewed, in English language, and included both a measure of physical activity during the COVID-19 pandemic and physical activity data for children aged 18 and younger. The search yielded 673 unique citations and, ultimately, 69 articles were included in the review. The results of the study found that during the COVID-19 pandemic, frequently reported physical activity included walking, unstructured play, and virtual physical activity through online platforms. Of the articles that reported changes in physical activity of children during the COVID-19 pandemic, 89% reported physical activity (e.g., frequency, intensity, duration, or the percentage of children who met physical activity recommendations) of children decreased. Boys, younger children, children who lived with other children, and children with more outdoor play space had higher levels of physical activity. From these results, it was concluded that the COVID-19 pandemic resulted in decreased physical activity among children around the world. The results of this review may be helpful in identifying barriers and facilitators to physical activity in children during the COVID-19 pandemic. Future work in policy and program development is needed to target physical activity of children beyond the COVID-19 pandemic.

References

1. Rundle AG, Park Y, Herbstman JB, Kinsey EW, Wang YC. COVID-19-related school closings and risk of weight gain among children. Obesity (Silver Spring). 2020;28(6):1008-9.
2. World Health Organization. Coronavirus disease 2019 (COVID-19): situation report. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports. Last updated Jun 17, 2024; cited Jul 3, 2024.
3. Nicola M, Alsafi Z, Sohrabi C, Kerwan A, Al-Jabir A, Iosifidis C, et al. The socio-economic implications of the coronavirus pandemic (COVID-19): a review. Int J Surg. 2020;78:185-93.
4. Advisory Committee on Childhood Lead Poisoning Prevention, Centers for Disease Control and Prevention. Low level lead exposure harms children: a renewed call for primary prevention. Atlanta, GA: US Department of Health & Human Services, Centers for Disease Control and Prevention; 2012.
5. Foster C, Moore JB, Singletary CR, Skelton JA. Physical activity and family-based obesity treatment: a review of expert recommendations on physical activity in youth. Clin Obes. 2018;8(1):68-79.
6. Thivel D, Tremblay A, Genin PM, Panahi S, Riviere D, Duclos M. Physical activity, inactivity, and sedentary behaviors: definitions and implications in occupational health. Front Public Health. 2018;6:288.
7. World Health Organization. Physical activity. Available from: https://www.who.int/news-room/fact-sheets/detail/physical-activity. Last updated Jun 26, 2024; cited Jul 3, 2024.
8. Chaput JP, Willumsen J, Bull F, Chou R, Ekelund U, Firth J, et al. 2020 WHO guidelines on physical activity and sedentary behaviour for children and adolescents aged 5-17 years: summary of the evidence. Int J Behav Nutr Phys Act. 2020;17(1):141.
9. Janssen I, Leblanc AG. Systematic review of the health benefits of physical activity and fitness in school-aged children and youth. Int J Behav Nutr Phys Act. 2010;7:40.
10. Poitras VJ, Gray CE, Borghese MM, Carson V, Chaput JP, Janssen I, et al. Systematic review of the relationships between objectively measured physical activity and health indicators in school-aged children and youth. Appl Physiol Nutr Metab. 2016;41(6 Suppl 3):S197-239.
11. Patterson R, McNamara E, Tainio M, de Sa TH, Smith AD, Sharp SJ, et al. Sedentary behaviour and risk of all-cause, cardiovascular and cancer mortality, and incident type 2 diabetes: a systematic review and dose response meta-analysis. Eur J Epidemiol. 2018;33(9):811-29.
12. Guthold R, Stevens GA, Riley LM, Bull FC. Global trends in insufficient physical activity among adolescents: a pooled analysis of 298 population-based surveys with 1.6 million participants. Lancet Child Adolesc Health. 2020;4(1):23-35.
13. Brazendale K, Beets MW, Weaver RG, Pate RR, Turner-McGrievy GM, Kaczynski AT, et al. Understanding differences between summer vs. school obesogenic behaviors of children: the structured days hypothesis. Int J Behav Nutr Phys Act. 2017;14(1):100.
14. Franckle R, Adler R, Davison K. Accelerated weight gain among children during summer versus school year and related racial/ethnic disparities: a systematic review. Prev Chronic Dis. 2014;11:E101.
15. Siebach MK, Piedimonte G, Ley SH. COVID-19 in childhood: Transmission, clinical presentation, complications and risk factors. Pediatr Pulmonol. 2021;56(6):1342-56.
16. Dhochak N, Singhal T, Kabra SK, Lodha R. Pathophysiology of COVID-19: why children fare better than adults? Indian J Pediatr. 2020;87(7):537-46.
17. Okuyama J, Seto S, Fukuda Y, Funakoshi S, Amae S, Onobe J, et al. Mental health and physical activity among children and adolescents during the COVID-19 pandemic. Tohoku J Exp Med. 2021;253(3):203-15.
18. Ghosh R, Dubey MJ, Chatterjee S, Dubey S. Impact of COVID -19 on children: special focus on the psychosocial aspect. Minerva Pediatr. 2020;72(3):226-35.
19. Shrestha R, Copenhaver M. Long-term effects of childhood risk factors on cardiovascular health during adulthood. Clin Med Rev Vasc Health. 2015;7:1-5.
20. Kallio P, Pahkala K, Heinonen OJ, Tammelin TH, Palve K, Hirvensalo M, et al. Physical inactivity from youth to adulthood and adult cardiometabolic risk profile. Prev Med. 2021;145:106433.
21. Ruegsegger GN, Booth FW. Health benefits of exercise. Cold Spring Harb Perspect Med. 2018;8(7):a029694.
22. Lavie CJ, Ozemek C, Carbone S, Katzmarzyk PT, Blair SN. Sedentary behavior, exercise, and cardiovascular health. Circ Res. 2019;124(5):799-815.
23. Booth FW, Roberts CK, Laye MJ. Lack of exercise is a major cause of chronic diseases. Compr Physiol. 2012;2(2):1143-211.
24. Nieman DC, Wentz LM. The compelling link between physical activity and the body's defense system. J Sport Health Sci. 2019;8(3):201-17.
25. Nieman DC, Pence BD. Exercise immunology: future directions. J Sport Health Sci. 2020;9(5):432-45.

26. Sallis R, Young DR, Tartof SY, Sallis JF, Sall J, Li Q, et al. Physical inactivity is associated with a higher risk for severe COVID-19 outcomes: a study in 48 440 adult patients. Br J Sports Med. 2021;55(19):1099-105.
27. Williams N, Radia T, Harman K, Agrawal P, Cook J, Gupta A. COVID-19 Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children and adolescents: a systematic review of critically unwell children and the association with underlying comorbidities. Eur J Pediatr. 2021;180(3):689-97.
28. Fernandes DM, Oliveira CR, Guerguis S, Eisenberg R, Choi J, Kim M, et al. Severe acute respiratory syndrome coronavirus 2 clinical syndromes and predictors of disease severity in hospitalized children and youth. J Pediatr. 2021;230:23-31 e10.
29. Gao YD, Ding M, Dong X, Zhang JJ, Kursat Azkur A, Azkur D, et al. Risk factors for severe and critically ill COVID-19 patients: a review. Allergy. 2021;76(2):428-55.
30. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.
31. Yomoda K, Kurita S. Influence of social distancing during the COVID-19 pandemic on physical activity in children: a scoping review of the literature. J Exerc Sci Fit. 2021;19(3):195-203.
32. National Heart, Lung, Institute aB. Study quality assessment tools. Available from: https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools. Last updated Jul 2021; cited Jul 3, 2024.
33. Alonso-Martinez AM, Ramirez-Velez R, Garcia-Alonso Y, Izquierdo M, Garcia-Hermoso A. Physical activity, sedentary behavior, sleep and self-regulation in spanish preschoolers during the COVID-19 lockdown. Int J Environ Res Public Health. 2021;18(2):693.
34. Androutsos O, Perperidi M, Georgiou C, Chouliaras G. Lifestyle changes and determinants of children's and adolescents' body weight increase during the first COVID-19 lockdown in Greece: the COV-EAT study. Nutrients. 2021;13(3):930.
35. Cachon-Zagalaz J, Zagalaz-Sanchez Mf, Arufe-Giraldez V, Sanmiguel-Rodriguez A, Gonzalez-Valero G. Physical activity and daily routine among children aged 0-12 during the COVID-19 pandemic in Spain. Int J Environ Res Public Health. 2021;18(2):703.
36. Chambonniere C, Lambert C, Fearnbach N, Tardieu M, Fillon A, Genin P, et al. Effect of the COVID-19 lockdown on physical activity and sedentary behaviors in French children and adolescents: new results from the ONAPS national survey. Eur J Integr Med. 2021;43:101308.
37. Delisle Nystrom C, Alexandrou C, Henstrom M, Nilsson E, Okely AD, Wehbe El Masri S, et al. International study of movement behaviors in the early years (SUNRISE): results from SUNRISE Sweden's pilot and COVID-19 study. Int J Environ Res Public Health. 2020;17(22):8491.
38. Gilic B, Ostojic L, Corluka M, Volaric T, Sekulic D. Contextualizing parental/familial influence on physical activity in adolescents before and during COVID-19 pandemic: a prospective analysis. Children (Basel). 2020;7(9):125.
39. Gilic B, Zenic N, Separovic V, Jurcev Savicevic A, Sekulic D. Evidencing the influence of pre-pandemic sports participation and substance misuse on physical activity during the COVID-19 lockdown: a prospective analysis among older adolescents. Int J Occup Med Environ Health. 2021;34(2):151-63.
40. Sekulic D, Blazevic M, Gilic B, Kvesic I, Zenic N. Prospective analysis of levels and correlates of physical activity during COVID-19 pandemic and imposed rules of social distancing; gender specific study among adolescents from southern Croatia. Sustainability. 2020;12(10):4072.
41. Zenic N, Taiar R, Gilic B, Blazevic M, Maric D, Pojskic H, et al. Levels and changes of physical activity in adolescents during the COVID-19 pandemic: contextualizing urban vs. rural living environment. Applied Sciences. 2020;10(11):3997.
42. Francisco R, Pedro M, Delvecchio E, Espada JP, Morales A, Mazzeschi C, et al. Psychological symptoms and behavioral changes in children and adolescents during the early phase of COVID-19 quarantine in three European countries. Front Psychiatry. 2020;11:570164.
43. Hommes F, van Loon W, Thielecke M, Abramovich I, Lieber S, Hammerich R, et al. SARS-CoV-2 infection, risk perception, behaviour and preventive measures at schools in Berlin, Germany, during the early post-lockdown phase: a cross-sectional study. Int J Environ Res Public Health. 2021;18(5):2739.
44. Konstantinou C, Andrianou XD, Constantinou A, Perikkou A, Markidou E, Christophi CA, et al. Exposome changes in primary school children following the wide population non-pharmacological interventions implemented due to COVID-19 in Cyprus: a national survey. EClinicalMedicine. 2021;32:100721.
45. Kovacs VA, Starc G, Brandes M, Kaj M, Blagus R, Leskosek B, et al. Physical activity, screen time and the COVID-19 school closures in Europe - an observational study in 10 countries. Eur J Sport Sci. 2022;22(7):1094-103.
46. Lopez-Bueno R, Calatayud J, Andersen LL, Casana J, Ezzatvar Y, Casajus JA, et al. Cardiorespiratory fitness in adolescents before and after the COVID-19 confinement: a prospective cohort study. Eur J Pediatr. 2021;180(7):2287-93.
47. Lopez-Bueno R, Lopez-Sanchez GF, Casajus JA, Calatayud J, Gil-Salmeron A, Grabovac I, et al. Health-related behaviors among school-aged children and adolescents during the Spanish Covid-19 confinement. Front Pediatr. 2020;8:573.
48. Medrano M, Cadenas-Sanchez C, Oses M, Arenaza L, Amasene M, Labayen I. Changes in lifestyle behaviours during the COVID-19 confinement in Spanish children: a longitudinal analysis from the MUGI project. Pediatr Obes. 2021;16(4):e12731.
49. Lopez-Gil JF, Tremblay MS, Brazo-Sayavera J. Changes in healthy behaviors and meeting 24-h movement guidelines in Spanish and Brazilian preschoolers, children and adolescents during the COVID-19 lockdown. Children (Basel). 2021;8(2):83.
50. Morgul E, Kallitsoglou A, Essau CA. Psychological effects of the COVID-19 lockdown on children and families in the UK. Revista de Psicologia Clinica con Ninos y Adolescentes. 2020;7(3):42-8.
51. Poulain T, Meigen C, Sobek C, Ober P, Igel U, Korner A, et al. Loss of childcare and classroom teaching during the Covid-19-related lockdown in spring 2020: a longitudinal study on consequences on leisure behavior and schoolwork at home. PLoS One. 2021;16(3):e0247949.
52. Ng K, Cooper J, McHale F, Clifford J, Woods C. Barriers and facilitators to changes in adolescent physical activity during COVID-19. BMJ Open Sport Exerc Med. 2020;6(1):e000919.
53. Orgiles M, Morales A, Delvecchio E, Mazzeschi C, Espada JP. Immediate psychological effects of the COVID-19 quarantine in youth from Italy and Spain. Front Psychol. 2020;11:579038.
54. Pietrobelli A, Pecoraro L, Ferruzzi A, Heo M, Faith M, Zoller T, et al. Effects of COVID-19 lockdown on lifestyle behaviors in children with obesity living in Verona, Italy: a longitudinal study. Obesity (Silver Spring). 2020;28(8):1382-5.
55. Pombo A, Luz C, Rodrigues LP, Ferreira C, Cordovil R. Correlates of children's physical activity during the COVID-19 confinement in Portugal. Public Health. 2020;189:14-9.
56. Predieri B, Leo F, Candia F, Lucaccioni L, Madeo SF, Pugliese M, et al. Glycemic control improvement in Italian children and adolescents with type 1 diabetes followed through telemedicine during lockdown due to the COVID-19 pandemic. Front Endocrinol (Lausanne). 2020;11:595735.
57. Roe A, Blikstad-Balas M, Dalland CP. The impact of COVID-19 and homeschooling on students' engagement with physical activity. Front Sports Act Living. 2020;2:589227.
58. Ruiz-Roso MB, de Carvalho Padilha P, Matilla-Escalante DC, Brun P, Ulloa N, Acevedo-Correa D, et al. Changes of physical activity and ultra-processed food consumption in adolescents from different countries during Covid-19 pandemic: an observational study. Nutrients. 2020;12(8):2289.
59. Schmidt SCE, Anedda B, Burchartz A, Eichsteller A, Kolb S, Nigg C, et al. Physical activity and screen time of children and adolescents before and during the COVID-19 lockdown in Germany: a natural experiment. Sci Rep. 2020;10(1):21780.

60. Schmidt T, Pawlowski CS. Physical activity in crisis: the impact of COVID-19 on Danes' physical activity behavior. Front Sports Act Living. 2020;2:610255.
61. Salzano G, Passanisi S, Pira F, Sorrenti L, La Monica G, Pajno GB, et al. Quarantine due to the COVID-19 pandemic from the perspective of adolescents: the crucial role of technology. Ital J Pediatr. 2021;47(1):40.
62. Ten Velde G, Lubrecht J, Arayess L, van Loo C, Hesselink M, Reijnders D, et al. Physical activity behaviour and screen time in Dutch children during the COVID-19 pandemic: pre-, during- and post-school closures. Pediatr Obes. 2021;16(9):e12779.
63. Theis N, Campbell N, De Leeuw J, Owen M, Schenke KC. The effects of COVID-19 restrictions on physical activity and mental health of children and young adults with physical and/or intellectual disabilities. Disabil Health J. 2021;14(3):101064.
64. Tornaghi M, Lovecchio N, Vandoni M, Chirico A, Codella R. Physical activity levels across COVID-19 outbreak in youngsters of Northwestern Lombardy. J Sports Med Phys Fitness. 2021;61(7):971-6.
65. Wunsch K, Nigg C, Niessner C, Schmidt SCE, Oriwol D, Hanssen-Doose A, et al. The impact of COVID-19 on the interrelation of physical activity, screen time and health-related quality of life in children and adolescents in Germany: results of the Motorik-Modul study. Children (Basel). 2021;8(2):98.
66. Zorcec T, Jakovska T, Micevska V, Boskovska K, Cholakovska VC. Pandemic with COVID-19 and families with children with chronic respiratory diseases. Pril (Makedon Akad Nauk Umet Odd Med Nauki). 2020;41(2):95-101.
67. Carroll N, Sadowski A, Laila A, Hruska V, Nixon M, Ma DWL, et al. The impact of COVID-19 on health behavior, stress, financial and food security among middle to high income Canadian families with young children. Nutrients. 2020;12(8):2352.
68. Ellis WE, Dumas TM, Forbes LM. Physically isolated but socially connected: psychological adjustment and stress among adolescents during the initial COVID-19 crisis. Can J Behav Sci. 2020;52(3):177-87.
69. Guerrero MD, Vanderloo LM, Rhodes RE, Faulkner G, Moore SA, Tremblay MS. Canadian children's and youth's adherence to the 24-h movement guidelines during the COVID-19 pandemic: a decision tree analysis. J Sport Health Sci. 2020;9(4):313-21.
70. Hemphill NM, Kuan MTY, Harris KC. Reduced physical activity during COVID-19 pandemic in children with congenital heart disease. Can J Cardiol. 2020;36(7):1130-4.
71. McCormack GR, Doyle-Baker PK, Petersen JA, Ghoneim D. Parent anxiety and perceptions of their child's physical activity and sedentary behaviour during the COVID-19 pandemic in Canada. Prev Med Rep. 2020;20:101275.
72. Mitra R, Moore SA, Gillespie M, Faulkner G, Vanderloo LM, Chulak-Bozzer T, et al. Healthy movement behaviours in children and youth during the COVID-19 pandemic: exploring the role of the neighbourhood environment. Health Place. 2020;65:102418.
73. Moore SA, Faulkner G, Rhodes RE, Brussoni M, Chulak-Bozzer T, Ferguson LJ, et al. Impact of the COVID-19 virus outbreak on movement and play behaviours of Canadian children and youth: a national survey. Int J Behav Nutr Phys Act. 2020;17(1):85.
74. Bazett-Jones DM, Garcia MC, Taylor-Haas JA, Long JT, Rauh MJ, Paterno MV, et al. Impact of COVID-19 social distancing restrictions on training habits, injury, and care seeking behavior in youth long-distance runners. Front Sports Act Living. 2020;2:586141.
75. Dunton GF, Do B, Wang SD. Early effects of the COVID-19 pandemic on physical activity and sedentary behavior in children living in the U.S. BMC Public Health. 2020;20(1):1351.
76. Garcia JM, Lawrence S, Brazendale K, Leahy N, Fukuda D. Brief report: The impact of the COVID-19 pandemic on health behaviors in adolescents with autism spectrum disorder. Disabil Health J. 2021;14(2):101021.
77. McGuine TA, Biese KM, Petrovska L, Hetzel SJ, Reardon C, Kliethermes S, et al. Mental health, physical activity, and quality of life of US adolescent athletes during COVID-19-related school closures and sport cancellations: a study of 13 000 athletes. J Athl Train. 2021;56(1):11-9.
78. Pavlovic A, DeFina LF, Natale BL, Thiele SE, Walker TJ, Craig DW, et al. Keeping children healthy during and after COVID-19 pandemic: meeting youth physical activity needs. BMC Public Health. 2021;21(1):485.
79. Tulchin-Francis K, Stevens W, Jr., Gu X, Zhang T, Roberts H, Keller J, et al. The impact of the coronavirus disease 2019 pandemic on physical activity in U.S. children. J Sport Health Sci. 2021;10(3):323-32.
80. de Matos DG, Aidar FJ, Almeida-Neto PFd, Moreira OC, Souza RFd, Marçal AC, et al. The impact of measures recommended by the government to limit the spread of coronavirus (COVID-19) on physical activity levels, quality of life, and mental health of Brazilians. Sustainability. 2020;12(21):9072.
81. Sa C, Pombo A, Luz C, Rodrigues LP, Cordovil R. Covid-19 social isolation in Brazil: effects on the physical activity routine of families with children. Rev Paul Pediatr. 2020;39:e2020159.
82. Siegle CBH, Pombo A, Luz C, Rodrigues LP, Cordovil R, Sa C. Influences of family and household characteristics on children's level of physical activity during social distancing due to Covid-19 in Brazil. Rev Paul Pediatr. 2020;39:e2020297.
83. Aguilar-Farias N, Toledo-Vargas M, Miranda-Marquez S, Cortinez-O'Ryan A, Cristi-Montero C, Rodriguez-Rodriguez F, et al. Sociodemographic predictors of changes in physical activity, screen time, and sleep among toddlers and preschoolers in Chile during the COVID-19 pandemic. Int J Environ Res Public Health. 2020;18(1):176.
84. Reece LJ, Owen K, Foley B, Rose C, Bellew B, Bauman A. Understanding the impact of COVID-19 on children's physical activity levels in NSW, Australia. Health Promot J Austr. 2021;32(2):365-6.
85. Cahal M, Amirav I, Diamant N, Be'er M, Besor O, Lavie M. Real-time effects of COVID-19 pandemic lockdown on pediatric respiratory patients. Pediatr Pulmonol. 2021;56(6):1401-8.
86. Chaturvedi K, Vishwakarma DK, Singh N. COVID-19 and its impact on education, social life and mental health of students: a survey. Child Youth Serv Rev. 2021;121:105866.
87. Ghanamah R, Eghbaria-Ghanamah H. Impact of COVID-19 pandemic on behavioral and emotional aspects and daily routines of Arab Israeli children. Int J Environ Res Public Health. 2021;18(6):2946.
88. Masi A, Mendoza Diaz A, Tully L, Azim SI, Woolfenden S, Efron D, et al. Impact of the COVID-19 pandemic on the well-being of children with neurodevelopmental disabilities and their parents. J Paediatr Child Health. 2021;57(5):631-6.
89. Munasinghe S, Sperandei S, Freebairn L, Conroy E, Jani H, Marjanovic S, et al. The impact of physical distancing policies during the COVID-19 pandemic on health and well-being among Australian adolescents. J Adolesc Health. 2020;67(5):653-61.
90. Nathan A, George P, Ng M, Wenden E, Bai P, Phiri Z, et al. Impact of COVID-19 restrictions on Western Australian children's physical activity and screen time. Int J Environ Res Public Health. 2021;18(5):2583.
91. Parker K, Uddin R, Ridgers ND, Brown H, Veitch J, Salmon J, et al. The use of digital platforms for adults' and adolescents' physical activity during the COVID-19 pandemic (Our Life at Home): survey study. J Med Internet Res. 2021;23(2):e23389.
92. Sciberras E, Patel P, Stokes MA, Coghill D, Middeldorp CM, Bellgrove MA, et al. Physical health, media use, and mental health in children and adolescents with ADHD during the COVID-19 pandemic in Australia. J Atten Disord. 2022;26(4):549-62.
93. Zhao Y, Guo Y, Xiao Y, Zhu R, Sun W, Huang W, et al. The effects of online homeschooling on children, parents, and teachers of grades 1-9 during the COVID-19 pandemic. Med Sci Monit. 2020;26:e925591.
94. World Health Organization. Adolescent health. Available from: https://www.who.int/health-topics/adolescent-health. Last updated Jun 10, 2024; cited Jul 3, 2024.
95. Wu X, Luo S, Zheng X, Ding Y, Wang S, Ling P, et al. Glycemic control in children and teenagers with type 1 diabetes around lockdown for COVID-19: a continuous glucose monitoring-based observational study. J Diabetes Investig. 2021;12(9):1708-17.
96. Zhang X, Zhu W, Kang S, Qiu L, Lu Z, Sun Y. Association between physical activity and mood states of children and adolescents in social isolation

during the COVID-19 epidemic. Int J Environ Res Public Health. 2020;17(20):7666.

97. Abid R, Ammar A, Maaloul R, Souissi N, Hammouda O. Effect of COVID-19-related home confinement on sleep quality, screen time and physical activity in Tunisian boys and girls: a survey. Int J Environ Res Public Health. 2021;18(6):3065.
98. Shinomiya Y, Yoshizaki A, Murata E, Fujisawa TX, Taniike M, Mohri I. Sleep and the general behavior of infants and parents during the closure of schools as a result of the COVID-19 pandemic: comparison with 2019 data. Children (Basel). 2021;8(2):168.
99. Xiang M, Zhang Z, Kuwahara K. Impact of COVID-19 pandemic on children and adolescents' lifestyle behavior larger than expected. Prog Cardiovasc Dis. 2020;63(4):531-2.
100. Yang S, Guo B, Ao L, Yang C, Zhang L, Zhou J, et al. Obesity and activity patterns before and during COVID-19 lockdown among youths in China. Clin Obes. 2020;10(6):e12416.
101. Elnaggar RK, Alqahtani BA, Mahmoud WS, Elfakharany MS. Physical activity in adolescents during the social distancing policies of the COVID-19 pandemic. Asia Pac J Public Health. 2020;32(8):491-4.
102. Jia P, Zhang L, Yu W, Yu B, Liu M, Zhang D, et al. Impact of COVID-19 lockdown on activity patterns and weight status among youths in China: the COVID-19 Impact on Lifestyle Change Survey (COINLICS). Int J Obes (Lond). 2021;45(3):695-9.
103. Prince SA, Butler GP, Rao DP, Thompson W. Evidence synthesis - where are children and adults physically active and sedentary? - A rapid review of location-based studies. Health Promot Chronic Dis Prev Can. 2019;39(3):67-103.
104. Kelso A, Reimers AK, Abu-Omar K, Wunsch K, Niessner C, Wasche H, et al. Locations of physical activity: where are children, adolescents, and adults physically active? A systematic review. Int J Environ Res Public Health. 2021;18(3):1240.
105. Weaver RG, Beets MW, Perry M, Hunt E, Brazendale K, Decker L, et al. Changes in children's sleep and physical activity during a 1-week versus a 3-week break from school: a natural experiment. Sleep. 2019;42(1):zsy205.
106. Marzi I, Demetriou Y, Reimers AK. Social and physical environmental correlates of independent mobility in children: a systematic review taking sex/gender differences into account. Int J Health Geogr. 2018;17(1):24.
107. Steene-Johannessen J, Hansen BH, Dalene KE, Kolle E, Northstone K, Moller NC, et al. Variations in accelerometry measured physical activity and sedentary time across Europe - harmonized analyses of 47,497 children and adolescents. Int J Behav Nutr Phys Act. 2020;17(1):38.
108. D'Angelo H, Fowler SL, Nebeling LC, Oh AY. Adolescent physical activity: moderation of individual factors by neighborhood environment. Am J Prev Med. 2017;52(6):888-94.
109. Alharbi M. Influence of individual and family factors on physical activity among Saudi girls: a cross-sectional study. Ann Saudi Med. 2019;39(1):13-21.
110. Lu C, Stolk RP, Sauer PJ, Sijtsma A, Wiersma R, Huang G, et al. Factors of physical activity among Chinese children and adolescents: a systematic review. Int J Behav Nutr Phys Act. 2017;14(1):36.
111. Reimers AK, Schmidt SCE, Demetriou Y, Marzi I, Woll A. Parental and peer support and modelling in relation to domain-specific physical activity participation in boys and girls from Germany. PLoS One. 2019;14(10):e0223928.
112. Best K, Ball K, Zarnowiecki D, Stanley R, Dollman J. In search of consistent predictors of children's physical activity. Int J Environ Res Public Health. 2017;14(10):1258.
113. Dishman RK, McIver KL, Dowda M, Saunders RP, Pate RR. Self-efficacy, beliefs, and goals: moderation of declining physical activity during adolescence. Health Psychol. 2019;38(6):483-93.
114. Burns RD, Bai Y, Fu Y, Pfledderer CD, Brusseau TA. Parent engagement and support, physical activity, and academic performance (PESPAAP): a proposed theoretical model. Int J Environ Res Public Health. 2019;16(23):4698.
115. Khan SR, Uddin R, Mandic S, Khan A. Parental and peer support are associated with physical activity in adolescents: evidence from 74 countries. Int J Environ Res Public Health. 2020;17(12):4435.
116. Haidar A, Ranjit N, Archer N, Hoelscher DM. Parental and peer social support is associated with healthier physical activity behaviors in adolescents: a cross-sectional analysis of Texas School Physical Activity and Nutrition (TX SPAN) data. BMC Public Health. 2019;19(1):640.
117. Cooper AR, Goodman A, Page AS, Sherar LB, Esliger DW, van Sluijs EM, et al. Objectively measured physical activity and sedentary time in youth: the International Children's Accelerometry Database (ICAD). Int J Behav Nutr Phys Act. 2015;12:113.
118. Craggs C, Corder K, van Sluijs EM, Griffin SJ. Determinants of change in physical activity in children and adolescents: a systematic review. Am J Prev Med. 2011;40(6):645-58.
119. Hu D, Zhou S, Crowley-McHattan ZJ, Liu Z. Factors that influence participation in physical activity in school-aged children and adolescents: a systematic review from the social ecological model perspective. Int J Environ Res Public Health. 2021;18(6):3147.
120. Corder K, Sharp SJ, Atkin AJ, Griffin SJ, Jones AP, Ekelund U, et al. Change in objectively measured physical activity during the transition to adolescence. Br J Sports Med. 2015;49(11):730-6.
121. Pate RR, Sallis JF, Ward DS, Stevens J, Dowda M, Welk GJ, et al. Age-related changes in types and contexts of physical activity in middle school girls. Am J Prev Med. 2010;39(5):433-9.
122. Rhodes RE, Guerrero MD, Vanderloo LM, Barbeau K, Birken CS, Chaput JP, et al. Development of a consensus statement on the role of the family in the physical activity, sedentary, and sleep behaviours of children and youth. Int J Behav Nutr Phys Act. 2020;17(1):74.
123. Edwards MJ, Jago R, Sebire SJ, Kesten JM, Pool L, Thompson JL. The influence of friends and siblings on the physical activity and screen viewing behaviours of children aged 5-6 years: a qualitative analysis of parent interviews. BMJ Open. 2015;5(5):e006593.
124. Loebach J, Sanches M, Jaffe J, Elton-Marshall T. Paving the way for outdoor play: examining socio-environmental barriers to community-based outdoor play. Int J Environ Res Public Health. 2021;18(7):3617.
125. Euler R, Jimenez EY, Sanders S, Kuhlemeier A, Van Horn ML, Cohen D, et al. Rural-urban differences in baseline dietary intake and physical activity levels of adolescents. Prev Chronic Dis. 2019;16:E01.
126. Rivera-Ochoa M, Brazo-Sayavera J, Vizmanos-Lamotte B, Manas A, Lopez-Taylor JR, Gonzalez-Gross M, et al. Health-related factors in rural and urban Mexican adolescents from the State of Jalisco: the HELENA-MEX study. Int J Environ Res Public Health. 2020;17(23):8959.
127. Adebusoye B, Phalkey R, Leonardi-Bee J, Chattopadhyay K. Association of the built environment with physical activity in children and adolescents in Africa: a systematic review protocol. JBI Evid Synth. 2020;18(3):553-63.
128. Gray C, Gibbons R, Larouche R, Sandseter EB, Bienenstock A, Brussoni M, et al. What is the relationship between outdoor time and physical activity, sedentary behaviour, and physical fitness in children? A systematic review. Int J Environ Res Public Health. 2015;12(6):6455-74.
129. Larouche R, Garriguet D, Gunnell KE, Goldfield GS, Tremblay MS. Outdoor time, physical activity, sedentary time, and health indicators at ages 7 to 14: 2012/2013 Canadian Health Measures Survey. Health Rep. 2016;27(9):3-13.
130. Lindsay AC, Greaney ML, Wallington SF, Mesa T, Salas CF. A review of early influences on physical activity and sedentary behaviors of preschool-age children in high-income countries. J Spec Pediatr Nurs. 2017;22(3):e12182.
131. Christiana RW, Bouldin ED, Battista RA. Active living environments mediate rural and non-rural differences in physical activity, active transportation, and screen time among adolescents. Prev Med Rep. 2021;23:101422.
132. Okazaki K, Suzuki K, Sakamoto Y, Sasaki K. Physical activity and sedentary behavior among children and adolescents living in an area affected by the 2011 Great East Japan earthquake and tsunami for 3 years. Prev Med Rep. 2015;2:720-4.

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Literature search results for Systematic Review on Covid-19 and Physical Activity in Children, 2020-present, English

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Embase Results: 263

(('exercise'/exp/mj OR 'sedentary lifestyle'/de OR 'physical activity'/exp OR 'play'/exp OR 'sport'/exp/mj OR 'screen time'/de OR 'physical inactivity'/exp OR 'sitting'/de OR 'sedentary time'/de OR 'youth sport'/de) OR ('fitness':ti,ab OR 'sedentary':ti,ab OR 'screen time':ti,ab OR 'screen use':ti,ab) OR (physical NEAR/2 (activit* OR inactivity)):ti,ab) AND ('juvenile'/mj OR 'boy'/mj OR 'girl'/mj OR 'child'/mj OR 'preschool child'/mj OR 'school child'/mj OR 'adolescent'/exp/mj OR 'minor (person)'/exp/mj OR 'adolescence'/exp/mj OR 'childhood'/exp/mj OR boy:ti,ab OR boys:ti,ab OR boyfriend:ti,ab OR boyhood:ti,ab OR girl*:ti,ab OR kid:ti,ab OR kids:ti,ab OR child:ti,ab OR child*:ti,ab OR children*:ti,ab OR schoolchild*:ti,ab OR schoolchild:ti,ab OR 'school child':ti,ab OR 'school child*':ti,ab OR adolescen*:ti,ab OR juvenil*:ti,ab OR youth*:ti,ab OR teen*:ti,ab OR under*age*:ti,ab OR pubescen*:ti,ab) AND ('coronavirus disease 2019'/exp OR 'severe acute respiratory syndrome coronavirus 2'/exp OR 'severe acute respiratory syndrome coronavirus 2' OR '2019 ncov' OR 2019ncov OR 'covid-19' OR '2019-ncov' OR 'sars-cov-2' OR '2019ncov' OR 'novel coronavirus') AND [english]/lim AND [2020-2021]/py 263

PsycInfo: 39

APA PsycInfo <2002 to March Week 4 2021>

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limit 9 to (english language and yr="2020 -Current") 39

CINAHL: 168

S9 S4 AND S5 AND S6 Limiters - Published Date: 20200101-20211231
Narrow by Language: - English 168

S8 S4 AND S5 AND S6 Limiters - Published Date: 20200101-20211231 168

S7 S4 AND S5 AND S6 179

S6 (MH "COVID-19") OR (MH "Coronavirus Infections+") OR (MH "Coronavirus+") OR (TX 'severe acute respiratory syndrome coronavirus 2' or '2019 ncov' or 2019ncov or 'covid-19' or '2019-ncov' or 'sars-cov-2' or '2019ncov' or 'novel coronavirus') 48,402

S5 (MH "Hospitals, Pediatric") OR (MH "Adolescence+") OR (MH "Maternal Age 14 and Under") OR (MH "Child, Preschool") OR (MH "Child Psychology") OR (MH "Pediatric Units") OR (MH "Intensive Care Units, Pediatric") OR (MH "Rehabilitation, Pediatric") OR (TX minors or minors* or boy or boys or boyfriend or boyhood or girl* or kid or kids or child or child* or children* or schoolchild* or schoolchild or school child or school child* or adolescen* or juvenil* or youth* or teen* or under*age* or pubescen* or pediatric* or paediatric* or peadiatric*) 1,237,921

S4 S1 OR S2 OR S3 380,492

S3 TX exercise or exercises or sedentary or "screen time" or "screen use" or fitness or "physical activity" or "physical inactivity" 302,701

S2 (MH "Life Style, Sedentary+") 8,845

S1 (MH "Physical Activity") OR (MH "Physical Fitness+") OR (MH "Exercise+") OR (MH "Dancing+") OR (MH "Play and Playthings+") OR (MH "Sports+") OR (MH "Life Style, Sedentary") OR (MH "Screen Time") 242,545

Web of Science: 168

TS=("severe acute respiratory syndrome coronavirus 2" or "2019 ncov" or 2019ncov or "covid-19" or "2019-ncov" or "sars-cov-2" or "2019ncov" or "novel coronavirus")

AND

TS=(minors or minors* or boy or boys or boyfriend or boyhood or girl* or kid or kids or child or child* or children* or schoolchild* or schoolchild or school child or school child* or adolescen* or juvenil* or youth* or teen* or under*age* or pubescen* or pediatric* or paediatric* or peadiatric*)

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TS=(exercise OR sedentary OR "physical activity" OR "physical inactivity" OR "activity level" OR sports OR "screen time" OR "screen use" OR fitness)

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IJMS INTERNATIONAL JOURNAL of MEDICAL STUDENTS

Case Report

Case Report: An Atypical Sellar Mass - Sellar Tuberculoma in a Young Patient

Arwa Moiz Jamali,[1] Rakeshkumar Luhana.[2]

Abstract

Background: Tuberculosis of the central nervous system is an uncommon but one of the most severe forms. It manifests as tuberculoma and tuberculous meningitis, with the majority of cases affecting children and immunocompromised patients. Overall, tuberculomas make up to 0.15–2 % of all intracranial lesions but sellar tuberculoma is extremely rare. **The Case:** An 18-year-old female patient presented with complaint of generalized weakness, eye pain and headache for 3-4 months. Magnetic resonance imaging (MRI) of brain showed sellar and suprasellar space occupying lesion. Trans sphenoidal approach was used to remove the lesion completely. A sellar tuberculoma was confirmed on pathological evaluation and the patient was put on postoperative anti-tubercular therapy. **Conclusion:** Although rare, intracranial tuberculomas, particularly those that originate in the sellar, are notorious for mimicking pituitary tumors by jeopardizing pituitary hormonal function and applying compressive forces on surrounding intracranial structures. However, a prompt assessment can help overcome this diagnostic difficulty with the timely initiation of anti-tubercular therapy (ATT).

Introduction

Worldwide tuberculosis(TB) is amongst the most lethal infectious diseases. In 2021, it was predicted that 10.6 million people worldwide would contract TB. More than two thirds of all cases of TB worldwide were found in eight countries highest being in India (28%).[1] Although TB is primarily a respiratory tract disease, 1% of cases also impact the central nervous system (CNS). These cases are the most severe form of the disease and have the greatest rates of morbidity and mortality.[2]

The most prevalent form of CNS TB is tuberculous meningitis, however in <5% of cases, TB of the CNS can manifest as a granulomatous mass lesion known as a tuberculoma.[3] Before the advent of chemotherapy, 30–50% of space occupying lesions(SOL) in both adults and children were tuberculomas.[4] The prevalence of intracranial tuberculomas has decreased as a result of chemotherapeutic drugs and improvements in socioeconomic situations. However, they still account for 0.15–4% of intracranial lesions, and the majority of the affected are individuals from low- and middle-income nations.[5,6]

Intracranial tuberculomas are usually found in the cerebellum and cerebral cortex, however they have also been reported in the thalamus, cerebello-pontine angle, brainstem, basal ganglion, pineal region, optic pathways, in the ventricles, and the aqueduct. Of this isolated sellar tuberculoma is quite uncommon.

This type of tuberculoma is characterized by growth of tuberculous lesion affecting the sellar region of the brain which houses the pituitary gland. Its clinical importance lies in its potential to cause a range of neurological and endocrine symptoms due to its proximity to the pituitary gland and optic pathways.

Highlights:

- This case involved a sellar tuberculoma, an extremely rare condition. Only 106 cases have been documented worldwide between 1924 and 2019, with 51 reported from India.
- Sellar tuberculomas often present with symptoms resembling other sellar region lesions, requiring careful attention in the diagnostic process.
- Early initiation of multidrug antitubercular therapy (ATT) and hormonal replacement therapy leads to favorable clinical outcomes.

As a result, understanding the presentation and diagnosis of sellar tuberculomas is crucial for providing timely and effective medical and surgical management. Given the limited existing literature on it, by delving into these aspects ,this case report aims to contribute valuable insights that can enrich the existing knowledge base surrounding this rare manifestation, ultimately fostering a better understanding of its nature and optimal approaches for addressing it.

The Case

An 18-year-old female patient presented to outpatient department with chief complaints of headache, eye pain and

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generalized weakness with an onset of 3-4 months. She denied any history of fever, cough, weight loss, or anorexia. There was no history of any known TB exposure, no notable comorbid conditions or pertinent social factors. No previous history of medication use was noted except analgesics. On examination, the patient was alert and fully oriented to time, place, and person. Vital signs were stable, with a pulse rate of 82 beats per minute, blood pressure of 110/80 mmHg, oxygen saturation (SpO2) of 98%, and body temperature of 98.6°F. No neurological deficits or abnormalities in other systems were noted during examination. On investigations low levels of T3, T4, TSH were found (*Table 1*). Magnetic resonance imaging (MRI) revealed a sellar and suprasellar space-occupying lesion measuring 1.4 × 1.9 × 1.0 cm (*Figure 1*).

On assessing the hormone profile hypopituitarism was noted (*Table 2*). After proper preoperative workup, endoscopic transnasal transsphenoidal approach with sellar and suprasellar space occupying lesion excision and sellar floor reconstruction with fat graft under general anesthesia was carried out (*Figure 2*). Intra operative and post operative period was uneventful. Post operative strict input output, thyroid profile and sodium were monitored to evaluate the function of the pituitary hormones. As the lesion was surgically removed the pressure on surrounding structures, such as the optic nerves and pituitary gland diminished leading to reduced intensity and frequency of patient's headache and gradually its resolution. Eye pain and weakness also improved gradually, and patient was vitally stable. Histopathology of the lesion revealed caseating granuloma. Ziehl Neelsen staining demonstrated acid-fast bacilli most likely tuberculoma. The patient was prescribed rifampicin (450 mg), isoniazid (300 mg), ethambutol (800 mg), and pyrazinamide (750mg) for 1 year (3 months intensive phase and 9 months continuation phase) and also prednisolone and thyroxine to address the endocrinological deficits. Regular monitoring and administration of prednisolone and thyroxine stabilized hormone levels.

Discussion

Pituitary adenomas are the most common lesions of the sellar region, but it is important to consider atypical non-adenohypophyseal lesions, including inflammatory and infectious conditions into account when making a sellar mass differential diagnosis. TB (tuberculoma) should be considered particularly in India. Sellar tuberculomas are fairly uncommon pathology.[7] From 1924-2019, 106 cases could be retrieved from the literature worldwide, out of which 51 cases were reported from India.[8]

Tuberculomas usually occur as part of a systemic infection, following hematogenous spread; however isolated lesions have been reported. In our case there was no evidence of systemic or primary active TB based on the patient's history and appropriate investigations. Also, patient's medical history revealed no prior diagnosis of immune compromise like HIV or immunosuppressive medications which are potential risk factor for this condition. In patients, headache is the most common symptom occurring earlier and is accompanied by visual disturbances. Variable levels of

Figure 1. **MRI Brain Coronal Study Showing Sellar Mass with Suprasellar Extension Causing Optic Chiasm Compression.**

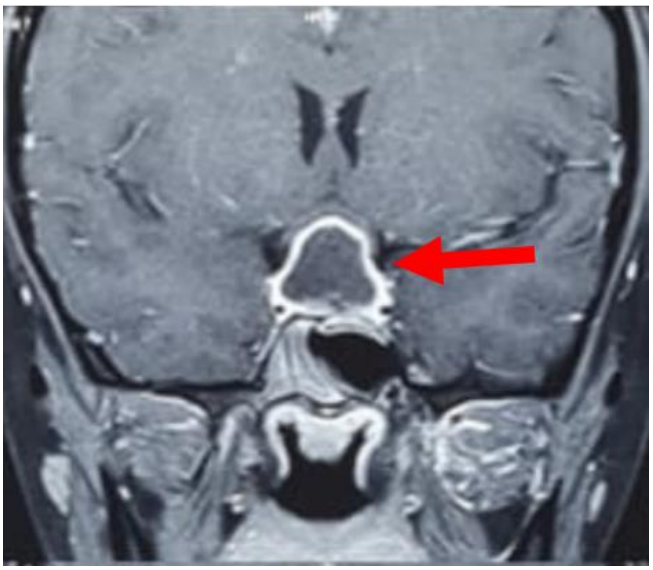

Figure 2. **MRI Showing Postoperative Sellar Floor Reconstruction with Fat Graft.**

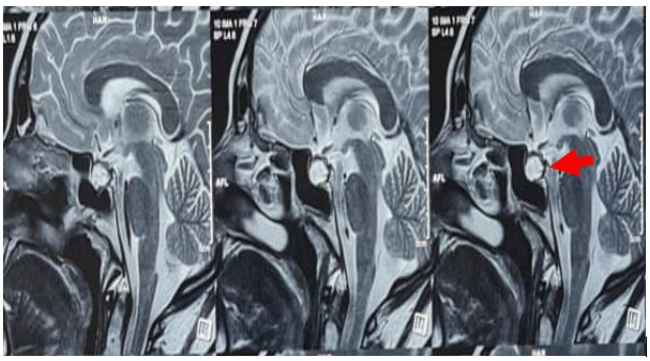

Table 1. **Complete Laboratory Profile of an 18-Year-Old Female with Sellar Tuberculoma.**

Investigations	Patient Values	Normal Ranges
Hemoglobin	12.40 g/dl	12.1–15.1 g/dL (females) and 13.8–17.2 g/dL (males)
Total leucocyte count	7860/µL	4000 to 11000/microliter
Platelet count	3.13 lakh/µL	150,000 to 450,000/µL
Random Blood Sugar	89 mg/dl	70 to 140 mg/dL
Serum creatinine	0.77 mg/dL.	0.6 to 1.2 mg/dL.
T3	1.2 ng/mL	0.8-2.0 ng/ml
T4	6 ng/dL	0.8 ng/dL to 1.8 ng/dL
TSH	0.13 microU/mL	0.4 to 4.0 microU/mL
HIV, HCV, HBSAG	Negative	

***Table 2*. Hormonal Profile of an 18-Year-Old Female with Sellar Tuberculoma.**

Hormone value	Patient Values	Normal Ranges
Serum cortisol	0.4 µg/dL	5 to 23 µg/dL
LH	0.5mIU/mL	Female (follicular phase): 1.9 to 12.5 mIU/mL Female (mid-cycle surge): 8.7 to 76.3 mIU/mL Female (luteal phase): 0.5 to 16.9 mIU/mL
FSH	3.5mIU/mL	Female (follicular phase): 3.5 to 12.5 mIU/mL Female (mid-cycle surge): 4.7 to 21.5 mIU/mL Female (luteal phase): 1.7 to 7.7 mIU/mL
Prolactin	129 µg/dL	2 to 29 µg/dL
GH	0.0536 µg/dL	0 to 10 µg/dL
IGF1	38.80 ng/mL	Age 0 to 18: 75 to 325 ng/mL

anterior pituitary dysfunction can later arise with or without central diabetes insipidus due to their compressive effects. Endocrinological evaluation varies from hypopituitarism to hyperprolactinemia. Majority of the patients are young females with a mean age of 36 years.[9]

Pituitary tuberculoma looks radiographically similar to an adenoma, making a straightforward identification of the disease challenging, particularly in the absence of a pulmonary TB history. Pituitary tuberculoma is known to cause thickening of the stalk. However, this nonspecific finding can also be found in inflammatory conditions like eosinophilic granuloma, granulomatous hypophysitis and sarcoidosis.[10] Additionally, the tuberculoma suprasellar extension renders a proper pituitary stalk evaluation on neuroimaging studies extremely challenging. Consequently, in order to make a precise diagnosis surgery is required and to decompress the optic chiasma. Trans-sphenoidal route is one the safest approach as it prevents cerebrospinal fluid contamination.[7] Sub-frontal approach after craniotomy is an alternative.

Histopathological examination is required to make the final diagnosis. Tuberculomas are classically characterized by a central area of caseation necrosis surrounded by epithelioid macrophages, lymphocytes, plasma cells and Langhans giant cells. On Ziehl-Neelsen staining, acid fast bacilli may or may not be visible. Cerebrospinal fluid and specimens can also be used for the diagnosis using the polymerase chain reaction technique. Anti-tubercular therapy (ATT) is mandatory, and in cases where hypopituitarism symptoms and signs are present, hormone replacement therapy may need to be started.[11] Our patient was prescribed ATT with 4-drug regimen of isoniazid, rifampin, pyrazinamide, ethambutol along with prednisolone and thyroxine. While it's prudent to obtain tissue diagnosis before initiating targeted treatment, in cases where pituitary tuberculosis is suspected, ATT can be commenced based on clinical suspicion alone. There are documented instances of significant reduction in the size of pituitary tuberculoma following initiation of ATT without confirmed tissue diagnosis.[12] This underscores the potential efficacy of medical management as a viable alternative to surgical intervention, particularly in cases where surgery poses significant risks or is not feasible due to patient factors.

Regular follow-up care is essential to monitor and manage any persistent symptoms or complications. In cases where treatment is delayed or ineffective, permanent endocrine dysfunction can be a challenging long-term outcome and can significantly compromise a patient's quality of life.[13] While this case report sheds light on sellar tuberculoma, its findings might lack generalizability and offer limited causality assessment due to uniqueness of individual cases. To address this, future studies could include case series and retrospective or prospective analyses to provide a more comprehensive understanding of the condition.

Patient Perspective

"My journey through treatment for a pituitary tuberculoma has been a rollercoaster of emotions. Planning my treatment involved discussions with my healthcare team, weighing the pros and cons of medications and potential surgery. The emotional impact was immense, as fear and uncertainty about the future consumed me. Support from my loved ones and healthcare professionals became my lifeline. I am quite satisfied with the treatment provided and my symptoms started to relieve few days after surgery. Coping with side effects, adjusting my lifestyle, and undergoing regular monitoring were challenging but necessary steps".

Conclusion

We report a case of sellar tuberculoma, an uncommon lesion that should be considered when making a sellar lesion differential diagnosis. Additionally, we also stress upon the importance of histopathological examination for the final diagnosis and postoperative anti-tubercular therapy in management of such cases. Prompt evaluation, rapid diagnosis, appropriate surgical management and timely starting of the anti-tuberculous regimen in patients result in great outcomes and noticeably improved clinical symptoms. This case emphasizes the diagnostic challenge of pituitary tuberculoma and the need for further research on specific diagnostic tools and long-term treatment efficacy.

References

1. Global Tuberculosis Report 2022. Geneva: World Health Organization; 2022.
2. DeLance AR, Safaee M, Oh MC, Clark AJ, Kaur G, Sun MZ, et al. Tuberculoma of the central nervous system. J Clin Neurosci. 2013;20(10):1333-41.
3. Ayele B, Wako A, Shewaye A, Tessema A. Sellar Tuberculoma: A rare presentation in a 30-year-old Ethiopian woman: case report. Afr J Neurol Sci. 2019;38(1):50-53.
4. Dastur HM. Tuberculoma. In: Vinken PJ, Bruyn GW, editors. Handbook of Clinical Neurology, vol. 18. New York: American Elsevier; 1975:413–26.
5. DeAngelis LM. Intracranial tuberculoma: case report and review of the literature. Neurology. 1981;31(9):1133-6.
6. Maurice-Williams RS. Tuberculomas of the brain in Britain. Postgrad Med J. 1972;48(565):679-81.
7. Ranjan A, Chandy MJ. Intrasellar tuberculoma. Br J Neurosurg. 1994;8(2):179-85.
8. Kumar T, Nigam JS, Jamal I, Jha VC. Primary pituitary tuberculosis. Autops Case Rep. 2020;11: e2020228.
9. Furtado SV, Venkatesh PK, Ghosal N, Hegde AS. Isolated sellar tuberculoma presenting with panhypopituitarism: clinical, diagnostic considerations and literature review. Neurol Sci. 2011;32(2):301-4.
10. Pereira J, Vaz R, Carvalho D, Cruz C. Thickening of the pituitary stalk: a finding suggestive of intrasellar tuberculoma? Case report. Neurosurgery. 1995;36(5):1013-5; discussion 1015-6.
11. Prabha BB, Rangachari V, Subramaniam V, Gopan TV, Baliga VB. Pituitary tuberculoma masquerading as a pituitary adenoma: interesting case report and review of literature. Asian J Neurosurg. 2021;16(1):141-3.
12. Dutta P, Bhansali A, Singh P, Bhat MH. Suprasellar tubercular abscess presenting as panhypopituitarism: a common lesion in an uncommon site with a brief review of literature. Pituitary 2006;9(1):73-7
13. Ben Abid F, Abukhattab M, Karim H, Agab M, Al-Bozom I, Ibrahim WH. Primary pituitary tuberculosis revisited. Am J Case Rep. 2017;18:391-4.

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Case Report

Successful Subungual Glomus Tumor Removal: A Case Report and Future Guidance on Diagnosis and Treatment

Made Bramantya Karna,[1] Richard Christian Suteja.[2]

Abstract

Background: Glomus tumors are rare benign hamartomas of the glomus body that occur mostly – though not limited to - the distal phalanxes of the digits. This article provides a real-life example of successful rare disease identification and treatment. It also provides a guideline that may help serve as future guidance on diagnosis and treatment. **Case**: A 41-year-old male came to our hospital presenting with a chief complaint of episodes of throbbing pain, which occurred spontaneously on the left thumb for the past two years. The pain had worsened in the past two weeks. The patient was positive for Hildreth's, Love's pin, and cold sensitivity tests. The previous x-ray showed no abnormalities in the left thumb. MRI found a hyperdense subungual lesion in the dorsal interphalangeal joint of the left thumb. We then performed an excision using the transungual approach. Histopathological findings found a relatively well-circumscribed lesion of the glomus apparatus absent of abnormal mitosis and necrosis. Two months after the excision, the patient reported no symptoms of recurrency, nail deformity, or other adverse outcomes. **Conclusion**: Patients typically present a chief complaint of chronic paroxysmal throbbing nail pain that persists for years, increases following exposure to cold environments, and is disproportionately exacerbated with the slightest touch. Hildreth's, Love's Pin, and cold sensitivity tests are special examinations that elicit or suppress pain. As with most benign tumors, complete excision usually yields good results. Adequate knowledge about diagnostic methods will help patients achieve early intervention and cure.

Introduction

Glomus tumors are rare benign hamartomas of the glomus body that occur mostly – though not limited to - the distal phalanxes of the digits.[1,2] Patients often present to the clinic with symptoms of paroxysmal pain in tissues below the nail.[3–5] The severity of the pain is proportional to the size of the tumor. The pain is exacerbated when touched or exposed to cold environments.[3–5] Studies report that glomus tumors only form about 1-5% of all hand tumors.[2] In most patients, initial pain is generally tolerable due to its paroxysmal and non-severe nature, However, as the tumor grows, the pain may be felt more frequently, with each episode being progressively painful. Furthermore, patients with chronic pain may develop a higher threshold when tolerating pain. This creates a delay from the patient's side in seeking treatment.

Highlights:

- Patients presenting symptoms of paroxysmal, throbbing pain exacerbated when exposed to a cold environment must be tested using all three provocation tests specific to the glomus tumor and transillumination test.
- T2-weighted MRI scan typically shows a well-demarcated hyperdense lesion and must be confirmed with further histopathology examination following excision.
- Periodic follow-up for recurrences, adverse effects, and impaired daily functioning must be done to provide comprehensive care for the patient.
- This article provides a real-life example of successful rare disease identification and treatment. It also provides a guideline that may serve as future guidance on diagnosis and treatment.

Studies report a mean length of time from initial symptom onset to diagnosis of around 7 years.[6] Aside from delays from the patient's side, it is reasonable to suspect our current knowledge on the disease. The lack of understanding and experience due to less to no contact to this disease during physician's training period may well contribute to the number of misdiagnoses. Albeit its lack of emergency, glomus tumors may reduce patient's quality of life, as there may be some limitation when performing specific movements such as gripping.

A knowledgeable and keen physician should be able to suspect a glomus tumor based on presented clinical symptoms. This is due to the disease's generally unique and distinguishable symptoms. Additionally, several specific tests may be performed to confirm the diagnosis. A transillumination test and MRI scan may also be performed on the affected digit.[7,8] However, a negative transillumination and MRI scan result do not necessarily exclude the possibility of glomus tumors when specific symptoms are present.[7,9–11] Prompt treatment may restore lost quality of life by

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allowing the patient to function as normal. In this article, we provide a case of successful glomus tumor diagnosis and removal. This case is uncommon, and therefore may serve as a learning material for medical students. This article is written while adhering to CARE guidelines.[12] This article will also propose a diagnostic scheme to help physicians diagnose glomus tumors.

The Case

A male in his 40s presented with a chief complaint of pain under the nail of his left thumb for the past two years prior to coming to our hospital, which worsened in the past two weeks. The pain was isolated and only felt on his left thumb. The patient described the pain as episodes of throbbing pain that occurred spontaneously. The patient felt that pain episodes were more prevalent during certain times of the year, and the throbbing felt greater when exposed to cold air from the refrigerator.

The patient reported that he had previously sought care from multiple doctors over the two years but to no avail. There are neither accompanying symptoms nor significant past, family, or social histories. There is also no history of trauma in the said location. Upon inspection, we found no discoloration, swelling, or deformity. However, tenderness was present and was localized to the dorsal side of the distal interphalangeal joint. Albeit localized within the joint, passive and active movement was not restricted. The presentation of paroxysmal, throbbing pain, exacerbated following exposure to a cold environment, warrants further provocation and transillumination tests, which, in our case, showed positive results (***Table 1***).

The patient came to our clinic with left thumb x-ray results from a scan he underwent after an appointment with his previous doctor. The x-ray showed no abnormalities in the left thumb and, in general, his left hand. A complete blood count found no significant results. Contrast-enhanced T2-weighted MRI scan found a well-demarcated 1.7 cm x 0.6 cm x 0.6 cm hyperdense lesion in the dorsal interphalangeal joint of the left thumb separate from the bone ***Figure 1.***

Initial findings and epidemiologic study made us suspect an early-formed ganglion cyst because it is one of the most prevalent soft tissue masses in hand surgery.[13] However, the feeling of pain was not typical of ganglion cysts and warrants further investigation. This makes our working diagnosis the glomus tumor of the hand, and further pathological examination was required to confirm this diagnosis.

Table 1. **Key Symptoms and Diagnostic Findings.**

Key Symptoms
• Chief complaint of subungual pain at left thumb.
• Pain was progressive (onset of two years, worsened in past two weeks).
• Pain exacerbated when exposed to cold air from the refrigerator or under cooler weather.
• Pain can be localized in the dorsal side of the distal interphalangeal joint.
• History of trauma was denied.
• Significant past medical history, family history, and social history was denied.
Key Diagnostic Findings
• Patient had positive Hildreth's, Love's pin, cold sensitivity, and transillumination tests.
• X-ray scan found no abnormalities. However, contrast-enhanced T2-weighted MRI scan found a 1.7 cm x 0.6 cm x 0.6 cm hyperdense lesion.
• Location based on clinical localization and MRI warrants excision via transungual approach.

We performed a surgical excision of the benign lesion using the transungual approach. This approach was chosen due to the location of the tumor as shown by MRI. Under local digital block, a finger tourniquet was used to exsanguinate the finger subjected to surgery. Antiseptic preparation was done on the surgical site, and then an incision was made along the lateral aspect of the proximal nail fold, followed by nail plate extraction. An exposed nail bed was then incised longitudinally right above the lesion site, allowing tumor exposure. Following the excision of the encapsulated tumor, the nail bed was then sutured, and the lifted nail was replaced on top of the nail bed. The nail was then sutured with the proximal nail fold, and wound dressing with gauze and antibiotic ointment was changed daily until the wound was dry, after which it was kept open.

Figure 1. **Contrast-Enhanced T2-Weighted MRI Scan; (A) Coronal, (B) Axial, and (C) Sagittal Sections of Left Hand.**

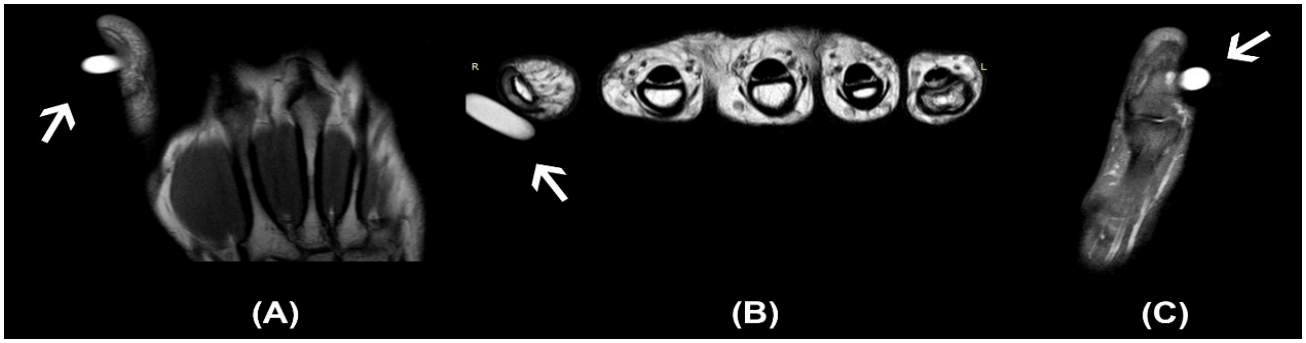
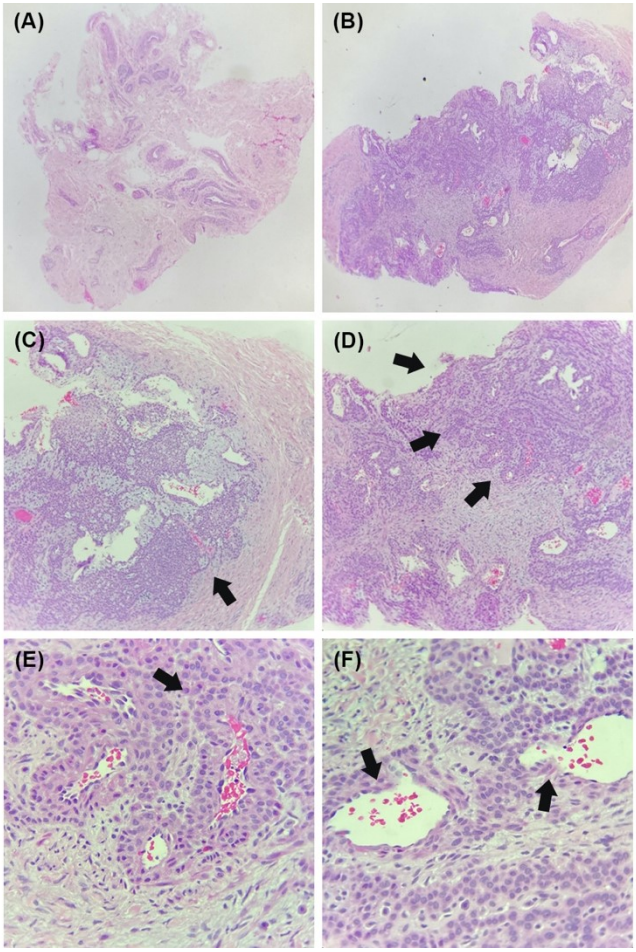


***Figure 2*. Histopathological Findings of Lesions.**



Legend: Histopathological Findings (A and B); Sample view under 40x magnification; (C and D) A sample view under 100x magnification shows a relatively well-circumscribed lesion with a solid nest and cuffing; (E) Sample view under 400x magnification, showing uniform rounded cells with pale eosinophilic and amphophilic cytoplasm, relatively sharp-defined cell border, centrally-located nucleus (arrow), surrounded with myxoid stroma; (F) Sample view under 400x magnification, showing that some cells (arrow) surround small and ectatic blood vessels, creating a staghorn appearance. There were no signs of abnormal mitosis and necrosis.

Following surgery, we successfully extracted two greyish-white tissues sized 0.4 cm x 0.2 cm x 0.2 cm and 0.3 cm x 0.2 cm x 0.2 cm, respectively. These tissues were then immersed in a 10% NBF (neutral buffered formalin). The excised tissue's pathological findings ***Figure 2*** correspond to the conventional morphology of the type II glomus tumor.

Two months following the excision, we monitored for any possibility of recurrence or post-treatment adverse effects. The patient reported no recurrence of symptoms such as pain, tenderness, or local inflammation. No nail deformity or any other adverse outcomes were reported. The patient was then able return to his work without any meaningful limitations. He can now carry things that require extensive use of his thumb symmetrically with his left and right hand. Provocation tests were performed again, this time showing negative results.

Discussion

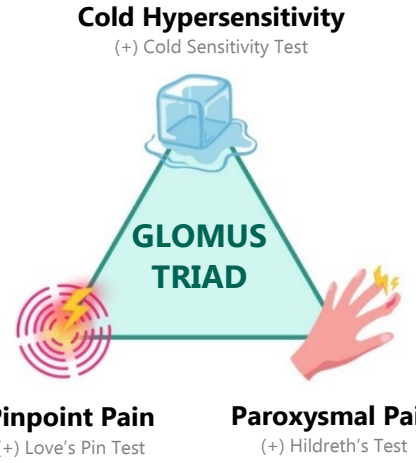
In our study, the patient presented symptoms which correlated to two of the three tests specific for the diagnosis of glomus tumor: paroxysmal subungual throbbing pain exacerbated when exposed to cold environments. These symptoms present in 90-100% of patients, as mentioned in several other studies which report 10 or more patients with digital glomus tumor.[14,15] Patients may also present with other symptoms such as nail disfigurement or discoloration.[14,15] However, these were not present in our patient. Following confirmation through physical and supporting examination, we decided that excision via transungual approach was the best surgical method due to the tumor being more centrally located. Albeit being the method which offers the best visualization and exposure, this technique is the most disruptive to the nail bed, increasing chances of complications such as inaesthetic nail, nail ridging, and nail splitting.[14,16,17] Other options include the lateral and volar approach, which were more restricted in visualization but are less disruptive towards the nail bed.[14,18,19] Structurally, a glomus apparatus consists of a single afferent arteriole and efferent venule, connected through multiple arteriovenous anastomoses (Suquet-Hoyer canals), altogether encapsulated with α-actin containing muscle fibers and glomus bodies.[20] The afferent arterioles are formed by endothelium, internal elastic lamina, and pre-glomic muscle cells, while efferent venules comprise a thin endothelium layer.[20] The glomus apparatus physiologically functions as a contractile neuro-myo-arterial unit that autonomically thermoregulates body temperature through shunting and maximizing blood flow within the cutaneous microvasculature.[20] On exposure to cold temperatures, a marked increase in norepinephrine results in constriction of blood vessels, shunting blood flow towards the apparatus.[21] Decrease of peripheral blood flow causes a reduction in convection-mediated heat loss. Hyperplasia of either one of the components within the glomus apparatus (i.e., blood vessel, glomus body, muscle) creates a condition known as a glomus tumor.[22] Generally, there are three types of glomus tumors based on their histopathological differences.

Although strictly differentiated into distinct types, there are cases where patients may present with multiple histopathological types concurrently.[23,24] The three main classifications are: (1) hyaline-mucoid type, (2) solid type, and (3) angiomatous type.[23,24] Hyaline-mucoid type glomus tumor is characterized by increased hyalinized connective tissue interspersed within islands of glomus cells and vascular spaces.[23,24] Solid-type glomus tumor is characterized by glomus cell masses and reduced vascular and muscle space.[23,24] This type was previously called the 'typical' glomus tumor histology. An increase in intracapsular vasculature characterizes the angiomatous glomus tumor and is the rarest among the three types.[23,24]

Although glomus apparatuses can be found in various parts of the body, a typical glomus tumor occurs as a solitary, benign lesion typically located on subungual tissues of the digits.[1] Patients typically present a chief complaint of chronic paroxysmal

throbbing nail pain, which persists for years, as it is often ignored or, sometimes, misdiagnosed.[3–5] This pain increases following exposure to cold environments and is disproportionately exacerbated due to the slightest touch.[3–5] In some cases, the tumor may present together with a bluish-pink nodule or longitudinal nail splitting.[4,5]

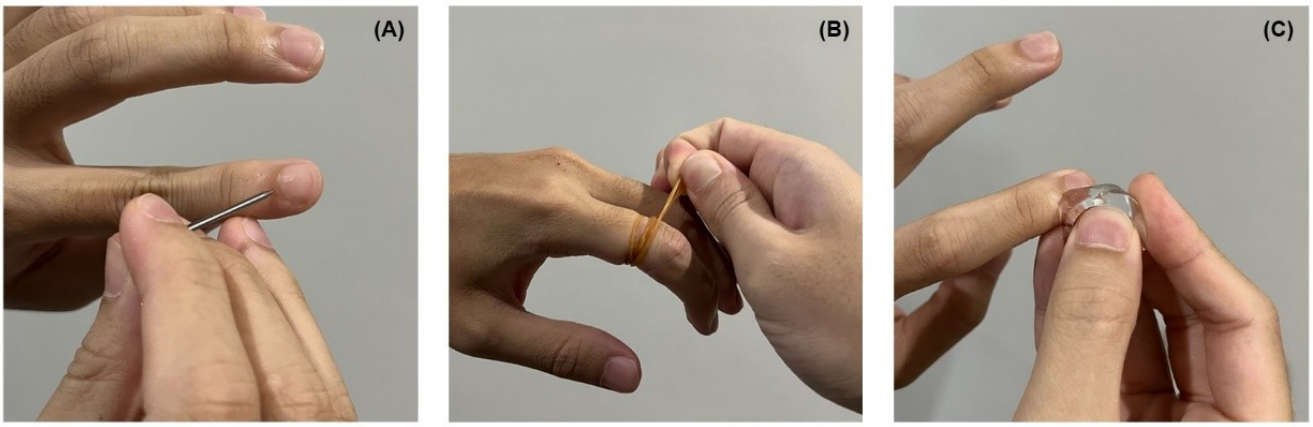
***Figure 3*. Glomus Triad.**



Legend: Cold Hypersensitivity (Elicited with cold sensitivity Test), Paroxysmal Pain (Elicited with Hildreth's Test), and Pinpoint Pain (Elicited with Love's Pin Test.

Owing to the relatively unique symptoms, the differential diagnosis of glomus tumor must be added following the presentation of paroxysmal throbbing pain, disproportionate pinpoint pain, and cold hypersensitivity, as shown in ***Figure 3.*** Physicians generally perform three special examinations that aim to elicit or suppress pain following exposure to certain conditions: Hildreth's Test, Love's Pin Test, and cold sensitivity Test. Love's pin test is performed by applying pressure to the mass using a rounded-tip object such as a ballpoint pen, pinhead, or the end of a paperclip.[25] Love's pin test is positive if the pain is elicited after applying pressure, a refractory hand withdrawal is demonstrated.[25,26] Love's pin test is also commonly used to roughly localize the lesion by identifying areas exhibiting the most severe pain.[26] Hildreth's test is performed by exsanguinating the affected digit using a tourniquet applied at the base of the digit.[27] The physician will then observe any signs of reduction in pain and tenderness, indicating a positive Hildreth test.[27] A surge of sudden pain may occur following the release of the tourniquet. Giele (2002) observed that this test was 92% sensitive and 91% specific to glomus tumors.[27] Reduced or absence of pain by repeating Love's pin test following application of tourniquet (sharpened Hildreth's test) also indicates a positive result.[26] Cold sensitivity test exposes the affected digit to cold environments, usually by applying an ice pack or cubes directly above the suspected lesion site. Induction of pain indicates a positive cold sensitivity test.[28] These tests can be seen in ***Figure 4.***

***Figure 4*. Provocation Tests: (A) Love's Pin Test, (B) Hildreth's Test, (C) Cold Sensitivity Test.**



Some studies also recommended the use of a transillumination test.[7] The test is performed by placing a flashlight on the palmar side of the affected digit and then looking for any inconsistencies in opacity within the nail plate and bed.[7] This method is an easy, non-invasive, cost-effective adjuvant diagnostic tool.[7] In addition to specific physical examinations, glomus tumors can be diagnosed using high-resolution magnetic resonance imaging (MRI). In a contrast-enhanced MRI scan, a typical glomus tumor is a hyperintense lesion with a well-demarcated border.[8] However, it must be noted that a negative MRI result on a clinically suspected glomus tumor patient does not exclude the possibility of a hidden tumor within the digits.[9–11]

Differential diagnoses include ganglion cysts, subungual melanoma, and subungual squamous cell carcinoma. However, ganglion cysts should be characterized as a non-painful lump except if they compress a nearby nerve.[29] In our case, the lesion was found to be more centrally-located and was not situated in a location highly possible for nerve compression.[30] Patients with ganglion cysts may also report preceding traumatic event or repetitive stretching of nearby capsular and ligamentous structure which stimulates production of tissue hyaluronic acid.[31,32] T2-weighted MRI of ganglion cysts may show hyperdense lesion(s) similar to glomus tumor. However, lesions are usually situated above joints.[30] Subungual melanoma was also

a possible differential diagnosis. However, it tends to manifest with nail discoloration, which was not present in our patient.[33] As they are more malignant, lesions which had a longer onset, such as in our patient, should include bone involvement, nail onycholysis, and erosion/ulceration of the nail bed.[34,35] This was not observed in our patient's X-ray and MRI results. Similar to subungual squamous cell carcinoma, lesions with a longer onset usually present larger mass with bony involvement, nail onycholysis, nail dystrophy, and other more destructive symptoms which were not present in our patient.[36] Keratotic/verrucous lesion may also be present on the nail bed following nail plate loss.[36]

As with most benign tumors, complete excision usually yields good results. There are several approaches to excision: the transungual, lateral, and volar approaches (shown in ***Figure 5***.[1,17–19,37] A transungual approach generally involves an incision along the lateral aspect of the proximal nail fold to allow nail plate extraction. Another longitudinal incision then allows tumor excision. The nail bed is then sutured again, and the lifted nail is be replaced on top of the nail bed. A lateral approach involves. making an incision along the side of the nail or finger, which allows for excision of the tumor with less disruption to the nail bed, potentially reducing the risk of nail deformity. The transungual approach generally provides better exposure to the tumor, increasing certainty towards complete excision with the expense of nail deformity due to massive manipulations.[17] Transungual approach is generally used for the typical centrally-situated subungual glomus tumor. A lateral approach involves a lateral high incision to the side nearer the tumor. The incision was then extended distally to cover the pulp.[1]

Thereafter, a deep dissection was performed, exploring subperiosteally to the distal phalanx, hence raising a dorsal flap of the nail matrix, nail bed, and nail plate in one single unit, and keeping the nail bed-to-plate integrity.[1] The magnitude of elevation depend on the proximity of the tumor.[1,37] A modification to this technique is the lateral subperiosteal approach, which omitted further incision towards the pulp.[37] This approach is advantageous as it is quicker and protects the nail against post-surgery deformity.[37] However, studies report that this approach may sometimes cause incomplete excision and early tumor recurrence. This approach is generally used for a more laterally-situated subungual glomus tumor.[17] The volar approach involves an incision on the palmar side of the digits and is used only when the mass is situated more towards the palmar or volar side.[18,19]

Based on the literature review and our personal experience in this case, we propose a diagnostic and treatment workflow, as shown in ***Figure 6***. We suggest performing all provocation tests alongside transillumination test even when only one symptom of the triad is present, especially on patients with a history of glomus tumor. The provocation procedures are relatively easy and cheap, sparing the patient of further loss.

Figure 5. **Various Approaches in Surgical Excision of Digital Glomus Tumor (A) Transungual Approach, (B) Volar Approach, (C) Lateral Subperiosteal Approach.**

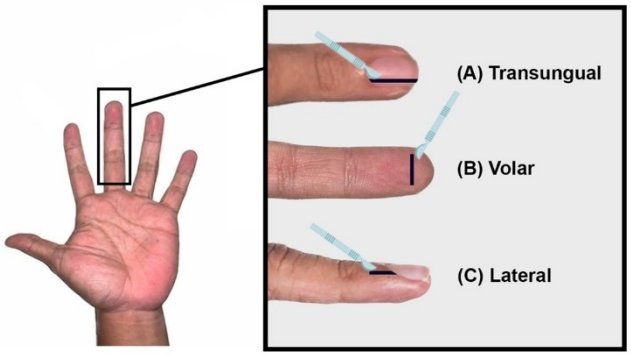
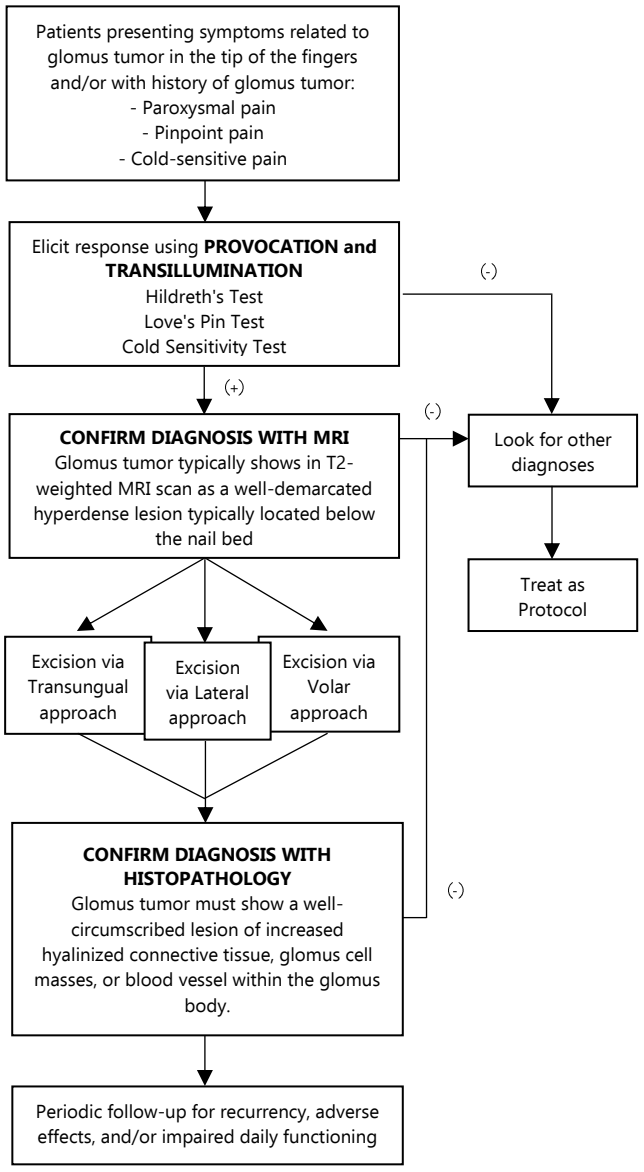


Figure 6. **Diagnostic and Therapeutical Algorithm for Glomus Tumors.**



Although the typical glomus tumor often occurs as a benign solitary nodule in the digits, it is anatomically possible for a glomus tumor to occur in other parts of the body, as other parts contain glomus bodies, too. These glomus tumors outside of the digits usually present with malignant-like characteristics such as multiple and large nodules, as well as atypical mitotic figures, infiltrative, and can metastasize.[38,39] These types of glomus tumors have a higher recurrence rate following excision.[39] Although this study reports a successful rare tumor removal, data regarding long-term (>12 months) recurrency or adverse effects follow up was not available. Literature reported that recurrence occurs in up to 18% of cases.[40] However, only tumors recurring after 24 months post-excision can be regarded as true recurrence rather than pseudo-recurrence which occurs due to inadequate excision.[41]

In conclusion, glomus tumors are rare benign hamartomas of the glomus body that occur mostly – though not limited to - the distal phalanxes of the digits. Patients typically present with a chief complaint of chronic paroxysmal throbbing nail pain that persists for years, increases following exposure to cold environments, and is disproportionately exacerbated due to the slightest touch. Hildreth's, Love's Pin, and cold sensitivity tests were special examinations that elicit or suppress pain. We suggest performing all provocation tests and the transillumination test even when only one symptom of the triad is present, especially on patients with a history of glomus tumor. The provocation procedures are relatively easy and cheap, sparing the patient of further loss. As with most benign tumors, complete excision usually yields good results. Adequate knowledge about diagnostic methods will help patients achieve early intervention and resolvent.

Upon follow up, the patient stated an almost 100% functional daily activity recovery. The patient reported that he is satisfied with the results, both cosmetically and functionally. Provocation tests specific for glomus tumor were redone and found to be negative.

Summary – Accelerating Translation

Glomus tumors are rare benign hamartomas of the glomus body that occur mostly – though not limited to - the distal phalanxes of the digits. Patients typically present a chief complaint of chronic paroxysmal throbbing nail pain that persists for years, increases following exposure to cold environments, and is disproportionately exacerbated due to the slightest touch. Hildreth's, Love's Pin, and cold sensitivity tests are special examinations that elicit or suppress pain. We suggest performing all provocation tests and transillumination test even when only one symptom of the triad is present, especially on patients with a history of glomus tumor. The provocation procedures are relatively easy and cheap, sparing the patient of further loss. As with most benign tumors, complete excision usually yields good results. Adequate knowledge about diagnostic methods will help patients achieve early intervention and resolvent.

References

1. Morey VM, Garg B, Kotwal PP. Glomus tumors of the hand: review of literature. J Clin Orthop Trauma. 2016;7(4):286–91.
2. Jawalkar H, Maryada VR, Brahmajoshyula V, Kotha GKV. Subungual glomus tumors of the hand treated by transungual excision. Indian J Orthop. 2015;49(4):403–7.
3. Bordianu A, Zamfirescu D. The hidden cause of chronic finger pain: glomus tumor—a case report. J Med Life. 2019;12(1):30–3.
4. Newman MJ, Pocock G, Allan P. Glomus tumour: a rare differential for subungual lesions. BMJ Case Rep. 2015;2015.
5. Carroll RE, Berman AT. Glomus tumors of the hand: review of the literature and report on twenty-eight cases. J Bone Joint Surg Am. 1972;54(4):691–703.
6. Kim DH. Glomus tumor of the fingertip and MRI appearance. Iowa Orthop J. 1999;19:136–8.
7. Tsiogka A, Belyayeva H, Sianos S, Rigopoulos D. Transillumination: a diagnostic tool to assess subungual glomus tumors. Skin Appendage Disord. 2021;7(3):231–3.
8. Al-Qattan MM, Al-Namla A, Al-Thunayan A, Al-Subhi F, El-Shayeb AF. Magnetic resonance imaging in the diagnosis of glomus tumors of the hand. J Hand Surg Am. 2005;30(5):535–40.
9. Bargon CA, Mohamadi A, Talaei-Khoei M, Ring DC, Mudgal CS. Factors associated with requesting magnetic resonance imaging during the management of glomus tumors. Arch Bone Jt Surg. 2019;7(5):422–8.
10. Chou T, Pan SC, Shieh SJ, Lee JW, Chiu HY, Ho CL. Glomus Tumor: Twenty-Year Experience and Literature Review. Ann Plast Surg. 2016;76 Suppl 1:S35-40.
11. Fazwi R, Chandran PA, Ahmad TS. Glomus tumour: a retrospective review of 15 years' experience in a single institution. Malays Orthop J. 2011;5(3):8–12.
12. Equator Network. CARE Checklist English 2013. Available from: https://www.care-statement.org/checklist. Cited Jun 26, 2023.
13. Zampeli F, Terzidis I, Bernard M, Ochi M, Pappas E, Georgoulis A. Ganglion cyst. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jul 17 [cited Dec 17, 2023]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK470168/
14. Shin DK, Kim MS, Kim SW, Kim SH. A painful glomus tumor on the pulp of the distal phalanx. J Korean Neurosurg Soc. 2010;48(2):185–7.
15. Shepherd JT, Rusch NJ, Vanhoutte PM. Effect of cold on the blood vessel wall. Gen Pharmacol. 1983;14(1):61–4.
16. Masson P. Le glomus neuromyoartérial des régions tactiles et ses tumeurs. Lyon Chir. 1924;21:257–80.
17. Tuncali D, Yilmaz AC, Terzioglu A, Aslan G. Multiple occurrences of different histologic types of the glomus tumor. J Hand Surg Am. 2005;30(1):161–4.
18. Looi KP, Teh M, Pho RW. An unusual case of multiple recurrence of a glomangioma. J Hand Surg Br. 1999;24(3):387–9.
19. Love JG. Glomus tumors: diagnosis and treatment. Proc Staff Meet Mayo Clin. 1944;19:113–6.
20. Tang CYK, Tipoe T, Fung B. Where is the lesion? Glomus tumours of the hand. Arch Plast Surg. 2013;40(5):492–5.
21. Yii NW, Elliot D. Hildreth's test is a reliable clinical sign for the diagnosis of glomus tumors. J Hand Surg Br. 2002;27(2):157–8.
22. Netscher DT, Aburto J, Koepplinger M. Subungual glomus tumor. J Hand Surg Am. 2012;37(4):821–3.
23. Kabakas F, Ugurlar M, Ozcelik I, Mersa B, Purisa H, Sezer I. Surgical treatment of subungual glomus tumors: experience with lateral subperiosteal and transungual approaches. Hand Microsurg. 2016;5(2):70–4.

24. Garg B, Machhindra MV, Tiwari V, Shankar V, Kotwal P. Nail-preserving modified lateral subperiosteal approach for subungual glomus tumour: a novel surgical approach. Musculoskelet Surg. 2016;100(1):43–8.
25. Mortada H, AlRabah R, Kattan AE. Unusual Location of Pulp Glomus Tumor: A Case Study and Literature Review. Plast Reconstr Surg Glob Open. 2022;10(3):e4206.
26. Senhaji G, Gallouj S, El Jouari O, Lamouaffaq A, Rimani M, Mernissi FZ. Rare tumor in unusual location—glomus tumor of the finger pulp (clinical and dermoscopic features): a case report. J Med Case Rep. 2018;12(1):1–5.
27. Binesh F, Akhavan A, Zahir ST, Bovanlu TR. Clinically malignant atypical glomus tumour. BMJ Case Rep. 2013;2013.
28. Folpe AL, Fanburg-Smith JC, Miettinen M, Weiss SW. Atypical and malignant glomus tumors: analysis of 52 cases, with a proposal for the reclassification of glomus tumors. Am J Surg Pathol. 2001;25(1):1–12.

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IJMS INTERNATIONAL JOURNAL of MEDICAL STUDENTS

Experience

Summer Surgical Elective in Hong Kong

Martin Ho,[1] Velda Chow.[2]

The Experience

Hong Kong is a coastal city in Southern China and a former British colony, located nearly 10,000 kilometers from my home country of Ireland. It's known by many names, including The Pearl of the Orient and Asia's Finest City. For me, it presented an exceptional learning experience within the field of plastic and reconstructive surgery, as I had the privilege of working with the esteemed team at Queen Mary Hospital, a prestigious institution situated in this vibrant city. Although Cantonese is the primary language spoken in Hong Kong, the doctors speak fluent English, which benefited me as an English-speaking medical student.

Summer elective attachments offer students a fantastic opportunity to gain real-world exposure to specialties of interest without the pressure of exams. Additionally, they demonstrate a student's organisational skills and early interest in a specialty which are valuable assets in future interviews. International electives also facilitate personal growth and cultural enrichment outside of the hospital. I would encourage all medical students to complete an elective attachment.

As a child, my father often told me stories about the positive experiences he had as a patient at Queen Mary Hospital. I yearned to work with the esteemed doctors there. As a penultimate-year medical student, I embraced the opportunity to do so. I applied for the elective eight months in advance via the Hong Kong University (HKU) website so that the relevant documentation and paperwork could be arranged.

Upon arrival, I immediately noticed differences between the healthcare systems in Hong Kong and Ireland. For instance, the scope of plastic and reconstructive surgery in Hong Kong exceeded that in Ireland. While I expected to learn about burn management, breast reconstruction, and skin excisions, I was surprised to see that the plastic surgery team also performed head and neck procedures such as thyroidectomies and lymph node dissections. This was impressive and spoke to the high quality of surgical training in Hong Kong. It ensured that patients with complex oncologic and reconstructive needs received timely, comprehensive care, while also minimising costs and logistical requirements of the surgery department.

To fully assimilate with the team, I attended all the early morning ward rounds, multidisciplinary team meetings, journal clubs, procedural clinics (Ultrasounds, Fine-Needle Aspiration Cytology), and outpatients. Because I showed a high level of interest and engagement, I was invited to teaching sessions with the HKU medical students where I learned new knowledge such as how to describe and spot-diagnose CT-TAPs and the procedural steps of Bilroth 1, 2, and Roux-en-Y gastric bypass surgeries. Upon conversing with the HKU students, I was surprised to learn that the final-year students had no summer holidays after their 4th-year exams. I wonder how my classmates in Ireland would react to this if implemented here. Such a change would likely face significant resistance, as it would exacerbate student stress and potentially increase medical school dropout rates. However, this issue may be less pronounced in Asian countries, which often have more intense working cultures compared to Western countries[1].

Figure 1. **An Exterior Photograph of the Entrance to Queen Mary Hospital Taken at 11 PM.**

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The most memorable operation I witnessed was a 13-hour total laryngopharyngoesophagectomy. Thanks to the broad scope and high standards of training, the surgical team excised the tumor and also performed the pectoralis major flap for the hypopharyngeal reconstruction. This was a lifesaving and life-changing operation for the patient and was breathtaking to watch. I was impressed and enthralled by the technical dexterity required to perform this procedure as well as the effective team dynamics which allowed for smooth problem solving. It was a privilege for me to be involved (in a minor way) in this patient's care. I left the hospital at 11 pm that night, knowing that helping patients through surgery was my calling in life (***Figure 1***).

The price of high-quality surgical care in Hong Kong is a grueling training scheme. Through conversing with "housemen" and interns, I was informed that 90–100-hour work weeks were routine[2]. While the average working hours of physicians in Ireland often exceeds the European Union's 2003 Working Time Directive[3] it allows for time to relax and pursue other interests, thus maintaining physician longevity. However, the increased intensity of surgical training in Hong Kong allows for faster career progression, which may be appealing to many trainees. Additionally, the remuneration of doctors in Hong Kong often exceeds that in European countries[4].

Amid the differences between the healthcare systems in Ireland and Hong Kong, I also noticed similarities. Public medical services in Hong Kong are provided by the Hospital Authority, which functions similarly to the Health Service Executive in Ireland, or the National Health Service in the United Kingdom. All of these public systems are said to be overcrowded and underfunded, resulting in increasing numbers of patients and doctors alike flocking to the private sector to work and receive care[5-7]. I wonder if this trend can be reversed or is it an inevitability for all governments who wish to provide a public health service?

In the evenings after work, I ate at local restaurants and food stalls dotted throughout Hong Kong. The Dim-Sum was second to none. I will forever remember the "Char-Siu bao", "Har Gow", and "Lai Wong bao". Highly recommended! As the population density in Hong Kong is almost 100 times that of Ireland, restaurants are extremely busy, and I was often told to eat right beside other diners to maximize restaurant space efficiency.

Throughout the elective, I appreciated the differences and similarities between Hong Kong and Ireland. The impactful cases I witnessed alongside the support I received from the surgical team strengthened my resolve to become a surgeon. The teaching I received helped to cement my understanding of surgical pathologies and treatments. Aristotle's timeless quote resonates with me, "Educating the mind without the heart is no education at all." This encapsulates the essence of my surgical elective in Hong Kong, where not only did I gain knowledge but also cultivated a deeper understanding of the human side of surgery.

References

1. Working Hours - Our World in Data [Internet]. cited 2024 May 27. Available from: https://ourworldindata.org/working-hours
2. Hospital Authority: Doctor Work Reform Recommendation Report 2007/08 [Internet]. cited 2024 May 27. Available from: https://www.ha.org.hk/visitor/ha_visitor_index.asp?Content_ID=1260&Lang=ENG&Dimension=100&Parent_ID=695
3. Directive 2003/88/EC - working time | Safety and health at work EU-OSHA [Internet]. cited 2023 Dec 18. Available from: https://osha.europa.eu/en/legislation/directives/directive-2003-88-ec
4. The Census and Statistics Department of the Hong Kong Special Administrative Region. Annual Statistical Survey Report. 2022 Report on Annual Earnings and Hours Survey. cited 2024 Jun 5; Available from: www.censtatd.gov.hk
5. Health Insurance in Ireland. cited 2024 May 25; Available from: www.hia.ie
6. Shah SA, Robertson C, Sheikh A. Effects of the COVID-19 pandemic on NHS England waiting times for elective hospital care: a modelling study. Lancet. 2024;403(10423):241–3.
7. Schoeb V. The Role of Health Professionals within a Social Model of Health. China Perspect. 2016(2016/4):51-58.

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Experience

Innovating Against Odds: A Medical Student's Research Journey in a Resource-Constrained Environment

Hamrish Kumar Rajakumar.[1]

The Experience

My research journey was sparked by a 1-hour phone call with a peer, where a discussion on a clinical case unraveled disparities in healthcare access, particularly in the early detection of cases. The clinical case we discussed became a catalyst to address these inequities and embark on a journey toward achieving health equity. As we sifted through databases in search of research topics aligned with our interests, we encountered numerous ideas. However, we had to discard many due to non-feasibility with challenges like lack of facilities, high costs, and a limited flow of eligible patients.

At this stage, I had many ideas in my mind, but I barely knew anything about the practical aspects of conducting research. The scary question of how to even start loomed large. This uncertainty is often a significant deterrent for many aspiring researchers. The lack of knowledge and experience in research can be intimidating, causing many to hesitate and fear that their efforts might be futile. This fear of the unknown prevents numerous individuals from taking their first step. I found myself at this exact point, contemplating whether to take the leap into the world of research or to continue with my familiar routine. However, my strong motivation to make a difference drove me forward. This motivation, I realized, is truly enough to set the wheels in motion and initiate the journey. Taking that first step into research, despite not knowing even the "R" in Research, is already halfway to success. The limited access to state-of-the-art laboratories and cutting-edge technologies forced me to explore unconventional avenues. Exploring local healthcare facilities unearthed a wealth of untapped data and patient insights, proving that groundbreaking discoveries could emerge from the most unexpected sources.

Balancing academic coursework, clinical postings, and the role of a principal investigator proved to be a formidable challenge as a medical student. The demands and stresses of these three facets necessitated the cultivation of meticulous planning, adaptability, collaboration, and a disciplined work ethic. Due to the finite nature of time, I had to prioritize tasks based on urgency and importance, allowing me to effectively manage research commitments alongside academic responsibilities.

The learning curve was steep, as theoretical classes on research methodology only provided a foundational understanding. However, theory alone could not prepare me for the practical world of research. The gap between theory and practice became apparent as I began literature reviews, proposal drafting, and hands-on project implementation. Under the guidance of mentors supplemented by online resources, each step became a learning opportunity, enhancing my skills in statistical analysis and scientific writing.

Choosing the right mentors is crucial for a medical student to start research. A good mentor was not just about offering professional guidance – they were also a source of encouragement, always there to keep me positive and offer constructive feedback on my mistakes. Their mentorship was invaluable in keeping me on track, offering insights and strategies that helped me overcome challenges. On the other side, I learned to avoid fake mentors who offered no genuine support and often seemed more interested in their agenda. A pivotal factor in sustaining my research journey was the collaborative experience with my research partner. As a synergistic duo, we became an unstoppable team facing challenges head-on, celebrating shared triumphs, and fueling each other's passions. Our collaboration extended beyond individual contributions, forging a partnership that is still a cornerstone of our achievements. This partnership not only accelerated the pace of research but also instilled resilience in facing challenges. Sharing the workload lightened individual burdens, making the research process more manageable and enjoyable. Beyond scientific exploration, we nurtured a connection that transcended the professional sphere, creating a foundation of trust, understanding, and unwavering support.

Our milestones echoed the progression of our research journey. From selecting impactful topics to securing ethical approval, collecting high-quality datasets, and proficiency in advanced statistical tools marked significant milestones. Presenting our

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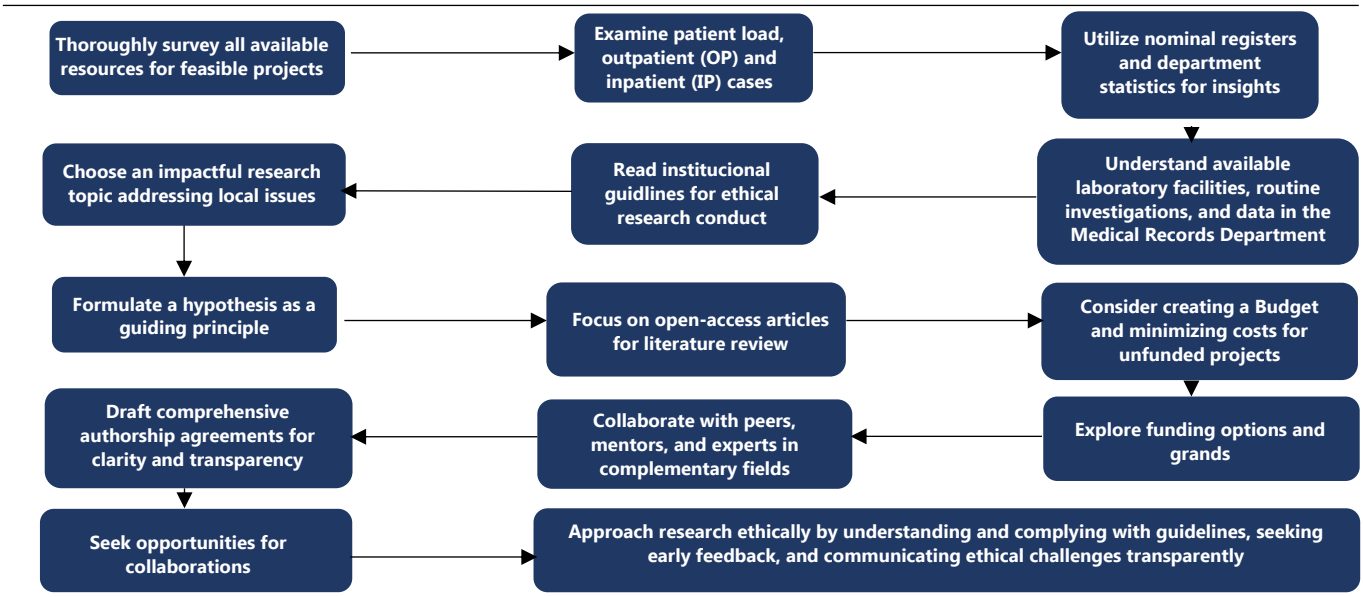
research at conferences was a rewarding milestone, allowing us to share insights, receive constructive feedback, and establish credibility within the academic community. Setbacks provided valuable lessons. Statistical challenges prompted extra efforts in attending online workshops and referring to YouTube videos to grasp the right statistical tests and their interpretation. The lack of specialized training opportunities highlighted the need for proactive skill acquisition. The issues of this research odyssey taught me the importance of effective communication and conflict resolution in maintaining a collaborative research environment.

In conclusion, my research journey from the inception of an idea born in a phone call to the presentation of research findings at conferences, each step has contributed to my growth, both academically and personally. Beyond academic pursuits, the shared odyssey with my research partner has created a lasting alliance that transcends professional spheres, a testament to the power of collaborative exploration in the pursuit of greater understanding and innovation. Figure 1 illustrates an easy guide that students facing resource constraints can adopt to initiate their research journey in similar environments. Additionally, I recommend students direct all available resources and focus their research on diseases with low prevalence in high-income nations where information is scarce. This encourages the exploration of less-studied areas, potentially yielding novel insights and innovative solutions that contribute significantly to medical knowledge and address global healthcare gaps.

Figure 1. **A Simplified Flowchart for Students: A Practical Guide for Initiating Research in Resource-Constrained Environments.**



Building Resilience in the Research Journey

Navigating the research journey has required resilience and a strategic mindset to overcome various challenges I have faced.

1. Time Management: Create realistic schedules that balance research commitments, personal life, and self-care. Specific time blocks should be assigned for research tasks, meetings, and relaxation. Setting boundaries helps prevent burnout and ensures sustainable progress.
2. Dealing with Rejection: Manuscript and conference rejections are common. Instead of taking them personally, view them as opportunities for improvement. Seek feedback from reviewers and refine your work. Each rejection can guide you toward enhancing your research quality.
3. Handling Unexpected Hurdles: Loss to follow-up, compliance issues, and other unforeseen challenges are part of the research. It is crucial to develop contingency plans and foster collaborative problem-solving to overcome these challenges.
4. Valuing Negative Results: We should not be disheartened by negative results, but value them as crucial in scientific research, as they play a significant role in refining hypotheses and guiding future investigations.
5. Team Dynamics: Differences of opinion among investigators or teammates, especially close friends, can arise in research. It is important to acknowledge and openly communicate about these issues to resolve conflicts and understand their potential impact on both personal and professional relationships. Separating personal relationships from professional endeavors is key to ensuring the longevity and success of collaborative research efforts.

Crafting a Presence

Completion of research objectives marks the transition to a phase where effective presentation skills become paramount. Medical conferences offer a valuable platform to share insights, gain exposure, and encourage collaboration. Many medical institutions host annual academic events that invite abstracts for paper presentations, case discussions, and poster presentations. Medical students must seize these opportunities and display their work to the wider scientific community.

A key aspect of impactful presentation lies in the creation of visually compelling slides that supplement the spoken narrative. Practicing the delivery of the presentation is equally vital, allowing for the refinement of timing, enhancement of clarity, and anticipation of potential questions. Stage fear can be overcome by thorough rehearsal, and presenting to fellow peers who offer insights to identify and rectify any shortcomings in the presentation. For those new to the stage, creating a script can serve as a backbone to the presentation. However, caution must be exercised to ensure that the script is not merely memorized and recited to the audience. Clear communication is imperative to tailor the message to resonate with the audience, avoiding unnecessary jargon while maintaining scientific rigor. Beyond the presentation itself, networking propels a researcher's career forward. Actively seeking opportunities to connect with peers, mentors, and professionals at conferences and academic gatherings not only provides avenues for collaboration but also contributes to the researcher's professional growth and exposure within the broader scientific community.

Breaking Down Barriers.

Institutional barriers to research are multifaceted, as evidenced by a study indicating the prevalence of challenges such as lack of awareness (53%), interest (54%), insufficient funds (62%), time constraints (59%), and difficulties in patient follow-up (67%).[1] However, an infrequently discussed yet critical barrier lies in the toxic research culture that permeates many institutions.[2]

This toxic culture presents a challenge to medical students who are often early-stage researchers and fall victim to its traps. The relentless pursuit of authorship, particularly in top-order positions, is driven by personal gains such as promotions. However, this pursuit can lead to the establishment of monopolies, especially in the ethics committees that unfairly reject research proposals. It has profound implications for medical students who are just beginning their journey in the field. Its implications are far-reaching, extending beyond the immediate challenges of rejection and hindrances to research proposals. An environment emphasizing personal gains and hierarchical authorship compromises the genuine spirit of collaborative and ethical research jeopardizing the development of the next generation of medical researchers.

This poses a substantial challenge for medical students, as they may find themselves navigating a landscape where academic credit and recognition are unfairly distributed. The initial stages of a research career are crucial for skill development and cultivating a passion for scientific inquiry. When faced with a toxic culture the potential for disillusionment and disengagement among medical students is heightened. As medical students venture into the realm of research, it becomes imperative to raise awareness about the existence of this toxic culture and its potential pitfalls.

References

1. Pallamparthy S, Basavareddy A. Knowledge, attitude, practice, and barriers toward research among medical students: A cross-sectional questionnaire-based survey. Perspect Clin Res. 2019;10(2):73-78.

2. Hamrish Kumar Rajakumar, Gaman M-A, Puyana JC, Bonilla-Escobar FJ. Transforming Toxic Research Cultures: Protecting the Future of Medical Students and Early Career Researchers – Part I. Int J Med Stud. 2024;12(2):128-32.

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Experience

VAXXED & BOOSTED: Increasing COVID-19 Vaccination Rates in West Greenville, NC, USA

Taylor Stamey,[1] Oluwafemi Opelami,[2] Janet Moye.[3]

The Experience

VAXXED & BOOSTED was a COVID-19 vaccination community campaign held in July, 2022 in West Greenville, NC. Through the use of community ambassadors and hosting events at convenient locations and times, the program aimed to combat vaccine misinformation and alleviate barriers to receiving the vaccine in order to increase COVID-19 vaccination rates

Introduction

Pitt County, North Carolina has an estimated vaccine hesitancy rate of 12.5%[1]. In the spring of 2022, Pitt County was ranked 48th out of the 100 counties in North Carolina for COVID vaccination rates, with only 53.8% of the population fully vaccinated[2]. West Greenville, located in Pitt County, is historically of lower socioeconomic status, which leads to poorer social determinants of health. Its residents face barriers to getting vaccinated such as transportation and getting time off of work. Additionally, misinformation and incorrect assumptions about the vaccine have been circulated throughout this community, as they have across the US.

In order to combat vaccine hesitancy and alleviate burdens preventing vaccination, a COVID-19 vaccination community campaign entitled VAXXED & BOOSTED was conducted during the summer of 2022. A similar campaign is the Sacramento County Vaccine Ambassador Program in California, which employed Vaccine Ambassadors to provide culturally relevant COVID-19 vaccine information[3]. They held vaccination events and used promotional methods such as phone banking, canvassing, and social media.

VAXXED & BOOSTED employed community ambassadors to educate people about the COVID-19 vaccine. Vaccination events were held at various times at two locations in West Greenville. ***Figure 1***,***2***,***3*** show pictures of the events and people getting vaccinated. The goal of VAXXED & BOOSTED was to increase COVID-19 vaccination rates in West Greenville.

Figure 1. **Patient getting vaccinated at VAXXED & BOOSTED event**

Methods

One important aspect of the campaign was to have influential members of the community serve as ambassadors to promote the vaccine and vaccination events throughout the community. Community ambassadors consisted of non-medical people who grew up in and were familiar with the community, as well as trained community health workers. They spoke to people about the importance of getting vaccinated and resolve any hesitancies they had with the vaccine. They were trained with evidence-based talking points from the CDC's "Benefits of Getting Vaccinated" page and "Myths & Facts About COVID-19 Vaccines" page to combat vaccine hesitancy. These resources provide information about the safety of the vaccine and dispel myths surrounding the vaccine We also equipped our ambassadors with resources, such as flyers made from the information from these websites, to provide people. They were also compensated for their time.

Five events were hosted throughout West Greenville at the Community Crossroads Center and the JOY Soup Kitchen. The Community Crossroads Center is the homeless shelter located in

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West Greenville. The JOY Soup Kitchen is a free soup kitchen located in West Greenville. The purpose was to place vaccine clinics in convenient locations. Most events were hosted at noon, while one event was hosted at 6 pm in order to accommodate varying schedules. Events were promoted on the VAXXED & BOOSTED website, Facebook page, and Instagram. Free food was offered to all event attendees at the events hosted at the Community Crossroads Center, $10 gift cards and goodie bags were provided to those who got vaccinated, and educational resources were provided to event attendees to share with others. Pfizer COVID-19 vaccines were provided by the ECU Pharmacy and given by EMTs and nurse practitioners under the supervision of physicians. Funding was provided by the Community-Campus Partnerships for Health NNICE Grant.

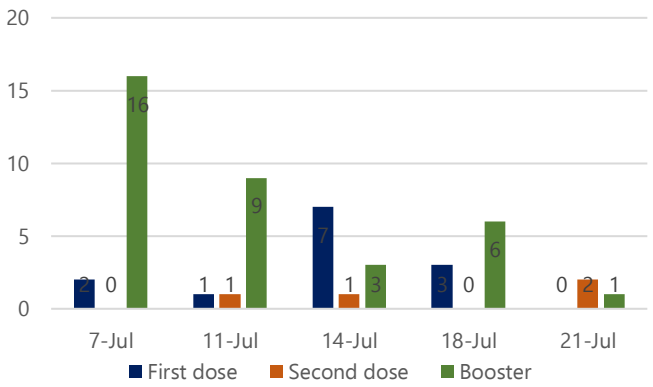
***Figure 2*. Co-director Taylor receiving her booster at a VAXXED & BOOSTED event**

A survey was implemented to gauge the efficacy of the event. Questions included in the survey were as follows: "Are you vaccinated for COVID? If yes, how many COVID vaccines have you received?" "Did you get vaccinated at today's event?" "Did the education provided at today's event influence your decision to get vaccinated?" "Did you learn something new at today's event?" "After today's event, do you plan to encourage others to get vaccinated?" "Did you find the use of community ambassadors helpful?" "Did you interact with a community ambassador before today's event?" Attendees circled "yes" or "no."

Results

Through VAXXED & BOOSTED, 52 people were vaccinated throughout 5 events that were held in a 1-month timespan. Of these 52 people, 13 people received their first dose of the vaccine, 4 people received their second, and 35 people received a booster ***Figure 4***. The feedback that we received from participants was generally positive. Out of 29 people who completed the survey, 24 people found the use of the community ambassadors helpful (82.8%, p <0.001) and 15 people interacted with a community ambassador before the event they attended (51.7%, p=0.855). The education provided at the event influenced the decision of 22 people (75.9%, p=0.005), 24 people learned something new at the event (82.8%, p<0.001), and 27 people plan to encourage others to get vaccinated (93.1%, p<0.001).

***Figure 4*. Vaccinations Given Through VAXXED & BOOSTED**



Discussion

Only one non-medical community member was able to be utilized as a community ambassador; however, community health workers were able to fulfill this role. Though they may not have been members of the community, they were already embedded in this space from other community health work and were familiar to the community. This is likely the cause of the low interaction rate of participants with community ambassadors prior to the events, as they spend less time in the community than a community member would. Because only 52% of the 29 people who completed the survey interacted with a community ambassador or health worker before the event, word of mouth likely played a big role in promoting the events.

Because the majority of people learned something new at the event, stated the education at the event influenced their decision to get vaccinated, and planned to encourage others to get vaccinated the events seemed to be successful in fighting vaccine hesitancy. By hosting events at convenient locations and various time, the campaign alleviated barriers to getting vaccinated for those who were already planning to get vaccinated.

One weakness of this study is the low response rate to the survey. Every attendee was provided with a survey; however, as

completing the survey was not a requirement to receiving the vaccine, many people did not respond. In addition, a few people asked for assistance with completing the survey due to poor literacy. People who asked for assistance were provided with it; however, we suspect that poor literacy rates in this community played a role in the low response rate. One in five adults in eastern North Carolina are illiterate, as opposed to one in seven in North Carolina as a whole[4]. Poor literacy rates likely also contribute to the poor vaccine rates in this community, as people are unable to verify information they hear from others. We tried to address this by providing our community ambassadors with talking points that can be explained verbally in simple language. In the future, it would likely be beneficial to conduct verbal surveys in this community.

***Figure 3*. Co-directors Taylor and Femi with two of the event vaccinators**

Compared to the Sacramento Vaccine Ambassador Program, VAXXED & BOOSTED vaccinated people at a slower rate. The Sacramento Vaccine Ambassador Program has vaccinated over 300,000 people since June 2020, in a county with a population of 1,584,000. In contrast, VAXXED & BOOSTED vaccinated 52 people in July 2022 in Greenville, NC, which has a population of 89,233. Specific census data for West Greenville is not available, but it comprises a small portion of Greenville's population. Several factors likely contribute to the disparity in vaccination rates, including the scale of the campaigns and pre-existing community attitudes toward vaccines. Communities with more favorable perceptions of vaccines before the program are more likely to achieve higher vaccination rates. Additionally, demographic differences may play a role. In Greenville, 39.3% of the population is African American, compared to 7% in Sacramento County[5,6]. The historical mistrust of the healthcare system among African Americans, stemming from past unethical medical practices, could contribute to lower vaccination rates in predominantly Black communities.Many people mistrust governments and health systems; however, when lifesaving medical interventions such as the COVID-19 vaccine become available, it is important that they gain public support and trust. Public health experts warn that is very likely that we have another global pandemic as travel has become so readily available[5]. When this happens, communities need to be prepared to fight it immediately, and the public needs to be on board. It was a goal of the VAXXED & BOOSTED campaign to not only instill trust in the COVID-19 vaccine, but to also instill trust in the medical system, which will make it easier for others to get behind public health initiatives in the future.

Conclusion

Through VAXXED & BOOSTED, 52 people in the West Greenville community received their COVID-19 vaccine. It was determined that the use of community ambassadors and educational events in convenient locations was helpful in educating people about vaccine safety and efficacy, as well as increasing the vaccination rates in this area. Improvements that can be made in the future include implementing verbal exit surveys instead of written surveys and recruiting more community ambassadors to increase interaction rates prior to events. The campaign sought to fight vaccine misinformation, alleviate barriers to getting vaccinated, and instill trust in the medical community.

References

1. CDC Vaccine Hesitancy for COVID-19 Available online: https://data.cdc.gov/stories/s/Vaccine-Hesitancy-for-COVID-19/cnd2-a6zw/ (accessed on 3 December 2023).
2. WNCT "Latest: Highest COVID-19 vaccination rates in NC." Available online: https://www.wnct.com/news/north-carolina/latest-highest-covid-19-vaccination-rate-in-nc/ (accessed on 3 December 2023).
3. Public Health Launches Vaccine Ambassador Program. Available online: https://www.saccounty.gov/news/latest-news/Pages/Public-Health-Launches-Vaccine-Ambassador-Program.aspx (accessed on 18 July 2024).
4. WNCT "Addressing the illiteracy rate in eastern North Carolina" Available online: https://www.wnct.com/news/addressing-the-illiteracy-rate-in-eastern-north-carolina/ (accessed on 18 July 2024).
5. U.S. Census Bureau. "QuickFacts: Greenville city, North Carolina." Available online: https://www.census.gov/quickfacts/fact/map/greenvillecitynorthcarolina/PST045219 (accessed on 18 July 2024).
6. U.S. Census Bureau. "QuickFacts: Sacramento County, California." Available online: https://www.census.gov/quickfacts/fact/table/sacramentocountycalifornia,US/PST045222 (accessed on 18 July 2024).

7. CEPI "How prepared are we to face a future pandemic?" Available online: https://cepi.net/news_cepi/how-prepared-are-we-to-face-a-future-pandemic/ (accessed on 3 December 2023).

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Experience

The Shame Is Not Mine: Addressing Abuse of Power Dynamics in Medical Training

Sierra Norman.[1]

The Experience

The concept and concern about mistreatment during medical school is a longstanding issue. In the early 1980s, a physician on faculty at a medical school noticed the stark contrast between the optimism and eagerness in incoming medical students and the cynicism and depression of graduating medical students.[1] His subsequent research revealed that medical student mistreatment, particularly during the clinical years, led to this significant and negative impact.[2] In 1991, the Association of American Medical Colleges began including questions about mistreatment in their annual Graduation Questionnaire.[3] Numerous studies have been conducted on best practices to address medical student mistreatment. In 2012, the David Geffen School of Medicine at UCLA published their results after analyzing 13 years of data on the incidence, severity, and sources of perceived mistreatment.[4] During this period, they had implemented multiple approaches to address medical student mistreatment, including creating formal and informal methods for reporting and resolving incidents, providing education on the topic to students, residents, and faculty (i.e. definitions of mistreatment), and promoting open discussion among all levels. Despite these efforts, there was no significant change in the culture of mistreatment, citing influence of the engrained "hidden curriculum" of unspoken norms in the academic-social environment.

My experience with mistreatment occurred on a surgery clerkship. Surgery clerkships have the highest rate of reported mistreatment from medical students, with faculty typically being the source.[5] Across all specialties, mistreatment of medical students is largely due to sex/gender, race/ethnicity, and sexual orientation.[3] The American College of Surgeons has recognized the problem of mistreatment within their specialty specifically, which uniquely also includes influence of student role and career choice.[6] This suggests individualization of mistreatment, which creates additional obstacles to relying solely on a generalized response to mistreatment.

An important part of responding to mistreatment is being aware it exists. However, many students do not feel comfortable reporting mistreatment. Common reasons include concerns about believing it was not significant enough, mistrusting their institution, and fearing retaliation.[7,8] And, unfortunately, these concerns are often justified.

My First Surgery Clerkship

I have carefully considered the decision to share my surgery clerkship experience. Having already faced retaliation and defamation for voicing my concerns, I worried that sharing publicly might further affect my future education and career. However, staying silent about this specific experience would make me feel like I am accepting the shame of it. But the shame is not mine.

During the summer of 2023, I began my third core clerkship in surgery. My approach to every core clerkship has been to make the most of my experience, realizing I may never do anything like it again. I knew there were stereotypes of the environment, but my approach to surgery was no different. However, the atmosphere was far worse than I could have ever anticipated.

The initial negative interactions were primarily with the physician assistants (PAs). I want to preface that these experiences were with individuals, not a profession. I have worked with some incredible PAs whom I admire and am grateful for their contributions to my medical education. During this clerkship, I was predominantly left to work with the PAs, and there was tension with them from the beginning. I was told incorrect times to arrive to cases, misdirected on which cases to participate in, and directly rejected when I tried to ask for help or clarity on expectations. I was not scheduled to participate in clinic with the attending physicians, being told "medical students slow things down," so my only interactions with them were in the operating room. During the end of one case, an anesthesiologist felt it necessary to step in on my behalf and diffuse a PA's mistreatment towards me after the attending physician had left. The expectations from the PAs often contradicted the document on medical student expectations that I had received from the site director. No matter how I tried to balance it, tensions continued to escalate. I have included the timeline of the negative interactions submitted to my university as a Supplementary file, highlighting two of note below.

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During Week 2 of 6, my interactions with the PAs had escalated to the point that I was concerned about their influence on my evaluation. I addressed this concern with the site director, who dismissed it. He reassured me that he was not worried about it impacting my evaluation and that I should not be either. He attempted to normalize tension within their surgical team by sharing some of the drama. Such as issues with a PA taking a "father-like" approach with students. And the practice needing offices on two separate floors due to contempt between some of the surgeons. And a surgeon writing inappropriate notes, like referring to a patient's pre-procedure shave as a "pornstar shave." He finished the conversation by advising me to keep trying with the PAs.

During Week 3 of 6, I was publicly humiliated for the second time by a PA, this time in front of the patient, a new attending physician, and the rest of the surgical team in the operating room. He continued to accuse me of skipping rounds, even after a brief explanation that I was not assigned to participate that morning. It was not the time or place to argue, so I waited until the next morning and asked to speak with him privately about it. I told him I was on the clerkship for my education first and foremost and would not intentionally skip opportunities. I acknowledged there was some confusion the day prior and asked if he had any concerns about my performance moving forward that he address them with me directly. Initially, he was receptive, then he abruptly started yelling. "Actually, I am upset now. I have never been called out by a medical student before. Do you want me to just ignore your existence? Because I can do that!"

After speaking to the site director about this interaction, he made adjustments to limit the PAs interactions with me. However, the negative encounters and toxic environment still continued. With about two weeks remaining in my clerkship, the site director completed my Mid-Rotation Student Feedback Form, giving me positive marks and indicating no concerns. He also mentioned several times that the other attending physicians had texted him that they had had a good day with me in the operating room. On my last day, I offered to discuss my clerkship experience with him, hoping for some follow-up about the environment. He did not accept but texted me that I "finished strong." I let him know I had a timeline of the negative interactions that occurred and would include it in my evaluation to the university, for the sole purpose of providing feedback to improve the learning environment for future students. He told me again that he was not worried. And I was simply relieved for the clerkship to be over and my break to be starting.

But It Only Got Worse

I wish I could say that the negative experience ended with the conclusion of the clerkship, but it only got worse. The knowledge of my timeline triggered retaliation from the site director, to a level of severity the university's designated advocate and other faculty members say they have never seen before. I mistakenly received an email from the site director intended for his colleague, stating he believed I would be giving him a negative evaluation and he would be failing me.

A few days later, I received the site director's evaluation, with a clinical grade of 34.1% (FAIL) and a comment stating, "it's a matter of time before she hurts a patient."

As an individual who made the choice to dedicate my life to a career helping people, receiving this comment was absolutely devastating. The days and months that followed left me to fall into a very dark place. For so many reasons, I struggled to share anything with anyone. The weight of it felt so heavy, I did not want to crush anyone else. I tried to keep the darkness to myself, but it was slipping through the cracks. And it broke my heart to watch as my behavior was misrepresented by my closest friends and twisted into damaging rumors, shredding the last bit of reputation I had and leading to more self-isolation.

I did make a half-hearted attempt to seek help. But when the university's counselor did not show up to our appointment, it just reinforced my belief that it was not that bad and I could handle it on my own, so I did not pursue further support. I knew I was not going to do anything, so I did not think I needed to tell anyone. I did not think I needed to tell anyone that my Juliette balcony seemed to taunt me with its symbolic and ironic possibility. I did not think I needed to tell anyone that I used to sleepwalk when overly tired and stressed. And that maybe fear of that led to waking up being unable to move, feeling like I was being choked by a shadowy creature. But mostly I did not say anything because I did not want anyone to think I was weak. And as a result, my body became weak.

I was not talking. I was not eating. I was not sleeping. I was having multiple panic attacks a day. And eventually that all caught up to me. I accidentally ate something I was allergic to, something that I have done dozens of times with only a mild reaction. This time, I thought I was just having an XL panic attack at the same time and practically begged for over an hour just to be left alone to go to sleep. By the time I let someone take me to the emergency room, my oxygen saturation was 77% and I was showing signs of stage 3 anaphylactic shock. The doctor gave an incredulous, but kind, lecture to this medical student, telling me that if I had gone to sleep, I would have woken up with brain damage, if I woke up at all. Being disturbed with thoughts of not existing anymore for weeks, and then having my actions almost unintentionally result in that, was such a violent wake-up call.

Starting To Heal

I was emotionally, mentally, and physically shattered, but I was alive. After my break, I started my Internal Medicine clerkship. As I was shown compassion and started to feel safe again, I slowly began sharing what I was going through. When I confided in my attending physician, she began to cry and shared something similar had happened to her during her surgery clerkship decades ago. She was promised the culture was not always going to be like this, but here it was still happening. Then she said something that brought on a fresh set of tears for me, "I want you to know that I wrote in your evaluation I would gladly let you care for my family members."

The attending notified the site director for the Internal Medicine clerkship, who offered me space to share what/if I wanted. When we met, she provided me with mental health resources outside of the university. She told me that even if there was truth to the comment, which she did not believe that there was, I was a student and a comment like that would be a reflection and failure of the educator. Then, she asked if she could give me a hug, which I accepted with more tears. Ultimately, I received a glowing evaluation with comments that reflected those from every other core clerkship (aside from the first surgery clerkship) and was offered a letter of recommendation.

Throughout this time, I had been appealing the evaluation and am disappointed to say that my abundance of evidence was not enough against the site director's word. I have included my appeal as a Supplementary file. I was never given a notification or explanation, but the comment "it's a matter of time before she hurts a patient" was removed from my evaluation. The rest of the evaluation and grade were left unchanged and, consequently, I had to repeat the six-week surgery clerkship at a different site. To my knowledge, it does not appear the site director has been or will be held accountable for his dangerous actions.

I needed answers to so many "whys" for acceptance and closure to move on. I met with several leadership members of the university, but each one redirected me to someone else for those answers. Eventually, all deferred the decision, and therefore any answers, back to the surgery clerkship director. I had only met with her once during the appeal process and when I reached out, she did not reply. After emailing her again, her response included "I will not be able to engage in more discussions about this matter" and she pointed me back to someone who had already pointed me to her.

I was terrified to return to the general environment that had almost destroyed my career and future. On the first day of my second surgery clerkship, my intern asked, "What are your goals for this rotation?" My goal was simply to survive, and not talk about my first surgery clerkship experience for six weeks. But being there was so much harder than I thought it was going to be. I made it six hours before I felt it was necessary to tell my chief resident how I was feeling and why. Her response was blunt and validating.

Although being there was a mental and emotional struggle, I did have a great experience. The biggest ghost of my first surgery clerkship was in the Mid-Rotation Student Feedback Form, where a disclaimer had been added: "***This is not a guarantee of your final grade, and it may change pending your future performance on subsequent shifts and your exam.***" It is an understandable statement, but another frustrating response from the surgery department to my experience, as my form from the first surgery clerkship was positive.

Overall, the second surgery clerkship was everything the first surgery clerkship should have been and more. From an attending physician joking with me for "calling out" a chief resident, to a chief resident gladly taking photos of me to capture the memories, and to a resident saying I had a "plastic surgeon's stitch," every interaction was the complete opposite to my first experience. I earned a clinical grade of 93.8% and a High Pass overall, again receiving comments consistent with every other clerkship, aside from the first surgery clerkship.

So What?

Words have value, and too often as medical students, we often feel we become the sum of words like PASS and FAIL, or "it's a matter of time before she hurts a patient." This makes the clinical years of medical school an especially vulnerable time for students, when a large portion of our grade can be arbitrarily decided. A weaponized fail or baseless comment can cause irreparable harm, and such behavior can have devastating consequences. It is not merely jeopardizing a student's career but also their very existence. Suicide rates among medical students are already three times higher than our peers,[9] without the added burden of being targeted by those who should be supporting us on our academic journey.

For this reason, more than any other, we must address the abuse of power dynamics in medical education to protect the well-being and future of every student. Unfortunately, it seems like some individuals in the medical field thrive on abusing power dynamics and see mistreatment as a rite of passage. Who excuse mistreatment as the method to strengthen resilience, because that is how it was done to them. But the desire to have others suffer as you have suffered is pathological. And the defensive nature of constructive criticism does not have a place in the future of medicine.

For decades, mistreatment of medical students has been condemned. But words are easy and often lack the necessary action to support them. My university says students are protected from retaliation, and I would imagine every institution has similar statements. I have unmistakable evidence that retaliation occurred, yet no action has been taken to protect me. It is often hard to prove when personal attacks bleed into professional spaces, but the designated advocate said this was the clearest and strongest case of retaliation they had ever seen. Still, it was not enough. So how are students supposed to feel safe coming forward when they have less or even no proof? When it is verbal, derogatory comments about their background or identity? Or physical, inappropriate moments of touch?

Isolation often serves as shame's closest companion, and that is a break-up I am working on. In the private conversations I have had, and other experiences shared, I know I am not alone in experiencing the pervasive culture of shame in our field. Unfortunately, as medical students, we have little power to do anything. I have been told I should have kept my mouth shut and head down, that the way I have been treated is just how things are. I do not accept that. I am not the kind of person to avoid doing the right thing just because it is the hard thing. And frankly, I would not want my future healthcare providers to do that either.

Moving Forward

What is being done to address medical student mistreatment, and subsequent retaliation for reporting, is not enough. We are still being exposed to negative educational experiences, and those in power to change that are not always supportive. The

burden should not fall to medical students to carve out a space for our own safety, but until the larger system and culture changes, it kind of does.

Over the past year, one of the most important things I have learned is the value of talking to people you trust. As medical students, I think our natural reaction is to keep our struggles to ourselves, likely fueled by imposter syndrome.[10] But it is a matter of time before every medical student faces some challenge during their training. Sharing experiences, advice, and encouragement can cultivate a supportive environment. Continuous, open communication among classmates may also help dismantle the negative effects of the "hidden curriculum" that perpetuate the culture of student mistreatment.

A student-led resource could offer a bottom-up approach to addressing medical student mistreatment by creating a space to facilitate these conversations. However, it is important to acknowledge that the act of sharing personal experiences of mistreatment could add stress to the already stressful experience of being in medical school. Feeling powerless to not only protect ourselves, but also our friends and classmates that we care about, from being mistreated can further add to the emotional burden of the experience. Utilizing this approach would require a strong partnership with and trust in the institution to enact the necessary change to end mistreatment.

Therefore, medical education institutions will always be at the center of change regarding learning environments. While many institutional responses to mistreatment have focused on a top-down approach, there is room for improvement in implementing and executing these policies and procedures. For example, I feel my situation could have been avoided with more proactive and protective policies, especially regarding retaliation. Students, and clerkship departments, should be notified if a student's clerkship performance is not at a passing level before the clerkship ends, to prevent students from being failed only after reporting a concern. Additionally, there should be specific procedures for addressing retaliation, such as involving a third-party to avoid any potential bias. And it is important that there be transparency about how the institution is addressing mistreatment.

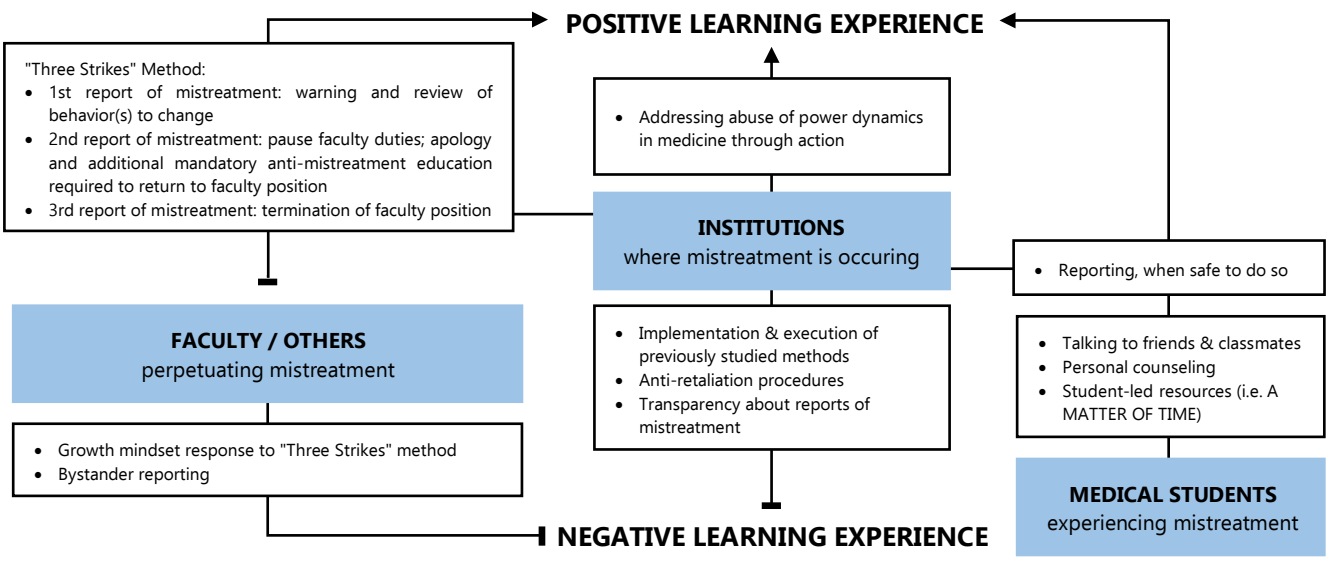
Bottom-up approaches can also be a response within an institution. Bystanders witnessing mistreatment should be encouraged to report. And those reported to be perpetuating mistreatment should be reviewed and held accountable, such as with a "three strikes" method. My suggestions are shown in *Figure 1*.

My hope in sharing my experience is to start a broader conversation about actively addressing the powerless position medical students are in during clinical years and the abuse of power dynamics in medical education. But I am only a fourth-year medical student, I do not have all the answers for the *how* to fix this. And more than anything, I do not have the power to fix this. This needs to be addressed by individuals with that power. I recognize this is complicated to navigate, but the implications are too important to ignore. Condemnation is a start, but it is action that really matters. We all deserve a safe, positive learning environment.

Conclusion

Healing from this experience has been a long process. Sharing this article is part of that conclusion, and it was suggested that I wait for my own well-being. I chose to wait until after re-completing the surgery clerkship and taking Step 2 CK, but I could not wait until after residency matching. I could not carry this alone for another year; I needed to let go to move forward. And I could not continue to play a part in maintaining the culture of mistreatment by staying silent any longer. Publishing this article has been healing for both me and others that have experienced mistreatment during their medical training, and I hope it will protect future students from similar exposures. Based on experiences shared from students, residents, and attendings, my experience could have, and has, happened at other institutions. I

***Figure 1*. Suggestions on How to Encourage More Positive Learning Experiences and Eliminate Medical Student Mistreatment.**



have chosen not to name my university or individuals involved because it is more than an isolated event. Mistreatment happens in many forms across different training sites and specialties and is allowed to occur because of the historic and systemic culture. Part of sharing my experience is to change that culture. I am hopeful that sharing this experience will be seen as a learning and growing opportunity, as I know it has been for me.

The comment "it's a matter of time before she hurts a patient" was truly devastating. Although I know it was written in retaliation and removed from my evaluation, living with that was one of the biggest challenges I had to overcome. I felt it was important to make a broader positive impact out of this negative experience. So, I am developing A MATTER OF TIME, a project intended to support mental health by creating a space for celebration during highs and support during the lows on the journey to physicianhood. As I approach the end of my time in medical school and will soon be focused on the demands of residency, I am hoping to partner with an organization that can help amplify the impact of A MATTER OF TIME. My vision is for it to become a student-led resource in medical schools nationwide to encourage supportive communication among medical students and contribute to a more positive and compassionate generation of physicians.

I did not fail my clerkship, but the clerkship department and university did fail me. And while this experience initially turned my imposter syndrome into a near-invincible beast, I have now slayed it. I know I am a badass medical student and will be an even better physician one day.

I did not choose medical school because it was easy, but it should not be this hard. While I have also had the best time of my life in medical school and thoroughly enjoy being a medical student, I have never felt as powerless as this experience has made me feel and was haunted by it for months. As medical students, we do not have much power. But I have my voice and will not let anyone silence it.

References

1. Silver HK. Medical Students and Medical School. JAMA. 1982;247(3):309–310.
2. Rosenberg DA, Silver HK. Medical Student Abuse: An Unnecessary and Preventable Cause of Stress. JAMA. 1984;251(6):739–742.
3. Hill KA, Samuels EA, Gross CP, et al. Assessment of the Prevalence of Medical Student Mistreatment by Sex, Race/Ethnicity, and Sexual Orientation. JAMA Intern Med. 2020;180(5):653–665.
4. Fried JM, Vermillion M, Parker NH, Uijtdehaage S. Eradicating Medical Student Mistreatment: A Longitudinal Study of One Institution's Efforts. Acad Med. 2012;87(9):1191-1198.
5. Breed C, Skinner B, Purkiss J, Opaskar A, Santen S, Reddy R, et al. Clerkship-Specific Medical Student Mistreatment. Med Sci Educ. 2018;28:477–482.
6. American College of Surgeons. It's Time to Address Student Mistreatment. Available from: https://www.facs.org/for-medical-professionals/news-publications/journals/rise/articles/student-mistreatment/. Cited July 16, 2024.
7. Bell A, Cavanagh A, Connelly CE, Walsh A, Vanstone M. Why do few medical students report their experiences of mistreatment to administration? Med Educ. 2021; 55: 462–470.
8. Kloos J, Simon E, Sammarco A, El-Nashar S, Bazella C. Neglect as an undefined and overlooked aspect of medical student mistreatment: A systematic review of the literature. Med Teach. 2023;45(12):,1-9.
9. Berkowitz C. Study of Medical Student, Resident, and Physician Suicide (Resolution 959-I-18). American Medical Association. Available from: https://www.ama-assn.org/system/files/2019-07/a19-cme-6.pdf. Last updated July 2019; cited July 16, 2024.
10. Maqsood H, Shakeel HA, Hussain H, Khan AR, Ali B, Ishaq A, et al. The descriptive study of Imposter Syndrome in medical students. Int J Res Med Sci. 2018;6(10):3431.

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Supplementary files

Timeline

(As it is not the intended focus, names mentioned in this document have been replaced.)

June 26/27: At the end of the day on June 26, I ran into PA1 and asked him some questions about the next day's schedule. Dr. A had said cases typically start at 7:30 am, but the status board for the next day showed a start time of 7:00 am with Dr. B. As it would be my first day starting in the OR, I wanted to confirm if that was the time the room started getting set up or if that was the time I should be there. He said I would be fine getting there at 7:30 am. The next morning, I showed up around 7:00 am to pre-round on the patient from the previous day before starting cases. I ran into PA2 and told him I would be in with Dr. B's cases that day and would be in the OR at 7:30 am. PA2 said the case was scheduled for 7:00 am and that I absolutely did not want to be late for a case with Dr. B. I hurried down to the OR and made it on time. The previous day, when everyone heard I would be working with Dr. B the next day, they all had some sort of warning. Dr. A had said he would try to intimidate me and I should "just stroke his ego for 5 minutes and all should be good." The morning of his case, when the scrub tech found out it was my first day with Dr. B, they told me to "stand behind [them] and don't say anything." At the time, I had attributed PA1 telling me to arrive late as a misunderstanding, but with all the events that continued to transpire, in hindsight, I believe he was trying to set me up for a bad first impression, especially with Dr. B.

June 27/28: At the end of the day on June 27, I again ran into PA1 and asked him some questions about the next day's schedule. There were overlapping cases with Dr. C and Dr. A on June 28. Dr. A had told PA1 on June 26 that he specifically wanted a PA in his first case as it was going to be difficult. I was under the impression after talking to PA1 the plan was for me to go to Dr. C's first case, while a PA would be in on Dr. A's first case as requested, and then I would go to Dr. A's second/last case. Sitting in Dr. C's case, he was telling the OR how PA1 and PA2 were fighting in the PA lounge that morning about which one would get to come assist with the end of that robotic case because neither wanted to go to Dr. A's breast case. He said they typically take turns and PA1 was in the robotic case the day before, so PA2 thought it should be his turn. However, PA1 was out of town the week prior and missed three of Dr. C's robotic cases, so he felt entitled to make them up this week. Partway through the case, PA1 came in to let Dr. C know he "won" coming to assist him later. He high-fived the nurses and me in celebration before leaving and returning later to close. After the case was over, I received a phone call from PA2, who was angry, saying that Dr. A had been all alone during his first case because they thought I was going to help and they didn't know where I was and that put PA2 in a position to have to go help. He said he was too busy to help with Dr. A's second/last case and was calling to make sure I went. I apologized for the confusion but explained I had understood that Dr. A wanted a PA's help on that case and that I had spoken with PA1 about watching Dr. C's robotic case (and that PA1 saw me in there) and assisting with Dr. A's second case. Because I had heard the backstory from Dr. C in the OR, I felt PA2 was trying to blame me for his not wanting to/not showing up to assist in Dr. A's first case.

July 3: I was working with PA3 and PA4. PA3 brought up how my notes were really not good and how they could never use them to bill as they were. In the Medical Student Expectations from Dr. A and when Dr. A was describing the note expectation during orientation, he specified they should be short SOAP notes, holding up his thumb and index finger which I took as indicating about a paragraph size. I had looked at previous notes from some of the doctors to get a better idea/example and found a recent paragraph size one from Dr. C that I modeled mine after. I tried to explain my understanding of the expectations from Dr. A. She said I was supposed to be doing my notes like theirs, which were longer daily H&P notes, and disregarded my explanation of the expectation from Dr. A. It was confusing and belittling, but I didn't want to argue or seem difficult, so I did H&P notes until after I was told to stop by Dr. A during our July 6 meeting.

July 5: At the clerkship site, I spend two weeks with acute care (I was scheduled for July 3-7 and July 24-28 by Dr. A). During these two weeks, I was expected to round with the on-call doctor and the PAs. This week, it was Dr. E. He rounds in the mornings and again later in the afternoon, but there is no set time that any of the doctors round. On July 5, we finished cases around 12 pm and Dr. E mentioned they would round again around 4 pm. There is a WWAMI study area at the hospital, so I told PA1 I would be going there to study until rounds and that I would be back at 4 pm. I asked if he would text me if they started rounds before 4 pm, he scoffed but said he would. I've noticed a large majority of communication within the hospital is texting, so I didn't think it was an unreasonable request but he made me feel that coming from me it was. He did text me around 3:30 pm telling me rounds were at 4 pm.

July 6: I knew all three PAs were working that day. Typically, I work on one of the computers in the PA lounge, which works out because that is where they/the doctors meet prior to rounds. However, there are only 3 computers in the lounge, so when all three are working, I have to go find a computer elsewhere. I ran into PA3 in the locker room and told her I would be at a different location to do my notes that morning and asked if she could text me when they start rounds. Again, there is no set time rounds begin. She proceeded to lecture me about how "we" can't be responsible for texting me all the time. I needed to be "independent" in figuring things out for myself and being where I needed to be and when. She said it was my responsibility to just keep checking in the lounge to see if they were there or not (which Dr. A during our meeting later that day told me not to do). Again I've noticed a large majority of communication within the hospital is texting, so I didn't feel it was an unreasonable request. Logging in and out of Epic while trying to complete the longer H&Ps every 5 minutes didn't seem logical. I felt I had been independent in completing my responsibilities,

there were just two special circumstances I was asking for help. But what shocked me the most was her use of "we." PA1 had been the only PA in the lounge the previous day, so I now knew they were complaining to each other about me. Dr. E was the previous site director, so when it was just us scrubbing in later that day, I asked if I could speak with him about some of my concerns since I would not see Dr. A for about a week. I said I felt there was growing tension with the PAs and wanted a better understanding of what our interactions were supposed to be in hopes of deescalating. He said he would have time to discuss it the next day.

- During the last case, Dr. E came in with PA1 and he was surprised to see me in there. He thought I would be in the case with Dr. B and Dr. G. Dr. G is a vascular surgeon who only comes once a month. In the Medical Student Expectations from Dr. A, it says to prioritize attending cases with Dr. G. But it also says to complete any acute care surgeries before scrubbing in for elective surgeries. I hadn't considered that I would be assigned to acute care when Dr. G was in town, so that was my mistake for it not to be on my radar. More on this during my meeting with Dr. A later that day.
- At the end of the case, Dr. E left me to close with PA1. I was doing a running subcutaneous stitch and hadn't buried my knot yet (so I hadn't yet checked the integrity of my stitch) before PA1 started pulling on the stitch and announcing that I had left a hole. He kept going on announcing the hole, saying he didn't know what I had done, asking if I could see the hole, saying he needed more suture to fix my mistake, etc. I acknowledged my mistake, but I didn't want to make excuses (though didn't feel I was given an opportunity to catch/correct my mistake) and was feeling publicly humiliated, so my responses to his comments were minimal. When he continued to carry on, the anesthesiologist peeked over the drape to step in, saying he remembered what it was like trying to suture as a medical student and was trying to be encouraging, telling me that I was doing my best. I was moved by his thoughtfulness and it did make me teary-eyed.
- As I was leaving, I ran into Dr. E who said he ran into Dr. A who wanted to chat with me. I assumed he had mentioned my request earlier to discuss the PA tension, so I went to Dr. A's office and after telling him my concerns, he said he wasn't aware and that he just wanted to do a 2-week mark check-in. He did say it technically wasn't their responsibility to be texting me for rounds, but it wasn't an inappropriate request and that I probably would have irritated them by popping my head in every 5 minutes. I told him I understood they were small, negative interactions, but my main concern was that it was escalating. That morning, I had learned they were talking poorly about me amongst themselves, and by the end of the day it was public humiliation in the OR to the point another doctor stepped in to defend me. I wasn't sure how evaluations were completed for this rotation, as most of my time was spent not with the doctors, but with their PAs. And if they were speaking poorly of me amongst themselves, I expected they would do the same with the doctors. I worried about how it would affect my experience and evaluation. Dr. A said they do typically rely on the PAs for feedback and tried to consider potential reasons for the tension:
    - He said the PAs are compensated for their involvement in teaching medical students, saying as the site director he gets twice as much as the other doctors and the PAs get half as much as the doctors (this conflicted with what he told me on my last day). He also mentioned they teach PA students, so maybe there was some role confusion.
    - I hadn't specifically mentioned any PA by name, but Dr. A asked if it was mostly PA1. He said there have been some issues with him in the past, but he just tries to take a "father-like" approach with the students that sometimes comes off the wrong way. That portrayal/mindset from Dr. A and PA1 made me uncomfortable and I felt it was not appropriate for a workplace or learning environment.
    - He asked if they knew I wanted to go into pediatric psychiatry, and when I said yes alluded that maybe they weren't taking me seriously because of that interest. I have been very clear on all my rotations when asked what specialty I'm interested in, that while I am pretty set on pediatric psychiatry, I am keeping an open mind. And at the very least, if I chose pediatric psychiatry, I will never do anything like this again so I want to make the most of my experience.
- We then shifted to more of a two-week check-in conversation. He looked at my notes and said they were good, however very long and detailed, more on the scale with expectations of a PA or PA student, and would take too much time for a medical student to do, as most of my time was supposed to be spent in the OR. He told me to return to doing a shorter SOAP note and shared his template with me. (I know the PAs read my notes, so I believe returning to shorter notes after they specifically told me to write longer ones contributed to the continued tension). On the topic of short notes, he shared that he dislikes how short Dr. B's notes are and it is hard to know what's going on when he takes over his patients. He said sometimes Dr. Bd's notes are also quite inappropriate, like saying the patient received a "pornstar" shave prior to the surgery. Dr. B and Dr. D have to be in separate clinic spaces/floors because of personal dramas. Dr. A made a comment that he doesn't like drama and I apologized for the drama with the PAs and he just brushed it off as not a big deal.
- With regards to missing Dr. G's case, Dr. A did say the PAs are supposed to be letting me know about his cases and other more interesting/unique opportunity cases, which they did not. (I also later went and looked at the Epic status board for Dr. G and it just had Dr. B's listed, so I am unsure how I could have known on my own that Dr. G was in town/assisting him.) He would not be back during my clerkship, so I was disappointed to miss out on that opportunity, likely due to this tension.
- Dr. A kept saying how medical students usually get along so well with the PAs. The conclusion of the meeting was to continue sticking close to the PAs, but if tension continued to just come and work in his clinic.

July 10: There were no scheduled elective surgeries that day, so when checking in with the PAs that morning, I told PA3 I would scrub in for Dr. F's (the on-call doctor) acute care case. When Dr. F and PA2 arrived in the OR, PA2 announced from the other side of the OR (in front of Dr. F, the nurses, the scrub tech, and the anesthesiologist) that I had skipped rounds that morning. I responded that I only round when I am on acute care, which was the previous week, to which he responded that I had missed 18 acute care patients that morning. I felt humiliated being accused of something I hadn't done, but didn't feel it was appropriate to argue about it across the OR room, so I went to scrub in. When PA2 came to scrub in as well, I explained to him again I was not assigned to acute care that week. Dr. F was present for the OR situation and would have been the rounding physician that morning, and I believe the PAs' portrayal of me was a direct cause of my interaction with Dr. F on July 25.

July 11: Still feeling the escalating tensions with the PAs and the new and continuing public humiliation attempts, I thought it was best to speak directly and privately. The morning after the incident in the OR with PA2, I asked if I could speak with him in the hallway. I told him I was on the clerkship for my education first and foremost and I would not intentionally skip opportunities. I understood there was some confusion the day prior, but asked that if he had any concerns about my performance moving forward that he come to me directly. Initially, he seemed receptive and understood where I was coming from. But suddenly, he flipped and said he "was upset now," that he had "never been called out by a student before." He asked, "Do you want me to just ignore your existence because I can do that." I felt like he was attempting to gaslight me about how the experience made me feel, but I didn't want to escalate the conversation anymore. So I just let him continue on and eventually, he calmed down. He said I was welcome to be joining them on rounds outside of my acute care weeks. I said it was tricky because they don't round at set times, to which he responded to just text about it. I was almost speechless since PA1 and PA3 have been so adamant about *not* texting for rounds.

- In between the two cases for the day, PA1 told me Dr. A wanted to speak with me and that I should go now. I went looking for Dr. A, and his office said he may have left for the day. I text him and he told me to call him that night. Since I was supposed to be in his cases the next day, I figured it had to do with my conversation with PA2 if it couldn't wait until the next day. When I called, I explained what happened with PA2 and he said that is about what Dr. B told him happened. I was a little confused about how Dr. B became a part of this but again wondered if the PAs were trying to get me on his bad side, especially due to his reputation. Dr. A said it is a dynamic rotation, switching back and forth between acute and elective care and when there isn't much going on, I am welcome to round with the team. He said he wasn't sure how "we" got off on the wrong foot with the PAs (which I did appreciate the use of "we"), but that he wasn't stressed about it and didn't want me to be stressed about it either. The resolution was for me to limit my interactions with the PAs. I no longer checked in with them in the morning or rounded. Dr. A would send me the cases to scrub into each week. Dr. A said they typically don't have medical students in the clinic, as it slows them down, but he did invite me to spend a couple of days there during the remainder of my rotation. Dr. C also invited me to his clinic once.

July 17: A small thing, but just another example of the constant contradictions between the PA's expectations and the expectations from Dr. A. I was working on my notes at a computer not in the PA lounge when I saw PA1. He told me PA2 said I was supposed to be signing my notes with a note about the attending I discussed them with. In the Medical Student Expectations document, with regards to giving the attendings a report on a patient, Dr. A says "It's great if you can find us don't waste time trying to track us down because we can be elusive!" I rarely saw the doctors outside of the OR, so I did not get many opportunities to present patients. There was also nothing in the Medical Student Expectations document about signing notes with "discussed with."

July 21: Since July 11, I saw the PAs less frequently. However, I never knew who/where/when I would be interacting with them again, which led to a lot of anxiety. When they were around, there was definitely tension that everyone seemed to ignore so I also tried to follow that lead. On July 21, I was left to close with PA3. I have watched the PAs close with the doctors dozens of times, and they have a rhythm assisting with dabbing oozing wounds when the doctor pulls a stitch through, cutting suture, etc. PA3 was watching me suture, holding the only Raytec in the field in her hand. I pulled a suture through and the wound was oozing, so I held the needle driver out of the way and asked PA3 if she would dab. I don't have the same rhythm with the PAs as the doctors do, so I try to be more verbal to avoid any accidental needle pokes. PA3 snapped that I should be "independent" and doing things on my own. I explained why I had asked her and then asked the scrub tech for another Raytec and finished independently. I believe surgery is arguably one of the most *inter*dependent specialties and that it is dangerous to have that mindset in the OR. As students, we are still learning and this continued narrative from PA3 could have been handled in a more helpful way.

- I closed with PA2 alone later, probably the first and only interaction I had with him since July 11 and for the remainder of the rotation. Without asking, he was very helpful while I closed and treated me in a professional and respectful manner.

July 25: I was supposed to be on acute care again this week (July 24-28), but Dr. A just had me do rounds with him on July 24 when he was covering for Dr. F and then participate in elective cases for the rest of the week. There were no scheduled elective cases for July 25, so when Dr. A asked me what my plan for the day was I told him I would text Dr. F in the morning to let him know I was on call, to which he agreed was a good idea (call requirements for the clerkships were one day a week and two weekends). When I text Dr. F on July 25, his response was "Take me off this list". I worry that is a direct result of what occurred on July 10.

July 27: I was left with PA1 alone to close. When the scrub tech was getting me a needle ready, PA1 told him he didn't want me to close. It was a robotic case, so I had only been watching for the rest of the surgery. When I saw Dr. A later, he asked how watching "robo-tv" and closing had gone. I told him PA1 didn't want me to close, and he didn't have a reply.

Aug 2: This was my last day and even though I had a poor experience, I still was appreciative of the opportunity. I have baked cookies to bring in with thank-you notes on my previous rotations and treated this one no differently. Dr. A thanked me for the cookies and mentioned how it was a nice gesture, as all the faculty are volunteers, and he was the only one that received a little compensation for having students as the site director (this conflicted with what he said during our meeting on July 6). We had a brief goodbye. I text him that I would be leaving that evening for a positive environment to finish studying for and to take this shelf exam. I offered to chat the next day about my clerkship experience, hoping for some follow-up/final clerkship feedback. He declined and his response included: "After a bit of a rough start to the rotation you finished strong." I also text PA2, saying "I know we have had our tensions during this clerkship, but I wanted to let you know I appreciate the way you have treated me during our last few interactions". His responses included "Don't think of it as tension, but rather confusion about roles and expectations."

Appeal

(As it is not the intended focus, names mentioned in this document have been replaced and location removed.)

I am disputing the clinical fail and evaluation I received on my surgery clerkship from June 26, 2023 to August 4, 2023. I believe the evaluation is the result of retaliation for sharing I would be voicing concerns about the site. There are also significant irregularities in the grading process of my evaluation.

Summary of Retaliation

Throughout my surgery clerkship, there was tension with the physician assistants (PAs), who were also referred to as Advanced Practice Clinicians (APCs). The tension started as small slights and eventually escalated to public humiliations. I spoke about this with Dr. A, the site director, on two separate occasions and he made changes to decrease their opportunities to interact with me. However, the interactions did not stop entirely and neither did the tension. Still, I was able to complete the clerkship.

Based on the written feedback I received during and directly after the clerkship, there were no concerns about my performance. On July 18, two weeks and one day before my last day, my Mid-Rotation Student Feedback Form was completed by Dr. A where he selected "meets expectations" for every category (Exhibit A - Mid-Rotation Feedback). On August 2, my last day of the clerkship, I offered to discuss my clerkship experience with Dr. A, hoping for some follow-up about the PA environment. Dr. A did not accept, but stated, "After a bit of a rough start to the rotation you finished strong" (Exhibit B - Dr. A Text). On August 4, two days later, I received a voicemail from Dr. A, where he said individuals I worked with shared they were "unfortunately, not overly impressed with [my] performance and just thought [my] knowledge base in the operating room wasn't super," but he was still waiting on feedback from Dr. E, the previous site director. Dr. A went on to add, "I thought you kinda got it together and finished at least okay" (Exhibit C - Dr. A Voicemail). At no point of feedback was there mention of concerns I was failing the clerkship.

As it was after hours, I responded to Dr. A's voicemail by email (Reference 1 - Voicemail Response Emails). I addressed his comments and shared that I had hoped for more discussion about my clerkship experience and the continued poor interactions with the PAs. I informed him I had been keeping a timeline of events that occurred during the clerkship and would be completing my evaluation of this experience. I had started the timeline in hopes I would have an opportunity to collectively discuss the experience with Dr. A at the end of the clerkship. On August 6, I submitted my evaluations, including the timeline, which I also sent directly to the Learning Environment department. The content of the timeline isn't relevant to this dispute, but for completion, it is attached as Reference 2 - Timeline. The events that followed informing Dr. A of the timeline highlight a shift from what appeared to be a successful completion of the clerkship to a failing grade, with serious allegations raised against me.

On August 7, I was discussing my concerns over the phone with Z, Director of the Learning Environment, when I received an email from Dr. X. The email was regarding a photo in an operating room that I had posted on Instagram from my OBGYN clerkship in Anchorage, AK. More information is included below in Additional Information. Dr. A was cc'd. Z advised sending a short reply simply stating no policy violation had occurred, and I did "reply all" with my response. Later that afternoon, I received a reply to the same email thread from Dr. A. However, it was addressed to Dr. X and I was the only recipient, suggesting Dr. A clicked "reply" to the conversation thread with the intent to respond to Dr. X, but instead responded to the most recent sender in the email thread, me (Exhibit D - Dr. X Emails). Notable comments in his email include: "Sierra was quick to tell me that she would also be giving me a poor evaluation as well....." and "she will be receiving a poor or failing grade from us." I shared this with Z, who stated this email thread warranted immediate escalation of this situation for Dr. Y, Surgery Clerkship Director. I agreed and gave my permission for her to do so.

On August 10, I received an email from Dr. Y with the failing grade and evaluation she had received from Dr. A (Reference 3A - Evaluation Email). For completion, I have addressed these comments point-by-point in Reference 3B - Evaluation Comments, but for conciseness, I will address the most pertinent to his retaliation in this dispute. Dr. A wrote an unnamed individual shared the following about me: "Failed on a personal and professional level. It's a matter of time before she hurts a patient and then what do we say? We are not liable if we tell the truth." This is a very serious concern that was never brought to my attention prior to receiving my evaluation. Nor had Dr. Y or the university been made aware of any concerns during my clerkship, or Dr. A it seems. If this were a valid concern, any one of them should have been notified immediately. And if it were a valid concern, my interaction with patients should have been adjusted, paused, or stopped immediately. Yet, on July 31, just two days before my last day, Dr. C, a surgeon at the site, directed me to drive the robot alone to suture the peritoneum after an inguinal hernia repair and then said I had done well. These concerns about patient safety were only made after I stated I was going to be sharing my experience with the university.

In conclusion, I feel my failed clinical grade and evaluation comments were due to retaliation as described above. I recognize that I did not excel on this clerkship due to the site not promoting a positive learning environment; however, I believe I was at least at a pass level according to Dr. A's comments throughout and immediately after my clerkship, with feedback such as "meets expectations," "at least okay," and "finished strong." Concerns about my performance and patient safety were only raised after I shared I would be completing my evaluation of the clerkship experience. This is supported by the attached mid-rotation feedback, text, voicemail, and, most importantly, the email accidentally sent to me where Dr. A shared I was going to give a negative evaluation and that he was going to give me a failing grade. There were also irregularities in the grading process, as described below.

Summary of Irregularities in the Grading Process

On August 29, I received an email from Dr. Y with her decision on the grade review/challenge and a summary of her conversation with Dr. A (Reference 4A - Grade Review Email). For completion, I have addressed these comments point-by-point in Reference 4B - Grade Review Comments, but for conciseness, I will address the most pertinent to the irregularities in this dispute. Several significant irregularities in the grading process are noted below, and the two I feel are most important to note are:

- The evaluation comment above ("Failed on a personal and professional level. It's a matter of time before she hurts a patient and then what do we say? We are not liable if we tell the truth.") was removed from my evaluation by Dr. Y. In my grade review meeting with Dr. Y, I expressed my distress about that specific comment, asking if she could get further insight from Dr. A. I have received no further clarification about the nature of the comment, but Dr. Y did not include it in my posted evaluation (Exhibit E - Surgery Evaluation). I do not believe the university would remove such a serious concern if they did not feel justified in doing so, pointing to the invalidity of the comment. I believe having to remove any part of the evaluation decreases the credibility of the evaluation as a whole.
- I feel both the student and clerkship department should not be surprised when a student fails a clerkship, especially if there are significant alleged patient safety concerns. I was not made aware of any concerns throughout or even directly after finishing the clerkship and was only notified I would fail in the email accidentally received on August 7. The surgery clerkship department was not made aware of any concerns regarding my performance or patient safety at any time during my clerkship.

Additional comments of significant note are included below:

- In his meeting with Dr. Y, Dr. A shared his Medical Student Surgery Clerkship Expectations document, stating I "did not utilize or pay attention to this information." Dr. Y shared the document with me, and it is not the same one I was provided by Dr. A prior to this clerkship. Exhibit F1 - Expectations is the document I received on June 22 and Exhibit F2 - Expectations is what Dr. Y received from Dr. A, with changes and additions marked and noted. In the document sent to Dr. Y, there are several changes and additions that seem to be directly related to my experience, particularly additional notes about the PAs.
- When Dr. Y questioned Dr. A about mid-rotation feedback (Exhibit A - Mid-Rotation Feedback) and the text he sent on my last day (Exhibit B - Dr. A Text), he argued two conflicting narratives about the sudden failure of my clerkship:
    - With regards to the mid-rotation feedback, he stated my performance "fell apart the last 3 weeks of the clerkship." If my performance had shifted so drastically and had been falling apart during the last 3 weeks of the clerkship (from July 12- August 2), it would have made sense that he noted it in the mid-rotation feedback form completed July 18; but, he did not. It also would have made sense that he bring the concerns about my performance to me, Dr. Y, and/or the university; but, he did not. If he thought my performance was deteriorating over the last three weeks, it would not have made sense for him to text that I had "finished strong" on my last day (August 2); but, he did.
    - With regards to the text he sent on my last day, he stated that it was sent before he received feedback from other individuals I worked with, shifting the reason for the sudden failure after the clerkship to other's feedback. However, I spent roughly as much time with Dr. A as I did with all the other surgeons combined. The approximate breakdown of the days spent with the surgeons from July 17-August 2 is: Dr. A: 7 days, Dr. B: 2.5 days, Dr. C: 2 days, Dr. D: 2 days, and Dr. E: 0.5 days (Reference 5 - Schedules). Therefore, his opinion that I had finished strong

on my last day should have held the most weight. Additionally, he was only waiting on Dr. E's feedback to finish my evaluation when he left the voicemail where no comments about failing or concerns about patient safety were made.

- Based on my relationship and tension with the PAs and the severity of some of the evaluation comments, I worried about their role in my evaluation. Dr. Y discussed this concern with Dr. A during their meeting, she said "he stated it was the surgeons not the APCs who provided feedback by the way." However, in his evaluation, he wrote at the beginning and end of that it was based on his conversations with his partners and the APCs, which included the PAs (Exhibit E - Surgery Evaluation).

In conclusion, there is an overwhelming amount of contradictions, inconsistencies, and irregularities regarding this clerkship and evaluation. For clarity and conciseness, I have included the ones I believe to be most pertinent, though many other ones are addressed in the attachments. Any one of these seems to make my overall final grade and evaluation unreliable.

Additional Information

Disinterest in a Surgical Specialty: My desired future in medicine does not include a surgical specialty, something that was brought up several times in my evaluation. I started medical school with an interest in pediatric psychiatry and have answered honestly about my intentions when asked. It has led other attendings to guide my experience to include opportunities related to my interest when they arise. I was asked several times during my first week what specialty I wanted to go into and believe the individuals at this surgery site came to certain conclusions about me because of my career interest. When discussing the PA tensions with Dr. A on July 6, he even postulated that was a potential cause for their behavior. Level of interest in a specialty is not the same as performance during a clerkship, which I believe I have made evident with my performance during my other clerkships, and interest should not be factored into the evaluation process. I have completed my OBGYN and family medicine clerkships, also specialties I am not interested in, but approached those clerkships the same way I did surgery: with an open mind and knowing, at the very least if I chose pediatric psychiatry, I would never do anything like this again and wanted to make the most of my experience. If I truly did not give clerkships I was not interested in pursuing a career in the serious effort they deserved, I would have done poorly on my other clerkships. Yet, even though OBGYN and family medicine were not specialties I was interested in, I had a great experience on the clerkships, learned a lot, and received very positive evaluations (see below) and clinical high passes.

- OBGYN Evaluation (Reference 6 - OBGYN Evaluation): "Sierra was an integral part of our medical team while on service. She was very compassionate and empathetic with patients. She took the time and extra effort to get to know our patients in labor and our patients knew her name and she was an active participant in the delivery. Sierra is on her way to becoming an amazing physician. She has the qualities you can not teach and she is works hard studying and learning all that she can. I have no doubt Sierra will be extremely successful in her career in medicine."
    - Additionally, I completed this clerkship on May 3. On August 8, several months later, W, a student I had met in Bozeman, started her OBGYN clerkship with one of my OBGYN attendings. I told her to tell the clinic doctors "hi" and she shared the resulting text: "They LOVED you and said to say hello back! I feel like I got brownie points for being your friend." (Reference 7 - W Text)
- Family Medicine Evaluation (Reference 8 - Family Medicine Evaluation): "Student Doctor Norman progressed through this family medicine rotation so that she was able to present oral and written cases in a consistently logical and organized manner especially with problems that became more familiar to her. She usually developed reasonable diagnostic plans reflecting appropriate clinical reasoning. She became comfortable performing common office procedural skills. Her patient centered communication skills really highlighted her strengths of emotional intelligence, discovering and guiding patients where their mental health needs affected their physical condition and suggesting practical ways to navigate those problems. She consistently sought evidence based management of her patients and read consistently to improve her knowledge base, showing great growths in this during the rotation. She was always professional in interactions with patients and staff and responsive to feedback."

Instagram Photo: Dr. Y has reviewed the concern and confirmed no HIPAA violation occurred. The photo in question was taken by an attending in Anchorage, AK during my OBGYN clerkship and posted on May 27, a month before I started my surgery clerkship in Bozeman, MT (Reference 9 - Instagram Post). I enjoy being a medical student and like taking pictures to commemorate this experience, but absolutely make sure it is done appropriately and respectfully. I feel it has been strongly suggested that the university likes us to capture these moments. When sending thank you notes to scholarship donors, there is a place to upload photos to let them know what we are up to. Also, the university Instagram page had requested to repost my OBGYN clerkship photo, and just the other day I received another request for additional photos to be shared by the university Instagram.

Surgery Shelf Exam Fail: I recognize I am not the strongest test taker, as evident by my previous shelf exams, earning a 62 with a passing threshold of 62 on my OBGYN shelf and a 68 with a passing threshold of 58 on my family medicine shelf (Reference 7 - OBGYN Evaluation and Reference 8 - Family Medicine Evaluation). External events do take an emotional toll on my exam performance. During my OBGYN clerkship, my grandmother passed away. When my surgery clerkship ended on August 2, I had to make a decision

on study quality vs quantity with my remaining time. Maybe quality was the wrong decision and I fully accept having to redo the surgery shelf exam. I missed passing by two questions, so I know with time to heal from this distressing experience, I will be able to pass the surgery shelf exam.

Additional Notes of Concern: This whole situation has been very distressing, but the accusation about hurting a patient in particular was the most distressing of it all. It has haunted me as a student and future caregiver and could seriously, negatively impact my career progression. In addition to the concerns included in this dispute, I have provided information regarding the environment of this site and my experience with the Learning Environment department, included for completeness (Reference 10 - Additional Notes of Concern).

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Letter to the Editor

Intricacies of Using Spaced Repetition Tools

Ahmed Ghani.[1]

I was intrigued by the article by Cooper et al.,[1] which described how spaced repetition study techniques improved GPA, USMLE Step 1, and COMLEX Level 1 scores. I also appreciate the authors' efforts to raise awareness of this valuable study method, which has been shown to enhance academic performance.[2] However, I would like to highlight a few concerns regarding the use of this approach, particularly the proper use of the software and factors that may have influenced the study's results.

First and foremost, Anki—like any software—must be used correctly and efficiently. As a medical student, I have spent hours trying to figure out how to use the program effectively. This can be frustrating, and the time lost could have been better spent on other learning strategies, such as active recall,[3] which is also known to improve grades. Furthermore, improper use of Anki may result in lower scores for students who don't have their settings optimized. For example, the option to configure timers for tracking the actual interval of "spaced repetition" is available, but the settings page can be difficult to navigate. Without external help, students are more likely to make errors. Your insights underscore the complexities of integrating Anki into medical education, emphasizing the need for user training. However, it's worth mentioning the availability of tutorials through various online resources such as blog posts, social media videos, and Anki's own support service.

Second, the results reported in the study may be more reflective of the intelligence of the students using Anki rather than the tool itself. To improve the study's objectivity, the authors should have addressed this factor in the statistical analysis. The article assumes a direct relationship between using Anki and higher scores, but it's possible that the students who use Anki are already more academically inclined. Distinguishing between correlation and causation regarding Anki usage and academic success is indeed crucial. Nonetheless, it's important to note that the study already acknowledges some limitations in establishing causality and calls for further investigation, which mitigates some concerns raised.
Finally, while the study represents a significant advancement in research methods, it's crucial to understand how to use the software properly when publishing data and to consider the unique characteristics of each student.

References

1. Cooper S, Twardowski N, Vogel M, Perling D, Ryznar R. The Effect of Spaced Repetition Learning Through Anki on Medical Board Exam Performance. Int J Med Students. 2023;11(4), 271–275.
2. Kang SH. Spaced repetition promotes efficient and effective learning: Policy implications for instruction. Policy Insights Behav Brain Sci. 2016;3(1):12-9.
3. Grijpma JW, Mak-van der Vossen M, Kusurkar RA, Meeter M, de la Croix A. Medical student engagement in small-group active learning: A stimulated recall study. Med Educ. 2022;56(4):432-43.

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