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Editorial Page

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Table of Contents

Editorial Page	3
Table of Contents	4
About JAMSA	6
Foreword	7
Asian Medical Students' Perspective on Medical Education Curricula Standards: A Qualitative Research	12
Sydney Tjandra ¹ , Ghina Tsurayya ² , Andrea Valerie Manik ¹ , Chaitanya Reddy ⁴ , Pratheek Kashyap ⁵ , Najiba Gina Nurisma ¹ , Niragh Sikdar ⁶ , Srinag Ritvik Nallam ⁷ , Rifkanisa Nur Faiza ⁸ , Giselle Clarissa Dsouza ⁹ , Muhammad Royyan Pranowo ¹⁰ , Louisa Patricia Sophia ¹¹ , Vindasya Almeida ¹	
Examining the Influence of Seasonal Changes on Mood: An Analytical Cross-Sectional Study of Local and Foreign Medical Students at Grodno State Medical University	32
Abeyasinghe Mudiyanseelage Himashi Neranjana Poddalgoda ¹ , Sevmini Upeksha Kumari Wijetunge ¹ , Balapuwaduge Shayami Michelle Mendis ¹ , Lahiru Vidushan Kulatunga ¹ , Akila Vinudha Goonesinghe ²	
Association Between Blood Pressure Levels and Diabetic Retinopathy Stage Among Patients at Karsa Husada General Hospital, Batu City: A Cross-Sectional Study	43
Yuliono Trika Nur Hasan ¹ , Nuril Farid Abhsori ² , Sakinah Baraja ³	
Addressing the Growing Concern of Substance Abuse Among Adolescents: A Call to Action	49
Rohan Singhal ¹ , Mannat Bery ²	
A Scoping Review of The Mental Health Support and Well-being Resources Provided to Medical Students by Australian Universities	51
Anton lu ¹ , Alexandra Yeoh ²	
Probiotics as adjuvant therapy with antidepressants vs placebo to treat major depressive disorder: a systematic review and meta-analysis of randomized controlled trials	63
Nathaniel Gilbert Dyson ¹ , Violine Martalia ¹ , Priscilla Geraldine ¹	
The Possibility of Using Modern Methods to Control Bubonic Plague Infection, A Highly Infectious Zoonotic Disease, Mongolia	80
Ryechindorj Erkhembayar ¹ , Jargatulga Ulzijargal ²	
Medical Students' Role in Anticipating The Psychosocial Effects of The COVID-19 Pandemic: A Narrative Review	86
Refa Rahmaddiansyah ¹ , Laila Isrona ² , Sukarsi Rusti ³	
The Efficacy, Side Effect, and Cost-effectiveness of Uperio for Heart Failure: A Literature Review	92
Amgalan Batbayar ¹ , Munkh-Ujin Dorjsure ¹ , Sodongoo Boldbaatar ¹ , Jargatulga Ulzijargal ¹ , Ayurzana Amgalanbaatar ²	
Understanding the Invisible Threat: The Progressive Escalation of Antibiotic Resistance in Pakistan	99
Maheen Nasir ¹ , Hadi Raza ¹ , Azqa Fatima ²	

About JAMSA

Journal of Asian Medical Students' Association (JAMSA)

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The Journal of Asian Medical Students' Association (JAMSA) is a peer-reviewed, international, and open-access biomedical journal led by students under the Asian Medical Students' Association-International (AMSA International). Published biannually, JAMSA is listed in the ICMJE and is a member of CrossRef. It is also indexed in reputable databases, including: Ulrichsweb, Google Scholar, ROAD (Directory of Open Access Scholarly Resources), Gale Cengage, BASE (Bielefeld Academic Search Engine), Genamics Journal Seek. JAMSA's vision is to promote student-led research throughout Asia, the Asia-Pacific region, and beyond.

Fostering Creativity in Medical Research

Medical student research is gaining global recognition, and AMSA International is committed to fostering this trend through its vision of Knowledge, Action, and Friendship. JAMSA encourages all forms of research and creative works from medical students, providing a platform for young, emerging researchers in the Asia-Pacific and other regions.

Scope of the Journal

The main goal of JAMSA is to document research activities across the medical student community. We encourage submissions in the form of: Original Research Articles, Review Articles, Case Reports, Feature Articles, Letters to the Editor. If you are interested in submitting a paper, please refer to the Author Guidelines and Submission Guidelines found on the Submission section of our website.

Who Can Submit?

JAMSA welcomes submissions from medical students worldwide, not limited to AMSA International members. We accept articles related to: All disciplines of medicine, Public health, Healthcare management. Any research with an impact on health is eligible for submission. However, the editorial board reserves the right to decline any article deemed unsuitable for publication.

Our priority is to minimize the processing time for submissions, and our online submission and article processing system has been designed with efficiency in mind.

Get in Touch

For any questions or inquiries, please feel free to contact us on j-amsa@amsa-international.org

Foreword



Rifkanisa Nur Faiza

Chief Editor
of JAMSA 2023/2024

Dear Readers,

I am delighted to welcome you to the 11th Volume of The Journal of Asian Medical Students' Association (JAMSA). This edition represents a milestone in our ongoing efforts to highlight groundbreaking research and emerging insights in the biomedical sciences. Our contributors have put in tremendous effort to advance knowledge in their areas, offering valuable contributions to the academic community.

This volume covers a broad spectrum of research articles spanning critical areas such as public health, mental health, infectious and non-communicable diseases, and medical education. Each piece is crafted to not only inform but also challenge your thinking, broaden your understanding, and ignite your passion for further exploration.

I extend my heartfelt appreciation to the contributors for their hard work and dedication. I am deeply thankful to my talented team, JAMSA Board 2023/2024, editorial team, management board, reviewers, and international research board members for their commitment to maintaining the high quality of this journal.

I invite you to delve into the rich content of this journal, engage with the ideas presented, and contribute your own insights to the ever-evolving field of biomedical science. May this volume inspire you to push the boundaries of your knowledge and embrace the journey of becoming the physician-scientists of tomorrow.

Sincerely,

Rifkanisa Nur Faiza
Chief Editor of JAMSA 2023/2024

Asian Medical Students' Perspective on Medical Education Curricula Standards: A Qualitative Research

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Background: Universal health care, a key aspect of the Sustainable Development Goals, requires effective, safe, and people-centered services ensured through comprehensive medical education. This education involves curriculum development, assessment, and innovation, requiring effective change management. While core knowledge is consistent, curricula vary in diverse global contexts.

Objective: This qualitative study combines panelists' and medical students' perspectives from Kyrgyzstan, Malaysia, Indonesia, and Macau to compare and contrast medical curricula as well as their ideal version envisioned by students.

Methods: This qualitative study employed a constructivist, phenomenological approach to explore medical students' perspectives on curricula. Data were gathered from an online event, featuring 48 participants from various countries. The event included a panel discussion and focus group discussions where attendees discussed curriculum design, admissions, learning media, clinical exposure, testing, standardization, and residency programs. Data were analyzed using open coding from transcriptions, with trustworthiness ensured through member checking. The figures and tables were drawn for correlation of data received using the online Datawrapper tool.

Results: Gaps in medical education curricula were observed globally. Medical students perceived curricula duration, format, and testing methods currently in place to be in accordance with their expectations. Earlier clinical exposure was favorable. Disparities in learning media usage exist, particularly between private and state universities. Financial burdens affect residency decisions universally.

Conclusion: To narrow gaps, international standards should encourage quality improvement, while taking into account the perspectives of medical students.

Keywords: global health workforce; medical curricula; medical education; medical students; qualitative study

Introduction

Universal health care is a fundamental right and humanitarian principle that should be accessible to all citizens worldwide.¹ The Sustainable Development Goals emphasize the need for universal health coverage, including financial risk protection and access to quality essential healthcare services and affordable medicines.² Quality health care must be effective, safe, and people-centered, requiring timely, equitable, integrated, and efficient services.³ Ensuring this quality depends on the meticulous training of healthcare providers through comprehensive medical education programs that transform students into professional physicians devoted to lifelong learning and improvement.⁴

Medical education is a multifaceted process that goes beyond imparting medical knowledge and clinical experience. It involves designing teaching programs based on societal needs, fostering innovation, and lifelong learning.^{5,6} Effective change management and a multi-perspective approach in teaching are crucial for the art of medical education, continuously improving the system.⁷ At institutions where they exist, Departments of Medical Education oversee curriculum development, assessment, and educational support, aiming to train healthcare professionals who will significantly impact future healthcare systems.^{8,9}

If we consider there exists a global desire for health, then healthcare is strongly influenced by globalization through its associated trends in travel, information, migration, poverty, disease, and socio-politics, as well as how we educate our future healthcare providers.¹⁰ In a world that increasingly serves the international exchange of information on medical training, many students, physicians, and educators encounter numerous variations in curricula, degrees, points of licensing, and terminology.¹¹ The processes involved in providing quality medical education to meet this goal vary significantly in countries around the world, as does the availability of resources to implement them. International accreditation of medical education programs is then appropriate to ensure global standards and quality in medical care.

Globalization and the diverse socio-political and cultural contexts significantly influence medical education. While basic medical knowledge is consistent globally, curricula vary to meet specific national needs. Internationalization of medical education requires balancing foreign cultural understanding with adherence to local cultural values.^{12,13} Comparative analysis of different countries'

medical education systems can identify advantageous and innovative teaching approaches for reforming and improving training.^{14,15} Educational strategies should focus on improving students' confidence and capabilities, aligning perceptions of ideal graduate attributes, and fostering a medical identity that meets societal needs.¹⁶

The countries in discussion, have structured medical programs that range from 5 to 6 years for undergraduate studies. Clinical training is an integral part of the curriculum in such programs. Furthermore, entrance exams and interviews are a common requirement for admission. There is ample evidence to show that there is a consistent influence of culture on the medical profession.* Hence, similar cultural and societal norms unite the medical systems set up in each of these countries.

Language instruction varies significantly with Malaysia primarily using English, while Macau, Indonesia, and Kyrgyzstan have multiple languages of instruction. Each country has varying levels of international recognition, which is determined by the quality and extent of clinical training. Globally, Malaysia has a highly recognized system at present. Hence, this qualitative study combines panelists' and medical students' perspectives from Kyrgyzstan, Malaysia, Indonesia, and Macau to compare and contrast medical curricula as well as their ideal version envisioned by students.

Method

This qualitative study employs a constructivist paradigm through a phenomenological approach, where the emphasis is on medical students' and key actors' perspectives. Data collection was done through the recording of an open event organised by medical students from India, Indonesia, Malaysia, Macau and Kyrgyzstan, part of Asian Medical Students' Association (AMSA) International, entitled "Medical Curriculum from Around the World." The webinar aimed to dive into divergencies and convergences within medical curricula across different regions. Hosted online using the Zoom platform, the event garnered participants from diverse corners drawing 48 eager attendees from various countries. Among these participants were aspiring medical students from different semesters of medical school who were keen on gaining insights into global medical education practices. The recording of this data is accessible through YouTube (<https://youtu.be/rzgznWR4yFw>).

In the first section of the event, a distinguished panel, including (1) Ms. HS, a medical student from Macau involved, (2) Mr. YJ, a medical student from Kyrgyzstan, (3) Dr. EGS, a medical association representative from Indonesia, and (4) Dr. ZN, a medical educationalist from Malaysia, brought forth their unique perspective and experiences on the following questions:

1. Could you elaborate on your country's medical education system in terms of admissions process, program structure, and residency training?
2. How is the medical education system adapting to meet the evolving needs of the healthcare system and emerging medical technologies, such as telemedicine, precision medicine, and artificial intelligence?
3. How does the national medical education system ensure standardized quality across all medical schools, considering potential variations in resources and faculty expertise?
4. How is the accreditation of medical schools graded? Are there certain thresholds that determine its grade quantitatively?
5. Are there both state-owned/public and private-owned medical schools in your country? If so, are there any differences in their public perception, quality,
6. What does testing look like in your country? Is it in the form of multiple-choice questions or essays, and why?
7. How is clinical exposure incorporated into your curriculum? Is it regarded as important?

Structured to encourage interactive engagement, the panel discussion served as the centrepiece and spanned for 1 hour and 15 minutes, facilitated by skilled moderators allowing attendees to probe further.⁷⁸ The format allowed a comprehensive exploration of key themes in medical education.⁹⁸

Subsequently, in the second section of the event, the attendees transitioned into breakout rooms where they were divided into 6 smaller groups for focus group discussions. Attendees were led by moderators to discuss the following prompts:

1. Characteristics: How long will medical school be? How long are the pre-clinical and clinical years? What will your curriculum look like (blocks/semesters/ etc.)? Add more details if you want!

2. Admission: How will students get accepted? Will they have to go through tests first? Do they have to take a bachelor's degrees first, or immediately into medical school after high school?
3. Media of learning: What would be the ratio of lectures to discussions? For example, if there were 100 hours to study about the cardiovascular system, how many hours of it would be lectures, practicals, discussions, etc.?
4. Clinical exposure: How much clinical exposure will the medical students get? Should they get exposure since their pre-clinical years?
5. Testing: What form of testing would be most ideal? Multiple choice? Essays? Practical exams (OSCEs)? Which will you put emphasis on?
6. Standardization: How will you ensure the quality output for each medical school? Will there be a certain test students have to pass before being able to become doctors? If yes, what will be tested?
7. Residency: What will residency acceptance look like? Do students have to pay to get in? How long will it take?

Leveraging Google Slides and Zoom breakout rooms, attendees were tasked with designing their ideal version of medical curricula tailored to address contemporary challenges and opportunities in healthcare.

The two sections of the event were chosen to firstly provide a similar baseline to all participants of how medical education takes place in flagship countries, and to encourage dynamic exchange in group settings when they delved deeper into the intricacies of the medical education curriculum design. Data saturation was reached through the number of participants and group iterations; trustworthiness was ensured through member checking as participants were requested to present their discussion results to other groups. Recordings and discussion notes were transcribed; open coding was employed to analyse the data. Thematic analysis approach was mainly utilised for the recordings while discussion notes were analysed with a content analysis approach. Ethical approval was not applicable as this event and its recording is publicly available as secondary data; all participants have consented to participate and to be recorded. Utilization of the data has obtained approval from AMSA. The data was analyzed and visualized in the form of figures (bar graphs, donut charts) and tables wherever applicable using the online Datawrapper tool.

Result

Shared experiences of medical curricula in four countries

Overall, the key comparisons of medical curricula between countries are summarized in **Table 1**.

Medical education system in Indonesia

Indonesia's medical education system includes public and private medical schools. Public schools, run by the government, offer admissions through a national exam or individual school exams, with the latter having higher fees. Private schools have higher fees overall and conduct their own entrance exams.

Residency training differs significantly from medical

school. The Medical College, or collegium—a body of experts and lecturers from various universities—oversees residency programs. They set national entrance exams, select candidates, develop curricula, and administer final board exams. The duration of training varies by specialty. Previously under the Medical Association, recent regulations have moved oversight to the Ministry of Health to reduce conflicts of interest and align with national health programs. This shift aims to improve residency program management and address issues like resident pay without compromising patient care.

Indonesia's medical faculties have not yet included artificial intelligence and palliative care in the national curriculum, which mandates 80% standardized content and allows 20% customization. Some universities are starting to consider these new subjects. The speaker

Table 1. Key comparisons between countries

Criteria/ Features	Countries			
	Indonesia	Macau	Malaysia	Kyrgyzstan
Admission Process	<ul style="list-style-type: none"> Public: national exam / individual school exams 	<ul style="list-style-type: none"> Eligibility criteria (science background, color blindness, etc.) Recommendation scheme; admission test; and international student pathways. Personal statement and multiple mini-interviews (MMI). 	<ul style="list-style-type: none"> Eligibility criteria from various high school certifications Ethnic quota English language requirements and interviews; varies between schools 	<ul style="list-style-type: none"> Evaluates academic achievements in biology, chemistry, and physics Interviews and aptitude assessments.
Residency Training	<ul style="list-style-type: none"> Medical collegiums set national curricula and exams. Duration of training varies by specialty. Shifting to hospital-based programs under MoH 	<ul style="list-style-type: none"> Vacancy based on residency demand Entry residency exam before training 	<ul style="list-style-type: none"> Two-year housemanship, rotating through six specialties. 4–6 years 	<ul style="list-style-type: none"> MDs/MBBSs pass an entrance exam and meet criteria, e.g. MoH endorsement Academic performance and exam results 2–3 years of residency
Adaptation to Evolving Healthcare Needs and Emerging Technologies	<ul style="list-style-type: none"> Artificial intelligence & palliative care not included yet in national curriculum (80% standardized; 20% customization) Might focus on tech utilization over creation 	<ul style="list-style-type: none"> Integrates teaching tools Updates tech advancements for relevant training 	<ul style="list-style-type: none"> Telemedicine training Emerging technologies (precision medicine and AI) in some schools Encourage lifelong learning through CPD 	<ul style="list-style-type: none"> MoH oversees updates, introducing modules on telemedicine, precision medicine, and AI

Criteria/ Features	Countries			
	Indonesia	Macau	Malaysia	Kyrgyzstan
Standardization of Medical Schools	<ul style="list-style-type: none"> National exam by Ministry of Education, contributed by lecturers nationwide 10% participants are retakers. Plans to increase from 100 to 300 medical schools 	<p>Since there is only one medical school in Macau, there is no standardization and accreditation</p>	<ul style="list-style-type: none"> Regulated by Malaysian Medical Council (MMC) and ensured by Malaysian Qualifications Agency (MQA) Non-compliant universities ineligible until improvements are made to meet standards. 	<ul style="list-style-type: none"> Overseen by the Ministry of Health Sets accreditation standards, program evaluations, and updates through international conferences. Investments in infrastructures are also done.
Accreditation of Medical Schools	<ul style="list-style-type: none"> Three categories: A (allowing supervision), B (minimum), C (two-year deadline to B) Will be simplified to accredited an 			<ul style="list-style-type: none"> Evaluated by Ministry of Health annually Accreditation for reputation (A, B, and C)
Perception of State-Owned VS Private-Owned Medical Schools	<ul style="list-style-type: none"> State universities are more reputable than private ones; able to offer residency programs Government has reversed the association's power, giving private universities equal opportunities. 	<p>The only medical school is part of a private university.</p>	<ul style="list-style-type: none"> Some people perceive government medical schools as better than private ones All schools meet the same curriculum standards. 	<ul style="list-style-type: none"> Public schools offer strong academic programs and extensive research opportunities with well-resourced facilities. Private schools provide more flexible, innovative curricula and personalized attention.
Clinical Exposure	<ul style="list-style-type: none"> 4 years focused on theory and basic clinical skills + 2 years of clinical rotations. One-year internship post-exam for licensing. Specialization: 3-6 years 	<p>Preclinical students observe hospitals and complete electives</p> <p>3rd–5th year: clerkships with hands-on experience</p>	<ul style="list-style-type: none"> Structured clerkships (3rd year), bedside teaching, and ward rounds. Simulated training 	<ul style="list-style-type: none"> 1st year: basic skills like injections. 3rd year: hands-on experience in various departments. 4th year: continue with hospital rotations and emergency duties.
Testing	<ul style="list-style-type: none"> Multiple choice questions OSCEs for practical examinations. National exam combines both. Block/module system 	<p>Multiple-choice, short answer, and OSCEs.</p> <p>Block system</p> <p>Block system</p> <p>MD exam to work in government hospital; 1.5 years of clinical training</p>	<ul style="list-style-type: none"> “Knows”: MCQs and OBAs “Know-hows”: OSCEs and simulations. “Shows how”: mini-CEX and direct skill observations 	<ul style="list-style-type: none"> MCQs, mid-term exams, and clinical assessments. Three government exams by the tenth semester: OSCE, a history exam, and another subject. Semester exams and oral assessments

notes that learning programming and developing health tech are challenging for medical professionals, suggesting it's more practical for them to focus on using technology rather than creating it. Skills in telemedicine are becoming vital, with programs like those at Harvard University teaching ethical practices, emergency differentiation, and appropriate patient referrals. Mastering these applied skills is seen as more beneficial for medical professionals.

In Indonesia, the Ministry of Education administers national exams for medical students, aiming to create unbiased, high-quality multiple-choice questions. Adapted from Singapore's system, these exams involve contributions from lecturers nationwide. Despite efforts, about 10% of participants fail and must retake the exam, sometimes multiple times, causing protests. Nevertheless, the exam ensures consistent standards for all doctors amidst a critical shortage of medical professionals.

Indonesia plans to increase its 100 medical faculties to 300 within five to ten years to address the shortage. With a doctor-to-population ratio of 0.5 per 1,000 people, well below WHO standards, and the pandemic highlighting a lack of specialists, expanding the medical workforce is essential.

In Indonesia, health-related faculties are currently accredited into three categories: Class A, B, and C. Class A, the highest grade, allows supervision of lower classes and establishment of medical specialties. Class B is the minimum requirement, while Class C is for new faculties, which must reach Class B within two years. Soon, this system will be simplified to just two categories: accredited and non-accredited, to streamline the process.

State universities in Indonesia have traditionally been more reputable than private ones due to their ability to offer medical residency programs. This was partly because the medical association previously blocked private universities from offering medical specialties. However, the government has now reduced the association's power. This change has enhanced the reputation of private universities, giving them equal opportunities and standards in medical education.

"For example, Pelita Harapan University has opened radiology and family medicine specialty programs. The national exam puts the private and public universities at the same level." (Dr. EGS, 2024)

In Indonesia, medical education begins with a four-year

bachelor's program focused on theory and basic clinical skills, followed by a two-year medical doctor's program with clinical rotations. After six years, students must pass a national exam and complete a one-year internship for their license. Testing is in the form of multiple choice questions and OSCEs for practical examinations. The national exam also comes in these two forms of testing.

Specialization involves a residency of three to six years and optional sub-residency training of two to four years. For example, Family Medicine Specialty includes one year of theory, one year of rotations and internships, and one year managing complex cases and supervising juniors, with possible independent practice in rural areas during the final year.

Medical education system in Macau

To be admitted to medical school, applicants need a science background with chemistry, no color blindness, and proficiency in English and Chinese. Admission pathways include:

- Recommendation Scheme: Based on high school grades and a recommendation letter.
- Admission Test: A written exam for local and international students.
- IB, SAT, A-level: For international students.

Applicants must also submit a personal statement and complete multiple mini-interviews (MMI).

To become a specialist doctor in Macau, one must first check for residency demand and vacancies. If available, they can apply, pass an exam, and complete specialized training to become a specialist. Interestingly, since there is only one medical school in Macau, there is no standardization nor accreditation. There are no differences in the perception as there is only one medical school, but the only medical school is part of a private university.

"We are the only medical school in Macau, and since we haven't graduated our first class yet, all doctors here were trained abroad, mainly in mainland China. Graduates will need to pass a test and complete an internship to become recognized general practitioners. Although we don't have local competitors to compare our curriculum with, we are indirectly competing with long-established institutions that have more comprehensive systems. We are working to tailor our education to Macau's needs, despite these challenges." (Ms. HS, 2024)

Since COVID-19, Macau has embraced new teaching

methods like Zoom and simulation labs. The medical school integrates interactive tools and stays updated with technological advancements, such as AI in radiology placements, to ensure relevant training.

Preclinical students gain early clinical exposure by observing at the university hospital and completing summer electives, including hands-on activities in settings like elderly homes. This early experience precedes formal clerkships. Starting in the third year, junior clerkships run until the fifth year, offering extensive hands-on experience and being favored by students over traditional lectures.

In Macau, tests include multiple-choice, short answer, and OSCEs. The program uses a block system, requiring students to pass a test after each block. Each year ends with a summative exam and OSCE. After earning their MD, students must pass an exam to work in a government hospital, then complete about one and a half years of training in major clinical subjects. Upon finishing this training and meeting all requirements, they are officially registered as licensed general practitioners.

Medical education system in Malaysia

In Malaysia, medical graduates must complete a two-year housemanship, rotating through six specialties: Internal Medicine, Surgery, Orthopedics, Obstetrics and Gynecology, Pediatrics, and either Family Medicine, Psychiatry, or Neurosurgery. During this internship, they gain hands-on experience under specialist supervision.

After housemanship, doctors can pursue further specialization or residency in fields like Internal Medicine or Pediatrics, with training programs lasting four to six years. These programs, accredited by the Malaysian Medical Council, are offered at local universities and focus on both academic and practical skills to prepare graduates for healthcare careers.

Medical schools in Malaysia are incorporating telemedicine training, teaching virtual consultations and remote diagnostics. Collaborations with telemedicine platforms provide hands-on experience, improving healthcare access. However, telemedicine should complement, not replace, in-person care for serious conditions. Challenges include tech barriers and data security. Schools are also adding courses on emerging technologies like precision medicine and AI, and encouraging lifelong learning through CPD to ensure healthcare professionals stay updated. This approach aims to produce skilled, technology-savvy doctors.

In Malaysia, the Malaysian Medical Council (MMC)

regulates medical education and practice, setting strict standards for curricula. Medical programs must meet these standards to be accredited, with non-compliant universities ineligible until improvements are made. The Malaysian Qualifications Agency (MQA) also ensures educational quality, requiring accreditation for medical graduates to practice. Universities undergo rigorous evaluations by the MQA, covering curriculum, students, facilities, and faculty. This collaboration between the MMC and MQA ensures that medical education meets international standards, preparing graduates for effective medical practice.

All medical schools in Malaysia must meet the standards set by the Malaysian Medical Council, achieving at least the minimum required. While some people perceive government medical schools as better than private ones, every medical school in Malaysia is required to meet the same curriculum standards.

Early clinical exposure is crucial to medical education, hence widely applied in Malaysia. Students engage with patients and healthcare professionals from the start, through structured clerkships, bedside teaching, and ward rounds. Clerkships begin in the third year, involving rotations in various specialties and hands-on patient care under supervision. Bedside teaching and ward rounds help students practice interviews, physical exams, and case discussions. Simulated training with task trainers and mannequins further enhances clinical skills. This comprehensive approach prepares students for clinical practice and promotes a patient-centered ethos.

A pyramid framework assesses clinical competence at various levels. At the base, "knows" focuses on fundamental knowledge through MCQs and OBAs. The "know-hows" level evaluates the application of knowledge with OSCEs and simulations. "Shows how" assesses competency through mini-CEX and direct skill observations. At the top, the focus is on independent performance in real-world settings, with workplace-based assessments like long-case and short-case evaluations to determine readiness for practice.

Medical education system in Kyrgyzstan

The admission process for medical schools in Kyrgyzstan involves evaluating academic achievements in biology, chemistry, and physics, along with interviews and aptitude assessments. This thorough evaluation ensures that only the most qualified and motivated candidates are admitted, upholding high standards for

future healthcare professionals.

In Kyrgyzstan, residency candidates must complete a five- to six-year MBBS or MD program. Foreign students may need additional language study. To join a residency in fields like surgery or internal medicine, candidates must pass an entrance exam and meet criteria such as Ministry of Health endorsement of their education. Applications are assessed based on academic performance and exam results. Residency programs last two to three years, with a rigorous selection process ensuring high standards in medical training.

Kyrgyzstan's Ministry of Health emphasizes standardizing medical education quality by collaborating with government agencies, academic institutions, and professional organizations. This includes establishing accreditation standards and regularly evaluating educational programs to ensure up-to-date curricula and knowledgeable faculty. At the speaker's university, the International Higher School of Medicine, faculty members attend international conferences in various specialties to stay informed. The Ministry also enhances infrastructure and resources in government medical colleges, prioritizing investments in simulation labs and research facilities. An annual accreditation system assesses and ranks medical colleges, aiming to continually improve the quality of medical education.

Medical education in Kyrgyzstan is evolving to include the latest advancements in healthcare and technology. The Ministry of Health oversees updates, introducing modules on telemedicine, precision medicine, and AI, available in English, Russian, and Kyrgyz. Medical universities feature simulation labs to aid patient care training, benefiting foreign graduates. Curriculum improvements involve collaboration with government, private sector, and NGOs, integrating modern technologies and practices to enhance healthcare quality and prepare graduates for contemporary challenges.

In Kyrgyzstan, medical school accreditation involves evaluating faculty qualifications, curriculum, student outcomes, and resources. Schools are assessed on their compliance with standards and continuous improvement, with no strict quantitative thresholds. The Ministry of Health conducts these evaluations, focusing on curriculum quality, clinical exposure, and online education effectiveness during the COVID-19 pandemic. Accreditation, which affects institutional

reputation and decision-making for students and employers, categorizes schools into A, B, and C. This process ensures the ongoing quality of medical education in Kyrgyzstan.

Public and private medical schools in Kyrgyzstan each have distinct roles in medical education. Public schools, funded by the government, offer strong academic programs and extensive research opportunities with well-resourced facilities. Private schools, with less government support, provide more flexible, innovative curricula and personalized attention, often with smaller class sizes and advanced digital technologies. Both types contribute to a diverse educational landscape, serving local and international students and preparing them for various medical challenges.

Medical students start clinical training in their first year with basic skills like injections. By the third year, they gain hands-on experience in various departments. In the fourth year, they continue with hospital rotations and emergency duties. This structured approach ensures they are well-prepared for medical practice by their final years. Moreover, Kyrgyz students are assessed using various methods including MCQs, mid-term exams, and clinical assessments. In a five-year program, students must pass three government exams by the tenth semester: OSCE, a history exam, and another subject. The curriculum includes preclinical and clinical phases, with final exams each semester and oral assessments. These methods ensure students are well-prepared for their medical careers.

Medical students' perspective

Participants' Characteristics

Participants were event attendees; a total of 47 people attended the discussions, of which 31 were preclinical students and 16 were clinical students. The distribution by country is 32 from Indonesia, 7 from Pakistan, 3 from Malaysia, 3 from China, 1 from Mongolia, and 1 from Vietnam. Randomization is conducted to divide the groups, with regards to nationality. Participants were well represented from each country in each group.

Question 1: Characteristics (duration, format of blocks/semesters)

All six groups (100%) had proposed 5 to 6 years of medical school, with distinct pre-clinical and clinical

periods, even though their requirements for the academic year component vary. All groups require 2-3 years of preclinical and 3–4 years of clinical experience in medical school. A one-year foundation term covering fundamental medical knowledge and an introduction to professionalism in the medical field was another period suggested by one of the groups. The other group (16.67%) added an internship period of one year following the clinical phase. An introduction to the basic sciences was provided during the preclinical phase, and one group additionally incorporated the curriculum with the concept of medical entrepreneurship. One group (16.67%) suggested four blocks carried out concurrently, whereas five groups (83.33%) adopted a block or module system for all courses. Another group (16.67%) stated that routine mental health assessments are necessary, in addition to faculty assessments of students' well-being.

Question 2: Admissions

The six groups highlighted the crucial roles of a comprehensive admission procedure in medical school, which includes evaluating the candidate's knowledge competency in subjects like biology, chemistry, and physics, as well as assessing their psychological readiness to enter medical school. Furthermore, two groups (33.3%) advocated an assessment of medical knowledge, with one of them citing the MCAT as an exemplar of an ideal test. Two approaches were utilized to search for methods or assessments that could identify the psychological features of candidates. Six groups (100%) suggested conducting psychological tests, such as the MMPI, while two groups (33.3%) emphasized the importance of using interviews as an essential component of this evaluation.

Duration of Study recommended (in years)

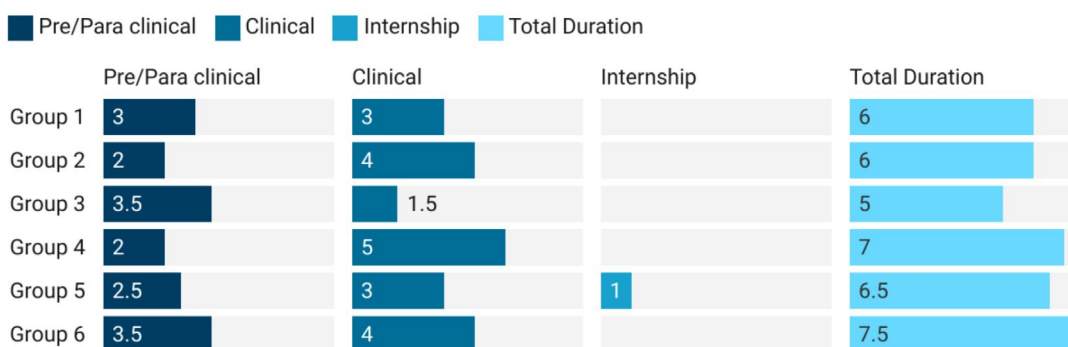


Figure 1: Split Bar Graph representing the suggested duration of study in Medical Schools in years.

In addition, another group incorporated a review of discriminatory factors during the applicant interview stage. One group indicated that interviews might potentially be undertaken afterward the preclinical phase. Some other points mentioned by one group were the pre-med period to prepare applicants in the disciplines of fundamental science, English, and medical knowledge. Age restrictions of no more than 25 years and an entrance test given once a year were also recommended by one group. These steps were provided with the same aim in each group, which is to guarantee that candidates are suitable and determined about their education and career route.

Question 3: Media of learning

More than half (66.6%) that is four out of six groups suggested that at least 40% of the curricula should be conducted offline and of interactive type. Two groups

demonstrated that a strong focus should be given to practicals (50%) where one group emphasized that 25% should be allocated to lab training and the other 25% to clinical interaction with patients. One group explained the importance of the inclusion of skills lab training which should be given 30% part in the curriculum so that pre-clinical year students can learn essential skills as they do not have clinical rotation experiences. Another group suggested that clinical case discussions should be allotted only 20% of time, especially during hospital visits that can serve as a source of clinical exposure to pre-clinical students. In contrast, only 50% suggest that discussions must comprise only 30% of the curricula but they should be given more consideration than the assessment tests/tools. Detailed description of various media of learning is provided in the form of a stacked bar graph (**Figure 2**).

Table 2. Mode of Admission into Medical School

	Group 1	Group 2	Group 3	Group 4	Group 5	Group 6
Entrance Test	Yes	Yes	Yes	Yes	Yes	
Interviews/ Personality Test	Yes	Yes	Yes	Yes	Yes	Yes
Psychological Test (MMI/MMPI)					Yes	Yes
Mandatory Pre-Med Course						Yes

Question 4: Clinical exposure

Out of the six groups, 90% (five out of six) showed strong consensus about pre-clinical exposure whereas one group suggested that the duration or length of clinical exposure should be increased in comparison to the pre-clinical exposure because few exposures such as Intensive Care Unit (ICU) and Emergency Rooms (ER) can turn out be overwhelming for pre-clinical students. However, a great alternative as reported by two groups was shadow work which refers to observing medical professionals provide care in clinical settings. Conversely, three groups (50%) commented on the frequency of

clinical exposure that must be provided during the pre-clinical years to enhance the smooth transition from pre-clinical to clinical years as shown in **Table 3**. Furthermore, one group suggested a dichotomization of clinical exposure, where pre-clinical students, that is the second and third-year medical students, must receive Basic Life Support (BLS) training and Objective Structured Clinical Examination (OSCE) should be a routine part of their assessment. Whereas, fourth and fifth-year students who have sufficient clinical exposure must interact daily with the patients and engage in discussions.

Time Allocation (%) for various Media of Learning

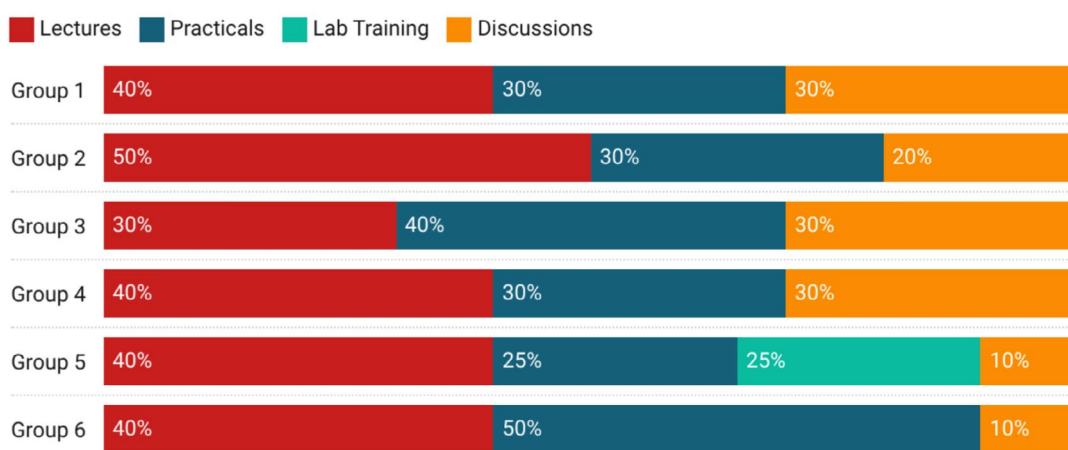


Figure 2: Stacked bar graph representing in percentages the time allocation suggested for lectures, practicals, and discussions as a medium of learning in medical schools.

Table 3. Frequency of suggested clinical exposure during pre-clinical year.

Group No.	Frequency
Group 1	Once a Week
Group 2	From Day 1 of Medical School
Group 3	Once a Year

Question 5: Testing

All six groups (100%) recognised that there should be a variety of tests implemented in each country's medical school system. Testings of both theoretical and practical types were discussed and suggested as seen in **Figure 3** below. Of the types of testing discussed, only 66.67% (four out of six) of the groups endorsed the use of essays as a testing method. As an alternative, however, one group suggested a slightly different approach to standard essay questions, the Modified Essay Questions (MEQ), where students instead analyze a clinical scenario in order to identify its clinical and ethical aspects. Another popular selection of theoretical tests include Multiple Choice Questions (MCQ) which were recommended by 83.33% (five out of six) of the groups. A supplementary recommendation regarding this type of testing was given by one group that suggests One Best Answer (OBA) or Extended Matching Question (EMQ), a type that encourages students to choose an answer that fits best instead of a seemingly correct one. Contrary to theoretical exams, the practical Objective Structured Clinical Examination (OSCE) was suggested by all (100%) groups, as each group sets it as a non-negotiable to recognise a doctor's competence in a clinical setting.

Question 6: Standardization

Of all groups, five out of six (83.33%) agreed to conducting national exams to assure the competency of medical school graduates. Groups 1, 2, 3, 4, and 5 stressed that these examinations must include both theoretical exams and practical exams that will allow the evaluation of all necessary clinical skills as seen in **Table 4**. Group 6 on the other hand, suggests otherwise. There should only be exit exams done for those interested in practicing in another country to ensure that their competency are in line with standards that were set in that country. In addition to this, groups 2 and 6 (33.33%) also recognized the need for standardizations to not just exist at the beginning or end of every students' education. Instead, there needs to be quality assessments done unto medical education providers. Group 2 suggested for there to be an accreditation done directly unto universities' in the matters of their approach to provide quality medical education. This is done based on an evaluation on the faculty's overall excellence, patient inload in their teaching hospitals, and supporting infrastructures for students to demonstrate practical skills. Group 6 supports the aforementioned point with suggestions that there be random-timing accreditations done unto faculty members, to ensure that their teachings are up to date with current developments in the healthcare industry.

Form of Testing suggested in Medical School (in %)

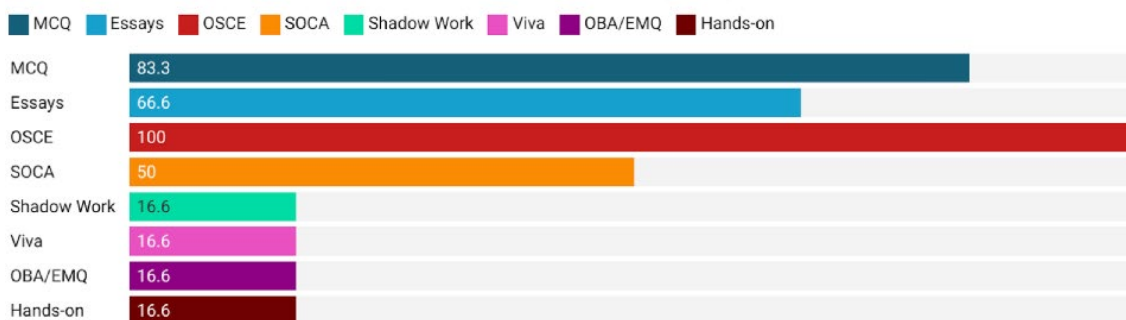


Figure 3 : Stacked bar graph representing in percentages the form of testing suggested by all six groups in Medical Schools.

Question 7: Residency

Of the six groups, 100% agreed on the importance of specific criteria for residency admissions, with all groups highlighting the importance of aligning residency admissions with a student's chosen residency. Specifically, 50% (three of six) emphasized adapted entrance exams for each specialization, while

another 50% (three of six) highlighted the use of diverse admission criteria, including final grades, multiple choice questions (MCQs), essays, and objective structured clinical examinations (OSCE). (Figure 4) Regarding the financial aspects of residency, 83% (five of six) of the group expressed concerns about financial problems to enter residency, specifically the need to pay entry fees or tuition fees. Two groups proposed paid residency

positions to reduce the financial burden. Additionally, 67% (four of six) recommended benefits or salaries for residents, recognizing them as workers and advocating for financial compensation during the residency period.

(Figure 5)

In terms of residency duration, all groups (100%) acknowledged that length should vary depending on residency, with suggestions ranging from 2 to 6 years. The proposed specific duration includes 3 years for clinical specialties and 2 years for paraclinical specialties. Additionally, 33% (two of six) of the group cited the need for flexible residency programs, both mandatory and

optional, with a focus on minimizing financial and time demands. One group pointed to a mandatory two-year residency program in Malaysia that covers basic disciplines as a model, emphasizing the importance of work-life balance and job satisfaction. Finally, 50% (three of six) groups proposed involving government agencies, such as the Ministry of Health, to provide scholarships and financial support for residents, highlighting the role of institutional support in facilitating residency training. The general consensus among all groups is that residency programs should be structured to help medical graduates enter desired specialties while balancing financial, time, and workload considerations.

Table 4. Quality Output Techniques for Standardization.

1	Group 1	Entrance Exams (MCQ + OSCE)
2	Group 2	Annual inspection of quality of medical education, patient inload, infrastructure of the medical school & affiliated teaching hospital MCQ, OSCE, Essay Test
3	Group 3	Entrance Exams (MCQ + OSCE)
4	Group 4	Entrance Exams (MCQ + OSCE)
5	Group 5	MCQ + OSCE after pre-clinical & final year completion
6	Group 6	Annual Inspection, Review curriculum & provide accreditation to medical schools as per their performance

Discussion

Setting the stage: the rise of international health worker migration

Many countries face challenges in recruiting skilled healthcare personnel for their own healthcare facilities. The shortage of healthcare workers leads to a decrease in the quality of patient care and an increase in workload for current healthcare workers. To tackle this issue, certain high-income countries, such as the United States and Canada, depend on health worker migration and actively recruit health professionals from low-to-middle-income countries like India and the Philippines, which contribute a substantial number of international health workers.^{17,18} International health worker migration refers to the relocation of health professionals across national borders for work opportunities, either temporarily or permanently.¹⁹ The issue has been a significant focus of global policy-making for many years, with multiple international organizations and bilateral agreements involved, including the WHO Global Code of Practice on the International Recruitment of Health Personnel, which aims to address these

issues by encouraging workforce self-sufficiency and discouraging active recruitment from countries with severe health personnel shortages.^{19,20} Various factors influence workers' decisions to leave their home countries, encompassing both push and pull factors. Push factors include limited employment prospects, financial difficulties, limited educational and career advancement, and even encouragement to migrate to another country. In contrast, pull factors include higher wages, better working conditions, access to advanced technology and training, and career advancement and personal development prospects.¹⁸

The emigration of workers abroad has sparked significant debate about its impact on the source country. Advocates highlight the potential advantages, citing instances where migrant health workers return with improved skills and knowledge, benefiting both their home country and their families through remittances.¹⁷ On the other hand, critics raise concerns about the potential drawbacks, such as a brain drain and the loss of skilled workers in the source countries who have to bear the cost of training. This can lead to heightened health disparities, as demonstrated in the WHO Africa Region.²¹

Admission Criteria for Residency Training

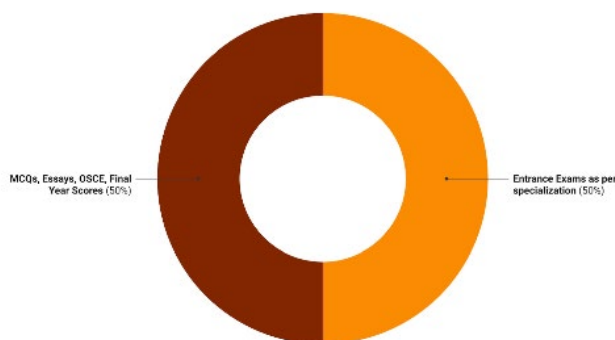


Figure 4 : Donut Chart representing in percentages the admission criteria suggested by all six groups for residency training.

Financial Aspects for Residency Training

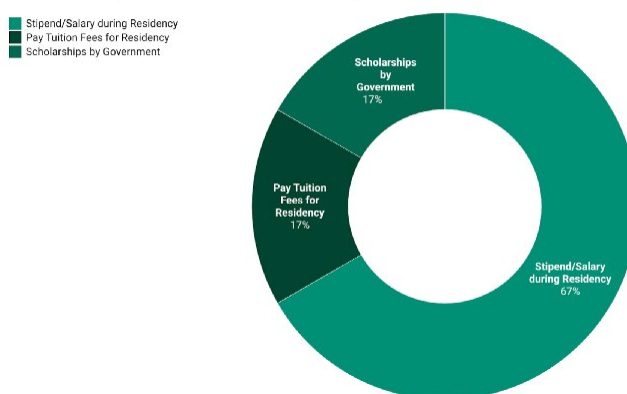


Figure 5 : Donut chart representing in percentages the suggested mode of financial aspects involved when considering residency training.

With the ongoing rise in health worker emigration abroad, it is imperative to address these concerns.¹⁷ One area that demands immediate attention is the role of medical education in each country and its ability to adapt to the increase in health worker migration. Changes in medical education—particularly the global orientation of education systems in source regions—significantly impact international health worker migration patterns. The Indian case exemplifies how education systems are aligned to produce globally oriented professionals, reflecting the global health worker labor market.²² However, some counterexamples, such as Cuba, place primary care and community health as their top priorities. They have developed a medical education system that efficiently generates a surplus of healthcare professionals willing to work in areas that lack adequate medical services, both domestically and internationally. This challenges the notion that all countries must align their medical education systems with global labor market demands to address health worker migration issues.²³ Each country, being unique, should decide how

their health education system should be oriented to meet the demands of their healthcare systems.

Students' perspectives versus best practices

Best practices for duration of medical education (see question 1)

The length of medical education programs is an important factor that shapes the skills and the preparedness of the students who are going to be future physicians. Standardizing the medical education curricula to the national and international standards is a vital factor in determining the right time frame for them. Nowadays, many countries and organizations, including the World Federation for Medical Education (WFME), have adopted the standards recommending five years for the basic medical degree, with one or two years of clinical training or internship as the minimum.²⁴ Following this generally accepted standard guarantees

the medics with a complete training and worldwide recognition upon graduation.

Medical education should be well-balanced between theoretical knowledge and practical clinical experience. The best practices include spending as much time as it takes for study rotations, clerkships and clinical experience in different medical specialties.²⁵ By providing students with this experience, they are able to acquire basic clinical skills, interpersonal competencies, and an understanding of real-world healthcare settings, which is an absolute necessity for their future practice.

Nowadays, medical schools put a lot of emphasis on interprofessional collaboration and teamwork. Curricula should be designed in such a way that medical students are provided an opportunity for interdisciplinary learning and interaction with other healthcare professionals like nurses, pharmacists, and therapists.²⁶ This exposure allows for a deeper understanding of the entirety of providing patient care and enhances communication and collaboration skills, which are essential in the current healthcare environment.

The medical education curricula should be made flexible enough to be able to accommodate emerging trends, new technologies, and evolving healthcare needs. The best practices include providing the electives, the research experiences, and the interdisciplinary learning.²⁷ This flexibility enables the students to design their education in a way they find interesting and in line with their future careers. As such, it assists them in meeting the challenges of the dynamic environment in healthcare.

The effective duration of the curriculum should be influenced by the continuous evaluation and improvement that is based on feedback from various stakeholders such as students, faculty, healthcare professionals, and accreditation bodies. Continuous evaluation and adjustments not only in the light of the latest medical knowledge, but also in the pedagogical approaches and the ever-changing needs of the society are necessary for the medical education programs to remain relevant and effective.²⁸

Best practices for admissions (see question 2)

In medical education in Asia, the best practices for admissions are very important in choosing talented and diverse students who can be successful in the medical curriculum and who will be part of the healthcare workforce. The implementation of a comprehensive admission process which takes into consideration a wide

range of factors such as academic excellence, personal qualities, life experience, and likelihood of succeeding in the medical field is one of the key best practices.²⁹ This strategy accepts that academic scores do not reveal all the aspects that an individual has.

The other important best practice is the promotion of diversity and inclusion in the student body in Asian medical school admissions. A student body that is diverse in its background leads to a learning environment that is so rich, that it enhances cultural competence and makes future physicians better able to serve the diverse communities in Asia.³⁰ Admissions committees ought to take into account aspects like socioeconomic circumstances, ethnicity, and individual experiences to make a diverse and representative cohort that mirrors the local community diversity.

Many medical schools in Asia have already included structured interviews like multiple mini-interviews (MMIs) or situational judgment tests as a part of the admissions process.³¹ Such interviews examine how applicants handle interpersonal relations, problem-solving, ethical reasoning, and communication, which are critical skills for successful performance in medical school and the medical profession.

Incorporating multiple stakeholders such as current medical students, faculty members and health professionals is also one key strategy in Asian medical school admissions.³² This collective method makes sure that the admission criteria and the procedures are consistent with the institutional values, mission, and needs of the communities that are served by the medical school.

Lastly, the assessment and improvement of admission processes shall be a part of the process. The criteria and practices for admission should be reviewed and refined regularly based on the data analysis, feedback from the stakeholders and the changes in the institutional priorities or societal needs.³³ This process of ongoing assessment enables Asian medical schools to identify and select the most capable of their students who can contribute to the health sector of the region.

Best practices for media of learning (see question 3)

The findings from our study shed light on the diverse perspectives among multinational medical students regarding the optimal composition of medical curricula, particularly concerning the balance between offline and interactive learning modalities, practical skills, laboratory

training, and case discussion. A notable consensus emerged among the majority of groups, advocating for a substantial portion of the curriculum (at least 40%) to be conducted offline and in an interactive lecture format. This inclination underscores the recognition of the value of face-to-face interactions, fostering engagement, active learning, and a theoretical foundation for medical practice. Previous study also emphasizes the essential role of student engagement in offline and interactive learning to ensure quality in medical education.³⁴ Student engagement is a psychosomatic state of motion making them feel triggered, and employ exertion in learning activities, which connects their state with medical education.³⁵ Thus, student engagement in medical education is positively allied with the outcomes of the learnings with utmost consequence on practical engagements than professionalism.^{36,37}

Practical training also emerged as a central theme, with a strong emphasis on hands-on experiences. A significant proportion of groups (50%) advocated for dedicating half of the curriculum to practicals, highlighting their pivotal role in bridging theoretical knowledge with real-world applications. Furthermore, the result also aligns with study that underscored the pivotal role of hands-on experiences in developing clinical skills and competence among medical students, supporting a Competency-Based Curriculum (CBC) with well-stated learning objectives for students to acquire essential clinical skills. Students should be provided with sufficient learning opportunities including a well-equipped clinical skills laboratory and individual attention, and constructive feedback should be given to students for building their confidence level during their learning process.³⁸ This aligns with another study that showed that skills training and practical simulation significantly lowers anxiety and increases confidence in medical students, enhancing their performance in patient care.³⁹ Moreover, the specific allocation of 25% each to lab training and clinical interactions with patients reflects a balanced approach, ensuring exposure to both laboratory techniques and clinical settings. This perspective acknowledges the needs of pre-clinical year students who lack direct exposure to clinical practice, emphasizing the importance of early skill acquisition to enhance preparedness for subsequent clinical training.

Moreover, discussions on clinical case presentations during preclinical studies received varying degrees of endorsement. While one group suggested a modest 20% allocation, underscoring the value of clinical exposure for pre-clinical students, contrasting opinions

were evident, indicating the need for further exploration regarding the optimal balance between clinical exposure and theoretical discussions. It is noteworthy that despite the emphasis on interactive learning modalities and practical training, discussions constituted a significant aspect of the curriculum according to half of the groups. A review also discusses the importance of theoretical foundations in medical education. Clinical teaching is fundamental to the training of physicians; however, it frequently lacks structure, being opportunistic and lacking a theoretical basis. Given the current landscape of healthcare provision, where accountability and patient safety are paramount concerns, medical education demands a rigorous scientific approach and evidence-based methodologies. Thus, theories play a crucial role in validating concepts through practical implementation, thereby enriching comprehension, application, and credibility in the learning process.⁴⁰ Overall, the multifaceted nature of medical education highlights the need for a balanced curriculum that integrates diverse learning modalities to optimize student learning and prepare future healthcare professionals effectively.

Best practices for clinical exposure timing (see question 4)

The results of our study revealed a predominant consensus among the majority of groups, with 90% expressing strong support for pre-clinical exposure within medical curricula. This result underscores the recognized importance of early clinical immersion in medical education, aligning with the principles of Early Clinical Exposure (ECE). ECE allows students to gain a deeper understanding of the healthcare delivery systems, patient care processes, and professional responsibilities, hands-on experience, develop empathy, and improve recruitment and retention by providing a more engaging and rewarding learning experience.⁴¹ ECE emerges as the most fitting concept to meet the needs of medical students in this study, as it integrates the knowledge of basic and clinical sciences and the psychosocial aspects of medical practice to move medical education towards the real context of practice, ultimately leading to the perfect training of professional physicians and smooth transition to the clinical phase.⁴²

Furthermore, alternative modalities for clinical exposure were proposed by two groups, emphasizing the concept of shadow work. Shadowing medical professionals in clinical settings provides students with valuable observational learning opportunities, enabling them to witness real-world clinical practice and contextualize

theoretical knowledge within clinical contexts. This perspective reflects a nuanced consideration of the balance between theoretical knowledge acquisition and practical clinical experience, highlighting the potential benefits of extended clinical immersion in enhancing students' clinical skills and readiness for professional practice.

Best practices for testing in medical school (see question 5)

Our research discovered that medical students perceived current exam formats to be ideal enough as they combined a variety of methods; nevertheless, measures must be taken to ensure these tests' reliability. For basic sciences in preclinical phases, multiple choice questions (MCQs), sometimes modified to have multiple possible answers, short answers, and laboratory practical exams, each assesses cognitive level with good reliability. In applying such knowledge into clinical settings, however, an oral exam (*viva voce*) is often used, but this test has high variability between scorers, leading to lower reliability. Direct observation in clinical practice and simulation-based assessments also require faculty training for optimal reliability.^{43,44} The "testing effect" should also be considered in all simulation-based assessments, including Objective and Structured Clinical Examinations (OSCEs).⁴⁴ Overall, assessment formats, scoring methods, stakes, duration, and frequencies should all be considered as they collectively affect students' learning.⁴⁵

Considering the marked interest in applying theories to clinical scenarios, simulated patients should be sufficiently prepared to provide authenticity, hence minimizing the risk medical students will pose on real patients.⁴⁶ Past studies have shown that students have perceived their medical education to provide less practical relevance than their expectations,⁴⁷ especially during the COVID-19 pandemic.⁴⁸ Nevertheless, educational theory dictates that formal theory should still be taught as a foundation for evidence-based practice.⁴⁹

Best practices for standardization (see question 6)

Medical students in our study mostly agree that a national exit exam is needed to ensure standardized doctors are competent for practice; scores for national CBT and OSCE have been found to demonstrate clinical performance quality, but complex factors over the years may have a greater role.⁵⁰ In India, a three-step National

Exit Test (NEXT), done in the (1) final year of the MBBS degree, (2) licentiate examination, and (3) PG entrance, is judged most feasible.⁵¹ Contrarily, in Vietnam, where medical licensure exams have not been required before 2024, medical schools are considered responsible for their graduates' competence. Nevertheless, the establishment of a National Medical Licensing Exam (NMLE) is deemed to be beneficial beyond its costs (human resources, infrastructure, and logistics).⁵² To tackle the high-stakes nature of such exams, progress testing can be conducted throughout medical education years to assess knowledge growth, reduce stress, and encourage deep learning.⁵³

Educational institutions should be monitored for quality even with the existence of exit exams,⁵⁴ through accreditation and the processes following it: post-accreditation monitoring, meta-accreditation, and meta-evaluation of the accrediting bodies.⁵⁵ Albeit often centralized, such systems should be designed to fit local needs and contexts, possibly through a fit-for-purpose framework.⁵⁶ Existing evidence shows that medical schools accredited by the World Federation of Medical Education (WFME) retrieved higher United States Medical Licensing Examination® (USMLE®) scores. However, implementing and maintaining meaningful accreditation systems requires substantial resources.⁵⁷ To prepare for accreditation, within medical schools, independent medical education units (MEUs) can be established and assigned for continuous quality assurance, given the authority to prescribe teaching interventions.⁵⁸

Best practices for residency (see question 7)

In our study, medical students expressed a variety of perspectives on how residency programs should be held in a well-structured system with diverse eligibility standards to allow postgraduate medical students to easily enter their desired medical residency. During this time, different countries used different methods for residency admissions, but the national exam remained the primary criterion in most countries.⁵⁹ However, the scores of the NMLE test are rarely placed in the top quartile on the research about factors that determine medical residents success during specialist training or throughout their career as a specialist.⁶⁰ Recent research about USMLE also reported the lack of representation of women and underrepresented minority groups (URM), showing disadvantages as the only criterion to embody diversity in residency programs. As emphasized by certain groups in our FGD, adapted entrance exams

for each specialization (interview, OSCE, or essay submissions) are suggested to be implemented to reduce inadvertent racial or gender bias and conduct a holistic admission process.^{61,62}

In addition, financial burdens and increasing amounts of debt during residency contribute to the rise of anxiety and stress levels among residents and unfortunately become one of the top reasons to not pursue or suspend their intention to join a residency program.⁶³ Adding the high tuition fees of residency programs to the list of other unpaid financial debts could be extremely burdensome for medical trainees, while some countries consider general practitioners to be just postgraduate students who are either unqualified to be paid or are paid less than the country's workers' standard salary. Ultimately, this has been shown to be a leading cause of the shortage of medical doctors in all countries, showing inequality in access to residency programs.^{64,65} Reformation of residency programs to regulate financial barriers is strongly needed, such as clarifying residents' status as healthcare workers, promoting scholarships and financial support for residents from government or private parties, and advocating the urgency for the government's financial assistance for giving financial compensation to universities or hospitals.⁶⁶ Certain nations that employ university-based residency programs urgently require financial support, and the conversion to hospital-based programs might also help to solve issues with paying medical trainees. After earning an adequate salary, it would be more visible for residents to be able to pay off their debts and overcome their financial problems, such that residency programs still remain the choice for postgraduate medical students. Since medical students are considered to have deeper concern on paying high amount of tuition fees throughout their educational year, recent research also reported the importance of financial management to be included in the medical curriculum.⁶⁷

Strengths and limitations

This paper encompasses the key aspects of medical education through the lens of its main stakeholders—medical students—through its qualitative nature that serves to describe the phenomenon comprehensively. However, limitations exist in its data source; as the discussions were conducted between AMSA members, subjects are mainly Asians who are interested in medical education and/or student activities. Such demographics may skew interpretation and the qualitative data accrued as we might have missed students who were not

involved in AMSA. Moreover, although Asian countries share similar collectivist values,⁶⁸ the four countries may not be representative for Asian countries beyond them.

Conclusion

Gaps between countries were observed in medical education curricula implementation. Block or module systems remained the leading methods in curricula with recommendations for improvement in annual mental health assessment for students and providing more clinical exposure since pre-clinical years. Furthermore, admission processes could consider psychological tests and MMI, which are still uncommon. Equitable use of learning media remains difficult due to curriculum differences and gaps between private and state universities reported in several countries. MCQs and OSCE are quite popular and meet the expectations of medical students to be continuously implemented as testing methods and national exit exams for requirements to enter residency programs. Medical students and all stakeholders agreed about financial burdens happening in all countries, affecting decisions to enter residency programs. Moving forward, solutions to advocate these issues to the government are still deliberated with much room for improvements to meet all parties' needs and expectations. WFME should create integrated medical education standards that can be applied globally with structured achievement targets, encouraging quality improvements. Nevertheless, implementation should remain context-sensitive in countries. In doing so, the perspectives of medical students as the main stakeholders in medical education should be considered.

A lengthy study must be carried out in order to identify medical education systems throughout Asia. Aspects that need to be evaluated are the comparison of curricula from different medical schools in Asia to identify best practices in career development, professional satisfaction, and patient outcomes in the healthcare environment. Evaluation can be done by investigating different teaching methods (problem-based, simulation-based, or conventional learning). The quality and quantity of student experiences and opportunities are some of the many points of student entitlement that need to be guided due to their impact on clinical competence and practice readiness.

Given technological advancements, medical education providers can investigate the function and efficacy of new systems, as well as the use of technology in medical

education, such as digital learning platforms and expanded telemedicine in daily practice. Public policy is essential for ensuring equity in faculty and curricular structures. Sustainable improvements in public policy can be implemented to improve medical training and health care.

In a fully involved world, student associations can play a leading role in medical student change. It can be achieved by speaking up and suggesting reforms to educational authorities. Students and staff can contribute to such changes by sharing their experiences and making ideas. This allows young organizations to organize and participate in discussions with officials about the issue. Finally, improvements and issues can be communicated and promoted through campaigns and idea exchanges. Peer support programs can also assist students in overcoming obstacles and advocating for institutional support structures on a broader scale.

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Conflict of Interest

ST was the Director of Global Health of AMSA International 2023/2024, RNF was the Chief Editor of JAMSA 2023/2024, and AVM was the Internal Global Health Officer 2023/2024 in charge of the interchapter collaboration event of which data was analysed in this article.

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Examining the Influence of Seasonal Changes on Mood: An Analytical Cross-Sectional Study of Local and Foreign Medical Students at Grodno State Medical University

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Background: Seasonal affective disorder (SAD) is known to cause negative effects on a person's life. This is more prevalent in the higher latitudes. Interestingly foreigners migrating to higher latitudes from lower latitudes had higher prevalence rate of SAD comparative to the indigenous population at that latitude.

Objective: There is a scarcity of research conducted on SAD among medical students. So, we aimed to examine the effect of seasonal mood variations among foreign (international) medical students relocating to regions with higher latitude and compare it to the changes of local medical students of that country.

Methods: This cross-sectional study was conducted in the Grodno State Medical University involving both local and foreign medical students. A pre-formed Google form with PIDS-SA was used for data collection. This data were then analyzed using Epi Info 7.6.2.0 Software.

Results: There were mood changes with seasons in both student populations (Foreign 70.2%, Local 64.2%). When considering the criteria to diagnose SAD, 11.3% were affected with SAD in Winter. Foreign students had 4 times more likelihood of been affected with Winter SAD relative to the local medical students. (OR=4.12, p 0.04). There were no cases of summer SAD in this sample.

Conclusion: Increased vulnerability of foreign students to SAD upon relocating to higher latitudes presents an additional challenge to a medical student's life. Raising awareness, teaching coping mechanisms and ensuring treatment access will foster a supportive environment for both local and foreign students' wellbeing.

Keywords: Seasonal Affective Disorder, Medical Students, Undergraduate Students, Eastern Europe, Local and International Students, Latitude

Category: Original Research

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Introduction

Changes in the mood, behavior, sleep, appetite, and activity that is influenced by the length of the daylight hours is known as seasonal affective disorder (SAD). Reports of such changes date back to classical times ¹. According to DSM-5 criteria, SAD is a depression with a seasonal pattern. This include having depression during a specific season each year, either in winter or summer with full remittance during other seasons, for at least two years and having more seasons with depressive episodes than seasons without depression over a lifetime ². SAD manifests in two primary forms as, Winter SAD and Summer SAD. Winter SAD (W-SAD) is more common, appearing during late autumn or early winter with decreasing daylight hours, and disappearing during the months of spring and summer. Less often symptoms appear in spring or early summer, known as Summer- SAD (S-SAD) and resolve by autumn or winter months ³. A large number of hypotheses has been made on the pathophysiology of SAD ⁴. Literature emphasizes more on the role of sunlight in the presentation of W-SAD symptoms. This could be due to a decrease in serotonin activity, an increase in melatonin production, disrupted circadian rhythms, and/or a low level of Vitamin D. ³

Studies also show that W-SAD is more prevalent in the higher latitudes ¹. But this influence of latitude was seen more in North America compared to Europe. Other factors like climate and socio-cultural factors have been shown to play a role as well ⁵. Interestingly, individuals migrating to higher latitudes from lower latitudes had a higher prevalence rate of SAD ⁶. Contrast to this, when an individual had lived in a higher latitude for a longer time there was a low prevalence of SAD ⁷. A significant number of people living with debilitating effects of SAD are not aware of this condition. And they do not realize that they are not functioning at their full potential ⁷. Students are one such affected population. SAD has been studied in undergraduate and postgraduate student ⁸⁻¹⁶. And it was evident that some students were not even aware of their condition ⁹.

A study done among undergraduate students in America noted that students from non-seasonal (with less seasons) hometowns had a higher likelihood of SAD than students from seasonal hometowns ¹⁵. A study done among Nambian students in a Russian university, suggests that migration will play a role in increasing the level of SAD ¹⁶. Medical students are a subset of students who are highly prone to stress throughout their academic careers. And it is also evident that mental

well-being declines during this period ¹⁷. This is a main reason why the effect of seasonal changes should be evaluated in this high stress prone student population. We only found a few published studies done specifically on medical students. These were limited to medical students of Russia¹¹, Korea¹⁸ and China^{13,14}. Studies done in the Asian population were comparatively limited. Summer variation of SAD was the pattern noted in all the Asian samples that were studied at large ^{13,14,19}. And this was what was noted among Chinese Medical Students as opposed to the Russian medical students who had a higher incidence of W-SAD ^{11,13,14}.

According to our knowledge, none of the previous studies had compared the foreign medical students who had migrated to a higher latitude with their local student population originating in that higher latitude.

Objectives

Our aim was to examine the effect of seasonal mood variations among foreign (international) students relocating to regions of higher latitude and compare it to the changes of their local counterparts within the same country.

Based on the current literature, we hypothesized that students originating from countries with minimal seasonal variation and lower latitude will have a higher likelihood of been affected by SAD when immigrating to a higher latitude ^{15, 16}.

Additionally, by conducting the study we hope to raise awareness about changes that come simultaneously with seasonal changes which may sometimes bear significant hindrance to a person's daily activities.

Method

Study Design and setting

A cross sectional descriptive and analytical study was conducted between the months of December 2022 to February 2023 in Grodno State Medical University, Belarus. Local and international students of the faculty of medicine from year one to year six participated in this study. A Google form questionnaire was distributed among this student population, and data was collected on a voluntary basis. Initial consent was taken from the participants through the Google form itself. IRB approval of the University was taken to collect data from the above-mentioned students. (Reference number - 2401)

Study size and participants

An initial sample of 200 students were chosen to allow for the elimination of invalid data while ensuring that at least 50% of the original sample (100 students) remains available for analysis. Half of the sample was collected from the local student medical faculty, and the other half from the foreign medical student faculty of the same university. Medical students, from either the local or foreign medical faculty who were above 18 years of age were eligible to participate in the study. Exclusion criteria included students without any exposure to seasonal changes for at least 2 years of duration (first- and second-year students of the foreign student population), students that were diagnosed previously with a major depressive disorder, and/or currently on medication for any mental disorder were excluded.

Data collection and bias

The independent and dependent variables were collected through a Google form that was distributed among the study sample. In order to reduce the volunteer bias, the questionnaire was distributed through various WhatsApp groups, ensuring a more diverse and inclusive representation of the study population. To reduce the language bias, the questionnaire was provided in English to the foreign students and in Russian to the local students.

Data sources and variables

The independent variables collected from all students were data on demographics, any chronic medical

conditions, any prior diagnosis of psychological illnesses, current use of any medications, seasonal changes in the student's county of origin, previous exposure to seasonality and coping mechanisms for seasonal changes. Prior diagnosis of any physical and psychological illnesses was crucial to remove any potential confounders and effect modifiers from the study sample. As literature showed an association of Depression and SAD ¹² we excluded students with depression and any physical illness with depressive symptoms. The foreign student's category included students from tropical countries who had not experienced seasonal changes. Thus, data about seasonality of the country, prior exposure to seasonal changes and coping mechanisms for seasonal changes were additional information that were collected.

The dependent or the outcome variable was SAD. The Personal Inventory for Depression and SAD, Self-Assessment Version (PIDS-SA) was used to collect data on SAD ²⁰. This Assessment tool was developed by Michael Terman, PhD, and Janet B.W. Williams, DSW of the New York State Psychiatric Institute and Department of Psychiatry of Columbia University. PIDS-SA is a four-part, self-rated screening tool, which had been developed as a clinician tool to pre-screen the patients and reduce the interview time ²¹.

The four parts of PIDS-SA are the likelihood of having depression according to DSM criteria, identification of depression as seasonal or non-seasonal, identification of months worst and best in a calendar year and the magnitude of atypical symptoms with winter exacerbation ²². (**Table 1**)

Table 1 - PIDS parts, interpretation and reference of adaptation

Part of the screening tool	Description	Interpretation criteria	Source of Adaptation by the PIDS-SA
Part A	DSM criteria for major depression in the past year	If score is ≥ 5 , individual may have MDD symptoms	Prime-MD Clinician Evaluation Guide, developed by Robert L. Spitzer, MD, and Janet B.W. Williams, DSW.
Part B	Magnitude of key symptoms of SAD (from NIMH SPAQ)	<ul style="list-style-type: none"> • If <6 Non seasonal, probably do not have SAD. • If between 7 to 11 may have mild SAD. • $f \geq 12$ may have clinically significant SAD. 	Seasonal Pattern Assessment Questionnaire developed by Norman E. Rosenthal, MD, Gary J. Bradt, and Thomas A. Wehr, MD.

Part C	Identification of months worst and best (from NIMH SPAQ)	<ul style="list-style-type: none"> Score ≥ 4 per month in a series of 3-5 months from September to January in Column A (feel worst), Column B (feel best) higher scores in March and June \rightarrow Fall or Winter SAD Feel worst in July and August (summer), feel better in winter \rightarrow Summer SAD 	Seasonal Pattern Assessment Questionnaire developed by Norman E. Rosenthal, MD, Gary J. Bradt, and Thomas A. Wehr, MD.
Part D	Magnitude of atypical symptoms with winter exacerbation	Higher the score, more likely have experienced winter symptoms. (But possible to be depressed in winter without the symptoms as well)	

(PIDS-SA - Personal Inventory for Depression and SAD, Self-Assessment Version 21, MDD – Major Depressive Disorder, NIMH SPAQ – National Institute of Mental Health SPAQ)

Since most SAD research was done using SPAQ²³, and as it is incorporated into PIDS, we were able to use PIDS-SA as the assessment tool. The sensitivity of SPAQ is not enough to use it as a diagnostic instrument, but it has been shown to be accurate enough to be used as a screening tool²⁴. SPAQ (Part B and Part C of PIDS-SA) evaluates retrospectively the degree of seasonal variation in mood and behavior. It describes months of the year when subjects would feel worst and feel best. This is relative to six parameters namely sleep length, appetite, weight changes, energy level, mood (overall feeling of well-being), and social activity. The degree of change in these 6 parameters are assessed from a scale of 0 to 4, and the total is summed up. The GSS score is thus calculated from 0 to 24.

Screening of data

The sample population of this study included 100 local students and 121 foreign students. Data was screened for validity (Figure 1). Following the removal of invalid data, the sample comprised 67 local students and 57 foreign students. (Figure 1)

Statistical methods

Data obtained from the Google forms were transferred and processed in Microsoft Excel. These were then analyzed using the Epi Info software 7.2.6.0. Chi-square and T-test were done to understand the association between the different student populations and W-SAD. A p value ≤ 0.05 was taken as statistically significant and $p \leq 0.10$ as marginally significant value.

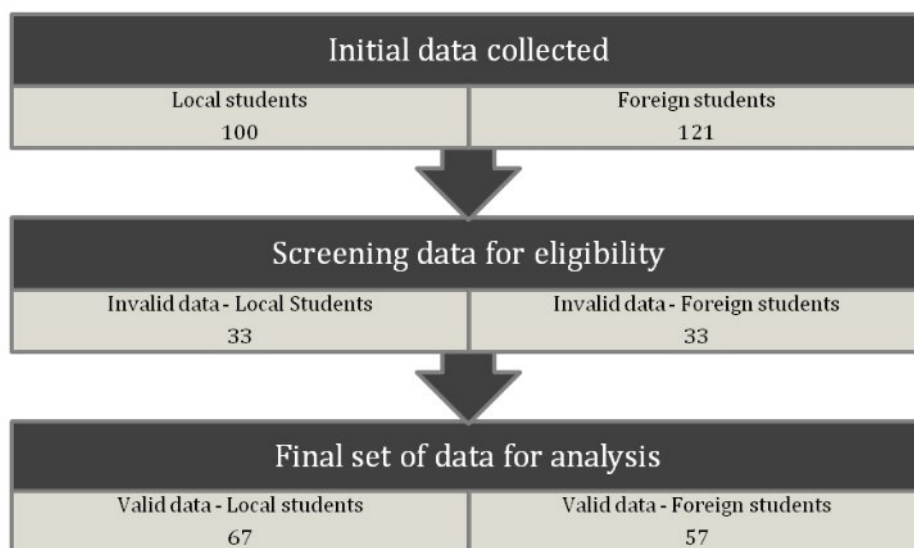


Figure 1 - Screening process for data validity.

one group additionally incorporated the curriculum with the concept of medical entrepreneurship. One group (16.67%) suggested four blocks carried out concurrently, whereas five groups (83.33%) adopted a block or module system for all courses. Another group (16.67%) stated that routine mental health assessments are necessary, in addition to faculty assessments of students' well-being.

Results

Characteristics of the sample (Table 2)

In the final sample of 124, consisting of both local and foreign students, approximately 80% were females and 20% were males.

Among the 67 students of the local population three nationalities were observed. This included 88% of Belarussians, 6% of Russians and 6% of Polish nationality. Among the 57 foreign student population, 77% were Sri Lankans, while 11% were Indians and 5% were Maldivians. There were minor but equal representations of Nigerians (2%), Tanzanians (2%) and Turkman (2%) nationalities as well.

In this study sample, the majority of the local students were in the 3rd year of studies (54%), while among the foreign student population equal distribution of 3rd, 4th and 5th year of students were seen (approximately 30% each). The first- and second-year students were excluded from the foreign student sample, as they had not had at least two years of exposure to seasonal changes.

In both the student populations there was a near normal distribution of the age ranging from 17 to 26 years among the locals (median 20) and 19 to 27 years among the foreign students (median 23). The majority (mode) of local students were 20 years of age, but most foreign students were 23 years. Thus, a more older student population was represented among the foreign students.

Among the local student population, the mean age was 20 years (SD = 1.64), while among the foreign student population it was 23 years (SD = 1.83), of age. When considering the place of residence, half of the local students resided in the hostel (52%) while the other half stayed in apartments or other housing arrangements (48%). Among the foreign students the majority lived in the hostel (68%), while the rest resided in apartments (32%).

According to religion, majority of local students were Orthodox Christians (49%), while 31% were either Christian, Catholic or Protestant. Within the rest of the local students, 26% were Atheist or an Agnostic, while a minority was Islamic (2%). In contrast, majority of the foreign student population was Buddhist (53%). Among the rest 21% were Islamic, 16% Christian and 10% Hindu. When considering the relationship status in both the student populations, the majority were single (61% among the locals, and 70% among the foreign). Only one individual (2%) in the local student group reported to be married.

One Way analysis of the PIDS-SA parts (Table 3)

Since PIDS-SA has four parts, analysis was also done in these four parts to see characteristics of each student population. The PIDS guidelines were taken for the interpretation (Table 1) 20.

When comparing both the local and foreign student populations, foreign students had more depressive symptoms in Part A with a mean score of 4.85 (SD 2.46) compared to 4.43 (SD 2.71) in the local student group. Additionally, a greater number of students from the foreign group (58%) were affected compared to the local counterparts (47.8%).

In Part B, a higher percentage (70.2%) of foreign students had seasonal effect in the mood with a mean score of 9.88 (SD 5.55) when compared to the local students who had a lower percentage (64.2%) with a lower mean of 9 (SD 4.71). It was also noted that among those foreign students that were affected, a higher percentage had a significant effect on their mood (52.5%) unlike the local group.

In the Part C of the analysis, neither the foreign students nor the local students had a summer variation of SAD (S-SAD) (Figure 2). Winter variation of SAD (W-SAD) was seen among 14 students out of the 124 population (11.3%). A higher percentage of these students affected with W-SAD were foreign medical students (n=10, 17.5%) as opposed to the local medical students (n=4, 6%). Out of the winter months most of these students were affected in December and January (Figure 2).

Comparison of the two student populations with PIDS-SA Scores – Two-way analysis (Table 4)

Analysis of Part A between the two student populations

Table 2 - Demographical characteristics of the study population

Characteristic	Local students n (%)	Foreign students n (%)
Gender		
Female	54 (80%)	45 (79%)
Male	13 (20%)	12 (21%)
Year of Study		
1st Year	4 (6%)	0 (0%) *
2nd Year	0 (0%)	0 (0%) *
3rd Year	36 (54%)	17 (30%)
4th Year	11 (16%)	18 (32%)
5th Year	6 (9%)	19 (33%)
6th Year	10 (15%)	3 (5%)
Nationality		
Foreign students -		
Sri Lankans	0 (0%)	44 (77%)
Indian	0 (0%)	6 (11%)
Maldivian	0 (0%)	3 (5%)
Lebanon	0 (0%)	1 (2%)
Nigerian	0 (0%)	1 (2%)
Tanzanian	0 (0%)	1 (2%)
Turkman	0 (0%)	1 (2%)
Local students -		
Belarussian	59 (88%)	0 (0%)
Russian	4 (6%)	0 (0%)
Polish	4 (6%)	0 (0%)
Residence		
Apartment	31 (46%)	18 (32%)
Hostel	35 (52%)	39 (68%)
Other	1 (2%)	0 (0%)
Religion		
Buddhist	0 (0%)	30 (53%)
Christian	11 (16%)	9 (16%)
Hindu	0 (0%)	6 (10%)
Islam	1 (2%)	12 (21%)
Orthodox	33 (49%)	0 (0%)
Catholic	9 (13%)	0 (0%)
Atheist	9 (13%)	0 (0%)
Agnosticism	3 (5%)	0 (0%)
Protestant	1 (2%)	0 (0%)
Relationship status		
In a relationship	25 (37%)	17 (30%)
Single	41 (61%)	40 (70%)
Married	1 (2%)	0 (0%)

*Since there was no exposure to seasonal changes for at least 2 years, 1st and 2nd years were excluded among the foreign students. (SD – Standard Deviation, IQR – Interquartile range, n – frequency, % - percentage)

Figure 2 - Part C Analysis

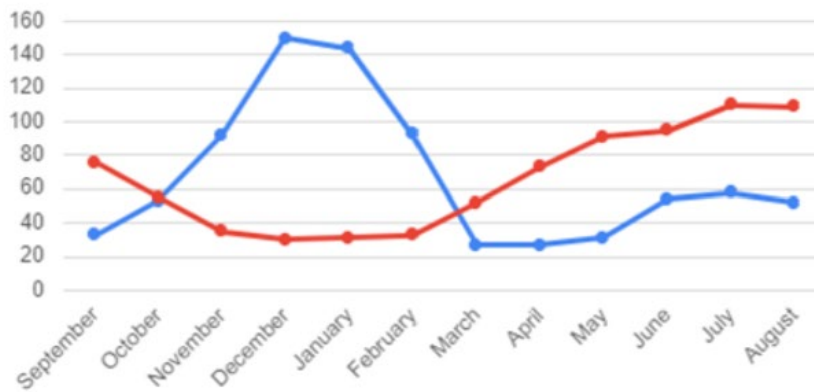


Figure 2a: Effects of seasonal changes in foreign students Blue: Column A (depressive symptoms) Red: Column B (opposite to depressive symptoms)

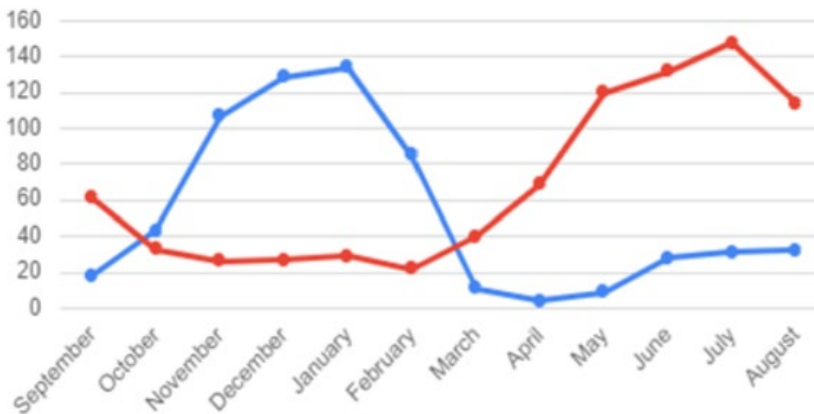


Figure 2b: Effects of seasonal changes in foreign students Blue: Column A (depressive symptoms) Red: Column B (opposite to depressive symptoms)

According to the PIDS-SA there was no cut off value for Part D, and only a numerical value to understand magnitude of atypical symptoms with winter. Foreign students had a higher mean score with a greater effect in winter than the local students. (Foreign student Mean 5.02 with a SD 1.89, Local student Mean 4.23 with a SD 2.36).

was not statistically significant. When considering the Part B of Analysis, according to PIDS-SA a score of 12 is taken as the cutoff 21. According to the original SPAQ guidelines, the cutoff value is 11 and is calculated as the GSS score 25. Neither of these cutoffs were statistically significant. When comparing the results of Part C, foreign students were 4 times more likely to have W-SAD compared to their local student population (OR=4.12) and this was statistically significant. (p 0.04)

In Part D of the analysis, there was a significant difference of winter effect between foreign students and local students with a p value of 0.04, which is statistically significant. Foreign students had a higher mean (t value = 2.04) of Part D than the local students. This meant they had more impact of the winter than the locals. Comparison of the two student populations with

PIDS-SA Scores – Two-way analysis (**Table 4**)

Analysis of Part A between the two student populations was not statistically significant. When considering the Part B of Analysis, according to PIDS-SA a score of 12 is taken as the cutoff 21. According to the original SPAQ guidelines, the cutoff value is 11 and is calculated as the GSS score 25. Neither of these cutoffs were statistically significant. When comparing the results of Part C, foreign students were 4 times more likely to have W-SAD compared to their local student population (OR=4.12) and this was statistically significant. (p 0.04)

In Part D of the analysis, there was a significant difference of winter effect between foreign students and local students with a p value of 0.04, which is statistically significant. Foreign students had a higher mean (t value

Table 3- Summary of data in the four parts of PIDS-SA

Characteristic	Local students n (%)	Foreign students n (%)
Part A score-		
MDD Value (>5) YES	32 (47.8%)	33 (58%)
MDD (<5) NO	35 (52.3%)	24 (42%)
Part B score-		
No seasonal changes	24 (35.8%)	17 (29.8%)
Mild seasonal changes	24 (55.8%)	19 (47.5%)
Significant seasonal changes	19 (44.2%)	21 (52.5%)
Part C (yes/no)-		
Winter SAD	4 (6.0 %)	10 (17.5%)
Summer SAD	0 (0%)	0 (0%)

(n - number of students, % - percentage)

Table 4 - SPAQ Analysis – Foreign students relative to Local students

Part of SPAQ	Odds Ratio (95% CI)	Stat Test
Part A	1.50 (0.73- 3.06)	X ² = 1.27
Part B	1.31 (0.62 – 2.80)	X ² = 0.50
Part B – Significant	1.47 (0.69 – 3.14)	X ² = 1.01
Part B – GSS Score	1.49 (0.72 – 3.09)	X ² = 1.18
Part C	3.35 (1.00 – 11.34)	X² = 4.12*

*p-value ≤ 0.05

Among the different parts of PIDS-SA scores, Part C was taken as the dependent variable for further analysis to understand the relationship of SAD with the student population.

Table 5 – Different student populations, latitude of the country of origin and W-SAD Affected students’ comparison

Nationality	Latitude in degrees	Seasonality of country as reported by students	Total number of students in the sample n (%)	Number of students affected with Winter SAD n (%)
Local Student Population (Higher Latitude) :				
Belarussian	54 °	Yes	59 (47.5%)	4 (28.6%)
Russia	62 °	Yes	4 (3.2%)	0
International Student Population (Lower Latitude) :				
Sri Lanka	8 °	No	44 (35.4%)	6 (42.9%)
India	21 °	Yes	6 (4.8%)	2 (14.3%)
Maldivian	3 °	No	3 (2.4%)	0
Nigerian	9 °	No	1 (0.8%)	1 (7.1%)
Turkey	39 °	Yes	1 (0.8%)	1 (7.1%)
Lebanon	34 °	Yes	1 (0.8%)	0
Tanzania	-6 °	No	1 (0.8%)	0

*Latitude taken from one common Google Dataset 26 , n = frequency, (%) = percentage

= 2.04) of Part D than the local students. This meant they had more impact of the winter than the locals.

Analysis of Winter SAD in the two student groups

In our study, we observed a noteworthy pattern among foreign medical students diagnosed with W-SAD (Table 5). Specifically, all these students had originated from countries situated at lower latitudes than that of Belarus. Additionally, among the 10 foreign students identified with W-SAD, only 3 reported prior exposure to seasonal changes in their respective country of origin before enrolling in studies in Belarus.

We further analyzed the foreign student population to understand the association of prior exposure to seasons (seasonality) in their country of origin to W-SAD (Table 6). There was a 4 times likelihood (OR=3.6) of foreign students with no seasonal changes in country of origin having W-SAD relative to the foreign students who had seasonal changes in their country, but it was only marginally statistically significant. (p-value =0.10)

To remove any confounders, we also asked the foreign students if they have lived outside of their country before relocating to Belarus, to see if they had prior exposure to seasons. Chi-Square analysis of this to W-SAD had no statistically significant value.

Open Ended Question Analysis

Among all 124 students in the sample, 43 students (34.7%) stated they had negative impact from seasonal changes in their daily lives. Coping mechanisms were asked from them as an open-ended question. A detailed statistical analysis was not done on this qualitative variable. Different themes were identified when summarizing these answers.

Some of the positive coping mechanisms mentioned were getting involved in social activities (talking with family and friends), spiritual/religious activities, physical activities, hobbies, entertainment, and wellness activities. The negative coping mechanisms could be categorized mainly to unhealthy eating habits and substance use including smoking, alcohol, drugs, and sedatives.

Table 6 - Foreign student specific characteristics and association with having W-SAD

Characteristic	Odds Ratio (95% CI)	Test Value, p Value
If the motherland had any distinct seasons	3.60 (0.70 – 18.56)	$\chi^2 = 2.56$ (p 0.10)
If they have lived outside the country before	0.41 (0.05 – 3.64)	$\chi^2 = 0.67$ (p 0.41)

X² = Chi-square test

Discussion

In this study, we aimed to understand the effect of seasonal mood variations among foreign (international) medical students relocating to regions with higher latitude and compare it to the changes of their local counterparts within the same country. It was evident that both the local and foreign students had mood changes with seasons, but we observed a significant difference among the two populations when comparing the PIDS-SA scores.

There was a higher winter effect on the foreign students when compared to the local students, as evident by the statistically significant difference in Part C and Part D scores of PIDS-SA. It was also evident that foreign students had a 4 times likelihood of been affected with W-SAD relative to the local students.

Foreign students in our study who were affected by W-SAD were all from lower latitude countries that had

relocated to Belarus which was in a higher latitude. This finding is consistent with two previous studies done among college students in America ^{10, 27}.

The foreign students in our study were mainly Sri Lankans, Indians, and Maldivians. Our mainly Asian sample shows a similar finding to the study done in England comparing the non-indigenous Asian women to the indigenous Asian women living in a higher latitude ⁶. The mood effect was more in the non-indigenous Asian sample comparative to the indigenous sample. The Asian sample in this study involved mostly Indian, Pakistani, and Bangladeshi ethnicities.

In our study, majority of participants in the foreign student sample were Sri Lankans, and notably the highest percentage of foreign students with W-SAD were also Sri Lankans. To gain a comprehensive understanding of mood effect among different nationalities in a foreign setting, future research should strive to include a more balanced representation of

other nationalities.

The only study involving Sri Lankans regarding SAD was a study done in Oslo, Norway ^{7,28}. In this study Sri Lankans were the least affected by W-SAD, but in our study the Sri Lankan student population were the most affected with W-SAD. In the qualitative part of the study in Oslo ²⁸, it was noted that close family, social networks and better economic prospects had attributed to the decreased incidence of SAD among the Sri Lankan immigrants. And we believe that these protective factors were not seen among the Sri Lankan student population in Belarus who live away from home and are not financially stable.

In our study, seasonal changes in mood had negative effects on nearly 35% of the student sample. But it was evident that only some knew positive coping mechanisms, and some had taken up negative disruptive activities like substance abuse. This also shows the importance of raising awareness about the mood changes with season and the need to teach positive coping styles for students.

We believe that our study provides valuable insights into seasonal effects on medical students. It shows that non-indigenous students are affected at higher latitudes. We hope that this knowledge will help universities create policies so that their foreign student populations better understand their mood changes with seasons and learn coping mechanisms for it.

Limitation

Given the cross-sectional design of our study, there is a need for further future research adopting prospective longitudinal approaches. This will further strengthen the findings of this study and find causal relationship

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between foreign nationalities, relocation to higher altitudes and SAD.

Winter-SAD could be confused with “holiday blues”, brought on by the changes of the time in the year. Winter-SAD is specifically due to the change in daylight hours, and not the calendar with holidays and stresses ³. Among medical students this kind of holiday and stresses could have been a confounding factor or effect modifier, and more studies should be done to identify these.

SPAQ is not yet culturally validated. Since PIDS-SA has adapted SPAQ in the questionnaire, this study will also have cultural limitations. Further studies with cultural validation should be done to understand different ethnic groups involved.

Conclusion

Medical students have a stressful academic life. On top of this, foreign medical students have challenges arising from immigration. Especially when relocating to higher latitudes they have a higher tendency to be affected with seasonal affective disorder. Recognizing and addressing these unique challenges is paramount in supporting the well-being of foreign medical students across all universities.

Universities should understand the significance of seasonal mood effect on student's lives and prioritize increasing awareness about it, teaching effective coping mechanisms, and ensuring access to necessary treatment in severe forms of Seasonal Affective Disorder. By fostering an environment of understanding and assistance, universities can significantly contribute to the overall well-being of both local and foreign students.

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Association Between Blood Pressure Levels and Diabetic Retinopathy Stage Among Patients at Karsa Husada General Hospital, Batu City: A Cross-Sectional Study

Background: Diabetic retinopathy is a microvascular disease of the retina that is progressive and threatens vision. One of the risk factors that can influence diabetic retinopathy is blood pressure. High blood pressure can worsen retinal microvascular conditions as it can cause blood vessels to thicken, leak, and form new ones.

Objective: This study aimed to determine the relationship between blood pressure levels and the diabetic retinopathy stage at Karsa Husada General Hospital, Batu City.

Methods: This research is an analytical observational study with a cross sectional study design. Data was collected from hospital medical records. There were a total of 40 cases of diabetic retinopathy at Karsa Husada General Hospital, Batu City in 2020-2022. The sample size consists of 32 patients which met the inclusion and exclusion criteria. The data collection technique uses a non-probability sampling technique, purposive sampling type. Data analysis uses univariate and bivariate analysis.

Results: 28.1% of patients had normal blood pressure, 21.9% had normal-high blood pressure, 31.3% had hypertension grade 1, and 18.8% had hypertension grade 2. There were 14 (43.8%) diagnosed with Non-Proliferative Diabetic Retinopathy (NPDR), meanwhile there were 18 (56.3%) diagnosed with Proliferative Diabetic Retinopathy (PDR). Bivariate data analysis conducted using the Chi Square test yielded a p value of 0.315.

Conclusion: Despite the established understanding that hypertension can exacerbate microvascular complications in the retina, our findings suggest that there is no significant relationship between blood pressure levels and diabetic retinopathy stage.

Keywords: Diabetic Retinopathy, Hypertension, Vascular Diseases

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Introduction

Diabetic Retinopathy (DR) is a progressive microvascular disease affecting the retina of the eye which can threaten vision. This retinal disease is often associated with prolonged hyperglycemia⁽¹⁾ which is intricately associated with diabetic complications and other conditions, such as high blood pressure. High blood pressure can harm the structure of the retinal blood vessels.⁽²⁾ Chronic hyperglycemia can also change the structure of the retinal blood vessels, one of which is neovascularization in diabetic retinopathy.⁽³⁾⁽⁴⁾

In 2019, The International Diabetes Federation (IDF) found that the prevalence of diabetic retinopathy reached approximately 27% among diabetic cases from 2015 to 2018. The specific prevalence of this retinal disease in the Southeast Asia (SEA) region is around 12.5%. IDF also estimates that this prevalence will increase by approximately 12.2% 2030. This proves that countries in the SEA region have a high prevalence rate of DR.⁽⁵⁾

Diabetic retinopathy is the second most common microvascular complication after nephropathy in Indonesia. The prevalence in Indonesia is 43.1% with treatment rate of 26.1% among affected individuals.⁽¹⁾ In 2020, the East Java Province had approximately 11,008,334 patients with both diabetic retinopathy and hypertension. The number of DR cases are expected to increase every year, considering that 70% of Batu City residents are diagnosed with either diabetes mellitus or hypertension. Most of these patients range in age from 20 to 64 years old.⁽¹⁾⁽⁶⁾

Diabetic retinopathy is classified into two stage: the Non-Proliferative stage, which represents the initial phase of the disease and the Proliferative stage, which occurs in the advanced phase.⁽¹⁾⁽⁷⁾ The European Society of Cardiology (ESC) classifies blood pressure into: normal, normal-high, and hypertension grade 1 to 3.⁽⁸⁾ Hypertension is diagnosed if the Systolic Blood Pressure (SBP) is ≥ 140 mmHg and/or Diastolic Blood Pressure (DBP) ≥ 90 mmHg.⁽⁹⁾

The physiological changes in the retina caused by hyperglycemia may lead to microangiopathy and micro obstruction. These conditions can result in ischemia.⁽¹⁰⁾ Apart from hyperglycemia, ischemia can also be caused by hypertension, as it is considered to worsen the condition of diabetic retinopathy.⁽²⁾

Thus, the purpose of this study was to determine the relationship between blood pressure levels and diabetic

retinopathy stage in patients at Karsa Husada General Hospital Batu City.

Method

This research was conducted in January 2023 at Karsa Husada Hospital, Batu City using a cross-sectional approach with secondary medical record data. The target population for this study was Diabetic Retinopathy (DR) patients with a total minimal sample of 32 people who met the inclusion and exclusion criteria. Diagnosis of DR was established based on American Academy of Ophthalmology guidelines.⁽¹¹⁾ The research was carried out after obtaining approval from the ethics commission of the Karsa Husada Batu General Hospital. The study was assessed by Health Research Ethics Committee, Karsa Husada General Hospital, Batu, and obtained ethical approval on 24 November 2022 (ethical certificate 070/001/008/102.13/2022).

The inclusion criteria for this study were as follows: 1) Patients diagnosed with DR, either NPDR and PDR stages at Karsa Husada Hospital, Batu City,⁽¹¹⁾ 2) Patients diagnosed with blood pressure data classified as normal, normal-high, hypertension grade 1 and hypertension grade 2,⁽⁸⁾ 3) Patients' medical records containing information such as age, sex, blood sugar levels, BMI, education, occupation, smoking habits, history of other diseases and drug therapy.⁽¹⁾ Exclusion criteria included the following: 1) Patients suffering from immune diseases, 2) Patients having a history of malignant disease, 3) Incomplete medical record data. BMI was also categorised into four groups according to the conventional WHO classification: underweight (18.5 kg/m²), normal (18.5–24.9 kg/m²), overweight (25–29.9 kg/m²), and obese (≥ 30 kg/m²).⁽¹²⁾

The results of the study were presented in cross-tabulations and analysed using the chi-square test to determine the significant correlation between research variables. Significance conditions are met if the p-value is less than 0.05. In addition, this test is used because the blood pressure levels data is in ordinal scale while the stage of DR is in a nominal scale.⁽¹³⁾

The formula used to calculate the minimal sample for this cross-sectional study is as follows:

$$n = \frac{Z^2 p(1 - p)N}{d^2(N - 1) + Z^2 p(1 - p)}$$

Information:

n = Number of samples

N = Number of population

Z = Degree of confidence (95% level = 1.96)

p = Proportion of a particular case to a population, if the proportion is unknown then it is set at 50% (0.50)

d = Degree of deviation to a population expected to be 5% (0.05).

Based on calculations using this formula, the minimum number of samples is 32 with calculation as follows:

$$\begin{aligned}
 n &= \frac{Z^2 p(1-p)N}{d^2(N-1) + Z^2 P(1-p)} \\
 &= \frac{(1,96)^2 \cdot 0,5 (1-0,5) \cdot 40}{(0,05)^2 \cdot (40-1) + (1,96)^2 \cdot 0,5 (1-0,5)} \\
 &= \frac{38}{1,2} \\
 &= 32
 \end{aligned}$$

Result

Summary of the study

Based on **Table 1**, most of the patients comprised approximately 18 patients (56.3%), fell within the age range of 50-59 years. Male accounted for 18 patients (56.3%) and BMI obesity were dominant with around 15 patients (46.9%). Grade 1 hypertension was observed in approximately 10 patients (31.3%), while PDR was detected in 18 patients (56.3%). Based on **Table 2**, a p-value of 0.315 (> 0.05) was obtained for the correlation between blood pressure levels and the diabetic retinopathy stage.

Then the data underwent a Chi-Square analysis test to see the relationship between the blood pressure levels and the diabetic retinopathy stage. Based on the Chi-Square test result, p-value of 0.315 was obtained, which means that the significance value is > 0.05. Thus there is no relationship between blood pressure levels and the diabetic retinopathy stage in patients at RSU Karsa Husada General Hospital, Batu City.

Discussion

Consistency With Previous Studies

In this study, the gender most affected by DR was male, comprising 56.3% of the patients. This finding aligns

Table 1. General characteristics of respondents

Characteristics	Frequency
Age	
• 30-39 years	5 (15.6)
• 40-49 years	3 (9.4)
• 50-59 years	18 (56.3)
• ≥ 60 years	6 (18.8)
Gender	
• Male	18 (56.3)
• Female	14 (43.8)
Education	
• Diploma/Bachelor	6 (18.8)
• Senior High School	10 (31.3)
• Junior High School	12 (37.5)
• Elementary School	4 (12.5)
Occupation	
• Soldier/ Police	2 (6.3)
• Private	7 (21.9)
• Self-employed	10 (31.3)
• Not working	13 (40.6)
Body Mass Index (BMI)	
• Underweight	0 (0)
• Normal	12 (37.5)
• Overweight	5 (15.6)
• Obesity 1	14 (43.8)
• Obesity	1 (3.1)
Smoking habit	
• No	27 (84.4)
• Smoking	5 (15.6)
History of Other Diseases	
• None	16 (50.0)
• Tuberculosis	1 (3.1)
• Strokes	2 (6.3)
• Kidney failure	2 (6.3)
• Heart failure	11 (34.4)
Drug Therapy	
• Oral administration	14 (43.8)
• Insulin Injection	18 (56.3)
Fasting Blood Glucose (FBG) levels	
• < 100 mg/dL	5 (15.6)
• 100-125 mg/dL	3 (9.4)
• ≥ 126 mg/dL	24 (75.0)
Blood Pressure	
• Normal	9 (28.1)
• Normal-high	7 (21.9)
• Grade 1 Hypertension	10 (31.3)
• Grade 2 Hypertension	6 (18.8)
Diabetic Retinopathy Stage	
• NPDR	14 (43.8)
• PDR	18 (56.3)

BMI (Body Mass Index); FBG (Fasting Blood Glucose); NPDR (Non-proliferative Diabetic Retinopathy); PDR (Proliferative Diabetic Retinopathy)

Table 2. Bivariate analysis of the relationship between blood pressure level and stages of diabetic retinopathy

Variable	Blood Pressure					p value
	Normal	Normal-high	Grade 1 Hypertension	Grade 2 Hypertension	Total	
	n (%)	n (%)	n (%)	n (%)	n (%)	
NPDR	2 (6.3)	4 (12.5)	4 (12.5)	4 (12.5)	14 (43.8)	0.315
PDR	7 (21.9)	3 (9.4)	6 (18.8)	2 (6.3)	18 (56.3)	
Total	9 (28.1)	7 (21.9)	10 (31.3)	6 (18.8)	32 (100)	

NPDR (Non-proliferative Diabetic Retinopathy); PDR (Proliferative Diabetic Retinopathy)

with a research by Cherchi (2020) which states that the prevalence of diabetic retinopathy is higher in men than women, with rates of 22.0% versus 19.3%. The higher incidence in men is often caused by unhealthy lifestyles, hormones changes, smoking, alcohol consumption, and lower levels of compliance with blood sugar control compared to women.⁽¹⁴⁾⁽¹⁵⁾

The age group most commonly diagnosed with DR was 50-59 years. According to Reubun (2022), people aged 50 years and older are considered to be more prone to experience diabetic retinopathy. Correlatively, as a person's age increases, their level of glucose intolerance also increases, putting individuals with a long history of Diabetes Mellitus (DM) at a higher risk.⁽¹⁶⁾ In addition, as individuals age, their body function decreases due to the process of cell apoptosis, particularly in the retina. This decline can be accelerated by inflammatory reactions and increased oxidative stress.⁽¹⁷⁾

Respondents predominantly diagnosed with grade 1 hypertension, 10 respondents (31.3%). The results of this study are consistent with Liu (2020), who stated that among 2189 respondents with diabetic retinopathy from Chinese, Malay and Indian ethnic groups, 1,046 respondents (47.8%) dominated by normal-high hypertension patients with readings of 130- 139 mmHg. This occurs because abnormal Pulse Pressure (PP) is considered to increase shear stress within the blood flow, potentially leading to the destruction of retinal capillary endothelial in the eye. High blood pressure can cause leaks in the retinal vessels.⁽¹⁸⁾⁽⁶⁾

Based on the results of the analysis of diabetic retinopathy, it was found that the majority of patient with diabetic

retinopathy were in the Non Proliferative Diabetic Retinopathy (NPDR) stage, with 14 respondents (43.8%), while 18 respondents (56.3%) had Proliferative Diabetic degree were Retinopathy (PDR). The results of this study are consistent with Primaputri's research (2022), which indicates that patients with diabetic retinopathy are predominantly in the PDR stage compared to NPDR stage with a ratio of 68.0% versus 51.0%. This is because many individuals with chronic diabetes mellitus do not undergo regular eye examinations at existing health facilities, resulting in numerous cases remaining undiagnosed at an early stage.⁽¹⁹⁾ Many patients who come to the hospital are already in the PDR stage, which means that retinal neovascularization has happened.⁽²⁰⁾

Based on data analysis using the Chi-Square test, a p-value of 0.315 was obtained, ($p > 0.05$), indicating that there is no significant relationship between the blood pressure level and diabetic retinopathy stage.

The results of this bivariate analysis are also relevant to Tariq's (2023) research, which states that there is no significant relationship between hypertension and the diabetic retinopathy, as indicated by a p value of 0.804. This occurs due to a lack of awareness among the public and minimal access to healthcare. It does not rule out the possibility that, many patients with NPDR or PDR have normal blood pressure.⁽²¹⁾

This study yields similar result to those of Halim (2022), which suggests that there is no significant relationship between systolic and diastolic blood pressure and the diabetic retinopathy, as indicated by a p-value > 0.05 .⁽²²⁾ This occurs because the majority of diabetic retinopathy patients are already taking antihypertensive and anti-

diabetes medications. Consequently, when examined at a health facility, their blood pressure is often controlled or not as high as those who do not regularly take antihypertensive medications.⁽²³⁾

The results of this study are different from Nauli (2018), which stated that there is a significant relationship between hypertension and the diabetic retinopathy with a p-value of 0.043. Diabetes Mellitus (DM) is closely related to hypertension, with one of the interactions involving hormones controlling blood sugar levels through the Renin Angiotensin-Aldosterone System (RAAS). In diabetic patients, there is an increase in RAAS, which can lead to hypertensive conditions. The combination of diabetes and hypertension affects the microvascular condition of the retina, leading to the release of retinal pericyte cells.⁽²⁴⁾

Strength and Limitations

This study is the first cross-sectional study to explore the relationship between blood pressure levels and diabetic retinopathy stage in Batu City, particularly within the Malang Raya region, especially at Karsa Husada Batu General Hospital.

The limitations of this study, which may contribute to insignificant results, include the fact that hypertension is not the sole factor causing diabetes retinopathy. Diabetic retinopathy has multifactorial causes, with the chronicity of diabetes mellitus being the primary factor. Additionally, the authors did not conduct further analysis to correlate these factors. Secondly, since the majority of respondents were taking antihypertensive medication, many of them displayed normal blood pressure during the checks which may not accurately represent their hypertension condition. Thirdly, the influence of less detailed classification of diabetic retinopathy stages is another limitation, as medical records solely list NPDR and PDR stages. Meanwhile, it's essential to monitor the development of diabetic retinopathy starting from the mild, moderate, and severe NPDR stages, in order to understand the progress of diabetic retinopathy in detail, particularly in cases influenced by increased blood pressure.

Conclusion

The majority of patients with diabetic retinopathy were in the PDR stage with 18 respondents (56.3%), while the remaining 14 respondents were in the NPDR stage (43.8%).

The majority of patients with diabetic retinopathy and blood pressure problems were grade 1 hypertension, comprising 10 respondents (31.3%), and followed by 6 respondents (18.8%) with grade 2 hypertension.

There was no significant relationship between blood pressure levels and diabetic retinopathy type with a p-value of 0.315.

Recommendation

Suggestions for future research includes using responses from individuals who have not undergone anti-hypertensive or diabetes mellitus therapy and employing a more detailed DR diagnostic classification. In addition, it is expected to use a larger sample size in cross-sectional studies, in order to provide more representative results.

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Conflict of Interest

The authors declare no conflict of interest.

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No funding was obtained for this study.

Abbreviations

DR (Diabetic Retinopathy)

BMI (Body Mass Index)

FBG (Fasting Blood Glucose)

NPDR (Non-proliferative Diabetic Retinopathy)

PDR (Proliferative Diabetic Retinopathy)

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Addressing the Growing Concern of Substance Abuse Among Adolescents: A Call to Action

Adolescence is the transitional period between childhood and adulthood, spanning the ages of 10 to 19. Adolescents experience rapid physical, cognitive, and psychosocial changes, which influence their emotions, thoughts, and decision-making. Thus, it is a distinct period of development and a crucial one for laying the foundations for long-term health.¹

During this phase, adolescents can develop patterns of high-risk behavior and habits, of which substance abuse is the most damaging, adversely affecting their physical, psychological, and social well-being.² The use of tobacco, alcohol, and other substances among adolescents is a major public health concern in several parts of the world, including India. According to a survey conducted by the National Sample Survey Organisation, about 20 million children aged 10–14 are estimated to be tobacco users, with around 5500 new users being added every day.³ The average age for initiation of tobacco use was found to be

12.3 years and for alcohol usage at 13.6 years among adolescents.⁴ This leads to a vicious cycle in which these people become preoccupied by their addictions rather than functioning as productive members of society.

Multiple factors facilitate the susceptibility of young people to substance abuse such as peer pressure, family history, media influence, easy access, and mental health issues. Peer pressure from friends was reported as the single most common reason for initiation among nicotine users.⁵ Another study by Tsering et al. reported that the primary driver of continued drug use amongst urban users was the ease of access to substances, while rural users cited “relief from tension” as their main motivation.⁶ On the other hand, “moral sense” and “fear of health problems” were the most common reasons stated for quitting among both urban and rural users implying that parental attitude shaping and awareness of the negative effects of use can encourage users to cease their habits indirectly.⁶ Further, there is also a correlation between adolescent substance abuse and the patterns of disengaged family systems, parenting styles centered on rejection and overprotection, and the existence of incomplete family systems.⁷

Regular drug use by teenagers is known to be associated with alterations in brain function and diminished neurocognitive ability with heavy alcohol use in adolescents being linked to a decline in attention, executive functioning, and information processing.⁸⁻¹⁰ In contrast, marijuana use has been associated with lower levels of cognitive flexibility, visual scanning, error commission, and working memory.¹¹ Additionally, it has been shown to have a role in mental health conditions such as bipolar disorder, depression, psychosis, poor school performance, risk of motor vehicle accidents, and chronic illnesses like

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MI, stroke, and bronchitis.¹¹⁻¹⁴

To achieve wholesome adolescent health, we need to adopt a multidimensional approach with special emphasis on mental health, behavior change of communication towards a healthy lifestyle, and a positive social environment to acquire life skills to implement prevention programs against substance abuse for

children, which requires continuous community-based efforts and legislation. Prioritizing modifiable risk factors and strengthening protective variables through family, school, and community preventive programs should be the focus of these coordinated efforts toward early identification, awareness, and prevention initiatives.¹⁵

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A Scoping Review of The Mental Health Support and Well-being Resources Provided to Medical Students by Australian Universities

Background: In 2020, the Australian government provided \$660,000 to develop a mental health framework for universities to adhere to in support of the mental health of university students. To date, there has been no formal evaluation of the current University Mental Health Framework (UMHF). In this study, we aim to provide preliminary observations that will highlight the current state of mental health support provided to medical students at Australian universities and its alignment with the UMHF.

Methods: A total of 19 UMHF-based criteria for student mental health support across 21 Australian universities were assessed in January 2022 and reviewed in December 2022. Data was obtained from publicly available university pages via homepage traversal and Google Search. Linear regression analysis was performed between the mental health strategy variable and sum of other variables, while Fisher's exact test was performed across all independent variables.

Results: The majority of universities offered individual counselling, as well as mental health crisis line access. Most universities also offered mental health first aid (MHFA) training, mental health resources, and regular well-being sessions. However, there was a lack of support for rural students and students with physical disability. A published mental health strategy was found to significantly correlate with the number of supports provided by universities, along with international student support and well-being session provision. University crisis lines, MHFA training and mental health resources were all found to intercorrelate. LGBTQI+ support correlated with international student support and well-being sessions. Well-being sessions had significant correlation to low SES background student support.

Conclusion: Our study suggests that current mental health support for medical students at Australian universities, while promising, possess significant inadequacies in regards to the UMHF framework. Therefore, it provides grounds for further, more comprehensive research regarding UMHF policies and university support systems, where additional analysis is required particularly on non-public resources.

Keywords: Mental health, medical student mental health, mental well-being, medical education, student well-being

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Introduction

The modern era has seen a growing awareness surrounding mental health, and its role in global disease burden has been widely acknowledged.¹ This has only been exacerbated by the recent COVID-19 pandemic, which has led to a widespread deterioration in general mental health due to increases in social isolation, loss of income, and overall uncertainty.²⁻⁴ Young adults in Australia between the ages of 12-25 suffer the highest rates of mental illness whilst simultaneously having the poorest access to support.⁵ The mental health of tertiary students (individuals attending post-secondary educational institutions such as universities), many of whom fall comfortably into this age bracket, is a subject of great concern.⁶⁻⁸ In particular, medical students experience high levels of academic stress, burnout and overall low quality of life suffered by students, all of which are extremely strong predictors of poor mental health.⁹⁻¹² Poor mental health or mental ill-health in this study is defined as a series of "conditions that affect cognition, emotion and behaviour" causing distress and/or impaired function to the individual.¹³ Because medical students tend to have poorer mental health than the rest of the general population^{14,15}, this can further result in mood disturbance, substance abuse and even suicide.^{15,16}

In 2020, the Australian Government initiated the development of the University Mental Health Framework (UMHF) for universities to adhere to in support of the mental health of university students.¹⁷ This framework outlines six principles, which can be summarised as follows: 1) mental health support should reflect the needs and realities of students, 2) all members of the university community contribute to a healthy learning environment, 3) mentally healthy university communities encourage diversity, connectedness and inclusivity in their learning environment, 4) collaboration and coordination are key to strengthening the mental health response, 5) appropriate, effective and timely services are needed for accessibility, 6) evidence-based continuous improvement and innovation is needed for these services.¹⁸

To date, there has been no formal evaluation of the current UMHF. In this study, we aim to provide preliminary observations that will highlight the current state of mental health support provided to medical students at Australian universities and its alignment with the UMHF.¹⁸ At present, there is a dire lack of literature regarding mental health service provision specifically for

medical students. Therefore, the following 18 variables were chosen based on current literature regarding mental health supports in conjunction with the UMHF principles:

1. Mental health strategy. A documented mental health strategy is essential for promoting and protecting a community's mental health,¹⁹ and enables implanting practical solutions in healthcare.²⁰ This reflects UMHF Principles 1,2 and 4.
2. Individual counselling. Counsellors are often the first point of contact when a university student requires mental health support,²¹ and this variable is in line with UMHF Principle 5.
3. No cap on individual counselling. It is well established that the efficacy of counselling sessions increases with the number of sessions.^{22,23} This also reflects UMHF Principle 5.
4. University crisis line. Current literature suggests that crisis lines improve mental health outcomes,²⁴ and a university crisis line indicates adherence to UMHF Principle 5.
5. External crisis line. Directions for external crisis lines are a substitute for university-run crisis lines which may improve mental health outcomes²⁴ and reflect UMHF Principle 5.

Demographic-specific support. The following were considered forms of demographic-specific support:

Counselling services, as discussed previously, are an important form of mental health support for students, and were included.

Staff and student advisors, which have been shown to benefit the well-being of university students,^{25,26} were included.

Peer mentors, which have been shown to improve student well-being,²⁷ were included.

Support groups, which have been shown to aid university student mental health,²⁸ were included.

6. Medical student support. Medical students have been shown to benefit from mental health services tailored to medical students,^{29,30} and specific support reflects UMHF Principle 5.
7. LGBTQI+ support. LGBTQI+ tailored support significantly increases well being, and has been strongly endorsed to improve mental health.³¹⁻³³ There is a current lack in LGBTQI+ trained mental health professionals,³⁴ needed to address UMHF

Principles 1 and 5.

8. Aboriginal and Torres Strait Islander support. Mainstream services are often inappropriate for Aboriginal and Torres Strait Islander individuals,³⁵ and improving access to culturally sensitive mental health support reflects UMHF principles 1 and 5.
9. International student support. International students are subject to a different range of cultural, economic and academic pressures,³⁶ and are a vulnerable population in need of tailored support, as per UMHF Principles 1 and 5.
10. Physical disabilities student support. Physical disabilities have been linked to increased risk of poor mental health.³⁷ Specific support for this vulnerable group reflects UMHF Principles 1 and 5.
11. Support for students of a rural/remote background. Remoteness of location has been correlated with psychological distress with altered social infrastructure and geographic isolation,^{38,39} making students from rural backgrounds at risk for poor mental health. The UMHF Principles 1 and 5 indicate a need for specific support for this group.
12. Students on rural placement support. Students who are not from a rural background also experience remoteness of location and thus mental health risks,^{38,39} despite being a separate entity from students originating from rural and remote locations. Support is needed for this group under UMHF Principles 1 and 5.
13. Low SES background student support. Low SES has been linked to poorer mental health outcomes,⁴⁰ and UMHF Principles 1 and 5 suggest a need for tailored support for this group.
14. Mental health resources. Increased mental health literacy as a result of mental health resources and training has been shown to reduce stigma,⁴¹ which aids in improving mental health outcomes. This aligns strongly with UMHF principles 3 and 4.
15. Mental Health First Aid (MHFA) training. MHFA training is effective in improving mental health literacy,⁴²⁻⁴⁴ but faces many accessibility issues for university students.⁴⁵ MHFA training reflects UMHF Principles 3 and 4.
16. Well-being sessions. Physical activity, along with mindfulness and meditation have been supported in the literature as interventions helpful in alleviating

mental ill-health and stressors.⁴⁶⁻⁴⁸ This aligns with UMHF principles 3 and 4.

17. Well-being app. Literature is growing in support of university-wide applications (apps) that aim to promote mental health and mindfulness.^{49,50} Examining the presence of a Well-being App scrutinises adherence to UMHF principles 3 and 6.
18. Overall score. Current literature lacks any numerical overall analysis framework for university mental health supports. Consequently, the present study utilised a sum total of binary values from the other 17 variables to create this proxy variable as a crude measure of the overall provision of these mental health support types.

In addition to these 18 variables examining types of university mental health support, university social media use was also investigated. UMHF Principle 6 emphasises the need for mental health literacy promotion, and social media has been shown to improve mental health literacy and increase the likelihood of young adolescents reaching out for help.^{51,52} Facebook and Instagram were the two platforms investigated as they are the two most commonly used platforms in Australia.⁵³ Posting frequency was utilised as a measure for social media use, as posting increases visibility, and therefore increased outreach with greater potential for health literacy education. However, social media posting frequency is poorly suited to a binary characteristic, and it was deemed necessary to separate this from the cumulative total of the first 18 variables.

Method

Search Method

Criteria for student mental health support was assessed in January 2022 and reviewed in December 2022 via a combination of Google search and homepage traversal. The two investigators independently traversed the public home page of each university website, searching for the presence of each variable. If a particular service or item could not be found on the university student home page, a Google search of "[insert university] [insert service]" was performed, e.g. "Bond University MHFA training". Identified mental health strategies are catalogued in Appendix 1.

The number of mental health and well-being-related posts within the last 2 years were manually counted

on the university Facebook and Instagram pages, as a surrogate marker of mental health promotion by each university. This was performed independently by the two investigators, and any discrepancies were resolved with discussion.

Inclusion Criteria

Only universities and tertiary institutions registered by the Royal Australian College of General Practitioners (RACGP) were investigated as Australian medical schools.⁵⁴

Since medical students tend to be on-shore students, only services accessible to on-shore students were

assessed. As we are investigating university-provided support services, those offered by student unions and clubs have been excluded.

Due to access restrictions, support resources gated by a university login were not assessed, unless referred to elsewhere; it was adjudged that general awareness around resources that were not alluded to on the public website was likely to be low, and so they were not “readily and obviously” accessible per our research question.

For the purposes of the study, only specialised, qualified counsellors and psychologists were accepted towards the student counselling criteria. Many universities offered student advisors for various target demographics,

Table 1. Variable definitions

Variable	Operational Definition
Mental health strategy (MH strategy)	A page or document was found to be publicly available, referring specifically to the university’s goals/aims relating to mental health and well-being within its community, including students. Identified university mental health strategies are listed in Appendix 1. An incomplete score for this category was assigned where the full strategy was alluded to, but only a summary was publicly accessible.
Individual counselling	The university offers individualised psychological counselling for all students with qualified counsellors.
No cap on individual counselling	There is no hard limit defined on the university’s website for the number of counselling sessions available to students.
University crisis line	The university offers an after-hours crisis line accessible to students for emergency purposes, such that support is available 24/7.
External crisis lines	The university website pertaining to urgent support and emergencies offers direct links to external 24/7 crisis lines for students in times of need.
Medical student support	The university offers counselling services, staff and student advisors, peer mentors or support groups specifically tailored towards assisting medical students.
LGBTQI+ support	The university offers qualified psychological counsellors who have completed some form of LGBTQI+ training, or who are LGBTQI+ Allies; alternatively, there is an established ally network, dedicated safe spaces, advisors, peer mentors or support groups specifically tailored towards assisting LGBTQI+ students.
Aboriginal and Torres Strait Islander support	The university offers counselling services, staff and student advisors, peer mentors or support groups specifically tailored towards assisting Aboriginal and Torres Strait Islander students.
International student support	The university offers counselling services, staff and student advisors, peer mentors or support groups specifically tailored towards assisting international students.
Physical disabilities students support	The university offers counselling services, staff and student advisors, peer mentors or support groups specifically tailored towards assisting students with physical disabilities.
Rural/remote student support	The university offers counselling services, staff and student advisors, peer mentors or support groups specifically tailored towards assisting students from rural and/or remote backgrounds.
Students on rural placement support	The university offers counselling services, staff and student advisors, peer mentors or support groups specifically tailored towards assisting students on rural placements.
Low SES background student support	The university offers widely available financial counselling, and/or financial assistance in the form of loans and grants specifically tailored towards assisting students from low socio-economic status backgrounds. Programs with restricted availability, such as scholarships and exclusive grants, have been excluded due to their lack of availability to the wider student population.

Variable	Operational Definition
Mental health resources	The “mental health resources” variable was defined as the following: The university offers direct access to online materials and information aimed at increasing mental health literacy, including information sheets, checklists and educational videos.
Mental Health First Aid (MHFA) training	The university offers MHFA training courses to students.
Well-being sessions	The university offers regular interactive sessions or programs aimed at student psychological well-being, including wellness workshops, mental health seminars and mindfulness exercise classes (e.g. meditation, yoga).
Well-being app	Our paper defines the “well-being app” variable as the following: The university offers exclusive access to students for a mobile app specifically targeted at improving student mental health and well-being (e.g. TalkCampus or university-specific apps).
Overall score	The sum total of the binary values of the previous 17 variables. Variables that were provided by a university were assigned the value “1”, those that were not found were assigned the value “0”. A proxy for overall mental health support.
Social media use	The university’s number of posts promoting mental health and well-being on the respective official university social media pages (Facebook and Instagram) over the past 2 years. These posts can include, but are not limited to, advertising “R U OK” days, reminding students of mental health resources and support available, and access to counselling services at the university.

but as these functioned primarily as more generalised (logistical or academic) assistance rather than mental health support, they were excluded.

Variables

The variables examined are summarised in the **Table 2**

Statistical analysis

Data was analysed using the Statistical Package for Social Science (IBM Corp. Armonk, NY) version 28.0.0.0. Linear regression analysis was performed on the mental health strategy variable and overall variable score, to examine correlation between presence of the mental health strategy and the numerical magnitude of the overall score. Fisher’s exact test was performed across each of the independent variables. $P < 0.05$ was considered significant.

Of Australia’s 21 medical schools, only 13 universities offered published mental health strategies on their websites. 2 of these were incomplete summaries, and 3 were published more than 5 years prior to 2022. All universities publicly offered individual counselling to medical students; however, only 8 universities did not specify a session limit, and of these 8, 3 defined the service as “short-term” in nature. Most of the other 13 universities imposed a 6-session limit, though this varied between semesterly, yearly and in total. The majority of universities publicised access to a mental health crisis

line from their website, whether run by the university itself or via redirection to external providers.

Around half (11) of the universities publicly offered medical student-specific support for their students. The vast majority of universities (19) demonstrated LGBTQI+ student support, whilst all universities offered support for Aboriginal and Torres Strait Islander students. The majority of universities (18) were observed to offer support for international students. All universities offered support for students with physical disabilities, though no university offered support for students from rural or regional backgrounds; the University of Melbourne and the Australian National University, however, offered student union-organised rural student clubs. Only the University of Notre Dame offered support for students on rural placement. The majority of universities offered support for low SES background students (19).

The majority of universities (18) publicly offered free mental health resources to students, as well as MHFA training courses (13). MHFA training courses offered by the University of Sydney and ANU via their public sports and staff websites were counted in the table, as there were no restrictions specified preventing students from taking these. Curtin University’s MHFA training program was not counted, as this was only available by enrolling in a specific subject. Most universities hosted regular well-being sessions (17), but less than half (8) offered a welfare app for students to download. Of these, 4 utilised the TalkCampus app platform. University social

Table 2. A summary of all independent variables at each university as per UMHF principles.

OVERALL TOTAL	15	13	14	14	12	13	12	12	13	13	13	10	11	12	11	9	10	8	9	8	8	
App	V	V	V	X	X	X	X	X	X	X	X	X	V	V	X	V	X	V	X	X	V	8
Well-being Sessions/Programs (e.g. meditation, yoga, seminars, workshops)	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	X	X	X	X	17
Mental Health Training Available (MHFA)	V	V	V	V	V	V	V	V	X	V	V	X	X	X	V	X	V	X	V	X	X	13
Mental Health Resources (info sheets, checklists, information videos) - increasing health literacy	V	V	V	V	V	V	V	V	V	V	V	X	V	V	V	X	V	V	V	X	V	18
Low SES background student support	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	X	X	19
Students on rural placement	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	V	X	X	1
Rural/remote students support (from rural background)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	0
Disabilities students support	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	21
International student support	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	X	X	X	V	V	18
Aboriginal and Torres Strait Islander support	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	21
LGBTQI+ support	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	X	X	V	V	19
Medical student support	V	X	V	V	V	V	X	V	V	V	X	V	X	X	X	X	X	X	V	V	X	11
Links to External Crisis Lines (on crisis page)	V	V	X	V	V	V	V	X	V	V	V	V	V	V	X	V	V	X	V	V	V	17
University Crisis Line 24/7	V	V	V	V	V	V	V	V	V	V	V	X	V	X	V	X	V	V	X	X	X	15
X Cap on Individual Counselling	V	X	V	V	X	X	X	X	V	X	V	X	X	V	X	X	X	V	X	V	X	8
Individual Counselling Available	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	V	21
Mental Health Strategy	V	V	V	V	X	V	V	V	V	V	V	V	X	V	V	X	X	X	X	X	X	13
University	ANU	Sydney	Adelaide	Monash	Melbourne	Western Australia	Flinders	Queensland	Newcastle	New South Wales	Griffith	Deakin	Macquarie University	Western Sydney	Wollongong	Curtin	Tasmania	New England	Notre Dame	Bond	James Cook	Total

media use for mental health promotion varied greatly, particularly on Facebook, but was generally lower on Instagram.

University mental health promotional activity on social media varied significantly, as shown in **Table 2**. The number of well-being-related Facebook posts between 2020-2021 ranged from 1-9, while the number of well-being-related Instagram posts in the same period generally ranged from 0-3, with notable outliers being Griffith University (8) and the University of Melbourne (10).

MH strategy and overall score

Linear regression analysis yielded significant correlation between universities having published a mental health strategy and their total overall score according to the criteria ($b=3.317$, $p<0.001$, $CI = 2.011, 4.623$).

MH strategy and other variables

Fisher's exact test revealed that a university's mental health strategy availability was significantly correlated with the following variables:

1. International student support ($df=1$, $N=21$, Fisher's Exact Test= 0.042)
2. Well-being sessions ($df=1$, $N=21$, Fisher's Exact Test= 0.012)

All variables

Fisher's exact test performed across each of the resource variables revealed significant correlations in universities offering the following resources ($df=1$, $N=21$):

1. University crisis line and MHFA training (Fisher's Exact Test= 0.014)
2. University crisis line and mental health resources (Fisher's Exact Test= 0.015)
3. LGBTQI+ support and international student support (Fisher's Exact Test= 0.014)
4. LGBTQI+ support and well-being sessions (Fisher's Exact Test= 0.029)
5. Well-being sessions and low SES background student support (Fisher's Exact Test= 0.029)
6. MHFA training and mental health resources (Fisher's Exact Test= 0.042)

All other correlations were found to be insignificant (Fisher's Exact Test > 0.05).

Discussion

Mental health supports and services provided to medical students varied greatly between each university. We acknowledge that our findings are based on information published on publicly available sites, including academic institutions' social media pages and websites, and may not be in line with information available to students on their home institutions' intranet and servers limited to staff and students. Thus, the comparison between each medical institution's available mental health services may not be accurate. However, a report by Levitz⁵⁵ has highlighted the importance of up-to-date and user-friendly websites for academic institutions for prospective students to have easier access to information. Moreover, a study by Rowan-Kenyon et al⁵⁶ highlights the importance of social media in engaging with tertiary students. Our findings advocate for medical institutions to not only keep their publicly available sites up-to-date with the mental health services they offer for staff and students' accessibility, but also encourage them to perhaps identify gaps in their services so that there is a standardised level of mental health support offered to medical students across all universities. Future research could include analysing each medical institution's internal supports, investigating students' perspectives on their institutions' available mental health services and correlating this information to the findings of this study.

The presence of a published mental health strategy was found to be significantly correlated with the overall mental health support provided by a university. There is no existing literature regarding the efficacy of mental health strategies and no documented correlation between a published mental health strategy versus the number of publicly available supports provided by a university. However, current literature accepts that strategic planning aids focus and implementation of change.⁵⁷ Our findings support this, suggesting that mental health strategies aid in the identification and provision of mental health supports as directed by the UMHF principles.

A publicised mental health strategy was found to be significantly correlated with international student support. 27.1% of university students in Australia are international students.⁵⁸ International students in healthcare professions are more likely to be subjected to increased discrimination and social isolation.⁵⁹ As such, appropriate mental health support for international students is crucial. Moreover, a study by Martirosyan et al

Table 3. Number of official university mental health and well-being-related social media posts between 2020 and 2022.

University (posts since 2020)	Facebook	Instagram
ANU	8	0
Sydney	6	3
Adelaide	1	1
Monash	9	3
Melbourne	8	10
Western Australia	3	2
Flinders	5	2
Queensland	9	0
Newcastle	3	2
New South Wales	6	2
Griffith	5	8
Deakin	6	3
Macquarie University	7	0
Western Sydney	5	1
Wollongong	6	0
Curtin	5	0
Tasmania	3	0
New England	7	0
Notre Dame	4	0
Bond	2	0
James Cook	5	2

suggests that support should be tailored to international students' academic and personal needs, both of which can often be overlooked without a strategy in place.⁶⁰ Once again, our study highlights the importance of a publicly available mental health strategy, particularly in the context of addressing the needs of international medical students.

The availability of a mental health strategy was also found to be significantly correlated with well-being sessions. There is limited literature on this topic, but existing literature suggests well-being sessions are helpful for medical interns.⁶¹ As aforementioned, physical activity, mindfulness and meditation all play a role in improving mental health, in line with UMHF Principles 3 and 4.⁴⁶⁻⁴⁸ Our findings suggest that a publicly available mental health strategy is important in implementing well-being sessions for students, which have been shown to improve students' mental health.

Significant correlations were found between the availability of a university mental health crisis line and MHFA training, between a university mental health crisis

line and mental health resources, and between MHFA training and mental health resources.

The presence of crisis lines has been shown to lead to improved mental health outcomes and MFHA training has been shown to improve mental health literacy,^{24,42-44} which in turn results in better mental health outcomes for students and young adults.⁶² All in all, our findings show that universities that have made a mental health crisis line available to their students are likely to also publicise mental health first aid training resources and other mental health resources for their students, which shows a holistic approach towards mental health emergencies. While there is limited literature on the synergistic effect of mental health crisis lines, MHFA training and other mental health resources on the mental health of students, our findings should encourage more medical institutions to implement these resources given the literature on its efficacy as individual interventions.

Our results also showed significant correlation between well-being sessions and a number of specialised counselling supports. That well-being sessions were correlated with both LGBTQI+ and low SES student supports suggests that well-being supports reflect a broader, overarching university mental health program – this reflects the correlation found between well-being sessions and a publicised mental health strategy. LGBTQI+ support was also observed to correlate with international student support. International and low SES student well-being supports are poorly characterised in the current literature. However, there is evidence to suggest that current resources for LGBTQI+ university students remain lacking.⁶³ Therefore, perhaps as the remaining 8 universities place increased emphasis on a published mental health strategy for the wider student community, this will empower the provision of appropriate well-being services for vulnerable student populations, as per UMHF principles 1, 4, and 5. Our results suggest that specialised student supports appear to reflect a broader mental health strategy, rather than being isolated entities.

The vast majority of universities offered individual counselling, as well as mental health crisis line access. There was also strong, widespread support for LGBTQI+, Aboriginal and Torres Strait Islander, international, and low SES background students, as well as students with physical disabilities; most universities also offered MHFA training, mental health resources, and regular well-being sessions. However, a limit to the number of sessions students could access was observed in many instances. UMHF principle 5 emphasises the importance

of availability for well-being supports, and it has been shown that the efficacy of such supports increases with the number of sessions attended.^{22,23} Therefore, despite many of these supports being offered, there is a need for development of these services to deliver longer-term care to achieve best mental health outcomes for students.

No specialised well-being supports were seen for rural students (whether from rural or those on rural placement), or those with physical disability. Rural students experience geographical and social risk factors for poorer well-being³⁹, while physical disability is strongly linked to poor mental health outcomes.³⁷ That these populations are so unanimously overlooked by the tertiary institutions studied is a worrying sign. Despite the present study only examining publicised information, support services were identified for all other vulnerable student populations. Therefore, there is perhaps a need to re-emphasise UMHF principle 1 in the context of increasing awareness and service provision for the well-being of rural students and students with physical disabilities.

Noticeably, no correlations were seen between a university well-being app and other mental health supports. Current research regarding well-being apps for university students has shown significant improvements to well-being.^{64,65} This lack of correlation suggests that app implementation is a somewhat isolated measure, rather than part of a cohesive mental health strategy. There is scope for further research regarding the interplay between well-being apps and supports such as counselling and crisis lines, and how they might be utilised in concert to provide appropriate mental health support for university students, as per the UMHF. Social media promotion of mental health varied greatly among the universities.

Currently, there is a dearth of research in this field; the optimal frequency of social media posting for commercial businesses has been identified as around 6-7 times per week,⁶⁶ wherein user engagement is maximised. This is incomparable to mental health promotion by universities, which are educational institutes first and foremost, which precludes absolute judgments of the posting frequencies found. However, the wide range of social media posting frequencies indicates different approaches by universities in addressing mental health promotion. Further research is therefore warranted into the effects of these approaches, and student well-being as a result.

Limitations

The authors' investigation was hindered by their lack of access to university websites. Due to feasibility and ethical considerations, data was restricted only to that which was accessible to the public. This information may not be the most accurate or updated, and universities may offer mental health support not described in their public domains, which eluded the authors. Additionally, ambiguities were present in variable stratification; for example, the decision was made to include the University of Notre Dame's rural clinical school well-being services as part of "rural placement supports", despite this not being explicitly to support the rural placement aspect of the students' experience.

Additionally, though the study's criteria were strictly modelled on the UMHF, there exists no official standardised framework or criteria with which to analyse and evaluate mental health support. These factors may have impacted the significance of our findings.

Strengths

Our paper examined all Australian universities with medical institutions in a nation-wide comparison, allowing for a comprehensive examination of a combination of mental health and well-being supports. In particular, our study analysed mental health and well-being supports in line with six core principles from the 2020 Australian Department of Health-commissioned university mental health framework. These included investigating the availability of specific programs, such as Mental Health First Aid Training, well-being sessions, well-being applications amongst many others. Therefore, our analysis allowed for observation of the strengths and deficiencies within each institution's mental health supports, both individually and as a national collective.

Our study also provides the only current evaluation of the UMHF within published literature. The evidence yielded, albeit limited, indicates a need for more rigorous evaluation of mental health support in Australian universities, given the lack of literature and nation-wide deficiencies in the UMHF's outlined approach. More specifically, given that only 13 universities have published a mental health framework and even fewer an updated guideline, this study may show a potential lack of commitment to students' mental health at certain institutions. Therefore, our paper serves as a basis for further research.

Conclusion

Australian medical students should consider the publication of a mental health strategy to provide more aspects of well-being support for students. Targeted support is provided for many vulnerable groups, but more resources are perhaps required for rural students and students with disability, as well as longer-term counselling services. Current adherence to the UMHF is promising, but there is space for further improvement to support the nation's medical students, as well as further research regarding current well being measures.

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Conflict of Interest

None.

Abbreviations

MH: Mental Health

MHFA: Mental Health First Aid

UMHF: University Mental Health Framework

LGBTQIA+: Lesbian, Gay, Bisexual, Transgender, Queer, Intersex, and Asexual

SES: Socio-economic Status

RACGP: Royal Australian College of General Practitioners

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Probiotics as adjuvant therapy with antidepressants vs placebo to treat major depressive disorder: a systematic review and meta-analysis of randomized controlled trials

Introduction: Despite improvement in antidepressant treatment, half of the major depressive disorder (MDD) patients fail to achieve remission. Increasing evidence suggests the role of modulating the microbiome-gut-brain axis through probiotics in mental health therapy. We aimed to compare the efficacy and safety of probiotics as adjuvant therapy with antidepressants compared to placebo in patients with MDD.

Methods: A systematic literature search was performed in several databases, such as PubMed, Cochrane, EBSCOHost, CINAHL, Scopus, and Google Scholar from inception until November 18th 2022. The literature search aimed to find clinical trials that tested the effectiveness of probiotics as a supplement to antidepressants in treating MDD. Studies were excluded if they lacked a control group, used probiotics alone, had no full text available, were not original research articles, or were written in languages other than English. The quality of studies was evaluated using Cochrane Risk of Bias 2.0 tools. We performed a meta-analysis using Review Manager v5.4.

Results: Five randomized controlled trials with a total of 369 participants were included. Statistical analysis showed that the pooled standardized mean difference among studies was favourable to the probiotics group (-0.43; 95%CI: -0.71, -0.14) with statistically significant results ($p=0.003$). Gut microbiota dysbiosis plays a role in the pathogenesis of depression through inflammation and modulation of the hypothalamus-pituitary axis. Probiotics modulate gut microbiota by reducing inflammation and improving the intestinal barrier. In addition, probiotics also improve the metabolism of tryptophan to serotonin and reduce kynurenine accumulation, which is also implicated in depression pathogenesis. The limitation of this study includes the use of varying types and doses of probiotics, which could impact their effectiveness. Additionally, the geographical diversity of the studies, reflecting different genetic and microbial environments, may also affect how individuals respond to probiotic treatment.

Conclusion: In conclusion, probiotics are beneficial for patients with MDD as an adjuvant to antidepressant drugs.

Keywords: adjuvant therapy, antidepressants, depression, probiotics, meta-analysis

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Introduction

Currently, more than 264 million people are still struggling with major depressive disorders (MDD) according to the World Health Organization data. This has put depression as the most common cause of disability worldwide. People with MDD are living with massive distress and dysfunction from daily activities that other healthy people can do.¹ With the ongoing threat from the COVID-19 pandemic, people are forced to face difficult situations, both physically and mentally. There are plethora of internal and external factors as the root causes, from loss of loved ones, changes in daily activities and routine, or even directly from the viral infection.^{2,3}

The good news is that most cases of MDD and other mood related disorders are treatable with the right drugs or psychotherapy methods. However, despite the progressive development of dozens of novel antidepressant agents, more than half of all patients treated with antidepressant monotherapy fail to achieve a remission of their depressive episode. This condition is also known as treatment-resistant depression (TRD). Therefore, it is very important to explore a safe well-tolerated, yet effective treatment alternatives that would bring more efficacy on depression remission in patients, not only in TRD patients, but also in common MDD patients.^{4,5}

There has been increasing scientists' attention on commensal gut flora effects to the central nervous system (CNS), specifically between the gut flora, the intestine, and the CNS. It suggests that this interaction is recognized as the microbiome-gut-brain axis.^{4,5} Therefore, imbalance or disequilibrium state of the gut microbiota may play a vital role on the pathophysiology of many gastrointestinal disease, but more importantly, on CNS disease, including major depressive disorder. Accordingly, regulating the gut microflora balance by daily probiotic intake has a crucial benefit on the function of the brain and prevents the development of several mood-related disorders. Probiotics is found to be a safe and natural way to modulate the gut microbiome by stimulating the growth of some beneficial bacterial species in human intestine.⁶⁻⁸

In recent years, there has been a great body of evidence proving the potency of probiotics as adjuvant therapy with antidepressant in alleviating depression, including the treatment-resistant one. By consuming probiotics with current antidepressant drugs, the efficacy of the therapy become much greater, thus, may also increase

patients' compliance to the drugs because patients will be satisfied of the improvement they feel after taking the medication.⁹ However, to our knowledge, the variety of probiotics species used are very diverse, yet there are still no comprehensive study to compare the efficacy and safety of each of them. Therefore, through our systematic review and meta-analysis, we would like to qualitatively present the comparison of efficacy of each study regarding the use of probiotics as adjuvant vs. placebo, followed by a thorough discussion of its safety profile as a recommendation for clinical use.

Method

This study was conducted according to the Cochrane Handbook 6.2 and the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA). Furthermore, this study has been registered to The International Prospective Register of Systematic Review (PROSPERO) according to the regulation for conducting systematic review and meta-analysis (ID: CRD42022379331).

Information sources and search strategy

The search strategy for this systematic review was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist. Multiple electronic databases, consisting of PubMed, Google Scholar, Cochrane Central Register of Controlled Trials (CENTRAL), EBSCO, CINAHL, and Scopus, were screened by three independent reviewers up to November 18th 2022. The keywords used in the pursuit were customized according to the database used, as shown in Appendix 1. Suitable advanced search techniques were applied whenever appropriate. The literature search was limited by the language, as the authors were only compatible with the English language. Availability of full text articles was also one of the limitation criteria used in the literature searching process. The planned procedure is illustrated in **Figure 1**.

Study eligibility criteria

We applied the following criteria: (1) clinical trial, (2) general population with depression without age and gender limit, (3) received probiotics as adjuvant therapy to antidepressant drugs, and (4) assess outcome in depressive symptoms improvement. The exclusion criteria for our literature search includes: (1) study without control group, (2) study which give

probiotic as sole therapy, (3) studies with irretrievable full text, (4) articles including reviews, commentaries, letters, conference abstracts, and (5) studies written in languages other than English.

Data extraction

We predetermined the outcome sheet in tabular form (MS Excel MS Excel® for Mac; Microsoft Corporation, Redmond, WA, 2018) to include the following data to be extracted: (1) author and year of publication; (2) study characteristics, including study design and location of study; (3) study population, including sample size, severity of depression, mean age, and sex ratio; (4) intervention, type of probiotics used and duration of follow-up; and (5) study outcomes, including comparative indicators, values pre- and post-intervention, as well as significance (*p*) values. Qualitative characteristics were extracted by two reviewers, and an independent third author rechecked accuracy of extracted data meanwhile performing statistical analysis.

Risk of bias assessment

Quality of each study was assessed using the Cochrane Risk of Bias 2.0 (Cochrane Methods, 2021), which evaluates 5 domains including randomisation bias, bias due to deviations from intended interventions, missing outcome data, outcome measurement, and bias in reporting results. The overall quality of study is then converted based on the Agency for Healthcare Research and Quality (AHRQ) standards. This assessment was performed by three independent reviewers and if there is any disagreement, resolution would be made based on consensus by the three reviewers.

Statistical analysis

We performed statistical analysis using Review Manager ver. 5.4 (The Nordic Cochrane Center, The Cochrane Collaboration, Copenhagen). The mean differences and standard deviations (SDs) were extracted from studies and we interpreted the pooled effects. We utilized the inverse variance, DerSimonian-Laird random effects model as proposed by Riley et al, since we considered that indecipherable heterogeneity could be discovered from studies. Heterogeneity was further evaluated using I^2 statistics, with cut-off limits of 0%, 25%, 50%, and 75% as insignificant, low, moderate, and high heterogeneity, respectively. (Higgins et al., 2003) Additionally, we performed sensitivity analysis following the Duval and Tweedie's trim-and-fill method to identify any outlier study.

Quality of evidence

The quality of evidence was assessed using the GRADE approach. Risk of bias was evaluated using the Cochrane Risk of Bias 2.0 tool. Inconsistency was assessed by assessing the variation in study results. Indirectness was considered if the populations, interventions, and outcomes were directly applicable. Imprecision assessed by examining the width of confidence intervals. Publication bias investigated using funnel plots and statistical tests. Thereby, the study provided high-quality evidence rating for probiotics as adjuvant therapy with antidepressants based on the GRADE criteria.

Result and Discussion

Search results and study selection

Upon database searching, 539 records were identified, after which 171 duplicates were removed. Primary filtering via title and abstract screening removed 290 articles and 38 articles, respectively. Finally, 40 articles are assessed for full-text eligibility. Overall, we found 17 studies with unsuitable design, 5 studies with incomplete outcome data, and 13 irretrievable full-text articles. Final search resulted in 5 eligible studies included in this review. Screening of titles and abstracts of studies was carried out by three independent reviewers. The planned procedure is illustrated in **Figure 1**.

Study characteristics and design

All 5 studies included are finished clinical trials, conducted in several countries including 1 in Russia, 2 in Iran, 1 in Japan, and 1 in the United Kingdom. The dates of publication range from 2018 – 2021, with follow-up durations ranging from 6 weeks – 8 weeks. Among the included studies, participants were mild to moderate depression patients which are diagnosed by certified healthcare workers based on diagnostic statistical manuals for psychiatric disorders. Moreover, participants were randomized into two groups, one that takes a probiotics supplement as adjuvant therapy to common antidepressant drugs and another that takes placebo with antidepressant. Outcomes are measured via parameters including reduction in depression by established mental health questionnaires, both in pre- and post-intervention. The complete characteristics of included studies are shown in **Table 1**.

Study quality assessment

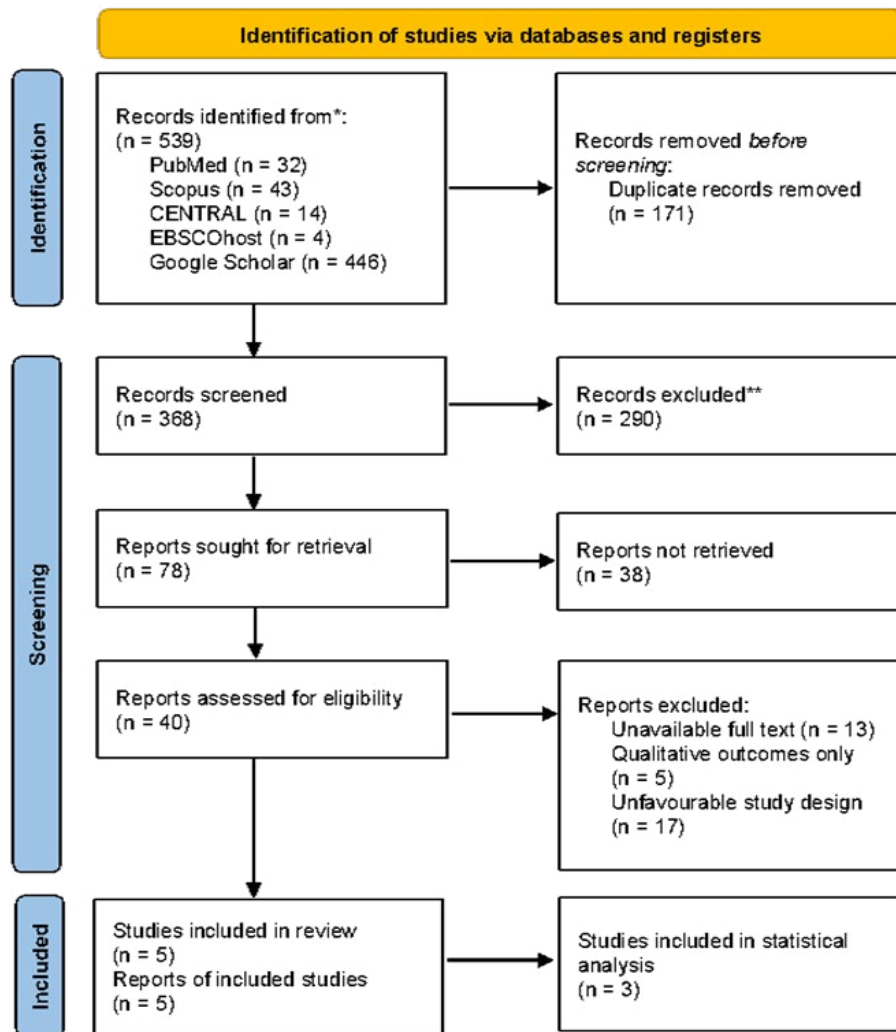


Figure 1. Diagram Flow of Literature Search Strategy

Risk of bias assessment, as shown in **Figure 2** and with the details as shown in Appendix 2, demonstrates that most studies are good quality, except for some concerns in Rudzki et al's study, particularly in the second domain.²¹ In this study, the patients were supposed to be aware of their assigned interventions, such that the blinding was not possible. Therefore, there might be a bias due to deviation from the intended interventions. The results of this study have less significant outcomes, and thus can be explained due to the risk of bias during the intervention process.

Efficacy of probiotics for treatment of depression

The included studies assessed the efficacy of probiotics to reduce depressive symptoms in terms of depression questionnaire's score, especially the Hamilton Depression Rating Scale (HAM-D) and the Beck Depression Inventory (BDI). **Figure 3** depicts the forest plot from 3 studies, namely Ghorbani et al⁹, Kazemi et al¹⁰, and

Rudzki et al¹¹. Statistical analysis showed that the pooled effect estimate of standardized mean difference among studies was favourable to the experimental group (-0.43; 95%CI: -0.71, -0.14) with statistically significant results (p=0.003). Moreover, the overall heterogeneity is negligible (I²=0%) and therefore sensitivity analysis was not performed. In conclusion, probiotics as adjuvant treatment to antidepressive agents provide better efficacy on alleviating depression compared to placebo.

Probiotics role in depression: a novel therapy

It is estimated that nearly 60% of people with depression worldwide are resistant to pharmacological therapy.¹⁴ In fact, remission after pharmacological treatment occurs in 1 in 3 patients.¹⁵ The pharmacological therapy usually targets the monoamine dysregulation in the brain. Resistance towards pharmacological therapy suggests other factors that may contribute to developing depression in some patients, including the brain-gut

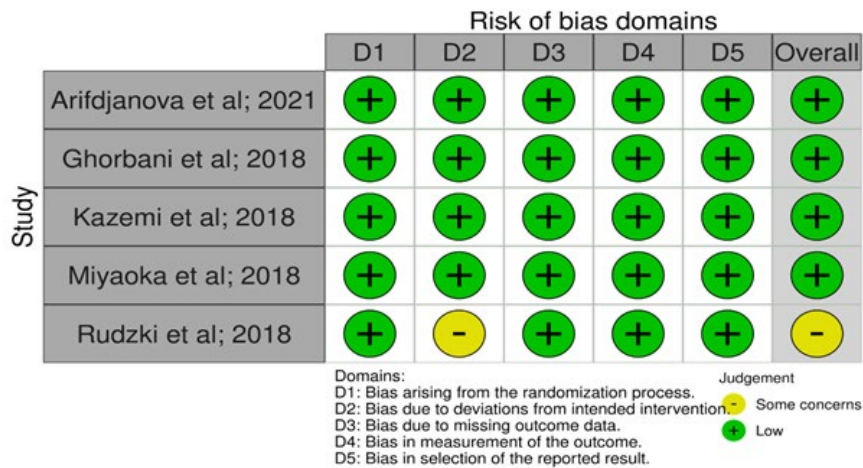


Figure 2. Risk of Bias Assessment

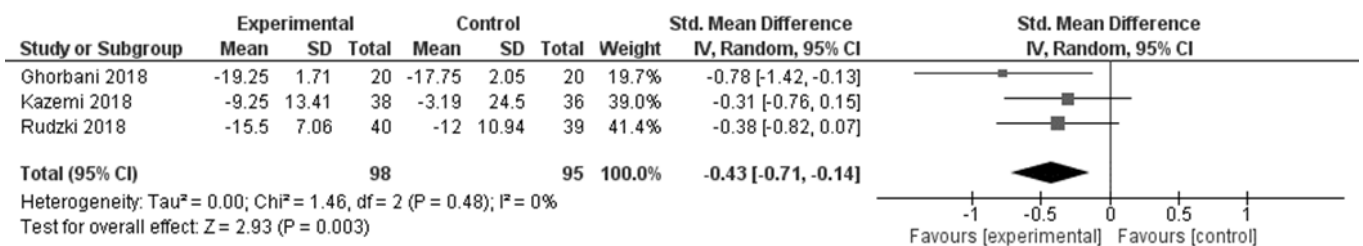


Figure 3. Forest plot of reduction in depressive symptoms post-treatment

axis.¹⁴ Disturbances in the brain-gut axis are associated with alterations in overall behavior and stress-response. Because of that, other therapies have begun to be developed that target the brain-gut axis modulation system.¹⁶

The role probiotics have in relation to mental health has been extensively studied due to promising effects of microbiota-gut-brain axis (MGBA) modulation to mental health.¹⁷ The gut-brain axis is a network that links the central nervous system and the enteric system, involving endocrine, humoral, metabolic, and immune routes at the same time. Evidence suggests that microbiota of the gut have influences on mental state, emotional regulation, neuromuscular function, and function of the hypothalamus-pituitary axis. In depression, low grade intestinal inflammation is observed, leading to increasing proinflammatory cytokines such as IL-1b, IL-6, TNF-a, and IFN-g. Gut microbiota influence the transcription of these cytokines. In addition, gut microbiota also influence the integrity of tight junctions in enterocytes, so dysbiosis of the gut also affects intestinal permeability, leading to low grade inflammation. Inflammation is thought to play a role in the pathogenesis of depression, in which inflammation alters neurotransmitter metabolism and activates the HPA axis, which affects the availability of neurotransmitter precursors and causes clinical depression.¹⁸

According to several studies conducted on rats, consumption of probiotics also reduces corticosterone, adrenaline, noradrenaline, and the effect of increasing ACTH due to stress induction, which tend to be high in depressed patients. Probiotics also increase the expression of BDNF or brain-derived neurotrophic factor that functions in plasticity, memory, and neuronal health, which is generally under-expressed in depressed patients. In addition, consumption of probiotics is also known to increase the level of tryptophan (a precursor of serotonin) in plasma, and decrease the level of 5-hydroxyindoleacetic acid or 5-HIAA (the main serotonin's metabolite). This effect is very similar to the mechanism of action of citalopram. Therefore, it can be concluded that the administration of probiotics has a positive impact on the central nervous system's function by regulating important neurotransmitters that contribute to developing depression. In some studies, the use of probiotics also improves memory, reduces anxiety and depressive-like behaviors.¹⁸

Probiotics as adjuvant therapy

The result of our systematic review is consistent, in which most studies reported significant difference in reduction of depression scores between treatment with adjuvant and control group. Probiotics as adjuvant treatment is especially relevant in treating treatment-

Table 1. Study Characteristics

Studies, year	Location	Sample characteristics			Intervention		Control; Blinding
		Sample Definition	Severity	Sample size (n)	Mean Age (y)	Duration	
Arifjanova et al ¹² , 2021	Simferopol, Russia	MDD, DSM-V	Mild to moderate	119	32.9	6 weeks	Bac set forte (multi-probiotic containing <i>Lactobacillus</i> and <i>Bifidobacterium</i>) + antidepressant (cipralez) Antidepressant: 10 mg/day (90 days), Placebo + antidepressant; double-blinded
Ghorbani et al ⁹ , 2018	Hamedan, Iran	MDD, DSM-V	Moderate	40	35	6 weeks	Familact (<i>Lactobacillus caseae</i> and <i>L. rhamnosus</i> 3x10 ⁸ CFU, <i>L. acidophilus</i> 2x10 ⁸ CFU, <i>L. bulgaricus</i> 2x10 ⁹ CFU, <i>Bifidobacterium breve</i> 2x10 ⁸ CFU, <i>B. longum</i> 1x10 ¹⁰ CFU, <i>Streptococcus thermophilus</i> 3x10 ⁸ CFU) Fructooligosaccharide 100 mg (prebiotic) + antidepressant (fluoxetine), Placebo + antidepressant; double-blinded
Kazemi, et al ¹⁰ , 2018	Shiraz, Iran	MDD, ICD-10	Mild to moderate	110	36.47	8 weeks	<i>L. helveticus</i> ROO52, <i>B. longum</i> R0175 10 x 10 ⁹ CFU (probiotic) or Galactooligosaccharide (prebiotic) + antidepressants (fluoxetine, sertraline, citalopram, or amitriptyline) dose as usual (20-80 mg/day) Placebo + antidepressants; double-blinded
Miyaoka, et al ¹³ , 2018	Izumo, Japan	TRD, DSM-IV	Moderate	40	44.2	8 weeks	CBM588 60 mg/day + Antidepressants (SNRI or SSRI) dose as usual Placebo + antidepressants as usual; double-blinded
Rudzki, et al ¹¹ , 2018	Scotland, UK	MDD, DSM-IV	Moderate	60	39.13	8 weeks	LP299v 10x10 ⁹ CFU + antidepressants (SSRI) Placebo + antidepressants; double-blinded

*Abbreviations: NR = Not reported; MDD: major depressive disorder; DSM-V: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition; CFU: colony forming unit; TRD: treatment-resistant depression; SSRI: selective serotonin reuptake inhibitor; SNRI: selective norepinephrine reuptake inhibitor.

Table 2. Summary of study outcomes

Studies; year	Outcome Parameter	Value with Intervention		Value without intervention		Significance (p-value)	Adverse events
		Value at baseline (SD)	Value post-treatment (SD)	Value at baseline (SD)	Value post-treatment (SD)		
Arifdjanova et al ¹² , 2021	HAMD-17	12.4±4.6	declined 56%	11.9±4.9	declined 44%	0.083	Not reported
Ghorbani et al ⁹ , 2018	HAM-D	22.90 (22.08 - 23.72)	3.65 (2.92 - 4.38)	22.55 (21.80 - 23.30)	4.80 (4.16 - 5.44)	0.013*	Bloating and nausea (20%). Diarrhea (10%). Abdominal cramp (15%). Difference were not significant between intervention and placebo group
Kazemi, et al ¹⁰ , 2018	BDI Scale	18.25 (14.15 - 21.62) SE: 1.90	9.0 (7.43 - 14.12) SE: 1.70	18.74 (14.11 - 23.13) SE: 3.92	15.55 (11.36 - 21.26) SE: 2.52	0.042*	Gastrointestinal complaints, nausea, fever, body aches, increased appetite.
Miyaoka, et al ¹³ , 2018	HAMD-17	31.9 (2.8)	declined >50%	31.8 (4.0)	NR	0.001*	Mild, transient headache. Difference were not significant between intervention and placebo group
	BDI Scale	43.8 (4.3)	declined >50%	41.4 (4.8)	NR	0.001*	
	BAI Scale	32.8 (5.8)	declined >50%	33.3 (4.7)	NR	0.001*	
	HAMD-17	21.53 (6.03)	6.03 (3.68)	22.00 (7.92)	10.00 (7.54)	0.205	
Rudzki, et al ¹¹ , 2018	SCL-90	2.41 (0.64)	1.1 (0.73)	2.67 (0.64)	1.56 (0.92)	0.684	Gastrointestinal complaints, headache, palpitations. Difference were not significant between intervention and placebo group
	PSS-10	28.27 (4.91)	14.86 (6.47)	29.70 (3.95)	19.23 (8.24)	0.214	

NR = Not reported; SD: standard deviation; SE: standard error; HAM-D: Hamilton Depression Rating Scale; HAM-D-17: Hamilton Depression Rating Scale 17 item; BDI: Beck's Depression Inventory; BAI: Beck's Anxiety Inventory; SCL-90: Symptom checklist 90; PSS-10: Perceived stress scale.

resistant depression (TRD), with study by Miyaoka et al reporting 70% of TRD patients responding to treatment and a remission rate of 35%¹³. On the other hand, prebiotics also cause greater reduction in depression scores, but this result is not significant. Therefore, probiotics remains the more superior method of treatment compared to probiotic.¹⁰

In addition to depression scores, supplemental probiotics also have positive effects on other parameters. Study by Kazemi et al showed that probiotics also reduces serum kynurenine/tryptophan ratio. Tryptophan is metabolized into serotonin, so shunting of tryptophan to the kynurenine pathway can cause serotonin deficiency, which leads to depression. Here, probiotics play a role in reducing the enzymes responsible for converting tryptophan to kynurenine, therefore driving tryptophan along the serotonin pathway.¹⁰

Another mechanism is that probiotics affect the synthesis of enzymatic cofactors in kynurenine metabolism towards NAD⁺ and ATP synthesis, such as vitamin B2 and B6. Inflammation and stress is related to accumulation of kynurenine, so this may be another benefit of probiotics in reducing inflammation.¹¹ Another study by Akkasheh et al also showed that supplemental probiotics decreases serum hs-CRP levels, a biomarker of systemic inflammation. Probiotics increase the production of short chain fatty acids (SCFA) and decrease the expression of IL-6, therefore playing a role in reducing inflammation.⁵

Arifdjanova et al also found that supplemental probiotics provided a more pronounced effect in limiting stress response.¹² Elevated cortisol is a physiological biomarker for emotional disorders, including depression. Along with noradrenaline and adrenaline, these hormones activate the hypothalamus-pituitary-adrenal axis (HPAA), which causes hyperactivity of the sympathetic system. This is a key in the development of depression. Increasing adrenaline and noradrenaline also increase the growth of Bacteroides and other opportunistic gut bacteria, leading to a vicious cycle of increasing production of catecholamines. The use of probiotics decreases HPAA activity, therefore correcting inadequate stress response.¹²

Various probiotics are shown to benefit major depressive disorder. Lactobacillus and Bifidobacteria are often used as evidence suggests they inhibit growth of pathogenic bacteria and fungi, improve intestinal barrier, enhance synthesis of SCFA, and modulates inflammatory cytokines.¹¹ Studies showed that *L. rhamnosus* and *L.*

helveticus have positive effects on intestinal barriers following psychological stress, and combination with *Bifidobacterium longum* resulted in improvement in mental health.^{5,10,11} *L. plantarum* were shown to also significantly influence kynurenine concentration and metabolism in depressed patients. However, it does not improve depression score parameters significantly.¹¹ Others such as *L. acidophilus*, *L. casei*, and *B. animalis* were also shown to improve depression parameters and reduce inflammation.^{5,18}

Clostridium butyricum (CBM588) was also used and provided antiinflammatory and neuroprotective effects, including neurogenesis, antioxidation, and anti-glutamate excitotoxicity.¹³ Based on studies included in this systematic review, combination of probiotics seems to have better results in significantly reducing depression scores, compared to single type probiotics such as in Rudzki et al's study.¹¹ Several fixed dose combination is available, such as the Bac set forte and Familact, as well as yogurts and capsules containing multiple probiotics.^{9,12} There is no consensus on the amount of probiotics needed to improve depression as an adjuvant therapy, but in general, a minimum amount of 10⁹ CFU has been recommended to yield health benefits.¹⁷

Studies cited in our systematic review reported minimal adverse effects, good tolerability, and good compliance. No significant difference in adverse effects were reported between placebo and probiotic group.^{5,9-11} Some of the most common side effects were gastrointestinal complaints such as bloating, nausea, or cramps. Neurological effects such as headache and tremor, fever, and increased in appetite were also reported.⁹⁻¹¹ Interestingly, Rudzki et al's study showed that gastrointestinal complaints were seen only on patients using SSRI as antidepressant, so it is likely that SSRI also contributed to that side effect.¹¹

Drugs interaction: probiotic and SSRI

Until now, there has been no definite statement that can describe the microbiome-drug interaction, hence the interaction between probiotics and SSRIs cannot be described with certainty. However, it has been suggested that some SSRI drugs can affect the balance and integrity of the gut microbiome, so that the side effects and therapeutic effects of these drugs can be altered. This is also thought to explain why some patients require higher doses than others even though it does not result in a significant increase in SERT binding.¹⁹

In addition, various types of probiotics and SSRIs also provide different interaction mechanisms, which have not been fully studied and still cannot be ascertained. Abdrabou A, et al conducted a study on rats by giving Citalopram (SSRI) and Lactobacillus showed that the concurrent administration of Lactobacillus and Citalopram had a positive effect on depressive symptoms. It was stated that Lactobacillus was able to lower kynurenine levels in brain tissue, which cannot be done by taking citalopram alone. In addition, the study also showed that mice given citalopram and Lactobacillus showed a better effect than those given Citalopram or Lactobacillus alone.²⁰

Strengths and limitations

This study is the first systematic review that explores the efficacy and safety of probiotics as adjuvant in depression therapy. Studies included in our review uses a variety of antidepressants including SSRI, SNRI, and tricyclic antidepressant, therefore the difference of effect due to different antidepressants is minimized and the result of this study may be generalized across all depressed patients using antidepressants. The use of probiotics as an adjuvant may also be beneficial in reducing the amount of antidepressants used, therefore reducing side effects from antidepressants, and also as an alternative for treatment-resistant depression before undergoing more aggressive and invasive treatment.

This study is not without limitations. First, the probiotics selected in the studies cited are not the same, with different doses and different combinations of probiotics, therefore this may have affected the results. Second, studies are located in different countries, where genetics and microbial exposure may influence individual response to probiotics.

Conclusion

This review focuses on the use of probiotics as adjuvant therapy in depressed patients. It can be said that

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probiotics have the potential to enhance therapeutic effects in patients with depression who are taking antidepressant drugs. Probiotics alone are known to have positive effects on the central nervous system such as anti-inflammatory, reduces stress hormones (adrenaline, noradrenaline, corticosterone, and ACTH due to stress induction), increase the expression of BDNF which has neuroprotective effect, increase the level of tryptophan, and decrease the level of 5-HIAA due to the brain-gut axis.

However, using probiotics alone or antidepressant drugs alone does not give a significant effect on treating depression, even though probiotics have their own potential health benefits. Several studies have shown that given probiotics with antidepressant drugs improves overall patient's depressive symptoms and gives significant difference in reduction of depression scores between control group and treatment with adjuvant, especially in TRD patients. Because of that, further research is recommended because of the variability in gut microbiome in each country. In addition, further research is also needed regarding the appropriate dose given to patients.

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Conflict of Interest

The authors declare no competing interests/conflict of interests in the making of this manuscript.

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Supplementary Files

Probiotics as adjuvant therapy with antidepressants vs placebo to treat major depressive disorder: a systematic review and meta-analysis of randomized controlled trials

Appendix 1. Table of keywords used in literature search

Database	Keywords	Hits
PubMed	((("Depressive Disorder, Major"[Mesh]) OR "Depression"[Mesh]) AND (probiotics OR "probiotics"[MeSH Terms] OR probiotic[Text Word] OR probiotics prophylaxis) AND (adjuvant OR combination therapy OR adjunctive therapy OR "adjuvants, pharmaceutical"[All Fields] OR "adjuvants, immunologic"[All Fields] OR "adjuvants, pharmaceutical"[MeSH Terms] OR "adjuvants, immunologic"[MeSH Terms] OR adjuvant[Text Word]))	32
Scopus	TITLE-ABS-KEY ((probiotics OR prebiotics) AND (depression OR depressive AND disorder OR mdd OR "major depressive disorder" OR "treatment-resistant depression") AND (adjuvant OR adjunctive OR combination)) AND (LIMIT-TO (PUBSTAGE, "final")) AND (LIMIT-TO (DOCTYPE, "ar")) AND (LIMIT-TO (LANGUAGE, "English"))	43
CENTRAL	(Major depressive disorder or mdd or major depression) AND (probiotics or probiotic therapy or probiotic prophylaxis) AND (adjuvant therapy OR adjuvant OR adjunctive) AND (placebo or placebo effect or nocebo or placebos)	14
EBSCOhost	(Major depressive disorder or mdd or major depression) AND (probiotics or probiotic therapy or probiotic prophylaxis) AND (adjuvant therapy OR adjuvant OR adjunctive) AND (placebo or placebo effect or nocebo or placebos)	4
Google Scholar	(Major depressive disorder or mdd or major depression) AND (probiotics or probiotic therapy or probiotic prophylaxis) AND (adjuvant therapy OR adjuvant OR adjunctive) AND (placebo or placebo effect or nocebo or placebos)	446

Appendix 2. Cochrane risk of bias tools 2.0

Domain 1: Risk of bias arising from the randomization process

Signaling questions	Response options	Arifdjanova et al, 2021	Ghorbani et al, 2018	Kazemi et al, 2018	Miyaoka et al, 2018	Rudzki et al, 2018
1.1 Was the allocation sequence random?	Y / PY / PN / N / NI	Y	Y	Y	Y	Y
1.2 Was the allocation sequence concealed until participants were enrolled and assigned to interventions?	Y / PY / PN / N / NI	Y	Y	Y	Y	Y
1.3 Did baseline differences between intervention groups suggest a problem with the randomization process?	Y / PY / PN / N / NI	N	N	N	N	N
Risk-of-bias judgement	Low / High / Some concerns	Low	Low	Low	Low	Low

Abbreviations: Y: Yes; PY: Probably yes; PN: Probably no; N: No; NI: No information

Domain 2: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention)

Signaling questions	Response options	Arifđjanova et al, 2021	Ghorbani et al, 2018	Kazemi et al, 2018	Miyaoka et al, 2018	Rudzki et al, 2018
2.1. Were participants aware of their assigned intervention during the trial?	Y / PY / <u>PN</u> / N / NI	N	N	N	N	N
2.2. Were carers and people delivering the interventions aware of participants' assigned intervention during the trial?	Y / PY / <u>PN</u> / N / NI	N	N	N	N	N
2.3. [If applicable:] If Y/PY/NI to 2.1. or 2.2.: Were important non-protocol interventions balanced across intervention groups?	NA / <u>Y</u> / <u>PY</u> / <u>PN</u> / N / NI	NA	NA	NA	NA	NA
2.4. [If applicable:] Were there failures in implementing the intervention that could have affected the outcome?	NA / Y / PY / <u>PN</u> / N / NI	PN	N	N	N	NA
2.5. [If applicable:] Was there non-adherence to the assigned intervention regimen that could have affected participants' outcomes?	NA / Y / PY / <u>PN</u> / N / NI	PN	N	N	N	PY
2.6. If N/PN/NI to 2.3. or Y/PY/NI to 2.4. or 2.5.: Was an appropriate analysis used to estimate the effect of adhering to the intervention?	NA / Y / PY / <u>PN</u> / N / NI	<u>Y</u>	<u>Y</u>	<u>Y</u>	<u>Y</u>	<u>Y</u>
Risk-of-bias judgement	Low / High / Some concern	Low	Low	Low	Low	Some concerns

Abbreviations: Y: Yes; PY: Probably yes; PN: Probably no; N: No; NI: No information

Domain 3: Missing outcome data

Signaling questions	Response options	Arifdjanova et al, 2021	Ghorbani et al, 2018	Kazemi et al, 2018	Miyaoka et al, 2018	Rudzki et al, 2018
3.1 Were data for this outcome available for all, or nearly all, participants randomized?	Y/PY/PN/N/NI	Y	Y	Y	Y	Y
3.2 If N/PN/NI to 3.1: Is there evidence that the result was not biased by missing outcome data?	NA/Y/PY/PN/N	NA	NA	NA	NA	NA
3.3 If N/PN to 3.2: Could missingness in the outcome depend on its true value?	NA/Y/PY/PN/N/NI	NA	NA	NA	NA	NA
3.4 If Y/PY/NI to 3.3: Is it likely that missingness in the outcome depended on its true value?	NA/Y/PY/PN/N/NI	NA	NA	NA	NA	NA
Risk-of-bias judgement	Low / High / Some concerns	Low	Low	Low	Low	Low

Abbreviations: Y: Yes; PY: Probably yes; PN: Probably no; N: No; NI: No information

Domain 4: Risk of bias in measurement of the outcome

Signaling questions	Response options	Arifdjanova et al, 2021	Ghorbani et al, 2018	Kazemi et al, 2018	Miyaoka et al, 2018	Rudzki et al, 2018
4.1 Was the method of measuring the outcome inappropriate?	Y / PY / <u>PN</u> / N / NI	N	N	N	N	N
4.2 Could measurement or ascertainment of the outcome have differed between intervention groups?	Y / PY / <u>PN</u> / N / NI	N	N	N	N	N
4.3 If <u>N</u> / <u>PN</u> / <u>NI</u> to 4.1 and 4.2: Were outcome assessors aware of the intervention received by study participants?	NA / Y / PY / <u>PN</u> / N / NI	N	N	N	N	N
4.4 If <u>Y</u> / <u>PY</u> / <u>NI</u> to 4.3: Could assessment of the outcome have been influenced by knowledge of intervention received?	NA / Y / PY / <u>PN</u> / N / NI	NA	NA	NA	NA	NA
4.5 If <u>Y</u> / <u>PY</u> / <u>NI</u> to 4.4: Is it likely that assessment of the outcome was influenced by knowledge of intervention received?	NA / Y / PY / <u>PN</u> / N / NI	NA	NA	NA	NA	NA
Risk-of-bias judgement	Low / High / Some concerns	Low	Low	Low	Low	Low

Abbreviations: Y: Yes; PY: Probably yes; PN: Probably no; N: No; NI: No information

Domain 5: Risk of bias in selection of the reported result

Signaling questions	Response options	Arifdjanova et al, 2021	Ghorbani et al, 2018	Kazemi et al, 2018	Miyaoka et al, 2018	Rudzki et al, 2018
5.1 Were the data that produced this result analysed in accordance with a pre-specified analysis plan that was finalized before unblinded outcome data were available for analysis? Is the numerical result being assessed likely to have been selected, on the basis of the results, from...	Y / PY / PN / N / NI	Y	Y	Y	Y	Y
5.2 ... multiple eligible outcome measurements (e.g. scales, definitions, time points) within the outcome domain?	Y / PY / PN / N / NI	N	PN	N	N	N
5.3 ... multiple eligible analyses of the data?	Y / PY / PN / N / NI	N	N	N	N	N
Risk-of-bias judgement	Low / High / Some concerns	Low	Low	Low	Low	Low

Abbreviations: Y: Yes; PY: Probably yes; PN: Probably no; N: No; NI: No information

The Possibility of Using Modern Methods to Control Bubonic Plague Infection, A Highly Infectious Zoonotic Disease, Mongolia

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Mongolia is a natural habitat to numerous zoonotic diseases including bubonic plague, anthrax, rabies and others. Lack of CDC-like structure, limited government capabilities and nomadic pastoral farming reflect high risk of future emerging and re-emerging outbreaks. Rapid risk assessment of outbreaks is conducted by the National Center for Zoonotic Diseases, meanwhile local and central governmental capacity of disease control remain unsatisfactory. With an AI-based disease control platform and instant mapping of hotspot locations should enable the rapid control and containment strategies. Furthermore, these dashboards and platforms will enable advanced level cooperation and management of emerging and re-emerging infections occurring within the intersection of nature, domesticated animals, wildlife and people in Mongolia and beyond. Ultimately, we aim to incorporate One Health approach and other International Health Regulations under the project outcomes. Mobile phone uses are above 90 per cent among Mongolian adults. In addition, connectivity is essentially well connected across the country.

Keywords: Bubonic plague, re-emerging infection, machine learning, artificial intelligence, Mongolia

Category: Original Research

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Introduction

Bubonic plague

The plague, sometimes referred to as the Black Death, was a zoonotic illness caused by *Yersinia pestis* that spread over the world.¹ Due to its high mortality rate and strong infectivity, it presents a serious risk to both people and animals. Bubonic, pneumonic, septicemic, meningial, and pharyngeal plague are the five main types of the illness. It can cause skin ulceration, carbuncles, and ulcers, along with pustules, spots, petechiae, bruises, and gangrene. It can also be spread through flea bites, respiratory droplets, eating raw, tainted meat, and handling infected animals. Patients risk dying from shock and heart failure if treatment is delayed.²

Epidemiology

Mongolia is a nation in central Asia that is bordered by China to the east and south and by Russia to the north and northwest. With a population of over 3.4 million, Mongolia is the 19th-largest and fewest densely populated independent nation in the world. Its total area is 1,564,116 km². 30% of the population live a nomadic or semi-nomadic lifestyle. With the Gobi Desert to the south and chilly mountainous areas to the north and west, Mongolia's landscape is diverse. Steppes make up the majority of the remaining land in Mongolia. Echinococcosis, plague, tularemia, anthrax, foot-and-mouth disease, and rabies are a few important emerging infectious diseases in Mongolia.³ In 28.3% of Mongolia's total area, there are natural plague foci, and 47.1% of them are highly active. More than 3000 plague cultures have been identified from host animals and their ectoparasites, and highly active foci of the plague are mostly found in western Mongolia. Between 640 to 3500 meters altitude level, plague foci can be found between latitudes 88°00 and 120°00 and longitudes 50°00 to 43°00.⁴ Because there are so few confirmed instances, it appears that human-to-human transmission of the disease is just a small factor.³ In 1980, the World Health Organization received the first reports of human cases in Mongolia.⁵ Each year, particularly in rural Mongolia, 40 people have been diagnosed with plague cases caused by *Yersinia pestis* infection. Hunting marmots (*Marmota sibirica*), huge rodents that are particularly common over the vast steppes of Central Asia, appears to be the primary source of transmission.³ One probable way for Mongolians to contract the plague is through

the practice of consuming diseased raw marmot flesh. As *Y. pestis* is effectively inactivated by cooking, eating raw meat is the cause of illnesses in Mongolia, not eating boodog that has been cooked. In Mongolia, close contact with infected marmots is the main route of *Y. pestis* infection. As rodents play a significant role in the spread of the plague, Mongolia is the perfect place to conduct in-depth research on their function as *Y. pestis* epizootic and enzootic reservoirs.⁶

A total of 12 endemic mammal species and 1 species of bird had ectoparasites that included 27% of all plague cultures. Fleas' ectoparasites were the source of the majority of isolates of plague cultures (91.5%). Sixty-four percent of the flea cultures that were isolated were from marmot fleas. The *Oropsylla silantiewi* marmot flea is thought to be the main plague carrier. The primary disease hosts in Mongolia are Siberian marmots. Mountain steppe and steppe zones are home to marmots. On marmots, 71 flea species and subspecies (5 families, 19 genera), 10 tick species, and 1 species of louse were discovered. On marmots, *O. silantiewi* fleas were nearly constantly present (95.8–100%). *Ctenophyllus hirticrus*, *Citellophilus tesquorum*, *Oropsylla alaskensis*, *Neopsylla mana*, *Neopsylla pleskei*, *Frontopsylla luculenta*, *Amphalius runatus*, *Frontopsylla hetera* and *Rhadinopsylla li transbaikalica*, were also commonly found on marmots.⁴ Six *Yersinia pestis* subspecies have been shown to be present in Mongolian among populations of voles and picas, according to recent investigations. It was important to detect the Analytical Profile Index 20E (API20E) test agent using classic biochemical methods in previous studies that clarified the phenotypic heterogeneity of *Y. pestis* strains in Mongolia. The isolation of multiple resistant strains in addition to those known from Madagascar is alarming and highlights the importance of bacterial cultivation and susceptibility testing.⁷

AI-based solution

AI refers to a set of modern technologies that enable computers to accomplish very complicated jobs that would need intelligence if performed by a human. Moreover, the distinction between AI and other methodologies, such as big data analytics, can be hazy.⁸ Intelligence is defined as a "agent's capacity to attain goals in a variety of environments", and AI is defined as any created agent (i.e. software or robot) that demonstrates intelligence. In the public sphere, AI is sometimes characterized as sentient computers with human-like capabilities, but the state-of-the-

art falls short of this ideal. Existing AI is 'narrow,' with computers learning to do just certain functions and not being able to apply their intelligence more broadly. Improved georeferenced datasets would be beneficial for quantitative analysis, such as the reconstruction of regional transmission networks or maybe the identification of probable historical plague reservoirs.⁹ Integrating plague data from various sources to address regional and temporal gaps may help to lessen the problem of spatial and/or temporal representativeness and increase our understanding of the spatio-temporal spread. Integrating plague data from various sources to address regional and temporal gaps may help to lessen the problem of spatial and/or temporal representativeness and increase our understanding of the spatio-temporal spread. Consistency in data definition and collection, on the other hand, is critical. Understanding the spatiotemporal dynamics of the past and current plague pandemics is a large task that is best approached collaboratively and transdisciplinary, and in the spirit of open data. Researchers see the opportunity that AI provides for advancement and, as a result, for saving lives. Stopping and thinking about the datasets utilizing, as well as the ramifications of apparently innocuous decisions, will allow us to get the most out of this bright, new technology.¹⁰

Method

Theory of the change

Detecting and tracing the spread of the disease is crucial for preventing outbreaks and controlling the spread of the disease. Artificial intelligence (AI) technology has the potential to revolutionize bubonic plague contact tracing and detection by analyzing large datasets and identifying patterns that might otherwise be missed. This theory of change outlines the steps necessary to develop and implement AI technology for bubonic plague contact tracing and detection.

Step one - Identify the Problem and Need

The first step in developing AI technology for bubonic plague contact tracing and detection is to identify the problem and the need. The bubonic plague is a highly infectious disease that can spread rapidly, making it difficult to control. Traditional methods of contact tracing and detection rely heavily on human labor, which can be time-consuming and slow. Additionally, the disease is often misdiagnosed, which can further delay treatment and contribute to the spread of the disease. Mongolia

has unique problems where it is illegal to hunt marmots, while it is consumed widely in the countryside. People often neglect and hide exposure that has life threatening hazards (**Figure 1**).

Step two – Develop the AI Technology

The second step in implementing AI technology for bubonic plague contact tracing and detection is to develop the technology. This involves building AI algorithms that can analyze data from a variety of sources, including medical records, social media, and public health surveillance systems. The AI algorithms must be trained on data specific to the bubonic plague and must be capable of identifying key indicators of the disease, such as symptoms and geographic locations. This approach will highly concentrate on mobile phone data based on proximity of cellular phones and chances of marmot exposure.

The development of AI technology for bubonic plague contact tracing and detection requires collaboration between public health officials, data scientists, and software developers. Data scientists must work closely with public health officials to identify the key data sources that are most relevant to the bubonic plague. Software developers must then build the necessary infrastructure to collect, store, and analyze the data. Public health officials must also ensure that the technology complies with ethical and privacy standards.

Step three – Implement the Technology

The third step in implementing AI technology for bubonic plague contact tracing and detection is to deploy the technology to public health agencies and healthcare providers. The AI algorithms must be integrated into existing public health surveillance systems and healthcare provider workflows to ensure that they are used effectively. Implementation also requires addressing potential ethical and privacy concerns. AI technology for bubonic plague contact tracing and detection must be developed in a way that protects patient privacy and confidentiality. Additionally, public health officials must ensure that the use of AI technology does not result in discriminatory practices or exacerbate existing health disparities.

Provincial health departments and Local zoonotic disease centers will be directly invited to selected local areas. Four provinces of Mongolia will be selected for geographical coverage.

Step four – Monitor and Evaluate the Technology

The fourth step in implementing AI technology for bubonic plague contact tracing and detection is to monitor and evaluate the technology. This involves tracking the performance of the AI algorithms and identifying areas for improvement. Public health officials must establish key performance indicators (KPIs) to track the effectiveness of the technology, such as the number of cases identified and the timeliness of response.

Evaluation should also include stakeholder feedback, including feedback from healthcare providers and patients. This can help identify any challenges or limitations associated with the use of AI technology for bubonic plague contact tracing and detection. Public health officials must also continually assess the ethical and privacy implications of the technology.

Step five – Articulate Assumptions

The fifth or final step will focus on policy development and formal introduction to the health system in Mongolia.

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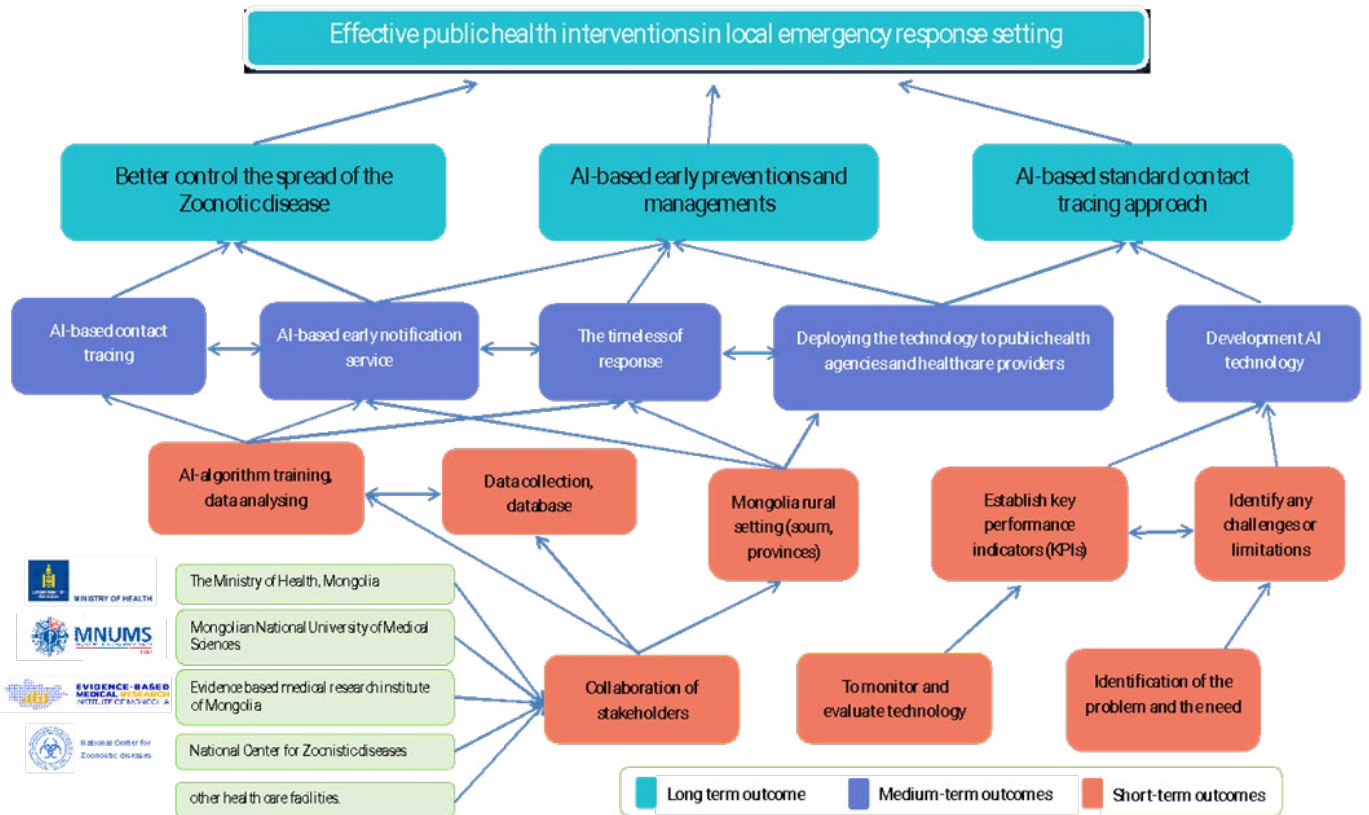
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Supplementary Files

The Possibility of Using Modern Methods to Control Bubonic Plague Infection, A Highly Infectious Zoonotic Disease, Mongolia

Appendix 1

Figure 1. Zoonotic Diseases Outbreak Monitoring and Control Platform Through AI -Based Notification and Contact Tracing in Mongolia, and Beyond



Medical Students' Role in Anticipating The Psychosocial Effects of The COVID-19 Pandemic: A Narrative Review

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The COVID-19 pandemic has affected learning activities in medical educational institutions all over the world. The world has managed to rise to the challenge of the global health crisis including mental health and well-being. Rethink the role that health students play during their education, not only in maintaining the continuity of their learning process but, also as agents of change who are part of health actions and responses. This literature review focuses on the role of medical students in anticipating the psychosocial impacts from the COVID-19. The main and supporting articles are search results from indexed international journal databases from Pubmed, ScienceDirect, or Google Scholar databases. Articles were searched using specific keywords with full text written in English, open access, EBM articles with a minimum level 3, and published in the last 5 years. Medical students can take part in ensuring the correctness of circulated information and prevent the spread of hoaxes, and be advised to educate the public to carry out activities for maintaining mental health. Students with stakeholders can create a database to support the health team and share it with other students at medical institutions, design and build information storage databases, create support teams for students for academic counseling, and mutual emotional support through a group under supervision by practitioners to equalize perceptions about everything that happens using interprofessional collaboration principal. A holistic approach based on community intervention is very possible for medical students to minimize the psychosocial impact after the COVID-19 pandemic era.

Keywords: COVID-19; medical education; medical student; post-pandemic; psychosocial.

Category: Review Articles

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Introduction

The definition of health according to WHO is a state of well-being that includes physical, mental, and social well-being that is not simply free from disease, disability, or death.¹ In line with this, ensuring a healthy life and supporting prosperity for all ages is one of the absolute things in realizing sustainable development scheduled until 2030.² The world has managed to rise to the challenge of the global health crisis that has affected almost all countries, namely the COVID-19 pandemic. The pandemic era has brought significant changes in almost all areas of life. In organizations, these challenges include increasing levels of stress in communities worldwide, and a greater need to protect mental health and well-being.³

The health profession as the main actor in organizing health efforts is required to be ready to face this challenge. However, the condition of global health human resources is overshadowed by crises such as shortage of personnel, maldistribution, mismatch, imbalance in the number and quality of health professions, mismatch between the competence of health professions and the needs of the population, poor teamwork, and weak collaboration and leadership.⁴

The COVID-19 pandemic has also disrupted the education sector throughout the world and affected learning activities in medical and other health science educational institutions.⁵ Therefore, it is time to rethink the role that health students play during their education, not only in maintaining the continuity of their learning process but also as agents of change who are part of health actions and responses.⁶ The medical faculty has formative and social goals which are the basic idea of ensuring the welfare and health of the community.⁷ Study from Ashcoft et al proposes a course and assessment structure for medical students' COVID-19 instruction, and it shows that medical students with the right training could be crucial to pandemic treatment later on.⁸

However, when COVID-19 broke out, it didn't mean that other diseases stopped threatening them. WHO also warned of a global mental health crisis due to the COVID-19 pandemic. The mental illness and mental health crisis may escalate as millions of people around the world are surrounded by death and disease and forced into isolation, poverty, and anxiety.⁹ WHO states that 12% of the global burden of disease is caused by mental health problems. This figure is greater than diseases with other (physical) causes.¹⁰ Mental health

itself is a state of mental well-being that enables harmonious and productive living as an integral part of a person's quality of life by paying attention to all aspects of human life.¹¹

Further research into mental health during the outbreak has proven that emotional distress is ubiquitous and threatens everyone. The Personal Growth Counseling Center recorded 327 cases of mental health problems in 22 categories on its free online counseling platform from March to May. It found that 33 percent of the 327 complaints were related to COVID-19.¹² Optimistic steps are needed by focusing on providing funding for a more efficient health system, better sanitation and hygiene, and efficient access to health services so that significant progress can be made in helping save the lives and well-being of millions of people, their physical and spiritual well-being.¹³

Indonesia lacks mental health resources to meet the country's needs. With a population of about 250 million in 2016, our country only has about 773 mental health workers, roughly one for every 323,000 people.¹⁰ This figure is far from the WHO recommendation of having one mental health worker for every 30,000 people.¹⁴ Amid the COVID-19 pandemic which also has an impact on mental health, the Association of Indonesian Psychiatric Medicine Specialists provides online self-examination services for psychological problems. So far this service has been used by around 1,522 users. The three psychological problems encountered were anxiety, depression, and psychological trauma. The number of service users showed that 63% of them experienced anxiety and 66% depression.¹⁵

Medical students have the opportunity to take part in this, of course by being trained by professionals such as psychiatrists. Students are pioneers with the knowledge they possess and high social commitment, making it possible to join in various formal activities and volunteer to work together during and after this crisis.¹⁶ A patient-centered approach ensures that they have professional competence, safety, and efficiency through each phase of care and beyond. Therefore, this literature review needs to examine the role of medical students in anticipating the psychosocial impact of the COVID-19 pandemic.

Method

In this paper, the author uses a narrative review method to study the role of medical students in anticipating the psychosocial impact of the COVID-19 pandemic.

The main and supporting articles are search results from indexed international journal databases such as Pubmed, ScienceDirect, and Google Scholar search engine. The keywords used are COVID-19, medical education, medical student, post-pandemic, and psychosocial. The reference inclusion criteria used are original research and meta-analysis published in medical and health journals. Criteria for literature searches for main articles are articles that can be accessed openly, in English, EBM articles of at least level 3, and published less than the last 5 years.

Discussion

Medical Education During and After the COVID-19 Pandemic

Students who are competent and have high social commitment can be invited to work together during and after this crisis period. A patient-centered approach can presumably ensure that they have prior professional competence, safety, and commitment including knowledge of the patient, diagnosis, intervention, and follow-up. Therefore, it is necessary to review the requirements for participation, not forgetting that for all health teams (including students), patients are a shared and primary responsibility.¹⁷

It is important to note that, due to the severity of the health crisis, students should be trained to become health professional reserves who can take action, especially in resolving psychosocial problems that occur, at least as promotive and educational personnel who respond quickly in various conditions.^{16,18}

The COVID-19 pandemic has changed dimensions and lifestyles. Online mode has become the primary means of obtaining up-to-date information and continuing medical education while maintaining social distancing. However, these benefits may not be generalizable to all forms of online teaching such as recorded lectures. Providing classical written material or note-taking, limited interaction and discussions with other students are important challenges for online learning.¹⁹

In the wake of the COVID-19 pandemic, medical schools can evaluate what was learned during the pandemic to create new opportunities and further faculty development. Baker et al. Divide the four themes driving post-pandemic faculty development into four themes: (1) Faculty development must better support work-life balance; (2) Academics must re-evaluate promotion processes, including tenure and promotion

timing, and Recognition of other scholarly activities beyond peer-reviewed publications, especially for women and underrepresented faculty; (3) The need to better leverage community engagement and learning through expanded dialogue and collaboration as community organizations There may be similar goals. (4) Information sharing should be expanded to the global community, and faculty development can create avenues for opportunities, collaborations, and open dialogue beyond campus to validate and corroborate research and scholarly activities.²⁰

A hybrid approach that combines face-to-face teaching with online learning can leverage the best of both approaches. Lessons learned from virtual learning for faculty development include setting realistic expectations for program development since time, technology, and resources may be limited.^{21,22} Even now, Indonesia itself has implemented full face-to-face lectures in line with the elimination of the COVID-19 pandemic status. This is also a breath of fresh air for medical education in Indonesia.

The Role of Pre-Clinical Stage Medical Students in Addressing Psychosocial Problems in the Pandemic Era and Post-COVID-19 Pandemic

Medical students can take part in supporting the dissemination of scientifically based information to the public about disease prevention measures. Includes nutritional, physical, and emotional health strategies during the isolation period.¹⁶ Students are encouraged to actively participate in identifying accurate, scientific evidence-based information about the pandemic while producing audiovisual or textual content that can be disseminated through various means of communication. Ensure the correctness of the information circulating and prevent the spread of hoaxes, both regarding medical matters and other matters in general. This problem becomes serious because during the pandemic everyone becomes intense with technology.^{23,24}

The rise of fake news and rumors is a factor that worsens the quality of people's welfare and mental health which will have an impact on poor health.²⁴ The public should limit excessive acquisition of information from news whose truth is not yet known, the public also needs to sort information by obtaining it from trusted sources.²³ Apart from that, to maintain mental health and overcome various emotions, medical students are also advised to educate the public to carry out simple

activities, for example by relaxing by breathing or by doing light exercise.²⁵

Students together with stakeholders can also create a database of national and international activities where students work to support the health team and share it with other students at medical institutions. Students have the capabilities needed to design and build information storage (databases) so that they can obtain an overview of the cases that occurred and the psychosocial dynamics experienced by the community so that the interventions carried out can be more optimal and by the reality of what is happening.^{26,27}

Students through organizations can also create support teams for students that reduce the physical and social impacts of isolation. Creating groups with various functions, such as sessions for academic counseling and sharing cases encountered virtually, meetings to provide mutual emotional support, a "Check-in" network system for classmates who want to ensure each other's well-being, as well as other initiatives organized by students for students through a group under supervision by practitioners to equalize perceptions about everything that happens.²⁸

It is hoped that students can help each other and collaborate safely and comfortably to produce policy outcomes in their respective regions that meet expectations. Caring for and protecting the population, making colleagues feel safe, ensuring that the information received by the public does not increase anxiety under strict supervision, and reminding family doctors of previous involvement are optimistic steps that can be taken.^{20,29}

Support activities for health workers can be carried out, such as campaigns and educating the population about clinical warning signs so that they can seek medical help. Includes a 24/7 hotline for online consultations and community-based webinars for mental health education. The students who are responsible here can not only help provide direct understanding to the public regarding information about the outbreak, but they can also develop their soft skills such as communication, negotiation, public speaking, leadership, and so on before entering the field and the professional world.²²

Activities can be carried out online by utilizing social media and cell phones or offline through house-to-house promotive preventive activities held with the Community Health Center and Regional Hospital.³⁰ Students can also provide recommendations regarding the referral flow for cases with risk factors or complications found

during the intervention. The students involved can detect, even remotely, relevant signs and symptoms to decide to refer a patient to second or third-level care.^{31,32}

As active learners, medical students should create clinical discussion groups. To develop clinical competencies related to critical thinking and decision-making, students are also encouraged to review, analyze, and discuss clinical cases including their consequences for the current psychosocial dynamics arising from the pandemic. Analyzing, summarizing, and distilling vast information about an emerging outbreak is a small thing that has a big impact.^{33,34}

Hundreds of articles, protocols, guides for managing the disease, news and reviews can be published every week. Systematic reviews of scientific evidence, publications and case reports, and scientific analyses performed can update data and assist healthcare professionals on the front lines of patient care about diagnosis, rehabilitation, and internal-external factors influencing the success of therapy.^{12,35} The concept of interprofessional education is important to make these various ideas a success. Medical students can attract colleagues from other departments or non-medical professionals.³⁶

The Role of Clinical Stage Medical Students in Addressing Psychosocial Problems in the Pandemic Era and Post-COVID-19 Pandemic

A key characteristic of clinical education is that students develop in a real professional environment, spanning first contact with patients in the outpatient setting through to hospital care, surgery, critical care units, and emergency rooms.^{34,37} Each student has varying clinical settings and perspectives, depending on what stage of education the student is in and their level of responsibility in decision-making. Therefore, analysis of student participation during activities must be based on academic grades and the level of proficiency in clinical competencies that students had before joining to maintain the quality of service.^{38,39}

Student activities must be supervised by clinical experts and ensure their safety with appropriate personal protective equipment. To direct students in making diagnostic decisions and therapeutic actions, students must follow the clinical observation algorithm with clinicians who treat patients with severe psychosocial disorders during the pandemic. During medical procedures, clinical stage students can provide emotional support to the clinician who is carrying out

the medical procedure in addition to the patient and their family as the main focus of care.⁴⁰

Students will learn to develop resilience, empathy, and leadership skills by contributing positively to the medical procedures provided. Doctor-patient communication can be improved by observing and communicating with family members and the patients themselves, providing emotional support to them, and providing an accurate understanding of the outbreak to overcome anxiety.⁴¹

Then, clinical students together with preclinical students who have been trained and under the supervision of a hospital or community health center can carry out screening to the community according to the directions set on a regional basis.⁴² Students can also remotely follow up on patients who are diagnosed with COVID-19 but do not require hospitalization. Supports patients and their families as well as professionals through follow-up reports that enable the expert nurse on duty to know the patient's situation.⁴³ Students can develop and strengthen clinical knowledge of evaluation, monitoring, and detection data that indicates disease that requires transfer of patient care to a hospital or emergency health center. Remote follow-up of outpatients who are isolating at home during the recovery phase of the disease.³⁸

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Students can monitor health status, provide emotional support, and become an extension of the doctor during this time. This activity can be carried out online or offline at the hospital or clinics closest to the students and is still carried out under the supervision of professional staff to minimize mobilization between regions to reduce the possibility of transmission.⁴⁴

Conclusion

The return of students to clinical areas must be supervised very carefully by lecturers and educational institutions, in this case, medical faculties, providing extraordinary training opportunities for students' professional and personal development, as well as realizing good collaboration with the social environment to create prosperity for all ages. especially psychosocial support after the pandemic. Solutions that include a holistic approach based on community intervention make it very possible for medical students to minimize psychosocial impacts to build a life structure that is in line with the WHO definition of health, physical, mental, and socially healthy to realize the 2030 sustainable development agenda.

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The Efficacy, Side Effect, and Cost-effectiveness of Uperio for Heart Failure: A Literature Review

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Heart failure is a clinical syndrome that results when the heart is unable to provide sufficient blood flow to meet metabolic requirements or accommodate a systemic venous return. HF is a costly condition that consumes 1–2% of the total healthcare budget. Recently, angiotensin receptor/neprilysin inhibitors (ARNIs; sacubitril/valsartan, Uperio®) showed a highly significant and clinically relevant reduction in mortality and heart failure hospitalizations, and improvement of quality of life when added to current standard drugs in patients with heart failure with reduced ejection fraction. Sacubitril is a neprilysin inhibitor to slow down natriuretic peptide (NP) breakdown, effectively increasing their vasodilation effect. NP levels are elevated in patients with HF and other cardiac diseases for restoring normal circulatory conditions. As for valsartan, this is an angiotensin receptor blocker. It blocks the vasoconstrictor and aldosterone-secreting effects of angiotensin II by selectively blocking the binding of angiotensin II. Although Uperio has fewer side effects, more effectiveness it is considered a high-priced heart failure medication and needs further economic impact.

Keywords: sacubitril/valsartan, heart failure, hypertension, side effects, cost

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Introduction

Heart failure (HF) is a syndrome resulting from cardiac disease, and is recognised clinically by a constellation of symptoms and signs produced by complex circulatory and neurohormonal responses to cardiac dysfunction.¹ Heart failure results from myocardial injury from a variety of causes including ischemic heart disease, hypertension, and diabetes.² In the United State of America (USA), the direct and indirect costs of total cardiovascular diseases (CVD), which include HF, were \$422.3 billion in.¹ There are several types of treatments available including Angiotensin-converting enzyme (ACE) inhibitors, Angiotensin-II-receptor antagonists (ARA), calcium-channel blockers (CCBs) and surgery. Angiotensin-converting—enzyme inhibitors reduce mortality and the need for hospitalisation and improve functional status in patients with heart failure. Despite such treatment, however, the mortality and morbidity rates associated with this condition are still high.³ Cough is a side-effect of ACE inhibitors in up to 4% patients and may require withdrawal of therapy.⁴ ARA could be used as an alternative to ACE inhibitors when side-effects that are specific to ACE inhibitors, such as cough, are encountered. Also, diuretics are undoubtedly successful at relieving breathlessness and oedema when overt fluid overload is present. Small randomised trials of older CCBs suggested no benefit or even a harmful effect in patients with heart failure.⁵ Heart transplants, for the lucky few, are a highly successful way of managing severe heart failure. Donor organ supplies are low and dwindling. Mechanical left-ventricular assistance devices are now available for patients with end-stage heart failure.⁶ Combination of an antagonist of the renin-angiotensin-aldosterone system (RAAS) has been introduced recently and effectively decreasing the blood pressure, with an inhibition of neprilysin, which is responsible for metabolising natriuretic peptides exerting antihypertensive and antifibrotic effects.

Uperio, which contains sacubitril and valsartan, is an angiotensin receptor-neprilysin inhibitor (ARNi). It's used to treat heart failure by enhancing the body's natural mechanisms to combat the condition. Sacubitril is a prodrug that inhibits neprilysin, an enzyme that breaks down natriuretic peptides. These peptides are important for blood volume and pressure regulation, promoting vasodilation and sodium excretion.⁷ Valsartan blocks angiotensin II receptors, countering vasoconstriction and aldosterone release, which can increase blood pressure.⁸ Together, they increase the

levels of beneficial peptides while blocking harmful systems, effectively reducing strain on the heart.⁷

Uperio is indicated to reduce the risk of cardiovascular death and hospitalisation for patients with chronic heart failure and reduced ejection fraction. It's usually prescribed alongside other heart failure therapies, often replacing an ACE inhibitor or another ARB.⁷ Clinical trials have shown that it significantly reduces the risk of death from cardiovascular causes and hospitalisation for heart failure compared to ACE inhibitor therapy alone.⁸

The purpose of this study is to conclude the efficiency of Uperio (valsartan/sacubitril combination), the cost difference with other drugs, the proper dosage of treatment, and the side effects for HF patients.

Method

With key words of ((heart failure) AND (uperio)) OR (angiotensin receptor-neprilysin inhibitor) OR (sacubitril/valsartan) results from Google scholar and PubMed were narrowed down and we excluded irrelevant topics and languages except for English. Inclusion criteria specified characteristics studies must have to be considered about uperio treatment for HF patients, and obviously described specific populations, interventions, outcomes, and study designs. However, articles that were not relevant to the research and did not present the participants and protocol in detail were excluded. We compared and summarised a total of 14 papers to each other.

Discussion

The natriuretic peptide system

The natriuretic peptide (NP) system is an endocrine system that maintains fluid and pressure homeostasis by modulating cardiac and renal function. Several types of NPs have been described: atrial (ANP) brain- (BNP) and C-type natriuretic peptide (CNP). Whereas ANP and BNP are synthesised and secreted mainly from the cardiomyocytes in response to myocardial stretch.⁹⁻¹⁰ CNP is released from endothelial cells in response to physiological agonists and by vascular injury NP levels are elevated in patients with HF and other cardiac diseases for restoring normal circulatory conditions.¹¹⁻¹³

Their actions are modulated through guanylyl cyclase-coupled receptors A and B (NPR-A and NPR-B) and the more abundantly expressed G protein-linked

NP-clearance receptor (NPR-C) ANP and BNP bind selectively to NPR-A, while CNP binds to NPR-B and NPR-C and leads to activation of intracellular pathways.^{9,14} By binding to NPR-C, natriuretic peptides are cleared from the bloodstream by endocytosis and intracellular inactivation.^{15,16} NPR-A and NPR-B induce the generation of the second messenger cyclic guanosine monophosphate (cGMP), which mediates via protein kinase G activation and serine/threonine kinases most of the physiological effects of the NPs including natriuretic and diuretic effects, as well as various cardioprotective and antihypertensive mechanisms such as vasodilation, a reduced sympathetic nervous system (SNS) activity, inhibition of the RAAS (all more acute effects), induction of apoptosis and inhibition of fibrosis (long-term effects).^{9,13,17} Unlike ANP and BNP, CNP does not act as an endocrine hormone, but as a paracrine factor in the vasculature, mainly as a vasodilator and inhibitor of vascular cell proliferation, although it is unclear whether CNP decreases blood pressure at physiological or pathological concentrations.^{14,18-20}

Natriuretic peptides play a similar role as in the periphery, directly counteracting the effects of ANG II. Overall, main effects of natriuretic peptides include decreased salt and water intake, and inhibition of vasopressin, resulting in a decreasing in body fluid and lowering of blood pressure.²¹

Nepriylsin

Nepriylsin is an ANP-degrading zinc-dependent endopeptidase.²² It was found that ANP was a substrate of NEP, also a multitude of other molecules such as ANP, BNP, CNP, angiotensins 1, 2, 3, 1-9, endothelin-1, endothelin-2, endothelin-3, adrenomedullin, and bradykinin.²³ NEP is expressed in epithelial cells, neutrophils and fibroblasts, and it has been located in many tissues, such as renal proximal tubules, the heart, the brain, lungs, blood vessels and thyroid.²⁴⁻²⁵ Inhibition of NEP activity, the goal is to slow down NP breakdown, effectively increasing their vasodilation effect.

Sacubitril/Valsartan (Uperio)

Sacubitril/Valsartan (previously known as LCZ696, and marketed under the name of Entresto®, Uperio®), a combination drug, has proven to be superior to conventional angiotensin-converting-enzyme (ACE) inhibition in reducing cardiovascular deaths and HF hospitalisation, in a large prospective randomised clinical trial.²⁶ The molecule consists of two active

moieties in a 1:1 ratio, the well-documented ARB, valsartan and a NEPi pro-drug sacubitril (AHU337). The new class is called angiotensin receptor/neprilysin inhibitor.

Valsartan is an ARB. By having a much greater affinity for AT1R compared to AT2R, valsartan can inhibit the BP-raising and pro-fibrotic effects that are triggered by AT1R-mediated overproduction of reactive oxygen species causing hypertrophic cell growth, cell senescence, endothelial dysfunction, and cardiovascular and renal remodelling, without interfering with the beneficial antihypertensive and cardioprotective effects of AT2R.²⁷

LBQ657 inhibits the neutral endopeptidase, an enzyme responsible for the degradation of NP. By preventing this process, the NP concentration increases and their cardioprotective and antihypertensive effects are enhanced.²⁸

Uperio in hypertension

LCZ696 can significantly reduce blood pressure in patients with heart failure. According to a meta-analysis study by Geng, Qiang et al., this meta-analysis to determine the antihypertensive effect of LCZ696 in patients with hypertension. Compared with angiotensin receptor blockers (ARBs), LCZ696 100 mg caused a significant reduction in systolic blood pressure (SBP) and diastolic blood pressure (DBP). LCZ696 200 mg caused a significant reduction in SBP, DBP, 24-h ambulatory SBP, and 24-h ADBP. LCZ696 400 mg caused a significant reduction in SBP, DBP, 24-h ASBP, and 24 h ADBP. Compared with LCZ696 200 mg, LCZ696 400 mg caused a significant reduction in SBP, DBP, 24-h ASBP, and 24-h ADBP. Research found that the blood pressure-lowering effect of LCZ696 is dose-related. It confirms the antihypertensive effects of LCZ696.²⁹

Three studies evaluated the effect of LCZ696 compared to olmesartan in the treatment of HT in Asian patients, in patients with essential HT not adequately responsive to olmesartan and elderly patients.²⁹⁻³¹ They all found LCZ696 to be superior in lowering the peripheral BP or CASP, although the effect seems to become non-significant over time.³¹ Furthermore, the studies all point towards the same level of tolerability and AE for LCZ696 as for olmesartan.

Uperio in Heart Failure

The largest completed study so far is the PARADIGM-HF trial.³² The study was a double-blinded, randomised,

phase 3 trial including 8442 patients with HFrEF (NYHA class II-IV) and with an EF of <40%. After a run-in period of 3–6 weeks, participants were randomised to an ACEi, enalapril (10 mg twice daily) or LCZ696 (200 mg twice daily) group in a 1:1 ratio. After a 27-month median follow-up period, the trial was stopped early because predetermined results for effects were achieved. The study showed a decreased hazard ratio of 0.8 (95% CI: 0.73–0.87; $p < 0.001$) for deaths due to CVD or hospitalizations and a reduction in physical symptoms ($p < 0.001$) with LCZ696. The study concluded LCZ696 to be 'superior to enalapril in reducing risk of death and of hospitalisation for heart failure'.³³ McMurray et al. later showed that LCZ696 caused a reduction in CVD mortality and hospitalisation even as additional medication on top of BAA and mineralocorticoid receptor antagonists.³⁴

Sacubitril was found to lessen cardiomyocyte cell death, hypertrophy, and impaired myocyte contractility by inhibiting PTEN, thus triggering a series of cascades that participate in cardiac remodelling. On the other hand, Valsartan improves cardiac remodelling by inhibiting the guanine nucleotide-binding protein family. More importantly, study found that the combination of Sacubitril and Valsartan acts synergistically against left ventricular extracellular matrix remodelling (LVEMR) and cardiomyocyte cell death, with Valsartan enhancing the effects of Sacubitril.³⁵

Beneficial effect on glycemic control

Type 2 diabetes mellitus (T2DM) and HF often coexist, and the presence of both conditions in a patient typically indicates a poorer prognosis than either condition alone. This is partly due to the metabolic imbalances caused by T2DM, which can exacerbate the pathophysiology of HF. Glycemic control, typically measured by glycosylated haemoglobin (HbA1c) levels, is crucial in managing diabetes severity. It has been shown to be associated with the development and progression of HF. Optimal glycemic control is essential to mitigate these risks. Clinicians must carefully manage glycemic control in HF patients with T2DM, considering the individual patient's risk factors, comorbidities, and response to treatment. This personalised approach is vital to improving clinical outcomes and quality of life for these patients.³⁶

There is evidence suggesting that treatment with a dual-acting angiotensin-receptor-neprilysin inhibitor (sacubitril/valsartan) resulted in improved glycemic control. This beneficial metabolic effect is most likely

secondary to NEP inhibition and consequent modulation of its circulating substrates.³⁷

Effect on Biomarkers of Extracellular Matrix Regulation

B-type natriuretic peptide (BNP) is a biomarker that plays a crucial role in the diagnosis and management of HF patients. Scientifically, BNP is a hormone produced by your heart's ventricles in response to excessive stretching of heart muscle cells (cardiomyocytes). This stretching can occur due to fluid overload, commonly seen in HF.³⁸

At baseline, the profibrotic biomarkers aldosterone, sST2, TIMP-1, Gal-3, PINP, and PIIINP were higher, and biomarkers associated with collagen degradation, MMP-2 and -9, were lower than published referent control values. Eight months after randomization, aldosterone, sST2, TIMP-1, MMP-9, PINP, and PIIINP had decreased more in the sacubitril/valsartan than enalapril group. At baseline, higher values of sST-2, TIMP-1, and PIIINP were associated with higher primary outcome rates. Changes from baseline to 8 months in sST-2 and TIMP-1 were associated with change in outcomes.³⁹

Biomarkers associated with profibrotic signalling are altered in HF with reduced ejection fraction, sacubitril/valsartan significantly decreased many of these biomarkers, and these biomarkers have important prognostic value. These findings suggest that sacubitril/valsartan may reduce profibrotic signalling, which may contribute to the improved outcomes.³⁹

Side effects

A phase 2 trial aimed to evaluate the safety and tolerability of LCZ696 for HF patients (NYHA class II-IV), NCT01922089. The study was conducted as a randomised, double-blind, multi-centre trial in the United States, Europe and Turkey. The 498 participants were randomised into two groups up-titrating to 200 mg LCZ696 twice daily in 3 or 6 weeks, respectively. Common side effects were ('condensed' vs. 'conservative') hypotension (9.7% vs. 8.4%), renal dysfunction (7.3% vs. 7.6%) and hyperkalaemia (7.7% vs. 4.4%) and adjudicated angioedema (0.0%), which occurred in patients.⁴⁰

Cost

As for the cost, it can vary depending on the region and the healthcare system. For example, in Pakistan,

Uperio 100mg tablets are available, and there might be discounts offered on purchases.⁴¹ Similarly, in Nigeria, the price for Uperio 100mg tablets (28 tablets) is listed, with potential discounts as well.⁴² It's important to note that prices can fluctuate and it's best to consult a local pharmacy or healthcare provider for the most current pricing information.

The actual price of the drug has to be discussed. The treatment with Entresto (400 mg) will cost 48.42DKK (6.89\$) a day. In comparison, equivalent doses of enalapril (20 mg) and valsartan (160 mg) will cost 0.27DKK (0.039\$) and 1.2DKK (0.17\$), respectively, per day. Therefore, the possible economic impact will need to be closely considered.

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Conclusion

Combination of Angiotensin–Nepriylsin Inhibition was beneficial in reducing hypertension, risks of death and hospitalisation for heart failure. Sacubitril was found to attenuate cardiomyocyte cell death, and hypertrophy, on the other hand, Valsartan improves cardiac remodelling. Also, they reduce profibrotic biomarkers which may contribute to improved outcomes. Uperio has a beneficial effect on glycemic control belongs to neprilysin inhibition. The proper dosage was 200 mg twice daily in 3-6 weeks. Although Uperio has fewer side effects, it is considered a high-priced heart failure medication and needs further economic impact.

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Understanding the Invisible Threat: The Progressive Escalation of Antibiotic Resistance in Pakistan

Antibiotic resistance is a global health problem and is quickly becoming a growing health concern in Pakistan. Rapidly increasing resistance to antibiotics in recent years has significant implications for the public health and the healthcare systems. Resistance develops when bacteria acquire certain characteristics which render antibiotics previously effective, obsolete. The primary cause of antibiotic resistance is the excessive and oftentimes inappropriate use of antibiotics. Antibiotics are often prescribed by healthcare workers without proper diagnostic tests and this misuse is contributing to the development of resistant strains. Lack of awareness and lack of access to healthcare in some regions of Pakistan prompt patients to search for quick solutions to their various illnesses. Antibiotic resistance has the potential to become a health crisis for the already crippling healthcare system of Pakistan. Therefore, a multifaceted approach must be adapted quickly to mitigate this issue. The distribution and sale of antibiotics should be controlled through implementation of strict regulations. Proper public awareness campaigns should be used as targeted interventions, to create a sense of responsibility in the general public about the prudent use of antibiotics.

Keywords: antibiotic resistance, global health crisis, healthcare system, Pakistan

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Antibiotic resistance is a silent global crisis which is intensifying and becoming an invisible threat to the public health of Pakistan. It is steadily gaining momentum and is rapidly spreading within our borders, leaving us apprehensive about what it means for the future of healthcare in our country. The discovery of penicillin was an unprecedented advancement in medicine which opened a floodgate for the development of antibiotics. This discovery which revolutionized the world of medicine, however, came with a host of side effects. Penicillin was sold over the counter in pharmacies for years which eventually led to the establishment of a population of resistant strains. The situation today is similar on a grander scale leaving us defenseless against life-threatening infections, when our most powerful and trusted weapons against bacteria become futile.¹

For instance, recently an article which evaluated the susceptibility of microbes to various antibiotics in Pakistan was published.² One key finding which was highlighted by the study was that multidrug resistance is rampant in Pakistan. The study also emphasized on the fact that antimicrobial treatment is very limited and that there are restrictions on the use of antibiotics which is a significant concern for the field of healthcare and medicine. This finding has great implications for a country like Pakistan which is home to more than two hundred million people and is currently grappling with the menace of antibiotic resistance which has deeply penetrated the country.³ The influx of low-quality antibiotic strains and their unchecked consumption is associated with the lack of clinical acumen as medications are sold without a prescription and worse due to a lack of standard treatment guidelines, the health workers are inclined to overprescribe antibiotics. Lack of awareness and education of the general public are major contributing factors to the rising resistance because of the lack of information about the consequences of the uncontrolled and unsupervised use of antibiotics. The general public is unaware of the hazardous effects of incomplete therapeutic courses and self-medication. The inadequate regulation and unchecked proliferation of antibiotics as over-the-counter medications are contributing to the formation of new resistant strains of bacteria.⁴

In Pakistan, the country with the highest rate of unnecessary antibiotic prescriptions, untreatable infections due to resistant bacteria have become a significant burden on the already crippling healthcare system. For example, *M. tuberculosis*, a pathogen that has plagued Pakistan for decades and is endemic in

the region, is an example of a superbug with multi-drug resistance. Pakistan ranks fifth among the TB high burden countries worldwide and reports more than five hundred thousand new cases of tuberculosis every year. The ramifications of this alarming number are further worsening due to the emergence of more than fifteen thousand drug-resistant cases of tuberculosis every year. The drug-resistant cases are exceptionally difficult to treat and require more expensive alternative treatments. This leads to inadequate control and cure of the disease leading to prolonged stay in the hospital further increasing the burden on the healthcare system.⁵

Antibiotic resistance is a complex problem that occurs when bacteria acquire the ability to continue to proliferate and survive even in the presence of agents designed to kill or inhibit their growth. The overuse of antibiotics puts a higher selection pressure on the bacteria to filter out the most resistant strains which leads to the diversification of the bacterial genome. This resistance to antibiotics develops through various mechanisms and it's imperative to understand them to develop strategies to combat this issue. One such mechanism is spontaneous mutations in the genetic material of bacteria which render the antibiotic ineffective against it. In addition, some bacteria produce enzymes which actively break down the antibiotics. This includes the enzyme β lactamase which is the leading cause of resistance against the pioneer antibiotic i.e. penicillin. Other mechanisms of resistance are efflux pumps which actively pump the drug out of the cell, modification in the target sites of the drug and the formation of biofilms which make the bacteria about one thousand times more resistant to antibiotics. One exceptionally important mechanism of antibiotic resistance which is becoming increasingly prevalent in the resistant strains is horizontal gene transfer (HGT) which is the exchange of genetic material within species without any sexual contact⁵. This exchange promotes collaboration among the bacterial population in the development of multi-drug resistance which leads to "superbugs" which can tolerate almost all antibiotics.

Antibiotic resistance is on track to becoming a large-scale medical issue and it is essential to adopt a multifaceted approach and to implement appropriate control measures to mitigate this rising threat. The most important tool to counter the situation that is proliferating out of control so rapidly is monitoring the usage of antibiotics which needs to be done at both a personal level and a national level. This can be achieved

by the implementation of regulatory measures that restrict the availability of antibiotics without prescription. Healthcare professionals including pharmacists should be properly educated about their role in the irrational use of antibiotics. Doctors should be strictly advised to not over-prescribe drugs and pharmacists should be in particular made vigilant to not provide antibiotics which require a prescription. A universal treatment guideline should be drafted by WHO to be followed

as a global prescription plan for antibiotics which all healthcare physicians must adhere to. In addition, targeted interventions should also be done at the national level and the government should play its role responsibly and effectively in mitigating this issue. The government should establish an antibiotic resistance surveillance and tracking system to monitor and track the emergence of new resistant strains to prevent this situation from getting out of control.

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Volume 11 | 2024 Release

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