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<b>Table of Contents</b>	i
<b>Journal of Health and Medical Sciences Editorial Board</b>	iii
<b>Innovating and Transforming the Healthcare Sector in Bangladesh: Challenges and Opportunities</b> H. M. Khalid Hossain Bhuiyan, Jannatul Ferdous	119
<b>Assessment of Three Multimedia Tools for Improving Patients' Understanding and Adherence to Orthodontic Treatments</b> El Mabrak Asmaa, Chafi Imane, Serhier Zineb, Bourzgui Farid	128
<b>Evaluation of Prevalence of Congenital Anomalies in Children and Infants Admitted to NICU and IPD of Banyan Provincial Hospital in 2018- 2023</b> Sherin Hemati, Jamila Jafari, Sayed Qasim Alavi	139
<b>Effect of PM2.5 Exposure among Children with Asthma: A Systematic Review</b> Clara Virginia Allun, Dian Andriani Ratna Dewi, Putri Aisyah Azhari, Suzandi Imam Pradana, Fitriana Nurul Aini, Wahyu Iman Utomo, Rafif Muzakki, Evania Marisa Rumbobiar	145
<b>The Role of Al-Hijamah in Efforts to Prevent Heart Disease and Blood Vessels: A Systematic Review and Meta-analysis</b> Angki Perdiyana, Dian Andriani Ratna Dewi, Lila Irawati Tjahjo Widuri, Arohid Allatib, Kelvin Dewantara, Ni Made Wiliantari, Karina Rahmawati Editya Putri, Lucy Laila Felicia, Farida Ulfa, Alexander	154
<b>Relationship Between Children's Cognitive Function and Type 1 Diabetes Mellitus (T1DM): A Systematic Review</b> Arohid Allatib, Dian Andriani Ratna Dewi, Shabrina Lathifatunnissa Rais, Muhammad Rakan Kabbani, Chiquita Jasmine, Kharissa Rahma Rindani, Taufik Hidayat, Andi Nadila Faatin, Farrasila Nadhira, Ni Made Wiliantari	166
<b>Ethanol Extract of Pomelo Peel to Prevent Dental Caries in Extracted Teeth In-Vitro</b> I Made Budi Artawa, I Gede Surya Kencana, I Nyoman Gejir	177
<b>Content and Antimicrobial Potential of Cambodia Flower (Plumeria sp.) Extract</b> I Nyoman Jirna, I Gede Sudarmanto, I Nyoman Gede Suyasa, Ida Ayu Made Sri Arjani, Cok Dewi Widhya Hana Sundari, I Nyoman Purna, Nyoman Mastra	185
<b>Analysis of Knowledge and Attitude regarding First Aid and CPR among Myanmar Seafarers</b> Tay Zar Lin, Rohit Kumar, Shwelinn Htet	192

<b>An Experimental Evidence for Antibacterial Activity of Propolis on Bacteria from Lebanese Patients</b>	199
Amena Allouch, Zainab Dagher, Dr. Ali Khalil Mezher	
<b>Gender Differences in Nutritional Status Among Adolescents Living with Family in Selected Slums of Dhaka, Bangladesh: A Mixed-Method Study</b>	210
Umme Haney, Tamanna Sharmin, Hridi, Nurhajan Akter, Barna Biswas, Mahmuda Ali, Zobaidur Rahman, Syed Shariful Islam, Fariha Haseen	
<b>“Yummy” Snakehead Sausage: Analysis of Nutrient Content and Acceptability of Fish Sausage in Lake Sentani Jayapura</b>	220
Sri Iriyanti, Budi Kristanto, Nia Budhi Astuti	
<b>Minimally Invasive Thoracoscopic Surgery of Lung Adenocarcinoma in Old Age People</b>	229
Sadam Hussain, Amna Abbasi, Li-Wei Zhang, Julaiti Ainiwaer	
<b>Gangs, Low Detection Rates, and Educational Achievement: Major Drivers of Violence</b>	237
Mandreker Bahall	
<b>Evaluating Heterogeneity in Meta-Analyses: A Review</b>	253
Rahman Hamze	

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# Innovating and Transforming the Healthcare Sector in Bangladesh: Challenges and Opportunities

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## Abstract

In Bangladesh, the public or government sector plays a vital role in determining the overall policies, funding sources, and modes of service delivery. Even though the health system encounters many insurmountable obstacles, it requires stronger national resource allocation priority. This study looks into the fundamental aspects of digitalisation and change in Bangladesh's healthcare industry. Additionally, it explores the relationship between digital technology and emerging elements of the existing healthcare system and offers suggestions for resolving ongoing crises within the healthcare framework. The authors decided to perform explorative research using secondary data to grasp better the fundamental concepts of Bangladesh's healthcare sector's digital transformation. This study examines Bangladeshi citizens' perceptions of the current 'Digital Transformation' in existing institutions and suggests an entirely new national health server-centric model for future solicitation.

**Keywords:** Health Service, MDG, SDG, Digital Transformation

## 1. Introduction

Bangladesh, which has 160 million people and ranks eighth in terms of population, has recently been praised for its outstanding performance in terms of health. The country has long been committed to enhancing healthcare services for the general public, resulting in significant advancements in the industry and the early acquisition of the Millennium Development Goals (MDGs). By 2032, hopes of the government to have all residents and localities have access to the affordable health care they require (CRI, 2018). The response of society to the social determinants of health is the health system. Every society holds to a set of factors that influence health, with science or reason seldom intervening. The worth of each individual is the core principle of every healthcare system. The human, material, and financial resources society allows for the health system are mainly determined by society's value of human life. A well-functioning healthcare system requires that services be readily available and accessible so that people can comprehend, accept, and put to good use. The constitution of Bangladesh mandates that the government "the provision all necessary healthcare needs to all kinds of individuals in the community"

and work to enhance the "nutritional and medical status" of the country." (Islam & Biswas, 2014). "Everyone has the right to a standard of living adequate for the health and well-being of himself and his family, including food, clothing, housing, medical care, and necessary social services, and the right to security in the event of unemployment, sickness, disability, widowhood, old age, or other lack of livelihood in society," states The United Nations General Assembly approved the International Covenant of Human Rights on December 10, 1948 (Sabur, 2021).

Since achieving independence in 1971, Bangladesh has had notable health advances, becoming a prime example of "good health at low cost." The government's plan offers a first road map that acknowledges the challenges of achieving universal coverage in a primarily informal economy with a heterogeneous health system and constrained fiscal space, despite its initial scepticism over the aim of universal health care. Maternal and child mortality rates have dramatically decreased since the middle of the 1980s. This remarkable success story also includes increased life expectancy, vaccination rates, the control of tuberculosis and diarrhoea, and other factors. A pluralistic health system with abundant stakeholders that pursues women-centric, gender-equity sensitive, and highly focused health interference in the planning for a family, the health of mother and child, immunisation, and nutrition interventions by the widespread work dispersed community health workers reaching entire households may be responsible for exceptional performance. Bangladesh offers lessons on how the innovation of work can be scaled up, how gender equity can enhance health outcomes, and how direct health interventions may partially overcome socioeconomic barriers (CRI, 2018).

One of the industries in Bangladesh that has experienced astounding growth in the five decades since independence is healthcare, gaining praise from the developed world in the process (Hasan, 2021). The People's Republic of Bangladesh's constitution states in the 15<sup>th</sup> article, "It shall be a fundamental responsibility of the State to attain, through planned economic growth, a constant increase of productive forces and a steady improvement in the material and cultural standard of living of the people, to secure to its citizens the provision of the necessities of life, including food, clothing, shelter, education, and medical care" (Sabur, 2021).

Given Bangladesh's massive population, the healthcare industry has always been plagued by infrastructural issues. The industry has traditionally struggled to deliver high-quality services because it is frequently underfunded, ill-equipped, and understaffed to meet the escalating requirements of a rapidly expanding population. The healthcare industry has long needed improvements to its organisational structure and method of service delivery. To promote efficiency and uniform quality, outdated models were in critical need of digital transformation (Huq, 2018). Although our healthcare system has undergone substantial improvement over the past 50 years, SDG 2030 also calls for quality and equity in healthcare to be attained. The population living in Bangladesh faces observable distinctions in health and longevity because of socioeconomic level variances, as has been shown in our nation in various methods and multiple times (Amanullah & Khatun, 2022). This study looks into the fundamental aspects of digitalisation and change in Bangladesh's healthcare industry. Additionally, it explores the relationship between the emerging elements and digital technology of the subsisting healthcare system as we offer suggestions for resolving ongoing crises within the healthcare framework.

## **2. Methodology**

The authors decided to perform explorative research using secondary data to grasp better the fundamental concepts of Bangladesh's healthcare sector's digital transformation. The report is based on a thorough analysis of data and information about Bangladesh's health system that has been published and unpublished. Scientific journal articles and research papers were also examined. The study is a retrieval article that is based on secondary data. However, the work solely relies on analyses of news stories, research reports, and articles written in English.

## **3. Health Sector in Bangladesh**

In terms of health-related accomplishments, Bangladesh has "outperformed" several of its South Asian neighbours, "convincingly defying the expert view" that economic strength and an abundance of medical resources are the primary factors influencing improved public health (The Financial Express, 2018). In the nation, maternal and

neonatal mortality have dramatically dropped while life expectancy at birth has improved (Hasan, 2021). In recognition of its outstanding accomplishments in achieving the Millennium Development Goals (MDGs), specifically in decreasing the child mortality rate, Bangladesh was given a UN award in 2010. In 2019, the rate of death was 28 per 1,000 births. In the same year, in every 1,000 live births, the child mortality rate was 21 and the rate of neonatal rate was 15 respectively. These factors helped Bangladesh reach a life expectancy of 73 in 2019. At the same time, 72 years was the average age of people worldwide, whereas it was 69 years in India, 67 years in Pakistan, 71 years in Nepal, and 76 years in Sri Lanka (Sabur, 2021).

According to a report demonstrated by the World Health Organization's (WHO) most recent rankings of healthcare quality in various nations worldwide, Bangladesh is ranked 88th. Only Sri Lanka is ranked 76 places higher than Bangladesh among the SAARC nations. India comes in at number 112, Pakistan at number 122, Bhutan at number 124, the Maldives at 147, Nepal at number 150, and Afghanistan at number 173 on the list. According to this ranking, Bangladesh's healthcare system appears superior to India's (Al Mamun, 2021).

The newborn mortality rate in Bangladesh has decreased from 9.4 percent in 1981 to 1.9 percent in 2019, as the maternal mortality proportion has decreased by 67 percent since 1990 (LightCastle Partners, 2022). Regular vaccination campaigns are carried out in the nation against diseases like diphtheria tuberculosis, maternal and neonatal tetanus, whooping cough, hepatitis B, Haemophilus influenzae-B, poliomyelitis, pneumococcal pneumonia, rubella, and measles. Through the EPI program, immunisations are given away free of charge to everyone in the nation. The vaccination rate has increased from two percent in 1985 to over 98 percent today (Al Mamun, 2021). Thanks to a highly well-organized network run by the Directorate General of Health Services (DGHS) executive, rural residents can access healthcare.

Additionally, community clinics are crucial in delivering crucial medical services to residents of rural places. There are currently 1,312 union-level sub-centres besides 87 union health and family planning centres, 424 upazila health complexes, 65 sadar or district hospitals, and 14,384 community clinics in Bangladesh, according to the DGHS. Thirteen thousand eight hundred eighty-one community clinics are currently open and operating nationwide. In contrast, just 35 dispensaries, a minimal number of community clinics, over 60 medical colleges, specialised hospitals, and many private hospitals may be found in urban regions (Hasan, 2021). To increase the effectiveness of program execution, the Ministry of Health & Family Welfare (MOHFW) started the Health & Population Sector Programs (HPSP) in 1998, which marked the beginning of Bangladesh's e-Health project. Because of the current government's Digital Bangladesh initiative, which provides particular precedence to delivering health services to residents through ICT, e-Health is receiving extra attention (CRI, 2018).

With a current market size of USD 6.6 billion, demand for healthcare services in the nation is still on the rise, especially in the wake of the COVID-19 epidemic. As the market for the healthcare business mounts, the government needs to reassess how to support the sector's future expansion. Although donor money has historically been a cornerstone of the healthcare sector's transformation, significant funding shortfalls remain in this industry (LightCastle Partners, 2022). Even if there may be concerns about how the government handled the COVID-19 epidemic, the world community and the nation's people have recognised the health sector's ability for a relatively low number of illnesses and fatalities. Bangladesh is now self-sufficient in producing life-saving generic as it gears up to become a nation that produces vaccines.

Additionally, its manufacturing of medical equipment is receiving some well-deserved attention (Hasan, 2021). According to reports, Bangladesh implemented a "pluralistic" health system in which non-governmental organisations were given resources from public monies to work in the nation's health sector. The UN, WB, and Asian Development Bank's support for the country's health sector has been a crucial source of funding generation. Exemplary, as part of its response efforts, the World Health Organisation (WHO) supplied Bangladesh with 100 venturi masks, 200 oxygen concentrators, 400 pulse oximeters, 100 nasal cannulas, and 65 patient monitors to 10 Covid specialised health institutions, as well as these items for 17 district hospitals. Similar to this, the World Bank and the Asian Development Bank have committed to provide \$100 million in assistance to the nation for emergency COVID-19 response (Fidai, 2021).



All public health-related industries must collaborate toward a common objective. Bangladesh is one of the nations with whom the World Health Organization collaborates closely to attain specific ambitious and challenging goals in the field of global health care.

Additionally, the adoption of such technology opens up several options and benefits. To manage and maintain such technology and processes, a system like this needs well-trained staff and management and a positive attitude from regular people. Technology was used to implement a telemedicine system in medical services as part of the creation of Digital Bangladesh. This allows residents of distant locations to provide expert medical advice to large hospitals in Dhaka via video conferencing. Additionally, these patients are treated by specialists via email and mobile devices. To receive medical care through a telemedicine facility, patients do not need to pay additional fees (Khan & Al Amin, 2021). The rural healthcare system has also received a lot of praise, particularly the Bangladeshi community clinic concept. However, because the health and local government ministries disagree, well-designed healthcare still needs to be built for the urban residents.

#### **4. Recent Innovations in the Health Sector in Bangladesh**

One crucial tactic for meeting the demand for health care in the twenty-first century is the usage of information and communication technologies (ICT). ICT in health care services can deliver services to people's doorsteps. It aids in addressing expanding demands, rising costs, finite resources, labour scarcity, and the distribution of best practices nationally and worldwide. ICT health services can also ensure the proficiency and efficacy of the health management system (Khatun & Sima, 2015). Striking drops in maternal, newborn, and childhood mortality rates have accompanied rapid expansions in the number of health interventions covered in Bangladesh. All these developments call for a careful examination of Bangladesh's strategy for providing healthcare during the past 40 years, hampered by pervasive poverty, political unrest, and frequent natural catastrophes. We examine health-service delivery techniques concerning success stories that have increased reach and enhanced health outcomes (El Arifeen et al., 2013). In Bangladesh, the digitalisation of the healthcare services industry is still in its infancy. In actuality, Bangladesh still needs to be ready to handle the usage of ICT in the medical and healthcare services industry effectively. There needs to be set standards and laws for utilising ICT in the healthcare sector effectively and efficiently. ICT usage in Bangladesh varies depending on the situation, and some ICT applications are more popular than others (Alam et al., 2020).

The greatest wonder that makes the computerisation of healthcare services in underdeveloped nations like Bangladesh possible is the expansion of the digital healthcare system. Digitalising healthcare delivery systems is far more complex in countries like Bangladesh, where resources are limited, and people are unwilling to accept challenges and appreciate recent technological advancements. Although Bangladesh has made significant progress in many areas of digitalisation, the progression in the healthcare and medical services era is significantly less for that country. However, with the right foundations, associations, and arrangements in place, ICTs can be a precious tool for those working to enhance healthcare services in Bangladesh. Modern business methods for an organisation's investment and development area for digitising the healthcare sector include digital online platforms, various apps, pay-per-click advertising, and pay-per-click campaigns (Khan & Basak, 2021). To increase the effectiveness of program execution, the Ministry of Health & Family Welfare (MOHFW) started the Health & Population Sector Programs (HPSP) in 1998, which marked the beginning of Bangladesh's e-Health project. Because of the current government's Digital Bangladesh initiative, which places a premium on providing health services to residents via ICT, e-Health is receiving extra attention. The five-year Health, Population and Nutrition Sector Development Program (HPNSDP) 2011-2016 for MoHFW was approved by the government of Bangladesh in 2011. One of the 32 operational strategies that make up the HPNSDP 2011-2016 is e-Health (CRI, 2018). Internet access was introduced across the total health locations down to the Upazila level by Bangladesh's Directorate General of Health Services (DGHS) in April 2009. This network has recently been expanded to include all community clinics and union health centres. To offer e-health services to the patients, community clinics and union health centres have laptop computers and internet connections. To improve e-health services in Bangladesh, community health workers have also been handed Android tablets (Hoque et al., 2014).

A system of technology allowing people to securely connect and exchange their health data with a network of recognised health experts is being developed in Bangladesh as part of the country's adoption of digital healthcare. It increasingly offers the knowledge and resources to help people better understand and manage their health. Bangladesh has created a strategic plan to support this sector, which is crucial to the nation's economy. The healthcare industry has a mixed response to digital change, though. In this light, it may be said that service providers are required to create a high-quality, broadly accessible health service based on ICT. Government policy guidelines should be developed for managing and monitoring the digitisation of the healthcare sector. Future research can focus specifically on e-health, m-health, telecare, telehealth, electronic health records, telemedicine, digital startups, and video conferencing. In any event, when there is simplicity, the whole digitalisation of the healthcare industry is possible. An essential benefit of people being aware of their health is that it helps organizations construct applications or programming specifically designed to monitor people's health and well-being. The key driving force for digitalization is the accessibility of the medical services sector from any necessary location (Khan & Al Amin, 2021).

### **5. mHealth**

In May 2009, the Ministry of Health implemented mHealth, widely known as Mobile Health Services, in all upazila and district hospitals nationwide. A cell phone has been issued to serve as a local call centre that offers citizens 24/7 access to medical advice. mHealth services have made it easier for people to access medical advice, especially those who are poor and live in rural areas. Now, even those who live far from a hospital and at odd hours can get medical advice (Ahmed et al., 2014). The ground-breaking mass SMS technology was launched in 2009. Bulk SMS was often used and driven by demand. All health managers' and employees' mobile numbers were gathered and organised into this system. Instantaneously broadcasting personalised text messages to one or more groups is possible (Hoque et al., 2014).

### **6. The Telemedicine Service**

Twenty-nine telemedicine facilities are operating, while telemedicine services were launched at eight hospitals in 2011. In 4,547 unions across Bangladesh, Union Information and Service Centers are run by Access to Information (A2I), which received the 2014 World Summit on Information Prize. Telemedicine is among the most well-liked value-added services in the individual UDCs, particularly for rural residents. The first of its type in Bangladesh, the telemedicine system was set up at CRP (Centre for the Rehabilitation of the Paralyzed) in July 1999. This was accomplished with the help of the UK-based Swinfen Charitable Trust. The Royal Hospital, Haslar in the UK, provides CRP access to consultants with various disciplines who have consented to offer consultations without charge. In 800 public hospitals, notice boards have been erected that explain how to text complaints to improve services. If patients or anyone visiting the hospital is dissatisfied with the service, they can text. The complaints are handled by designated staff members who receive the text messages through a web interface (CRI, 2018).

### **7. Geographical Information System (GIS)**

To test if the Geographical Information System (GIS) can be integrated into the health sector with the existing information personnel for mapping health facilities and services, the Health Ministry of Bangladesh launched a pilot study in the Nilphamari area of Bangladesh in 2009. The pilot program was successful, and policymakers were quite pleased with the report. Each divisional and district health office has been given a global positioning system (GPS) GIS device due to this pilot project. It aids service availability mapping and disease surveillance (Afroz, 2012).

### **8. Challenges of the Health Sector**

Despite these advances, the Bangladesh health system still faces many challenges. This year, the United Nations Survey gives special recognition to countries with over 100 million people who have put much effort into providing e-government services to their citizens despite their challenges. Indeed, when it comes to e-government advancement, every nation confronts its particular challenges (Uddin, 2012).

### *8.1. Low Budget*

The Bangladeshi public health system has long struggled due to a lack of funding from the government. Despite Covid issues, the country's allocation to the health sector this year is only 5.14% of the budget and less than 1% of GDP. Bangladesh has one of the lowest strata of public health spending worldwide, with 2.8% on average among lower middle-income countries and even 2.1% on average in South Asia. The nation's expenditure on the industry needs to be more reasonable and distributed across all geographic and residential divisions (Fidai, 2021).

### *8.2. Compromised Access*

Public hospitals provide a full range of hospital care services. On the other hand, a 3-level primary health care system has been established to serve the entire population (district, mass, and village levels). However, access to this network of health facilities is often severely hindered. It should be pointed out that although primary health care should be provided free in public hospitals and other facilities, people often have to pay for drugs, tests, and additional hidden costs themselves. Because of these costs, most state-funded health services are out of reach for the poor and disadvantaged. In addition, many public hospitals have ambulances that cannot be used or used by doctors and other staff. Patient access to ambulance services is restricted. In short, the accessibility of low-income people is significantly jeopardised in public health facilities due to a mismatch between concept and reality (Islam & Biswas, 2014).

### *8.3. Resistance of Change*

Older administrative workers in Bangladesh's medical sectors are accustomed to manual systems, and nobody wants to introduce new concepts into an established system. This problem of low motivation, frequently referred to as resistance to change or apprehension of new technologies, is well-documented. Administrative workers, policymakers, physicians, and nurses oppose using e-health for many causes. Two leading causes are that (1) they want to avoid accepting any form of change in their comfortable working environment, and (2) they are concerned that the computerisation of various healthcare operations may cause some redundant staff (Hoque et al., 2014).

### *8.4. Class Differences*

After independence, there has been an increase in the socioeconomic class disparities in access to care. Racial/ethnic, socioeconomic, and other health-related behaviours and status differences are well documented. Additionally, not everyone in our nation benefits equally from economic progress, which affects everyone's health. The rapid economic expansion has permanently impoverished disadvantaged people without social support systems and protection (Amanullah & Khatun, 2022).

People's lives are in danger in the delicate field of healthcare. To ensure safe practices of healthcare services, it is necessary to develop and adhere to suitable processes and guidelines before using any system. Otherwise, significant consequences could result. Hospitals had yet to benefit from the Bangladeshi government's national ICT policy in 2009. Bangladesh's regulatory and legislative structure still needs to be updated to meet the expanding demands of the technological world. However, emails have no official status and cannot be regarded legally as a legitimate means of communication in government institutions. Both rules for electronic authentication and regulations to prevent cybercrime are weak (Hoque et al., 2014).

### *8.5. Lack of Devolution*

The well-being framework has yet to experience a devolutionary preparation despite being decentralised. In other words, the UHCs were executing the plans and programs affirmed by the Service, with control and decision-making centralised at the MHFW in Dhaka. As a result, nearby substances need to be reflected in plans and programs. Also, the nearby wellbeing experts are regularly incapable of appropriately reacting to particular nearby crises or emergencies because of a need for a decision-making specialist (Islam & Biswas, 2014).

### *8.6. Inadequate ICT Infrastructure*

For e-Health, Bangladesh needs the essential ICT framework, counting computers, an online association, printers, and vitality. Moreover, only a tiny parcel of the populace has gotten to computers. According to a Bangladesh Telecommunication Regulatory Commission study, 4.5% of the crowd employ the web. In Bangladesh, the fetched web network is also over the top and must be more consistent. Also, there isn't an adequate sum of power accessible to back e-Health operations. On the other hand, because of the long delay between obtaining equipment and creating a custom computer program, the equipment is not significant when the computer program is usable (Hoque et al., 2014).

## **9. Recommendations**

To allow marginalised communities access to community healthcare administrations, the government of Bangladesh is serious about executing an open well-being card framework and shaping a consolidation with NGOs working in rustic districts and with powerless populaces. The availability of available well-being would move forward if the government successfully embraced this framework (Amanullah & Khatun, 2022). It needs to be more adequate to have an approach in hypothesis; controls and procedures must be put into hone. Within the various things that a few analysts have recorded, the noteworthiness of legitimate help, national benchmarks, and directions are also of significant concern. Rules and controls are pivotal for an unused framework or a framework currently in place. It has been proposed that creating a national approach serves as the establishment for the appropriation of e-health. To encourage the acknowledgement of e-health, Bangladesh's policymakers and government should make precise national e-health approaches and techniques.

### *9.1. Bridging the academia and industry gap can inspire innovation.*

Younger generations' transformational ideas can be sparked into startup endeavours by supporting innovative ideas in educational institutions (LightCastle Partners, 2022).

### *9.2. Budget Allocation*

The sector should receive an adequate budget. It's also crucial to stop the misuse of the resources that have been given. The number of secondary and tertiary hospitals is essential. Additionally, all hospitals at the district and upazila levels must have well-equipped intensive care units (Amanullah & Khatun, 2022).

### *9.3. Service Quality*

Quality should be at the core of all mHealth solutions to provide a high level of care for patients. Patients have the right to obtain high-quality medical care, whether provided in person or through contemporary ICT technology—poor quality results in difficulties and the requirement for extra care, significantly increasing expenditures. Due to the platform's lack of dependability and efficiency, the provider's lack of knowledge and expertise, the security and privacy of data or information, and its influence on consumers, there are growing concerns about the quality of these services (Akter & Ray, 2010).

### *9.4. Decentralisation*

Decentralisation can be accomplished effectively by incentivising healthcare professionals willing to work in remote and rural locations, with underprivileged groups, or both. The introduction of a patient referral system using digital communication and connectivity in primary, secondary, and tertiary hospitals, the provision of universal health insurance, and central monitoring and evaluation of the healthcare system to combat corruption and establish robust service are additional steps required for a modern design (Amanullah & Khatun, 2022).

### 9.5. Electronic Record

All healthcare institutions must maintain electronic patient records to provide quicker and higher-quality medical care (Khalifa, 2013). All parties involved in healthcare delivery can benefit from using electronic health records to store, process, and share medical data (Angst & Agarwal, 2009). As a first step, it is doable in the context of underdeveloped nations. Healthcare providers can use the voter list database for Bangladesh by supplementing it with extra data. Specialised urban doctors are well-positioned to use ICT or health records in their practice in rural areas.

## 10. Conclusion

The healthcare sector in Bangladesh is moving forward, but more is needed. Small data innovation has been implemented to increase the criteria of care, and it has to be more available for the general people and should be more efficient. The current investigation illustrates that Bangladesh's computerised well-being care administration segment needs to work more generally at a palatable level. The individuals accepting this benefit need to be recognised with these headways in healthcare administrations due to the absence of education, a need for mechanical know-how, and a hate to alter. These issues must be handled to improve the current healthcare framework and grant destitute and defenceless individuals better access to fundamental restorative treatment. No matter their financial level, everyone has the right to enjoy ideal well-being conditions since it could be a crucial human right.

On the other hand, the Bangladeshi government has executed a vital procedure to upgrade this industry, which could be a crucial component of the economy. The ponder emphasises the importance of a multisectoral, all-encompassing approach to making strides in the health system and the issue of reasonableness in well-being frameworks. Bangladesh's well-being framework critically needs inventive administration prepared to form and execute evidence-based approaches and activities. The well-being specialists ought to effectively empower remote ventures to update our healing centres, and moves should be made during international participation. At whatever point there's a dubious financial situation or a natural fiasco, the government should consider declaring a comprehensive social bundle. Generally, Bangladesh must endeavour to move forward with its positioning on the healthcare file and take all fundamental steps. The examination illustrates that Bangladesh's e-health environment is often favourable but needs to be improved. With these administrations, the benefit clients need to be more well-known. This leads to the conclusion that benefits suppliers must make strides in high-quality ICT-based well-being administrations that are broadly and effectively open nationwide. Analysts can conduct ponders on the use of e-health in Bangladesh.

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# Assessment of Three Multimedia Tools for Improving Patients' Understanding and Adherence to Orthodontic Treatments

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## Abstract

**Aim:** To assess the understanding and the recall of information using three communication tools: a video, a PowerPoint presentation and a flyer. **Methods:** We conducted a randomized clinical trial on a sample of 135 patients, divided into three groups (a) (b) and (c). Each group received a different form of information: a written pamphlet, a PowerPoint presentation and a video. The evaluation was conducted using a survey administered in two phases, in the short term (T1) and in the medium term (T2). **Results:** This study showed that all three tools were equally effective and valid in informing the patient. The results also showed that for some risks the audiovisual tools were better in terms of information including the risk of root resorption, and articular pain with a statistically significant difference. The effectiveness of these tools was different during the two stages T1 and T2 after one month of the first phase of information T1, the results showed no statistically significant difference between the information in the short and medium term. **Conclusion:** This study allowed us to verify the most effective information tool among the three tools used, which allows to establish a validated and reliable communication system within the care unit of Casablanca's department of orthopedics.

**Keywords:** Orthodontics, Consumer Health Information, Audiovisual Aids, Multimedia, Dental School of Casablanca, Morocco

## 1. Introduction

The reflection on the doctor-patient communication is generally important in the medical field; and particularly in the dental field. The evolution of modern medicine and the simplification and the keen interest in the electronic information in recent years has exposed the doctor and all the health actors to new challenges to result in the conception of the individual as being autonomous and responsible for his choices in the medical field. This special relationship, which is the subject of many investigations by doctors and human researchers, requires new skills in the field of communication that can be taught and learned by health professionals to care at best for their patients (Richard, 2005; Fournier, 2007).

In orthodontics, when a patient desires to receive an orthodontic treatment, the practitioner must provide him with as much information as possible about the necessary means of investigation, the procedures as well as all the risks inherent to this treatment, so that the patient can consent in a transparent environment. In dental practice, well-informed patients had more reasonable expectations of treatment outcomes and better involvement in therapy. This is particularly important in orthodontics because the long-term cooperation of patients during treatment improves clinical outcomes and the quality of life of patients; it also improves their satisfaction as well as that of the practitioner.

In addition, the involvement of patients in medical decisions reduces their anxiety and improves their cooperation and involvement, which is undoubtedly a guarantee of treatment success and a source of satisfaction for both the practitioner and the patient (Baird, 2003; Oudassi, 2010; Fraval, 2015). In this context, several studies have shown that patients who were well informed, adhered better to the proposed treatments (Fraval, 2015). In this context, the Department of Orthodontics of the dental treatment center Casablanca conducted a study on the recall rates and the understanding of the information transmitted during the informed consent in April 2010. This study showed that the consent process is well working on the diagnosis and the treatment basis. However, the results were unclear concerning the diagnosis of certain potential risks and sometimes irreversible, reported by the patients (Oudassi, 2010).

Knowing that most studies that have attempted to evaluate the recall rate of information related to orthodontic treatment have concluded that future research should focus on methods of improving communication with patients receiving orthodontic treatment (Patel, 2008). The use of other means than the written informed consent form; power point presentations, video or 3D media, could improve the understanding and the recall of information in patients (Fraval, 2015).

To meet this need, we have developed three information tools on orthodontic treatment: a PowerPoint support, a video and a flyer containing exactly the same information. In the present work, we will evaluate the understanding and the degree of recall of the information using these three communication tools to determine the most effective communication support so that we can integrate it into our daily practice within the department of orthodontics in the dental treatment center of Casablanca.

## 2. Topics and Methods

### 2.1. *The type of study*

This study is a randomized clinical trial that aimed the evaluation of the effectiveness of three multimedia tools, a written pamphlet, a PowerPoint presentation and a video in improving patients' understanding of the orthodontic treatment.

### 2.2. *The study population*

Our sample consisted of patients consulting within the orthodontics department of the dental treatment center in Casablanca, Morocco, patients aged 12 years and above. The reason we chose to conduct our study within the



center is due to the easy accessibility, as the need for communication and information was particularly noted in this population in a previous study.

### 2.3. *The survey*

The survey used in this study was developed on the basis of the results obtained from the previous study on recall rates and the *understanding* of informed consent information.

This questionnaire contained five sections:

- Patient identification
- Evaluation of the understanding of the diagnosis
- Evaluation of the understanding of the treatment plan
- Evaluation of the understanding of the risks of treatment
- Evaluation of the understanding of the means of prevention of these risks.

### 2.4. *Eligibility criteria*

#### 2.4.1. Inclusion criteria

- Patients older than 12 years old;
- Patients able to speak Arabic or French;
- Patients who consented to start orthodontic treatment;
- Patients being treated for less than three months.

#### 2.4.2. Exclusion criteria

- Psychomotor or learning development disorders
- History of orthodontic treatment
- Brothers or other close family members who had benefited from orthodontic treatment at the orthodontic department of the dental treatment center of Casablanca.
- Patient with a nearby dentist or orthodontist.

### 2.5. *Randomization method*

The randomization list was prepared by the statistician within the medical informatics laboratory at the Faculty of Medicine and Pharmacy of Casablanca, using the table of figures of the software Epi-info. The numbers of the three groups were distributed according to a list with a distribution according to the block method. A document describing the randomization procedure has been kept confidential in the Methodology and Data Management Center of the Faculty of Medicine and Pharmacy of Casablanca.

### 2.6. *Ethical approval*

We have submitted a local authorization application to the teachers responsible for the clinical sessions during which the survey will be conducted. Ethical approval was obtained on behalf of the patients in the orthodontic department of the dental treatment center of Casablanca.

### 2.7. *The study progress*

The first contact with the patients was made during the session of communication of the information by the attending physician. The patients answered the questionnaire the first time, it was the phase T0, and then they were invited to watch the information tools according to the distribution of groups as dictated by the randomization protocol methodologist, right after their attending physician explained the diagnosis, the treatment plan and the risks related to orthodontic treatment. Patients were allowed to ask questions, the same oral information was

provided to answer the different questions of the participants. Then, to evaluate the short-term recall rate, participants responded to the questionnaire a second time, during phase T1, and it was the previously calibrated interviewer who collected the responses. In order to evaluate the long-term recall rate, patients in group (a) kept the flyer, while patients in group (b) and (c) received the power point presentation and the video via a secure YouTube link which was communicated to them by email. The patients were called for the second care appointment, four weeks after the first test, in order to complete the same survey sheet used previously, it was the T2 phase.

### 2.8. Statistical analysis

The statistical analysis included a statistical description of the population studied; the comparison of the groups was made using the chi-2 test. Data entry, data collection and analysis used Epi-info 3.5.1.fr software within the Medical Informatics Laboratory of the Faculty of Medicine and Pharmacy of Casablanca.

## 3. Results

### 3.1. Evaluation of the understanding of orthodontic treatment risks (Phase T0)

Among the 135 patients who responded to the questionnaire,

- 2 (5.7%) patients reported that they knew that the orthodontic treatment has dental side effects, compared to 94.3% who ignored it.
- 7 patients (5.2%) said that caries risk is a potential risk inherent in orthodontic treatment compared to 94.8% who did not know it.
- 6 (4.4%) patients claim to know that the risk of tooth staining is a potential risk inherent to orthodontic treatment versus 95.6% who did not know it.
- All the respondents completely ignored the existence of possible periodontal adverse effects including gingival inflammation, recession and root resorption.
- All the patients were unaware of joint possible risks inherent to orthodontic treatment including blockage, pain and joint noise.
- All the patients stated that they were not aware of the potential risk of recurrence, failure or the possibility of preventing these risks during the orthodontic treatment.

Table 1: Evaluation of the understanding of the risks of orthodontic treatment (Phase T0)

	Frequencies	Percent
<b>Knowledge of dental effects</b>	n=2	5,7 %
carious risk	n=7	5,2%
risk of staining	n=6	4,4%
risk of necrosis	n=135	100%
<b>Knowledge of periodontal effects</b>	n=135	100%
Gingival inflammation	n=135	100%
Recession	n=135	100%
reduction		
<b>Knowledge of joint effects</b>	n=135	100%
blocking	n=135	100%
Pain	n=135	100%
Noise	n=135	100%
<b>Knowledge of the risk of relapse (Yes)</b>	n=135	100 %

<b>Knowledge of behaviour in relapse (Yes)</b>	n=135	100 %
<b>Knowledge of the risk of failure (Yes)</b>	n=135	100 %
<b>Knowledge of causes of failure (Yes)</b>	n=135	100 %
<b>Knowledge of prevention strategies (Yes)</b>	n=135	100 %

### 3.2. Evaluation of the understanding of the risks of orthodontic treatment (Phase T1)

#### 3.2.1. Assessment of the Knowledge of Dental Adverse Events (Table 2)

Our study showed that for all groups a, b and c, patients were aware that dental undesirable effects may be inherent to orthodontic treatment as well as carious and coloring risks with no significant difference between the three groups. For the risk of necrosis, group (a) was better informed (n = 28) or 80% who responded to this risk against 60% for both groups (b) and (c) with a non-significant difference ( $p > 0.005$ )

#### 3.2.2. Assessment of the knowledge of periodontal adverse effects (Table 2)

According to our study; the three groups were well informed about periodontal adverse effects, with a percentage of 100%. For the risk of gingival inflammation, the respondents in group (a) were the best informed, with a percentage of 100% against 97.14% for group (b) and 82.9% for group (c) and with a significant difference between the three groups. The highest information rate for the risk of gingival recession was noted in group (b) a percentage of 100% against 97.1% for the group (a) and 82.9% for the group (c) with a significant difference ( $p < 0.05$ ). No significant difference was found for the root resorption risk, between group (a) with a percentage of 51.4%, group (b) with a percentage of 65.7% and group (c) with a percentage of 57.1%.

#### 3.2.3. Assessment of the knowledge of articular effects (Table 2)

For the risk of blocking, an information rate of 85.7% for group (a), 65.7% for group (b) and 71.4% for group (c) with no statistical difference between the three groups. Regarding the risk of pain, the best rate of information was noted for group (b) with 100%, followed by group (a) with a rate of 97.1% and 77.1% for group (c) with a significant difference ( $p < 0.05$ ). For the risk of articular noise, there was a better information rate for group (b) with 100%, and 77.1% for group (a) and (c) with a statistically significant difference ( $p < 0.05$ ).

#### 3.2.4. Assessment of knowledge of the risk of relapse (Table 2)

An information rate of 100% was noted for the three groups (a) (b) and (c) with no noticeable difference between the three groups.

#### 3.2.5. Assessing the knowledge of behavior during relapse (Table 2)

An information rate of 100% was noted for the three groups (a) (b) and (c) with no noticeable difference between the three groups.

#### 3.2.6. Assessment of the knowledge of the risk of failure (Table 2)

An information rate of 100% was noted for the three groups (a) (b) and (c) with no noticeable difference between the three groups.

### 3.2.7. Evaluation of the knowledge of prevention (Table 5)

An information rate of 100% was noted for the three groups (a) (b) and (c) with no noticeable difference between the three groups.

Table 2: Evaluation of the understanding of the risks of orthodontic treatment (Phase T1)

	a	b	c	Chi-2 test
<b>Knowledge of dental effects</b>	n=35 (100%)	n=35 (100%)	n=35 (100%)	
carious risk	n=35 (100%)	n=35 (100%)	n=35 (100%)	
risk of staining	n=35 (100%)	n=35 (100%)	n=35 (100%)	
risk of necrosis	n=28(80%)	n=21 (60%)	n=21(60%)	0,122 ((NS)
<b>Knowledge of periodontal effects</b>	n=35 (100%)	n=35 (100%)	n=35 (100%)	
Gingival inflammation	n=35 (100%)	n=34 (97,14%)	n=29 (82,9%)	0,009 (S)
Recession reduction	n=34 (97,1%) n=18 (51,4%)	n=35(100%) n=23 (65,7%)	n=29 (82,9%) n=20 (57,1%)	0,009 (S) 0,476(NS)
<b>Knowledge of joint effects</b>	n=35 (100%)	n=35 (100%)	n=35 (100%)	
blocking	n=30 (85,7%)	n=23 (65,7%)	n=25 (71,4%)	0,143 (NS)
Pain	n=34 (97,1%)	n=35 (100%)	n=27 (77,1%)	0,001 (S)
Noise	n=27 (77,1%)	n=35 (100%)	n=27 (77,1%)	0,009 (S)
<b>Knowledge of the risk of relapse (Yes)</b>	n=35 (100%)	n=35 (100%)	n=35 (100%)	
<b>Knowledge of behavior in relapse (Yes)</b>	n=35 (100%)	n=35 (100%)	n=35 (100%)	
<b>Knowledge of the risk of failure (Yes)</b>	n=35 (100%)	n=35 (100%)	n=35 (100%)	
<b>Knowledge of causes of failure (Yes)</b>	n=35 (100%)	n=35 (100%)	n=35 (100%)	
<b>Knowledge of prevention strategies (Yes)</b>	n=35 (100%)	n=35 (100%)	n=35 (100%)	

### 3.3. Evaluation of the understanding of the orthodontic treatment risks (Phase T2)

#### 3.3.1. Assessment of Knowledge of Dental Adverse Effects (Table 3)

An information rate of 100% was noted regarding the knowledge of dental adverse effects, carious risk, staining and the risk of necrosis with no difference between the 3 groups (a) (b) and (c).

### 3.3.2. Assessment of knowledge of periodontal adverse effects (Table 3)

The three groups were well informed about the periodontal adverse effects, with a percentage of 100% with no difference between the three groups for risk of gingival inflammation, gingival recession, except for the risk of root resorption where the respondents of group (b) and (c) were better informed with a significant difference ( $p < 0.05$ ).

### 3.3.3. Assessment of knowledge of articular effects (Table 3)

For the knowledge of the joint adverse effects, and the risk of pain, the information rate was similar between the three groups (a) (b) and (c) with no difference. For the risk of blocking, the candidates in group (c) were better informed than group (a) and (b) with a non-significant difference ( $p > 0.05$ ). Regarding the risk of articular noise, the candidates were better informed with audiovisual tools, group (b) and (c) with a percentage of 100% against 85.7% for the group (a) either one with a significant difference ( $p < 0.05$ ).

### 3.3.4. Assessment of the knowledge of the risk of relapse (Table 6)

An information rate of 100% was noted for the three groups (a) (b) and (c) with no statistically significant difference between the three groups.

### 3.3.5. Assessing the knowledge of the behavior in case of a relapse (Table 3)

An information rate of 100% was noted for the three groups (a) (b) and (c) with no noticeable difference between the three groups.

### 3.3.6. Assessment of the knowledge of the risk of failure (Table 3)

An information rate of 100% was noted for the three groups (a) (b) and (c) with no noticeable difference between the three groups.

### 3.3.7. Evaluation of the knowledge of means of prevention (Table 3)

An information rate of 100% was noted for the three groups (a) (b) and (c) with no noticeable difference between the three groups.

Table 3: Evaluation of the understanding of the risks of the orthodontic treatment (Phase T2)

	a	b	c	Chi-2 test
<b>Knowledge of dental effects</b>	n=35 (100%)	n=35 (100%)	n=35 (100%)	
carious risk	n=35 (100%)	n=35 (100%)	n=35 (100%)	
risk of staining	n=35 (100%)	n=35 (100%)	n=35 (100%)	
risk of necrosis	n=35(100%)	n=35 (100%)	n=35(100%)	
<b>Knowledge of periodontal effects</b>	n=35 (100%)	n=35 (100%)	n=35 (100%)	
Gingival inflammation	n=35 (100%)	n=35 (100%)	n=35 (100%)	
Recession	n=35 (100%)	n=35 (100%)	n=35 (100%)	
reduction	n=27 (77,1%)	n=35 (100%)	n=35 (100%)	0,0001 (S)
<b>Knowledge of joint effects</b>	n=35 (100%)	n=35 (100%)	n=35 (100%)	
blocking	n=34 (2,9%)	n=34 (2,9%)	n=35 (100%)	0,601 (NS)

Pain	n=35 (100%)	n=35 (100%)	n=35 (100%)	0,005 (S)
Noise	n=30 (85,7%)	n=35 (100%)	n=35 (100%)	
<b>Knowledge of the risk of relapse (Yes)</b>	n=35 (100%)	n=35 (100%)	n=35 (100%)	
<b>Knowledge of behavior in relapse (Yes)</b>	n=35 (100%)	n=35 (100%)	n=35 (100%)	
<b>Knowledge of the risk of failure (Yes)</b>	n=35 (100%)	n=35 (100%)	n=35 (100%)	
<b>Knowledge of causes of failure (Yes)</b>	n=35 (100%)	n=35 (100%)	n=35 (100%)	
<b>Knowledge of prevention strategies (Yes)</b>	n=35 (100%)	n=35 (100%)	n=35 (100%)	

#### 4. Discussion and Conclusion

The purpose of this study was to produce and validate three patient communication and information tools ; a PowerPoint presentation , a video and a written brochure. The tools included General information on the definition of the orthodontic treatment, the means of diagnosis, the information of the patients on the diagnosis, the nature of the treatment, the fees and the duration of the treatment, as well as the explanation of the risks inherent to orthodontic treatment.

These tools were then evaluated through three groups (a) (b) and (c), of which each was given a different form to assess its reliability. This work comes to complete the study conducted in our care unit in April 2010, which has identified a real need for education and information of the patients on their orthodontic treatment and on the risks that may accompany it. Indeed, this study showed that the consent process works well regarding the diagnosis and the treatment plan. And much less concerning the knowledge of certain potential and sometimes irreversible risks, in particular the knowledge of the carious risk, the risk of necrosis, the risk of resorption and the risk of recession. Many of our patients were unaware of the risk of recurrence and the risk of failure of the orthodontic treatment.

The majority of our respondents (77%), preferred to consult the tools in Arabic. This suggests that it might be better to use these tools, while respecting the familiarity and sensitivity of the target population with regards to their mother tongue language, in order to facilitate communication of the message. The reliability of these tools was verified in two stages T1 and T2 after one month of the first phase of information T1, the results showed no statistically significant difference between the information during the short and the medium term ( $p > 0, 05$ ). The results showed that all three tools significantly improved patients' knowledge levels. Nevertheless, for certain risks, audiovisual tools were better in terms of information efficiency. In other terms the effectiveness of audiovisual tools was much better with regards to certain potential risks, in particular the risk of gingival inflammation, gingival recession (100%), root resorption (65.7%) and joint sound (100%) with a statistically significant difference ( $p < 0.05$ ).

Within same context, few studies have been conducted to validate the communication tools in the orthodontic treatment education. Moreover, several studies have evaluated the contribution of audiovisual tools to traditional information in the medical field, in order to determine the factors influencing patients' understanding. In this sense, a recent randomized controlled trial driven by Carter and Al. in 2022 aiming to compare the efficacy of 2 methods of delivering information for orthodontic patients, one by giving printouts with handwritten descriptions, and the

other via an audio-visual presentation (PowerPoint). Immediate and six-months Interviews of each group of patients were realized. At six-month follow-up, there were no significant differences between the two methods in terms of information retention and comprehension, and according to this trial, there is no better consent collection method to ensure that patient and parent information is preserved for months after starting treatment. (Carter, 2022).

Another randomized controlled trial was conducted by Ahn and al. (2019), to compare the effectiveness of three informative methods for short-term and long-term information recall for orthodontic patients and parents. In this trial, participants received an audiovisual presentation on orthodontic treatment by either leaflets, generic mind map, or participant's customized mind map. It was concluded that there was a small but significant improvement in information retention using mind maps compared to leaflets; and that there was no statistical difference between the type of mind map. And because of information recall degradation from short to long term in all groups, Ahn and al. suggested to repeat the information at follow-up appointments. (Hyun-baek, 2019)

A third study conducted in England by Patel J. et al (2008), aiming to determine the factors influencing the patients' recall of the information presented in different forms (PowerPoint and written brochures), the written information was a commercial flyer on orthodontic treatment which was produced by the British Orthodontic Society and was widely used in the UK and has been verified for better understanding for younger patients (Patel, 2008). The recall of the information was assessed using a short and long-term questionnaire. Age, gender, ethnicity, and the time taken to display or read the information were recorded. Variations in the participants' intelligence might also have an impact on children's understanding of information. The study showed that age was not an important factor affecting the retention of information, which is consistent with the results of our study, that showed good scores at all ages. This study showed that the recall of the information by the patients was better with the group informed using PowerPoint presentations with a percentage of 100% against 67.5% with the group informed using the flyer.

Results' analysis showed that the information tool was the only statistically significant factor in the short and longer term in each group, the mean scores were similar for both questionnaires, suggesting that time was not a major factor in the retention of information. Another study, conducted by Thomson et al which aimed the investigation on the degree of retention of the information on orthodontic treatment presented in 3 different forms (written, visual and oral), in the short and long term, using closed and open questions showed no statistically significant difference between the different groups as well as for the time factor, this is not consistent with the results of our study (Thomson, 2001). A multicenter, randomized, cross-sectional study published in 2016 by winter et al, that aimed the assessment of the contribution of video, media and portable media (PVM) in improving knowledge and satisfaction of patients during the consent process for cystoscopy and ureteral stent insertion in comparison with standard verbal communication (SVC) (Winter, 2016), showed a patients' preference for tools (PVM) in the consent process. PVM improves the patient's understanding of SVC and is considered an effective way to improve the knowledge acquired during the consent process which is consistent with the results of our study.

In another double-blind, randomized study by Dallimore et al, published in 2016, they compared satisfaction and recall of the information during physiotherapy rehabilitation sessions in patients who had hip surgery using two forms of information (Dallimore, 2016). The first group received information on the rehabilitation by means of an iPad and the second by a simple informative flyer. The study concluded that while both tools used have shown positive results on recalling the information and on patient satisfaction, the iPad remains the most effective tool for improving the understanding and the recall of the information and generated the most satisfaction ( $p < 0.01$ ), which is consistent with the results of our study, compared to the multimedia tools that we used in particular the PowerPoint presentation, and the video.

In parallel, and regarding the education of health professionals, another recent study conducted by Kam et al (2016), aimed to compare the contribution of PVM means of communication with traditional information tools such as conferences and tutorials, during the educational training of nurse assistants for the surgical block (Kam, 2016). To achieve this goal, they conducted a multicenter, cross-controlled, randomized trial. The acquisition of

knowledge was collected by means of a questionnaire, and the satisfaction of the method of delivery of the education was measured using another satisfaction questionnaire.

The study concluded that MLP information provides a new and effective method for providing nurses with the information in surgical procedures, improves recall of knowledge, and is more satisfying for the candidates. Thus, the three tools i.e.: the written flyers, PowerPoint presentation and video have been satisfactorily effective in terms of informing and educating patients during the consent process, and can be considered as valid, reliable and practical tools in informing patients on the orthodontic treatment, its ramifications and its potential risks. Nowadays, patient's information is above all, a right and a practitioner's duty which implies serious legal responsibilities.

These studies showed that the information tool remains the most important factor to consider during the informed consent process. The use of other tools than the traditional written information including PowerPoint presentations, a video and the simple access to information via the internet by taking advantage of the growing explosion of Android devices in particular among the youngest patients, could improve the understanding and the recall of information, as well as the level of motivation and therefore reduce the anxiety among patients. This can be a significant strength, which will improve the level of cooperation of patients, much desired for the sole purpose of offering and providing a better quality of care.

In sum, the disclosure of information requires communication skills on behalf of physicians, and requires new abilities that will require special attention. In light of the reading of published scientific literature on this subject, it can be concluded that the present study has shown that the use of audiovisual tools in the patient education process has positive effects on the recall of information. The use of video and PowerPoint presentations lead to significantly better recall scores especially regarding some risks. The use of modern technology for patient's education and facilitating the access to information is becoming a must for a good service delivery. A controlled, randomized trial by Fraval et al, published in 2015 that compared the quality of informed consent obtained in patients who were candidates for surgery; using two methods, traditional verbal and web-based educational tools showed that using the web has improved knowledge (86%) and reduced anxiety among patients (60%) (Fraval, 2015). As orthodontic patient's education is a component that has the potential to affect the outcome of treatment, including the perception of the quality of the patient's therapy. Patient education must, therefore be designed to meet the needs of the patients and the demands of the treatment.

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# Evaluation of Prevalence of Congenital Anomalies in Children and Infants Admitted to NICU and IPD of Bamyan Provincial Hospital in 2018- 2023

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## Abstract

**Background & Aim:** Congenital Anomalies are one of the most important causes of disability and death of infants in developing and advanced countries, and the cost of hospitalization and treatment of these children puts a heavy burden on the health system and their families. Therefore, in this research, it has been considered to determine the prevalence of congenital Anomalies in infants Admitted to NICU and IPD. **Materials & methods:** This is cross-sectional retrospective descriptive study, all infants and children who were admitted to the IPD and NICU of Bamyan provincial hospital from 2018 to September 15, 2023 with the diagnosis of one or more congenital Anomalies were studied. To collect data, after obtaining the permission, NICU's and IPD's register books were accessed. The required data were collected through these books, which included diagnosis and patients' demographic characteristics and additional information was collected through contact with physicians. Data were analyzed and presented for SPSS software version 20 and also using descriptive statistics (mean, standard deviation, frequency and frequency percentage). **Results:** from 679 infants and children diagnosed with congenital Anomalies, 172 cases (25.4%) were congenital heart diseases (CHD), with the highest frequency in the first degree, 153 cases (22.5%) were seizures and 115 cases (17%) were Neural tube defect (NTD) and 94 cases (13.8%) were Blood Disorders and also 94 cases (13.8%) were cerebral palsy (CP) and 44 cases (6.5%) were chromosomal disorders and 7 cases (1%) were cleft lip and Clift palate. Also, patients with chromosomal disorders were include Down syndrome and Nephrotic syndrome and patients with Blood Disorders included Anemia and thalassemia. Patients with Neural tube defect included three type, Encephalocoele, Anencephaly, Spina Bifida, Most of these patients died, or became paralyzed from the legs after surgery. Cerebral palsy patients also had seizures, and most of the statistical population was male with 398 cases (58%) out of all patients. **Conclusions:** The frequency of congenital heart diseases, seizures and nervous system disorders was higher compared to other congenital Anomalies. Therefore, in order to reduce the prevalence of the mentioned disorders, informing young mothers and families about the risk factors of these diseases to different ways is very important.

**Keywords:** Congenital Anomalies, Prevalence, Infants, Frequency, Bamyan

## 1. Introduction

Congenital Anomalies are developmental errors of the fetus that are present at birth and are divided into structural and functional types (Jennifer 2010). According to the report of the World Health Organization, three million babies are born with congenital Anomalies every year, and the disease is the cause of death of 495,000 children in the world. Congenital Anomalies are one of the most important causes of disability and death of children in developing and advanced countries. The cost of hospitalization and treatment or rehabilitation of these children and infants puts a heavy burden on the health system, society and their families (Shawky 2011). Many studies have suggested the multifactorial nature of the factors that cause congenital anomalies, which include genetics (Pediatric 2013), environmental factors, and the interaction of genes and the environment (Jenkins, Taparia 2007). Therefore, any serious action to determine the prevalence and identify the factors influencing the development of congenital Anomalies and their prevention will lead to the health and improvement of the future generation as much as possible and prevent social and economic damages (Zarante 2009). In the studies of Shawky and his colleague (2011) in Egypt, the prevalence of congenital Anomalies was reported as 13.5%. In the study of Jennifer (2010) in England, 3% of babies and from study of Linhart (2000) 8.7% of babies in Israel are born with congenital Anomalies. In the study of Abdi Rad and his colleagues (2008) in Urmia city, the prevalence of congenital Anomalies was reported as 187 cases in 10,000. In the study of Karbasi and his colleagues (2009) in Yazd, the prevalence of congenital Anomalies was 2.8%. Afghanistan is a traditional society that due to the high rate of family marriages, the prevalence of congenital Anomalies is more frequent than other societies. These diseases are difficult and expensive to treat, and affected patients must be under special care for the rest of their lives. For this reason, it is not possible for most families to provide medical and care expenses. The lack of professionals, the lack of specialized health centers, and the lack of availability of medicines for patients and appropriate medical attachment to diagnose the disease, and the lack of accurate statistics of patients in the Afghanistan, have multiplied the problems of these patient (Afghan Voice News Agency 2016). In the past 12 years, more than 24,000 children with heart holes have been registered in the Afghan Red Crescent Society; Up to 12,500 children with this disease have been treated, and 11,000 more children are waiting for treatment, and about 10,000 children died while waiting for treatment (motmaen 2023). Studies conducted in different parts of the world have shown that the prevalence of congenital Anomalies is different in different countries and even in different cities of the same country. Considering the geographical, environmental and cultural, social, racial and economic differences of societies, regional studies in different societies can be an effective step in preventing the spread of birth defects and death and subsequent disabilities. Therefore, the present study was conducted with the aim of determining the frequency of congenital Anomalies in infants and children Admitted in Bamyán Provincial Hospital during the study period.

## 2. Materials & methods

This is cross-sectional retrospective descriptive study, all infants and children who were admitted to the IPD and NICU of Bamyán provincial hospital from 2018 to September 15, 2023 with the diagnosis of one or more congenital Anomalies were studied. To collect data, after obtaining the permission, NICU's and IPD's register books were accessed. The required data were collected through these books, which included diagnosis and patients' demographic characteristics and additional information was collected through contact with physicians. Data were analyzed and presented for SPSS software version 20 and also using descriptive statistics (mean, standard deviation, frequency and frequency percentage).

## 3. Results

From 679 infants and children with congenital Anomalies who were admitted to NICU and IPD in Bamyán provincial hospital from 20018 to 15 September 2023, were included in the study. During this period, an average of 113 cases of Admitted infants and children were congenital patients. Demographic characteristics of infants and children are given in Table 1. According to the results, among these patients, 216 children (31.9%) were under 28 days old and 463 infants (68.1%) were over 28 days old. The minimum and maximum age of the patients was 1 day and 14 years, respectively. 397 (58.4%) patients were male and 282 (41.6%) were female.

Table 1: Characteristics of infants and children participating in the study

Characteristic		frequency	percentage
Age	Under 28 days old	216	31.9
	Over 28 days old	463	68.1
gender	Male	397	58.4
	Female	282	41.6

According to the Table 2, which shows the results of examining the type frequency of congenital anomalies. Among all the studied patients, 172 cases (25.4%) had congenital heart and 153 cases (22.5%) had seizures and epilepsy and 115 cases (17%) had Neural tube defect(NTD) and 94 cases had blood disorders, and also 94 cases had cerebral palsy (13.8%), 44 cases (6.5%) had chromosomal disorders, and 7 cases (1%) cleft lip and cleft palate. According to the data, congenital heart diseases with the highest frequency are in the first degree and other anomalies are in the second to sixth degree respectively. Also, patients with chromosomal disorders were include Down syndrome and Nephrotic syndrome and patients with Blood Disorders included Anemia and thalassemia. Patients with Neural tube defect included three type, Encephalocoele, Anencephaly, Spina Bifida, Most of these patients died, or became paralyzed from the legs after surgery. Cerebral palsy patients also had seizures.

Table 2: frequency distribution type of congenital Anomalies of infants and children under study

Types of congenital anomalies	frequency	percentage
Congenital heart diseases	172	25.4
Seizures and epilepsy	153	22.5
Neural tube defect	115	17
Blood disorders	94	13.8
Cerebral Palsy	94	13.8
Chromosomal disorders	44	6.5
Cleft lips and cleft palate	7	1
total	679	100

Chart 1 shows the percentage of frequency of congenital anomalies according to gender of the studied infants and children. The results show that among male patients with congenital anomalies, the most common congenital anomalies was seizure and epilepsy with the highest percentage (27.2%) and with few different, congenital heart diseases with (26.5%) was in the second degree. And neural tube defect, blood disorders, were ranked third and fourth with (13%, 12.5%) respectively.

Also, among the female patients who were suffering from congenital anomalies, the most common congenital anomalies was congenital heart diseases with (23.8%) and neural tube defect ,cerebral palsy, seizures and blood disorders. They were ranked second to fourth with (22.3%, 16.7%, 16%, 16%) respectively.

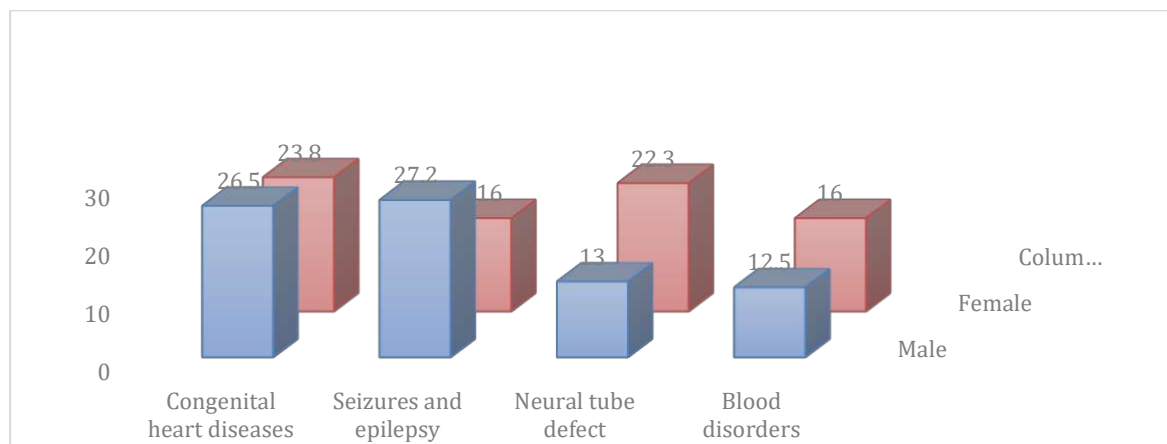


Chart 1: percentage of frequency of congenital Anomalies according to gender of the studied infants and children

In table3 (number of patients, number of anomalies, Mean, standard deviation) of the studied patients is given considering gender. According to Table 3, the number of male patients with an average of 56, standard deviation is 34, and the number of female patients with an average of 40, standard deviation is 20. Therefore, there can be a relationship between the gender of patients and congenital disorders.

Table 3: number of patients and number of anomalies and Mean, standard deviation of the studied patients considering gender

Gander	Number of patients	Number of anomalies	Mean	standard deviation
Male	397	7	56	34
Female	282	7	40	20

Table 4 shows the frequency and percentage of congenital Anomalies considering the age of the studied patients. According to the results, among the children with congenital anomalies, Neural tube defect, which is among the overt congenital Anomalies that can be diagnosed in new born, have been identified with the highest percentage (53.2%) in this research, and the diseases CP has not been diagnosed in children. Among infants, seizures with the highest percentage (29.4%) and congenital heart diseases with percentage (25.5%) are ranked first and second.

Table 4: frequency and percentage of congenital Anomalies with age under 28 days old (children) and age over 28 days old (infants)

congenital Anomalies	Children		Infants	
	frequency	percentage	frequency	percentage
Congenital heart diseases	54	25	118	22.5
Seizures and epilepsy	17	7.9	136	29.4
Neural tube defect	115	53.2	0	0
Blood disorders	12	5.6	82	17.7
Cerebral Palsy	0	0	94	20.3
Chromosomal disorders	14	6.5	30	6.5
Cleft lips and cleft palate	4	1.8	3	0.6
total	216	100	463	100

Table 5 (number, mean, standard deviation) of patients under study is shown yearly. According to the results, the highest and lowest number of patients with congenital anomalies were hospitalized in 2022 with mean of 23, standard deviation of 15.1 and in 2019 with mean of 12, standard deviation of 7, respectively.

Table 5: number and mean and standard deviation of patients under study

year	Number of patients	Mean	Number of anomalies	standard deviation
2018	111	16	7	11.2
2019	82	12	7	7
2020	105	15	7	7.9
2021	130	18	7	12.1
2022	164	23	7	15.1
2023	87	12	7	7.4

#### 4. Discuss

This study was conducted with the aim of investigating the prevalence of congenital anomalies in children and infants Admitted in Bamyan Provincial Hospital from 2018 to September 15, 2023. According to the results, 32% of the studied population was under 28 days old and 68% was over 28 days old, and most of the population was male (58%). Also, in the examination of the frequency of congenital anomalies, the most common congenital anomalies was congenital heart diseases, (CHD) (25.4%), with the highest frequency in the first degree and

seizures and epilepsy (22.5%), neural tube defect (17%) and blood disorders (13.8%), cerebral palsy (13.8%), chromosomal disorders (6.5%), and cleft lip and cleft palate (1%) were in the second degree to sixth, respectively. The results of this study were consistent with the studies conducted in Golestan province and Birjand city, where the most common congenital anomalies was congenital heart disease. While in the research conducted in the northwest of Iran, the most common disease was related to the nervous system. Also, in the studies of Tomater and his colleagues (2009) in Turkey, the most common congenital anomalies observed were disorder, related to the central nervous system and the skeletal and muscular system.

In this study, some less important congenital anomalies in infants and children may not have been diagnosed or recorded. Considering that the data of the study were extracted from the register books of the relevant departments, and in these books, the diagnosis of the disease, age, gender and place of residence of the patient are available. Therefore, it is suggested that in the future studies to determine the prevalence of congenital anomalies among newborns using patient files, although there are limitations in this method, because patient files are completed based on clinical needs and not based on. In research studies, some variables may not be included in the patient file. Therefore, it is better to identify and investigate the causes and factors of the disease within 24 hours of the birth of sick new born in order to obtain more accurate and useful results.

## 5. Conclusion

Considering the different prevalence and frequency of congenital anomalies and numerous regional factors related to these anomalies in the world; In order to reduce the high costs for individuals, communities and the health system due to the prevalence of congenital anomalies in infants, identifying the most common anomalies and its risk factors and conducting regional studies have an effective role in this field.

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# Effect of PM2.5 Exposure among Children with Asthma: A Systematic Review

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## Abstract

**Introduction:** Particulate matter (PM), which encompasses tiny particles (PM2.5) and inhalable coarse particles (PM10), is a significant environmental issue that carries potential health consequences, particularly for children, including those who have asthma. This systematic review aims to examine the association between exposure to PM2.5 and the exacerbation of childhood asthma, focusing on publications published between 2018 and 2023. **Methods:** A comprehensive PubMed search retrieved 147 records, leading to the selection of 11 articles for full-text assessment. Subsequently, four studies meeting the criteria were included in this review, following a meticulous selection process. These studies were rigorously assessed for methodology, study design, and key findings. **Results:** The chosen studies' findings indicate a negative correlation between short-term PM2.5 exposure and a range of lung function indicators in children diagnosed with asthma. This suggests that prenatal PM2.5 exposure may have enduring effects on respiratory health. **Discussion:** Childhood asthma, marked by complex pathophysiology involving chronic inflammation and hyperresponsive airways, is indeed influenced by PM2.5 exposure, underlining a multifaceted challenge for public health. **Conclusion:** This systematic review underscores the importance of addressing environmental PM2.5 as a critical public health concern, particularly for children with asthma. Although the studies in this analysis offer valuable insights, they also underscore the need for additional research to understand the intricate link between exposure to PM2.5 and the worsening of pediatric asthma.

**Keywords:** PM2.5, Exposure, Children, Asthma, Respiratory



## 1. Introduction

Particulate matter (PM) encompasses many components, including minuscule solid particles and tiny liquid droplets inside the Earth's atmosphere. The droplets or particles comprise several chemical compositions varying according to the emissions' source (Nevada Department of Environmental Protection, n.d.). Particle pollution is classified into two categories by the United States Environmental Protection Agency (USEPA) (Nevada Department of Environmental Protection, n.d.). "Fine particles," which include smoke and haze, have a diameter of no more than 2.5 microns. Another name for fine particles is PM<sub>2.5</sub>. Particles can be emitted into the atmosphere through two primary pathways: direct release from forest fires and indirect release through the atmospheric interactions of gases from industrial facilities, power plants, and vehicles. Because PM<sub>2.5</sub> is so tiny, it can travel incredibly long distances while remaining suspended in the atmosphere (Garrett, 2014). Areas with high traffic and dusty industries have been observed to contain inhalable coarse particles with a diameter bigger than 2.5 microns but less than 10 microns. In this context, the inhalable coarse particles are called PM<sub>10</sub> (Nevada Department of Environmental Protection, n.d.).

The National Ambient Air Quality Standards (NAAQS) encompass three regulatory standards specifically targeting PM<sub>2.5</sub>: (Nevada Department of Environmental Protection, n.d.) leading standard of 12 micrograms per cubic meter annually arithmetic mean ( $\mu\text{g}/\text{m}^3$ ), (Garrett, 2014) a supplementary standard of 15  $\mu\text{g}/\text{m}^3$  (annual arithmetic mean) and (Meghji et al., 2021) 24-hour average not to exceed 35  $\mu\text{g}/\text{m}^3$ . PM<sub>10</sub> has a 24-hour average of 150  $\mu\text{g}/\text{m}^3$  as the primary and secondary standard (Garrett, 2014). One of the most frequent childhood ailments is asthma. Low- and middle-income nations caused 96 percent of asthma-related fatalities and 84% of disability—adjusted life-years (Meghji et al., 2021). A Japanese study found peak expiratory flow dropped with each ten  $\mu\text{g}/\text{m}^3$  increase in PM<sub>2.5</sub> (PEF, changes: -2.96, 95% CI: -4.55, -1.37) (Zhou et al., 2022). An increase in PM<sub>2.5</sub> levels was associated with a significant reduction in forced expiratory volume in 1 second (FEV<sub>1</sub>) among children diagnosed with asthma, according to the findings of a birth cohort study conducted by the Columbia Center for Children's Environmental Health (CCCEH). This connection's regression coefficient ( $\beta$ ) was -0.15, with a 95% confidence interval from -0.29 to -0.01 (Zhou et al., 2022).

The relationship between PM<sub>2.5</sub> and pediatric asthma is complex and has multiple dimensions. PM<sub>2.5</sub> refers to diminutive particulate matter suspended in the air, characterized by a diameter of 2.5 micrometers or smaller. PM<sub>2.5</sub> particles possess a size that enables them to infiltrate the respiratory system profoundly. Upon inhalation, these particles have the potential to incite an inflammatory reaction. The presence of inflammation has the potential to impact the airways, rendering them more susceptible to sensitivity. Consequently, this heightened sensitivity may result in the manifestation of asthma symptoms among youngsters who possess a predisposition to this particular ailment (Sun et al., 2020). This contention is supported by an abundance of scientific research studies that have established a positive correlation between increased PM<sub>2.5</sub> exposure and a higher prevalence of asthma in children. The available evidence indicates that extended exposure to PM<sub>2.5</sub> is linked to the exacerbation of pre-existing asthma symptoms in pediatric populations (Pothirat et al., 2019).

Examining the correlation between PM<sub>2.5</sub> and childhood asthma holds excellent significance due to the widespread prevalence and substantial impact of this public health concern. Gaining a comprehensive understanding of the function of PM<sub>2.5</sub> in the development and worsening of asthma will facilitate the formulation of efficacious preventative measures, thereby mitigating the burden of this respiratory condition among children. Research endeavors can facilitate the identification of demographic groups that exhibit heightened susceptibility to the impacts of PM<sub>2.5</sub> exposure. Such children possess pre-existing respiratory ailments or individuals residing in regions with elevated pollution levels. This information has the potential to advise and guide targeted actions and healthcare strategies for these specific demographic groups. In conclusion, examining the correlation between PM<sub>2.5</sub> and childhood asthma holds significant importance in safeguarding the well-being of children, enhancing air quality, and extending our comprehension of respiratory ailments, yielding advantageous outcomes for public health.

## 2. Method

### 2.1 Search Strategy

The systematic review followed the principles outlined in the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA). The utilization of the “Participants,” “Exposure,” “Comparator”, and “Outcome” (PECO) framework was employed in order to construct a precise study subject. The current systematic review sought to answer the question: "Is exposure to PM2.5 associated with asthma exacerbation in children?". Research investigating the correlation between exposure to PM2.5 and asthma in children has been documented in two prominent English databases, PubMed and Google Scholar. Our search strategy used combinations of air pollution terms ("air pollution, "particulate matter," "air pollutants") and respiratory disease terms ("asthma," "bronchitis," and "bronchiolitis").

The PubMed search string used turned into as follows:

```
((children) AND ((particulate matter 2.5) OR (pm2.5))) AND (((asthma) OR (bronchitis)) OR (bronchiolitis)) OR (lower respiratory infections [MeSH Terms])
```

### 2.2 Eligibility criteria and study selection

The researchers applied the following inclusion criteria in order to identify and choose pertinent papers: (i) original peer-reviewed journals; (ii) published in full-text; (iii) studies published in 2017 until 2023; (iv) studies that identify objective measures of PM2.5; (v) the subject is a child with asthma. Studies were excluded if they met any of the following criteria: (i) not related to PM2.5 exposure; (ii) no quantitative results for the effects; (iii) with insufficient data.

### 2.3 Data extraction

In the initial search, after deleting duplicates, the first reviewer (CVA) assessed the title and abstract to ensure that the inclusion and exclusion criteria were met. To minimize bias, relevant studies were separately examined by the first and second reviewers (CVA and FNA) using Covidence (an online software for primary screening and data extraction created by the Cochrane Community) to examine the entire text of publications against the inclusion criteria. Before extracting data, CVA and FNA addressed all selected studies and unresolved issues between the two and the third reviewer, PAA. The details are shown in **Figure 1**.

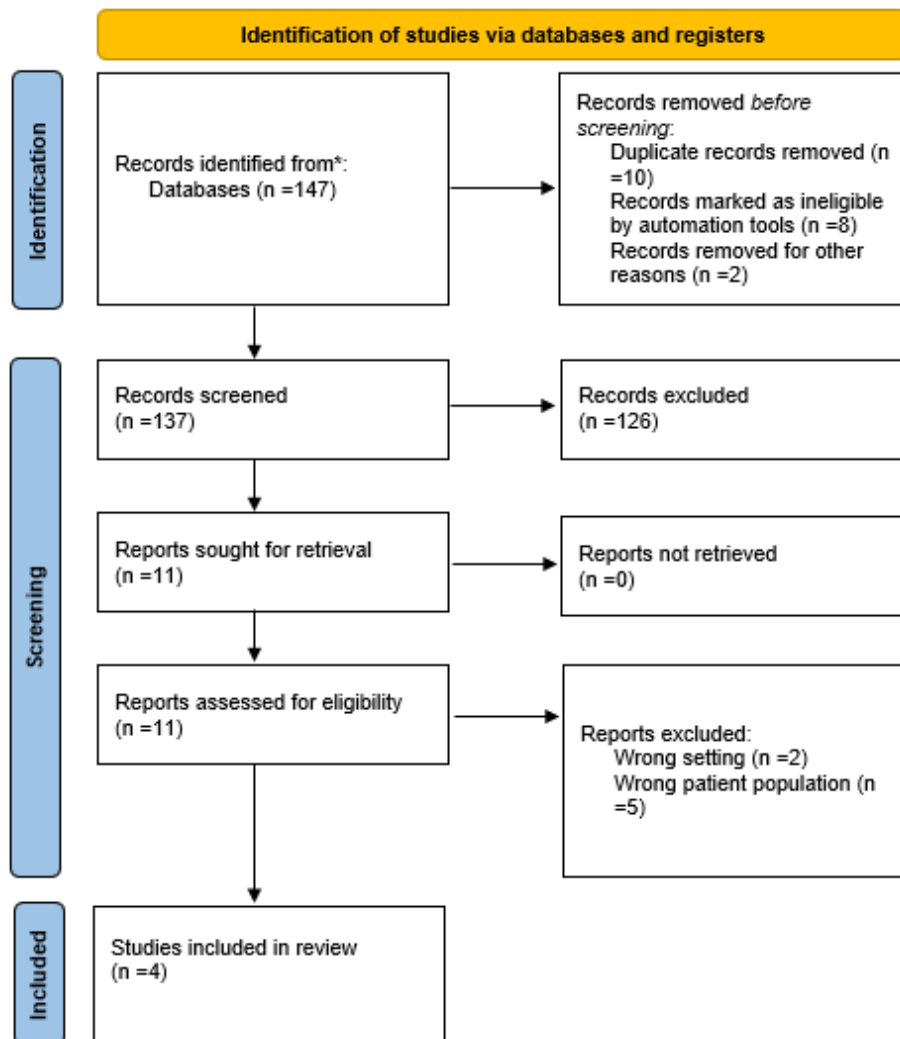


Figure 1: PRISMA flow diagram

#### 2.4 Methodological quality assessment

Due to the absence of a validated scale, it is presently impossible to assess the quality of time-series, panel, and case-crossover study designs. Consequently, the scale proposed by Mustafi et al., derived from the reputable NOS scale, was employed to evaluate the quality of the entities above (Mustafić et al., 2012) and the Cochrane risk of bias tool (Higgins et al., 2011). Mustafi's personalized scale consisted of three items, with the allocation of "0-3" points to the respective factors as follows: The validation of depression assessment, which is classified as either 0 to indicate the absence of valid criteria or 1 to indicate the existence of valid criteria, as well as the assessment of air pollutant measurement quality (0: the measurements were not conducted on a daily basis or there was a data deficiency of more than 25%; 1: the measurements were conducted on a daily basis, with a 25% occurrence of missing data), and the extent of confounder adjustments (0: long-term trends, season, and air temperature were not accounted for in the analysis; 1: only long-term trends, season, and air temperature were adjusted with a score of 2). A study was deemed of "high quality" if it achieved the maximum score of 5 points across all three categories. Conversely, if the study did not attain the greatest score, it was categorized as "low quality."

#### 2.5 Risk of Bias Assessment

Furthermore, a comprehensive assessment was performed to evaluate the potential risk of bias (ROB) associated with each individual study. The notion being discussed is a relatively recent development within the field of environmental health research, and it is intricately connected to, yet distinct from, the evaluation of methodological rigor. The utilization of the Risk of Bias (ROB) assessment tool developed by the National Institutes of

Environmental Health Sciences National Toxicology Program Office of Health Assessment and Translation (OHAT) was employed to evaluate the potential bias in cohort and cross-sectional studies ("Welcome to the 2015 Annual Meeting," 2015). In light of the lack of a recognized and validated instrument for evaluating the risk of bias (ROB) in time-series and case-crossover studies, we undertook an assessment of their ROB using the OHAT tool and the University of California, San Francisco (UCSF) Navigation Guide (Lam et al., 2016). Critical factors, including confounding bias, exposure assessment, and outcome assessment, were evaluated in the selected studies utilizing the OHAT instrument and the UCSF Navigation Guide. Additional methodological criteria were taken into account, encompassing selection bias, attrition/exclusion bias, selective reporting bias, conflict of interest, and other potential causes of bias. The studies chosen for each of these domains were assessed and categorized as having a level of evidence classified as "low," "probably low," "probably high," or "high." Per the recommendations of the Navigation Guide's OHAT (Office of Health Assessment and Translation) tool, the scholarly journals utilized in our study exhibited a low degree of bias.

### 3. Results

#### 3.1 Study and participant characteristics

The studies in the analysis were conducted in three countries and employed various research approaches, including cross-sectional, cross-over intervention, and cohort designs. Two studies were undertaken in the People's Republic of China, one in the United States of America, and one in the Republic of Korea. Some studies did not indicate whether they were conducted in rural or urban areas.

The study and participant characteristics were comprehensively documented. The inclusion criteria specified that all participants were children. However, for this review, only data related to children were analyzed. No research reported relationships between religion, disability, or time dependence.

#### 3.2 Literature retrieval

The process of conducting research involves essential elements such as data analysis and reporting of the findings. All research reports need to include accurate, unbiased, thorough, and perceptive reporting of the analytical treatment of data (qualitative or quantitative). Psychologists use numerous ways to analyze data, and no methodology is universally accepted as long as it is suitable for the study questions being asked and the type of data being collected. The techniques employed must yield unambiguous, clear insights into the data and sustain their analytical demands, including robustness against assumptions that are violated.

Table 1: Summary of Selected Study Characteristic

No.	Title	Author, year (Country)	Study design	Aim of the study	Population	Results and Outcomes
1.	Early-life exposure to PM2.5 constituents and childhood asthma and wheezing: Findings from China, Children, Homes, Health Study	Zhang et al., 2022 (China)	Cross-sectional	To examine potential associations of early-life exposures to PM2.5 mass and its major chemical constituents with childhood asthma and wheezing.	30,325 preschool children aged 3-6 years	A total of 1205 children, comprising 4.0% of the sample, self-reported a medical diagnosis of asthma. The mean PM2.5 concentrations across all urban areas during the initial year following birth were recorded as $61.8 \pm 10.5 \mu\text{g}/\text{m}^3$ . These values exhibited a statistically significant correlation with an

						elevated likelihood of developing asthma.
2.	Personal exposure to PM2.5 oxidative potential in association with pulmonary pathophysiologic outcomes in children with Asthma	He et al., 2021 (China)	Cross-over study	To further examine the associations of health outcomes with personal exposures to PM2.5	43 children aged 5-13 years	The mass concentration of PM2.5 is 55.7 µg/m <sup>3</sup> . Variability in PM2.5 oxidative potential drives asthmatic children's airway resistance more than PM2.5 mass exposure.
3.	Long-Term Coarse Particulate Matter Exposure Is Associated with Asthma among Children in Medicaid	Keet et al., 2017 (US)	Cohort study	To understand the relationship between long-term fine and coarse PM exposure and asthma prevalence and morbidity among children	Children aged 5 to 20 years old	Asthma diagnosis prevalence increased with coarse PM exposure (RR = 1.006; 95% CI = 1.001-1.011), hospitalizations, and emergency department visits (RR = 1.017; 95% CI = 1.001-1.033), after adjusting for fine PM.
4.	Association between Peak Expiratory Flow Rate and Exposure Level to Indoor PM2.5 in Asthmatic Children, Using Data from the Escort Intervention Study	Kim et al., 2020 (Korea)	Cross-over intervention study	To evaluate the effects of indoor PM2.5 on children's peak expiratory flow rate (PEFR)	26 children aged between 6–12 years were diagnosed with asthma	They found a 6.5 µg/m <sup>3</sup> difference in indoor median PM2.5 levels between control and experiment groups. Asthmatic children with lower PEFR (0.2%, 95% CI = 0.1–0.5%) significantly increased indoor PM2.5 levels, even after controlling for other variables. Our multilevel model included a random intercept for each asthmatic child.

### 3.3 Increased risk of asthma through exposure to particular matter

There is still a dearth of definitive evidence establishing a conclusive association between exposure to PM2.5 and the manifestation of asthma outcomes in children. In their study, Kim et al. assessed PM2.5 and its impact on asthmatic children, finding a significant association between higher levels of exposure to PM2.5 and decreased peak expiratory flow rate (PEFR) (Kim et al., 2020). However, instead of focusing on asthma, the main focus of the study was on the simultaneous occurrence of acute respiratory symptoms and a mild decrease in lung function. In their study, Zhang et al. discovered a strong correlation between early-life exposures to a combination of primary PM2.5 elements and heightened chances of asthma and wheezing. However, no transparent relationships between specific compositions and wheeze were observed within the first year of life (Zhang et al., 2022). This finding aligns with a study conducted by He et al., which demonstrated that daily personal exposure to PM2.5 is associated with an elevated oxidative potential. This elevated oxidative potential is significantly correlated with increased small, significant, and total airway resistance, heightened airway impedance, reduced lung function, and lower scores indicative of specific asthma symptoms and overall symptom severity (He et al., 2021). According to a separate study conducted by Keet et al., it has been determined that there is a correlation between heightened

asthma prevalence and morbidity among children enrolled in Medicaid and increased exposure to elevated average levels of coarse particulate matter (PM). These findings underscore the necessity for direct monitoring of coarse PM and reevaluating long-term average levels of coarse PM pollution (Keet et al., 2018). Based on the research conducted by Kim et al., a noteworthy correlation has been observed between elevated levels of indoor PM<sub>2.5</sub> (particulate matter measuring 2.5 micrometers or smaller in diameter) on a daily or weekly basis and a reduction in peak expiratory flow rate (PEFR) among children diagnosed with asthma. The research study observed a decrease in peak expiratory flow rate (PEFR) by 0.2% (with a 95% confidence interval (CI) of 0.1 to 0.5) or by 1.2% (with a 95% CI of 0.1 to 2.7) for every 1 g/m<sup>3</sup> rise in indoor PM<sub>2.5</sub> concentrations (Kim et al., 2020).

#### 4. Discussion

Asthma is a multifaceted and diverse medical condition distinguished by persistent inflammation, temporary airflow limitations, and heightened airway sensitivity (Hirose et al., 2017). Around 300 million people globally have asthma (Huo & Zhang, 2018). Exposure to PM<sub>2.5</sub> has been linked to impaired lung function and the onset of acute asthma attacks in both children and adults, according to a growing body of epidemiological evidence. The current research conducted in Canada investigated the correlation between exposure to trace metals in PM<sub>2.5</sub> and heightened levels of exhaled nitric oxide among a group of school-age children diagnosed with asthma (Godri Pollitt et al., 2016). Duan et al. (Duan et al., 2021) found a negative correlation between short-term exposure to PM<sub>2.5</sub> and three respiratory health indicators: forced expiratory volume in one second (FEV<sub>1</sub>), forced vital capacity (FVC), and peak expiratory flow (PEF). Specifically, for every 10 g/m<sup>3</sup> increase in PM<sub>2.5</sub> at a lag of three days, FEV<sub>1</sub> decreased by 0.012 L, FVC decreased by 0.042 L, and PEF decreased by 0.061 L/s.

Currently, there is a widely held opinion that PM<sub>2.5</sub> has a substantial impact on the exacerbation of asthma, particularly in children who are considered to be more vulnerable in comparison to adults (Chi et al., 2019; Fan et al., 2016). According to projections made in 2015, it was estimated that PM<sub>2.5</sub> had contributed to a significant number of hospitalizations, ranging from 5 to 10 million, among individuals who have asthma. These hospitalizations accounted for around 4 to 9 percent of the global visits for this medical condition (Anenberg et al., 2018). Research findings have consistently indicated that PM<sub>2.5</sub> is the sole chemical compound that has exhibited an independent correlation with emergency room visits among individuals with asthma (Hsu et al., 2020). Furthermore, a research investigation in the South Texas region unveiled a positive correlation between elevated concentrations of PM<sub>2.5</sub> particles and an augmented probability of hospital readmissions in pediatric patients diagnosed with asthma (Baek et al., 2020). Research has indicated that individuals may have an elevated vulnerability to asthma development when exposed to small particulate matter measuring 2.5 micrometers or less (PM<sub>2.5</sub>) during their early childhood. Yan et al. (year) present findings that support the notion that prenatal exposure to PM<sub>2.5</sub> may have significant repercussions (Yan et al., 2020), raises the risk of asthma and wheezing in children and is more strongly related to the risk of asthma in children under the age of three. A recent comprehensive study conducted across multiple cities in the United States has provided evidence indicating that exposure to PM<sub>2.5</sub> pollution poses a significant risk to fetal lung development during the gestational period from 26 to 36 weeks. Based on the results of their study, an elevation of 2 g/m<sup>3</sup> in environmental PM<sub>2.5</sub> exposure was associated with a 1.29-fold rise in the likelihood of developing asthma (Hazlehurst et al., 2021).

From a research perspective, there exists a requirement for enhanced exposure assessment methods and precise asthma case definitions. Furthermore, utilizing a broader array of sampling methods for indoor and outdoor pollutants is crucial to fully understand the impact of asthma outcomes across the studies incorporated in the analysis. This is necessary as the findings of these studies were inconsistent and, in certain instances, lacked sufficient clarity in their definitions. Moreover, the existing data is insufficient to determine whether the potential elevation in asthma risk among youngsters varies by gender. Currently, there is limited comprehension of the potential danger associated with the inhalation of each substance. There were significant variations in the substances examined and the methodologies employed for their measurement across different investigations. However, the suitability of conducting a meta-analysis for this review may have been compromised not only by discrepancies in size and definitions but also by the heterogeneity in susceptibility among different individuals within the population and the diverse environmental contexts in which individuals spend their daily lives.

## 5. Conclusion

Individuals are subjected to a multifaceted amalgamation of biological, chemical, and physical components throughout their lifetimes. Although numerous nations have made advancements in air pollution regulation, the mitigation of environmental PM<sub>2.5</sub> continues to be a significant area of focus. This phenomenon is associated with an ongoing increase in morbidity and mortality rates across a range of disorders. Gaining insight into the impact of PM<sub>2.5</sub> on commonly occurring chronic respiratory conditions is an essential initial measure in preventing and identifying health issues associated with PM<sub>2.5</sub> exposure. Further multi-regional cooperation research is necessary to help mitigate the significant health burden caused by variations in PM<sub>2.5</sub> composition and concentration among countries and regions. This review highlights the necessity for more investigation into the impacts of indoor and outdoor air pollution on human health and well-being, employing objective measures. Additionally, it emphasizes the importance of maintaining uniformity in reporting research studies to facilitate comparability.

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# The Role of Al-Hijamah in Efforts to Prevent Heart Disease and Blood Vessels: A Systematic Review and Meta-analysis

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## Abstract

**Background:** Cupping therapy or Al-Hijamah is a traditional treatment the Prophet Muhammad SAW recommended. It has also become an effective alternative for ridding blood plasma of disease-causing substances, including cholesterol, which plays a role in cardiovascular disease. **Purpose:** To analyze the role of Al-Hijamah therapy or cupping in reducing cholesterol levels in the body as a preventive measure against heart disease and blood vessel disorders. **Methods:** Of the 513 articles collected, three articles were selected for analysis. Risk of Bias evaluated study quality for Randomized or RoB2 and ROBINS-I. Quantitative analysis using Review Manager 5.4.1, focusing on changes in total cholesterol, low-density lipoprotein, high-density lipoprotein, and triglycerides concentrations due to cupping therapy in healthy people. **Results and discussion:** Wet cupping therapy effectively reduced total cholesterol concentration (Pooled MD = -16.20, 95% CI (-16.20, -0.85), p=0.03, I<sup>2</sup> = 0%). Wet cupping effectively reduced low-density lipoprotein levels (Pooled MD = -17.48, 95% CI (-30.67, -4.30), p=0.009, I<sup>2</sup> = 0%), showing statistical significance. Wet cupping therapy effectively increased high-density lipoprotein levels (Pooled MD = 3.54, 95% CI (0.34,6.73), p=0.03, I<sup>2</sup> = 19%). Then, insignificant meta-analysis results for triglycerides concentration outcomes (Pooled MD = 3.58, 95% CI (-55.03,62.18), p=0.90, I<sup>2</sup> = 86%). **Conclusion:** Results from a systematic review and meta-analysis indicate that cupping therapy may be beneficial in managing cholesterol in healthy individuals, especially low-density lipoprotein. Further research with high-quality randomized control trials must confirm these findings and consider cupping a non-pharmacological intervention.

**Keywords:** Al-hijamah, Cholesterol, Low-Density Lipoprotein, High-Density Lipoprotein, Triglycerides, Cardiovascular Disease

## 1. Introduction

Cupping Therapy: Cupping in Arabic, known as Al-Hijamah, is a health therapy rooted in Islamic culture. The name Al-Hijamah itself comes from the word "Al-Haj," which means "to suck." The practice of Al-Hijamah or cupping has a special position in Islamic culture because cupping is a form of treatment recommended by the Prophet Muhammad SAW. Cupping therapy has even been around since the time of the Prophet Muhammad SAW, and this can be seen from the many hadiths that recommend Muslims to undergo cupping treatment (Umayyah, 2014). Cupping therapy is a historically popular treatment in Arab and Islamic countries. This therapy was recommended by Arab and Islamic doctors such as Ibn Sina (980-1037 AD) and Abu Bakr Al-Razi (854-925 AD) (Aboushanab & AlSanad, 2018).

The practice of cupping has become an integral part of Islamic medical practice, and this historical evidence illustrates the importance of cupping treatment in supporting the health and happiness of Muslims. As Rasulullah SAW said: "The medicine is found in three things, in cupping cuts, or drinking honey, or ironing tools (burning fire), and I forbid my people from ironing." (HR. Bukhari)(Muhammad Bin Isma'il Abu 'Abdullah Abu Al-Bukhari Al-Ja'fi n.d.). In another hadith, it is also said that Al-Hijamah (cupping) is the best treatment, as the Messenger of Allah SAW said: "Indeed the best method of treatment is cupping or the ideal method of treatment is cupping"(HR. At-Tirmidhi) (Ibnu et al.)

Al-Hijamah is a physical treatment method that acupuncturists and alternative medicine practitioners have long used. This method involves using glasses or plastic cups placed on the skin over the area requiring treatment or at specific acupuncture points. The main aim of this treatment is to create negative pressure by sucking air from the glass, which then produces a therapeutic effect. Cupping treatment has significant benefits that practitioners and patients generally accept. One of its main benefits is detoxification, which aims to eliminate waste materials and toxins from the body (S. Kim et al., 2018). This process is also seen as a harmonizing effort to overcome imbalances that may occur in the body system. Cupping is important in cleaning blood plasma from various disease-causing materials, such as free radicals, cholesterol, and other dangerous substances (Budi Sungkawa, 2019).

Two lipoproteins carry cholesterol throughout the body; low-density lipoprotein (LDL) cholesterol, sometimes called "bad" cholesterol, makes up most of the body's cholesterol. High levels of LDL cholesterol raise the risk of heart disease and stroke. High-density lipoprotein (HDL) cholesterol, sometimes called "good" cholesterol, absorbs cholesterol in the blood and carries it back to the liver. The liver then flushes it from the body. High levels of HDL cholesterol can lower your risk for heart disease and stroke. When the body has too much LDL cholesterol, the LDL cholesterol can build up on the walls of the blood vessels. This buildup is called "plaque," it can cause health problems, such as heart disease and stroke. Plaque is made up of cholesterol deposits. Plaque buildup causes the inside of the arteries to narrow over time. This process is called atherosclerosis. Triglycerides (TG) are a type of fat in the blood that the body uses for energy. The combination of high levels of TG with low HDL and high LDL cholesterol levels can increase the risk for health problems, such as heart attacks (Aryani et al., 2023) (Ayudia et al., 2023). Therefore, cupping treatment that can overcome cholesterol problems and cleanse the blood of harmful substances is important in maintaining body health and preventing cardiovascular diseases (CVDs) (Hidayat Fahrul, 2023).

## 2. Method

### 2.1 Research Methodology

We conducted this systematic review and meta-analysis research using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and the Cochrane Handbook for Systematic Reviews of Intervention, version 6.3, 2022.

## *2.2 Eligibility Criteria: Inclusion and Exclusion Criteria*

Before starting the literature search, we formulated strict inclusion and exclusion criteria to identify relevant studies. Our inclusion criteria included: 1) Studies with a Randomized Controlled Trials design, 2) Patients included in the healthy population according to the WHO definition, 3) Exclusive use of cupping therapy interventions, and 4) Studies that measured Cholesterol, LDL, HDL, and TG levels. On the other hand, exclusion criteria included 1) Not using English or not using a compatible language and 2) Not providing access to the full text. The entire paper selection process was carried out by two independent researchers (AA, AP), with joint consultation with another researcher (KD) in resolving disagreements, which is explained further in our method development.

## *2.3 Reference Standard*

Research with a Randomized Controlled Trial design showing the effects of cupping therapy in healthy populations is used as a reference.

## *2.4 Search Strategy*

In the literature search effort, independent researchers (AA, AP, KD) conducted comprehensive searches in several leading databases, such as Cochrane, PubMed, Google Scholar, Embase, and Scopus. The literature search process was carried out from 30 September 2023 to 8 October 2023 by referring to terminology according to the Medical Subject Heading (MeSH) browser. Specific keywords are used by following the boolean operator keywords guidelines, namely: [((“Cupping Therapy” OR “Cupping” OR “Hijama Therapy”) AND (“Healthy” OR “Well-being” OR “Fitness”) AND (“Cardiovascular” OR “Cholesterol” OR “HDL” OR “LDL”) AND (“Randomized” OR “Randomised”))]. A complete description is available in (attachment 1).

## *2.5 Study Selection*

From all the databases we used, we managed to collect 513 articles. We collect all these articles in confidence. After review, we found 131 duplicate articles, 123 articles that did not match the study because they were eBooks and books, and irrelevant articles. Furthermore, from the selection by reading all the articles, we excluded 257 articles because 84 of them did not use cupping therapy, 51 of them did not use healthy populations, 9 of them used incompatible language, 67 of them did not measure cholesterol concentrations (LDL, HDL, or TG), 26 of them did not have access to the full text, and 19 of them did not use a Randomized Controlled Trial (RCT) design. The final result of the literature selection was finding three articles that could be analyzed. The flow of literature selection that we carried out can be seen in (Figure 1).

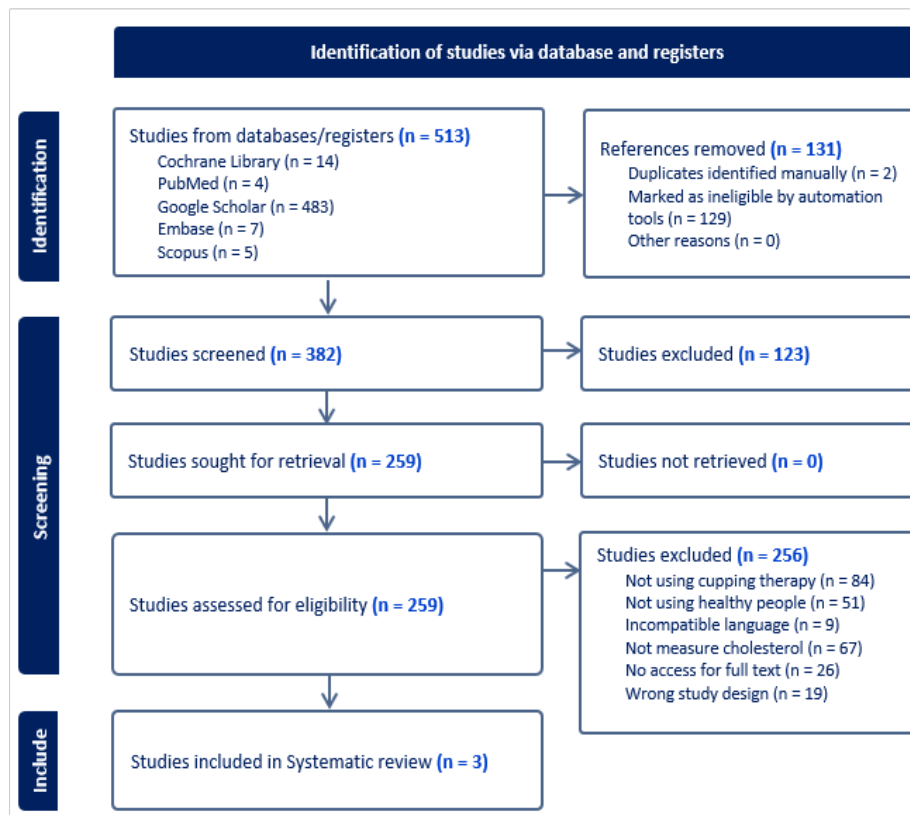


Figure 1: PRISMA Flow Diagram

### 2.6 Data Extraction and Analysis

A summary of the studies included in this review can be seen in Table 2. Data extracted from the selected studies were author, year, country, sample size, age, type of control, Number and location of cupping treatments, Treatment Sessions, Side Effects, Assessment Period, cholesterol concentration, LDL concentration, HDL concentration, and TG concentration. Meta-analysis was performed using RevMan version 5.4.

### 2.7 Risk of Bias in Individual Studies (Qualitative Synthesis)

The quality of the selected studies was assessed using the Risk of Bias for Randomized Trials (RoB2). RoB 2 consists of five domains and 28 questions that must be assessed. These questions refer to the randomization process, intervention, outcome data, and reported outcomes. The choices made are yes, maybe yes, maybe no, no, and not included, which, if added up, can be seen whether the researcher tends towards practicality, tends towards comparison, moves away from uncertainty, tends towards the unpredictable, and chooses no answer. Quality assessments were analyzed by three independent reviewers (AP, AA, KD). Scores are presented based on the RoB 2 algorithm and Robins, such as low risk, some concerns, and high risk. The bias assessment results showed that the two journals we used had several concerns. An indication of study quality is shown in (Figure 2).

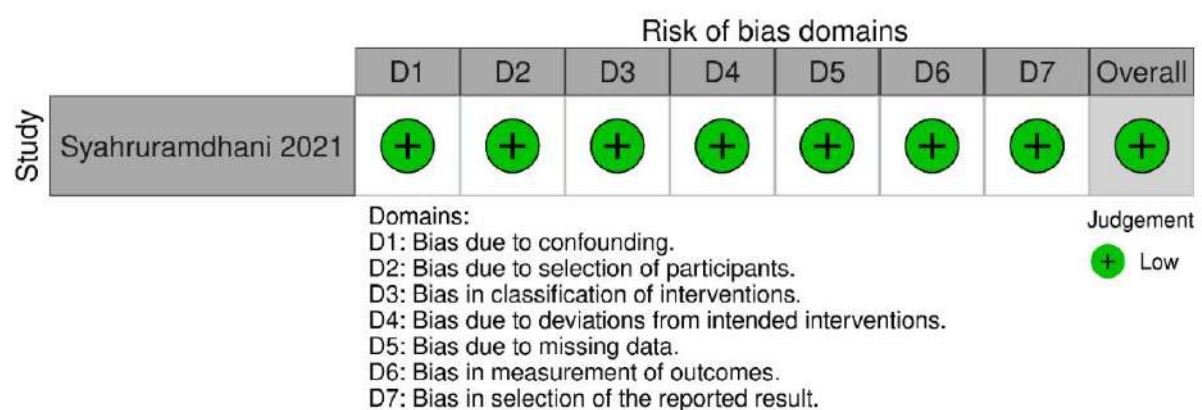
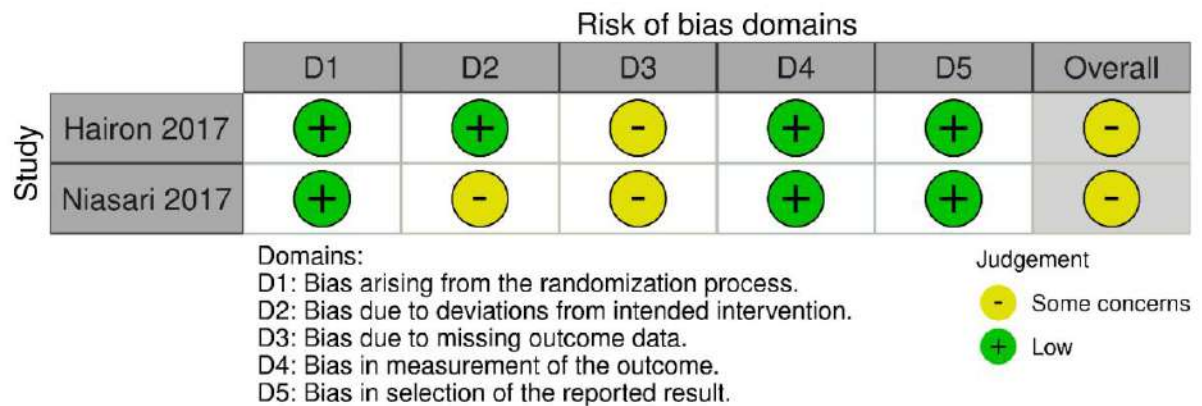


Figure 2: Risk assessment rob.2 and robins

2.9 Quantitative Data Synthesis (Meta-Analysis)

Review Manager 5.4.1. (The Nordic Cochrane Center, The Cochrane Collaboration, Copenhagen) was used for quantitative analysis of the data obtained. Mean differences (MD) and Standard Deviations (SD) for the intervention and control groups were extracted from previously included studies before and after treatment. The data used is continuous type. The statistical method used is inverse variance. Furthermore, the analysis model used is the fixed effect model (FEM) if the level of heterogeneity (I2) is < 50% and the random effect model (REM) if the level of heterogeneity (I2) is ≥ 50%. MD and SD for changes from baseline using cupping therapy for healthy individuals were assessed as primary outcomes guiding statistical analysis, as indicated by significant effects on LDL, HDL, and TG concentrations. Standardized mean differences (SMD) with study confidence intervals and a total is 95% (CI) were used to measure effects.

3. Results and Discussion

3.1 Screening Results and Study Characteristics

From all the inclusion articles we included, the number of participants reached 109 individuals who were divided into two groups: the intervention group, consisting of 54 participants, and the control group, which had 55 participants. The two studies came from Malaysia and Iran. The conclusions from each inclusion article can be seen in the extraction table in (attachment 2).

### 3.2 The Effect of Cupping on Cholesterol Levels Based on Type

A study (Sutriyono, 2019) states that cupping therapy has been proven to prevent cardiovascular disease (Rosyanti et al., 2020). This research shows that although cupping does not significantly reduce total cholesterol levels, it significantly reduces LDL levels and increases blood cholesterol levels HDL. So this can also reduce the risk of stroke (Wang et al., 2022). Significant meta-analysis results in the intervention group were obtained (Pooled MD = -16.20, 95% CI (-16.20,-0.85),  $p=0.03$ ,  $I^2 = 0\%$ ) (Figure 3).

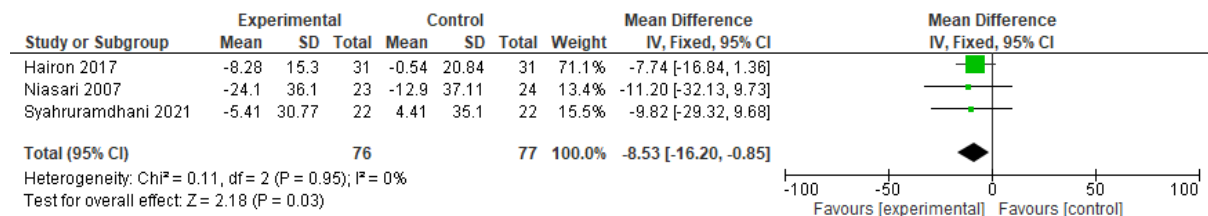


Figure 3: Meta-analysis for total cholesterol outcomes

In this review, we divided the meta-analysis into three subgroups to see more specific results regarding the data in the included articles. We have categorized the results of this meta-analysis based on the type of cholesterol component, namely Low-Density Lipoprotein (LDL), High-Density Lipoprotein (HDL), and Triglyceride (TG).

Cupping therapy is a method involving the removal of impure blood from the body through the skin's surface. This process is carried out by applying cupping therapy to specific meridian points, particularly on the right meridian points. This therapy significantly benefits reducing hypercholesterolemia, a condition characterized by elevated cholesterol levels in the blood. The administration of cupping therapy on the right meridian points has been proven to increase the number of leukocytes, lymphocytes, and the reticuloendothelial system. Additionally, this therapy stimulates the release of various substances such as ACTH, cortisol, endorphins, enkephalins, and other humoral factors. The effects of these releases include anti-inflammatory effects and reduction of serum fats, triglycerides, and phospholipids, especially LDL cholesterol. Furthermore, cupping therapy also stimulates the lipolysis of fat tissues and normalizes blood glucose levels. Thus, cupping therapy provides a holistic approach to addressing health issues related to cholesterol and fat metabolism. (Wibowo, et al. 2023)

### 3.3 The Effect of Cupping on Low-Density Lipoprotein (LDL) Levels

In the first subgroup, we assessed the effectiveness of wet cupping therapy in reducing low-density lipoprotein (LDL) levels. Significant meta-analysis results in the intervention group were obtained (Pooled MD = -17.48, 95% CI (-30.67, -4.30),  $p=0.009$ ,  $I^2 = 0\%$ ). LDL levels need to be lowered because they can increase the risk of coronary heart disease, stroke, and diseases related to blood vessels (Figure 4) (Ayudia & Imran, 2023).

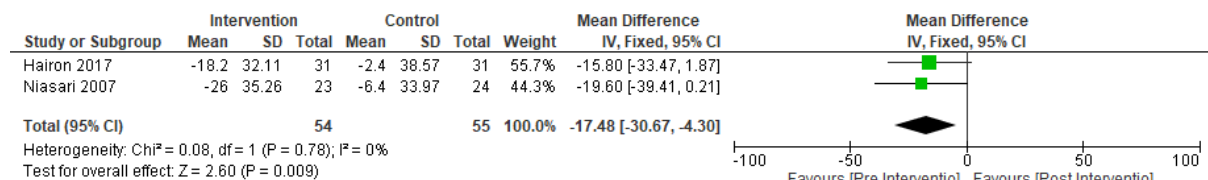


Figure 4: Meta-analysis of the effectiveness of cupping therapy in reducing LDL levels

Low-density lipoprotein (LDL) contributes to forming atherosclerotic plaques that block blood flow to vital organs, such as the heart and brain, which can ultimately cause a heart attack or stroke (KJ Kim et al., 2020). In addition, high LDL also stimulates arterial inflammation, which can worsen atherosclerosis and affect heart health in general. By lowering LDL levels, the risk of cardiovascular disease can be reduced, and overall heart health can be improved (Ayudia & Imran, 2023) (KJ Kim et al., 2020)

### 3.4 The Effect of Cupping on High-density Lipoprotein (HDL) Levels

In the second subgroup, we assessed the effectiveness of wet cupping therapy in increasing high-density lipoprotein (HDL) levels. We changed the position of the graph label for the outcome control on the left because a good outcome is an increase in HDL. Significant meta-analysis results in the intervention group were obtained (Pooled MD = 3.54, 95% CI (0.34,6.73), p=0.03, I<sup>2</sup> = 19%). HDL needs to be increased because HDL is a type of cholesterol that is often called good cholesterol (Figure 5) (Rampengan, 2015).

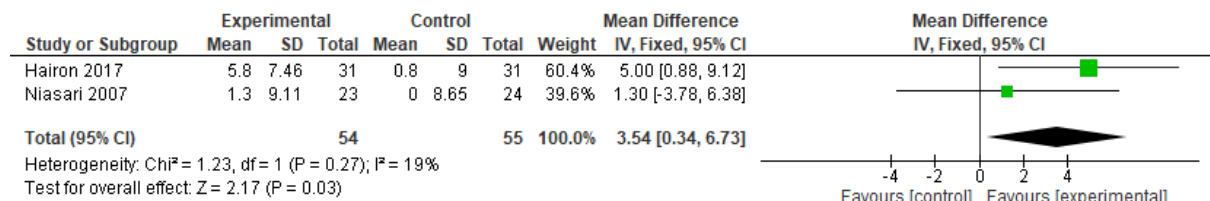


Figure 5: Meta-analysis of the effectiveness of cupping therapy in increasing HDL levels

Density Lipoprotein (HDL) helps transport excess cholesterol from the walls of the arteries and returns it to the liver to be excreted from the body (Rampengan, 2015). In other words, HDL helps clear cholesterol accumulated in the arteries, reduces atherosclerotic plaque formation, and improves blood flow. High HDL levels have been shown to protect against heart disease and stroke, so increasing HDL may reduce the risk of cardiovascular disease (Rampengan, 2015) (Kosmas et al., 2018)

### 3.5 The Effect of Cupping on Triglyceride (TG) Levels

We assessed wet cupping therapy's effectiveness in reducing triglyceride (TG) levels in the third subgroup. Insignificant meta-analysis results in the control group were obtained (Pooled MD = 3.58, 95% CI (-55.03,62.18), p=0.90, I<sup>2</sup> = 86%). However, the results of this forest plot cannot be concluded because the data is heterogeneous, and sensitivity analysis cannot be carried out because it will result in 1 article remaining being studied. This shows the need for other studies with homogeneous data to be able to conclude whether cupping can reduce TG levels to prevent cardiovascular disease. Triglycerides (TG) need to be reduced because high TG levels in the blood can increase the risk of cardiovascular disease, such as coronary heart disease (Figure 6) (Agung, 2021)

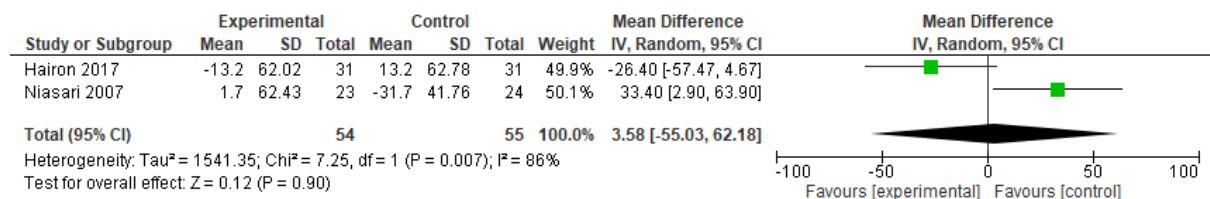


Figure 6: Meta-analysis of the effectiveness of cupping therapy in reducing triglyceride levels

Triglycerides are the main form of fat in the body, and the blood and high TG levels can lead to the formation of atherosclerotic plaque in the arteries. This plaque can narrow the arteries, restrict blood flow, and increase the risk of heart attack and stroke. In addition, high TG levels are also often associated with metabolic diseases, such as type 2 diabetes. By lowering TG levels, the risk of heart disease and health problems increases. Other related issues may be reduced (Aryani et al., 2023).

### 3.6 Implementation and Recommendations for Subsequent Implementation

Future implementation of cupping treatment offers enormous potential if it continues to be developed and implemented more widely. One of the main aspects that makes it stand out is the role of cupping as an effective alternative treatment for treating metabolic disorders in the body. According to the teachings of the Prophet, several essential points in the body are interconnected. When one point is cupped, it can provide a positive response that affects the other points. This concept became the basis for scientific developments in cupping treatment,

demonstrating the complex relationship between these points (Malik, 2015). Given the rich legacy of knowledge in cupping practice, further development and broader implementation may open up opportunities to provide health care to reduce Cholesterol, LDL, HDL, and Triglyceride levels and prevent the occurrence of Cardiovascular Diseases (CVDs). This development will allow cupping treatment to continue developing as a valuable alternative to maintaining health and overcoming various health problems.

### 3.7 Advantages and Limitations

Our study is the first meta-analysis study to discuss the effectiveness of cupping therapy to prevent increases in total cholesterol, LDL, and TG levels and increase HDL levels with significant results in reducing total cholesterol, LDL levels, and significantly increasing HDL concentration. In addition, this study uses RCT study references to obtain quality results. The limitations of this research are that the references used are very few, and the articles used have some bias concerns. It is hoped that several limitations of this research can serve as guidelines for future research.

## 4. Conclusion

A systematic review and meta-analysis indicate that cupping therapy positively affects cholesterol levels in healthy individuals. Although the results are significant, this research is limited in the number and quality of studies used. Therefore, further research with a high-quality Randomized Controlled Trial (RCT) design is needed to confirm these findings. In its application, cupping therapy has the potential to be an effective non-pharmacological intervention in managing cholesterol levels, especially in reducing total cholesterol, Low-Density Lipoprotein (LDL) levels, and increasing HDL concentration, and can be an alternative or addition to current pharmacological approaches in managing cholesterol.

**Author Contributions:** All authors contributed to this research.

**Funding:** Not applicable.

**Conflict of Interest:** The authors declare no conflict of interest.

**Informed Consent Statement/Ethics Approval:** Not applicable.

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**Attachment 1: Study Selection****Keyword:**

CENTRAL (Cochrane Library)

No	Search	Result
#1	MeSH descriptor: [Cupping Therapy] explode all trees	35
#2	Hijama therapy	13
#3	cupping	924
#4	#1 OR #2 OR #3	924
#5	Cholesterol OR Healthy OR Well-being OR Normal	309660
#6	Cardiovascular OR Cholesterol OR HDL OR LDL OR Triglycerides	160185
#7	#4 AND #5 AND #6	14

**Total: 14**

## PubMed

No	Search	Result
#1	Cupping therapy [MeSH Terms]	92
#2	((healthy) OR (well-being)) OR (fitness)	10,029,118
#3	(((((cardiovascular) OR (cholesterol)) OR (HDL)) OR (LDL)) OR (CRP))	2,471,654
#4	#1 AND #2 AND #3	4

**Total: 4**

## SCOPUS

TITLE-ABS-KEY (("Cupping Therapy" OR "Cupping") AND ("Healthy" OR "Well-being" OR "Fitness") AND ("Cardiovascular" OR "Cholesterol" OR "HDL" OR "LDL") AND ("Randomized" OR "Randomised"))

**Total: 5**

## EMBASE

("Cupping Therapy" OR "Cupping") AND ("Healthy" OR "Well-being") AND ("Cardiovascular" OR "Cholesterol" OR "HDL" OR "LDL")

**Total: 7**

## GOOGLE SCHOLAR

("Cupping Therapy" OR "Cupping") AND ("Healthy" OR "Well-being") AND ("Cardiovascular" OR "Cholesterol" OR "HDL" OR "LDL") AND ("Randomized" OR "Randomised") - Review -Systematic

**Total: 483**

**Attachment 2: Data Extraction**

Table 1. Data Extraction

Penulis, Tahun		Hairon et al., 2017	Niasari et al., 2007	Syahruramdhani et al., 2021
Country		Malaysia	Iran	Indonesia
Sample size, n (Trail/control)		62 (31/31)	47 (23/24)	44 (22/22)
Age ( $\pm$ SD) or Age Range	Trail	44.97 $\pm$ 6.44	18 - 25	18-23
	Control	43.23 $\pm$ 7.39	18 - 25	18-23
Type of Control		Untreated	Untreated	Untreated
Type of Cupping Therapy		Wet Cupping	Wet Cupping	Wet Cupping
Quantity (Cupping Location)		5 (in both scapulae, in both lumbar region and vertex region)	NI (interscapular area)	5 (across from T1-T3, two sites in mid-clavicular, and two sites in 3 cm from the vertebra)
Number of sessions of therapy		single session	single session	Single session
Adverse Event		-	-	-
Total cholesterol	Pre-Cupping	103.14 $\pm$ 16.56	163 $\pm$ 39.4	147.91 $\pm$ 31.73
	Post-Cupping	94.86 $\pm$ 13.68	138.9 $\pm$ 31.5	142.50 $\pm$ 29.71
	Pre-Placebo	104.4 $\pm$ 21.6	147.3 $\pm$ 39.2	154.45 $\pm$ 39.46
	Post-Placebo	104.94 $\pm$ 19.98	134.4 $\pm$ 34.6	158.86 $\pm$ 27.73
Triglyceride (Mean $\pm$ SD)	Pre-Cupping	161.1 $\pm$ 63.7*	116.2 $\pm$ 57.2	N/A
	Post-Cupping	147.9 $\pm$ 60.2*	117.9 $\pm$ 66.6	N/A
	Pre-Placebo	141.7 $\pm$ 58.4*	108.2 $\pm$ 48.2	N/A
	Post-Placebo	154.9 $\pm$ 66.4*	76.5 $\pm$ 25.3	N/A
LDL-C (Mean $\pm$ SD)	Pre-Cupping	136.5 $\pm$ 33.2*	96.7 $\pm$ 36.4	N/A
	Post-Cupping	118.3 $\pm$ 30.9*	70.7 $\pm$ 34	N/A

	Pre-Placebo	142.3 ± 42.5*	83.3 ± 35.8	N/A
	Post-Placebo	139.9 ± 32.8*	76.9 ± 31.8	N/A
HDL-C (Mean±SD)	Pre-Cupping	53.4 ± 6.6*	43.2 ± 9.4	N/A
	Post-Cupping	59.2 ± 8.1*	44.5 ± 8.8	N/A
	Pre-Placebo	53.7 ± 9.7*	42.4 ± 9.8	N/A
	Post-Placebo	54.5 ± 8.1*	42.4 ± 6.6	N/A
Results		The cupping group significantly improved Total Cholesterol, HDL-C, LDL-C, and triglycerides, while the control group showed no improvement.	Wet cupping may effectively reduce LDL cholesterol in men, potentially offering a preventive effect against atherosclerosis.	In the intervention group's post-test, the mean SBP and DBP were substantially different from the pretest (p = 0.01 and 0.03). Although there was no statistically significant difference in TC outcome, overall cholesterol decreased following an intervention.

NI = No Information

N/A = No Administered

\* = After conversion to mg/dL

# Relationship Between Children's Cognitive Function and Type 1 Diabetes Mellitus (T1DM): A Systematic Review

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## Abstract

**Background:** Type 1 diabetes mellitus (T1DM) is the most common type of diabetes in children and is caused by various factors, including immune system abnormalities, genetic factors, and environmental influences. T1DM usually occurs in early to mid-childhood when an autoimmune process damages the pancreas's beta cells, producing insufficient insulin. **Purpose:** Review several studies on T1DM associated with cognitive decline in children. **Methods:** The study systematically reviews five articles from randomized controlled trials, focusing on the cognitive function of children with T1DM. It specifically explored the relationship between T1DM, cognitive deficits, and the impact of diabetic ketoacidosis on cognitive function in children. **Results:** This review included five articles from randomized controlled trials between 1999 and 2023, distributed across two nations. The studies included 1.579 children with T1DM or with Ketoacidosis diabetic. Sample testing with cognitive function measurements in each article. **Discussion:** Type 1 diabetes patients had milder to moderate cognitive deficits on a variety of neuropsychological tests compared with nondiabetic control subjects. These cognitive deficits are primarily related to mental processing speed, executive function, and memory. **Summary:** Children with T1DM, especially those with a history of diabetic ketoacidosis, exhibited mild to moderate cognitive deficits, particularly

in mental processing speed, executive function, and memory. The review emphasized the potential impact of T1DM on children's cognitive development and academic performance, underscoring the need for early diagnosis and appropriate management to mitigate cognitive decline.

**Keywords:** Type 1 Diabetes Mellitus (T1DM), Cognitive Function, Children

## 1. Introduction

Type 1 diabetes mellitus (T1DM) is an autoimmune disorder involving multiple factors. It is characterized by T cell-induced destruction of  $\beta$ -cells in the pancreas, resulting in insulin production and release deficiencies. This condition has the potential to be severe and life-threatening (Akil et al., 2021). Type 1 diabetes mellitus, which is also referred to as insulin-dependent diabetes mellitus or juvenile-onset diabetes, accounts for about 5-10% of all diabetes cases (Banday et al., 2020). In studies conducted in the United States, 80% of diabetes cases were T1DM at ages <9 years and 6-76% between 10 and 19 years (Saraswathi et al., 2019). In 2021, the estimated global total of new cases of T1DM in children and adolescents is 355,900 diagnosed cases. This figure is predicted to increase to 476,700 cases by 2050 (Ward et al., 2022).

Type 1 diabetes mellitus is the most common type of diabetes in children and is triggered by factors such as immune system disorders, genetic factors, and environmental influences. T1DM usually begins to appear in early to mid-childhood, when the beta cells of the pancreas are damaged by an autoimmune process, leading to a lack of insulin production (Pasi & Ravi, 2022). The disruption in insulin production starts with the formation of auto-antibodies against pancreatic  $\beta$ -cells, eventually resulting in  $\beta$ -cell damage. When  $\beta$ -cells are damaged, insulin production is impaired. In the early stages of clinical symptoms, some functioning  $\beta$ -cells may take over, producing insulin, resulting in a temporary period of normalcy. Over time, T1DM patients will experience disease progression or may develop complications due to diabetes (Ward et al., 2022). Insulin deficiency leads to uncontrolled lipolysis and increased plasma levels of free fatty acids, thus suppressing glucose metabolism (Ozougwu, 2013). This is because insulin can restrain the use of fat as an energy source by inhibiting the hormone glucagon (Raghupathy, 2015). The hormonal changes that occur will increase glucose production from glycogenolysis and gluconeogenesis, causing an increase in acetoacetic and  $\beta$ -hydroxybutyric acids (ketones) that exceed the capacity of the equilibrium system in the blood. This complication is metabolic acidosis, referred to as diabetic ketoacidosis (DKA). It can progress to hyperglycemia, hyperketonemia, osmotic diuresis, severe vomiting, dehydration, electrolyte deficiency, and more severe insulin resistance (Wolfsdorf et al., 2006).

Type 1 diabetes mellitus is usually detected in childhood and adolescence, which is a period of rapid development of the central nervous system. Elevated blood glucose levels in non-diabetic and pre-diabetic patients have been associated with cognitive impairment. Diabetes is characterized by persistent elevation of blood glucose levels. Thus, hyperglycemia becomes a possible causative agent of cognitive impairment in diabetic patients (Feinkohl et al., 2015). There is concern that the developing brain may be more susceptible to extreme blood sugar fluctuations (Moheet et al., 2015). Some studies also suggest that complications of DKA may cause neurologic damage that subsequently affects cognitive function (Diabetes.co.uk, 2019; Lacy et al., 2020). Children with impaired cognitive development due to the rapid onset of T1DM can have a negative impact on their academic performance (Moheet et al., 2015). This article focuses on the association between T1DM and cognitive function in children with T1DM. We have conducted a literature search to provide a summary database on cognitive function in T1DM pediatric patients and added the latest literature to update the previous systematic review.

## 2. Methods

### 2.1. Selection Method

We conducted this *systematic review* and meta-analysis by PRISMA (*Preferred Reporting Items for Systematic Reviews and Meta-Analyses*) guidelines and the *Cochrane Handbook for Systematic Reviews of Interventions*, version 6.3, 2022.

## 2.2. Reference Standard

Research with a *Randomized Controlled Trial* design shows the prognosis of the effect of a history of diabetes mellitus on cognitive function.

## 2.3. Search Strategy

In the literature search effort, independent researchers (AA et al.) conducted a comprehensive search in several leading databases, such as Cochrane and PubMed. The literature search process was completed from October 12, 2023, to October 31, 2023, using terminology according to the MeSH (*Medical Subject Heading*) browser. Specific keywords were used by following the *boolean operator keywords* guidelines, i.e. : *((diabetic[Title/Abstract] OR diabetic OR hyperglycemia OR hyperglycemic) AND ((children[MeSH Terms] OR (child))) AND (cognitive OR cognitive impairment OR cognitive behavior))*. The full description is available in Appendix 1.

## 2.4. Eligibility Criteria

Before starting the literature search, we formulated strict inclusion and exclusion criteria to identify relevant studies.

Inclusion criteria:

- a. study with *Randomized Controlled Trials* design and prospective cohort,
- b. The patients included in the population were patients with type 1 diabetes mellitus or mild diabetic ketoacidosis,
- c. measuring IQ scores before DM diagnosis and after DM diagnosis, and
- d. have a control group in a healthy population. On the other hand,

Exclusion criteria:

- a. Not using English or not using a compatible language, and
- b. Does not provide access to full text. Three independent researchers (AA, SLR, KRR) conducted the entire paper selection process, with joint consultation with another researcher (MRK) to resolve disagreements.

## 2.5. Study Selection

From all the databases we used, we managed to collect 40 articles. We collected all the articles in evidence. After reviewing, we found eight duplicate articles, three unsuitable for studies because they were *eBooks* and *books*, and irrelevant articles. Furthermore, from the selection by reading the entire article, we excluded 24 articles because 17 of them did not use a history of diabetes as an intervention, two did not see the effect on cognitive function, and 5 of them did not have access to the full text. The final result of the literature selection was that we found five articles that can be used for qualitative analysis and two articles that can be used for quantitative analysis. The flow of our literature selection can be seen in Figure 1.

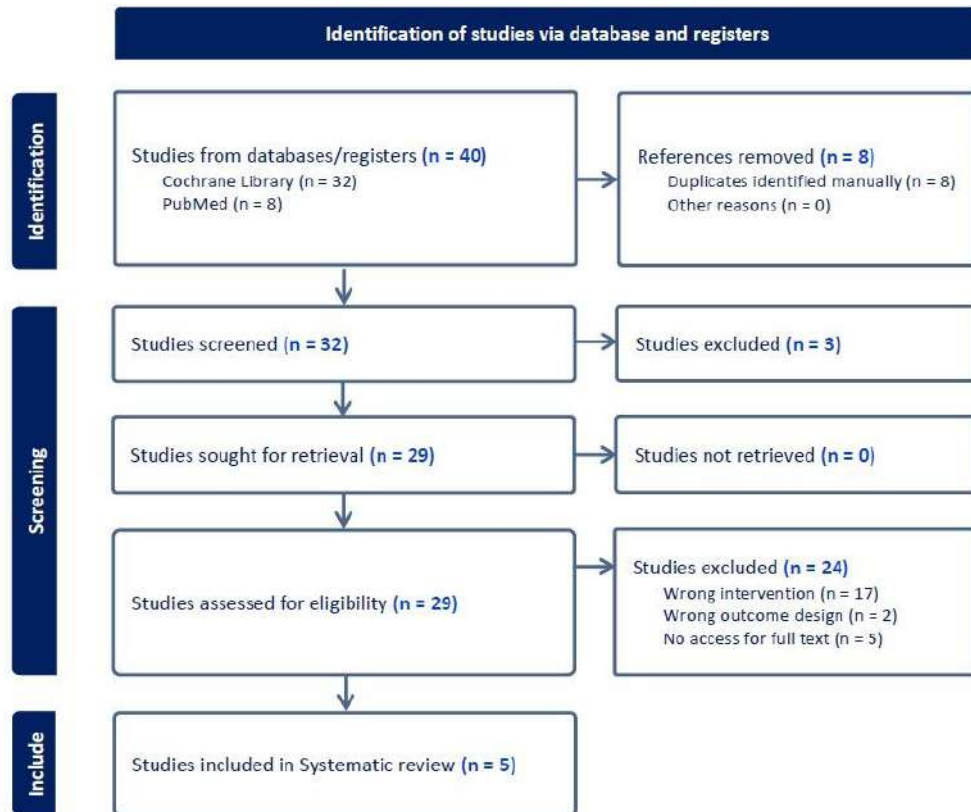


Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) flow diagram

### 2.6. Risk of Bias in Individual Studies (Qualitative Synthesis)

The quality of the selected studies was assessed using the *Risk of Bias for Randomized Trials* (RoB2). RoB2 consists of five domains and 28 questions to be evaluated. These questions refer to the randomization process, intervention, outcome data, and reported results. The choices made were yes, probably yes, probably no, no, and not included, which, when summed up, can be seen whether the researcher tends toward the practical, tends toward the comparator, moves away from uncertainty, tends toward the unpredictable, and chooses not to answer. Quality ratings were analyzed by one independent reviewer (AA). Scores were presented based on the RoB 2 algorithm, such as low risk, some concern, and high risk. The results of the bias assessment found that the two journals we used had results with some concerns. Indications of study quality are shown in table 1.



Table 1: Quality of Inclusion Articles

Study	Risk of bias domains					Overall
	D1	D2	D3	D4	D5	
Ghetti 2020	+	-	-	-	-	-
Ghetti 2023	+	-	-	-	-	-
Hershey 1999	+	-	-	+	+	-
Lin 2014	-	-	-	+	-	-
Kirchhoff 2016	-	+	-	+	-	-

Domains:  
D1: Bias arising from the randomization process.  
D2: Bias due to deviations from intended intervention.  
D3: Bias due to missing outcome data.  
D4: Bias in measurement of the outcome.  
D5: Bias in selection of the reported result.

Judgement  
- Some concerns  
+ Low

### 3. Results

Titles and abstracts were comprehensively scrutinized to verify their compliance with the established inclusion and exclusion criteria. The systematic search results yielded five articles by independent researchers (SLR, MRK). The search result extraction table will then describe the search results, starting from the author, country, year, study design, population and sample size, a method for measuring cognitive function, and findings in each article. The research description table can be seen in Table 2.

Table 2: Research description

Author (Year)	Country	Title	Study design	Population and Sample Size	Methods for Measuring Cognitive Function	Results
Ghetti et al. (2023).	United States of America	Cognitive Function Following Diabetic Ketoacidosis in Young Children with Type 1 Diabetes	RCT	Seventy-three children aged 3-5 years with newly diagnosed type 1 diabetes mellitus from 12 pediatric emergency centers.	This study measured IQ using the Wechsler Preschool and Primary Scale of Intelligence (WPPSI-III). Children aged 3 years received the WPPSI test with four subtests: block design, arithmetic, vocabulary, and comprehension. For 4-5-year-olds, the WPPSI test includes block design, information, matrix reasoning, vocabulary, picture concepts, word comprehension, and coding.	It was found that 22 children (30.1%) had moderate-severe diabetes mellitus and had IQs up to <105, and 24 children (32.87%) had medium-severity diabetes with IQs >105. While there were 27 (37.3%) children who were not diagnosed with diabetes had IQ >110
Ghetti et al. (2020).	United States of America	Cognitive Function Following Diabetic Ketoacidosis in Children With New-Onset or Previously Diagnosed Type 1 Diabetes	RCT	A total of 1,249 children were studied. Several children with type 1 DM aged 6-18 years were taken from the Pediatric Emergency Care Applied Research Network (PECARN). There were also some children with type 1 DM but no history of diabetic ketoacidosis also taken from PECARN.	Cognitive tests included spatial and color memory tasks, Wechsler Abbreviated Scale of Intelligence (IQ measured 65-160), forward number span, and backward tasks (numbers: 0-18).	The study found that patients with moderate/severe DKA had a lower adjusted mean IQ score of 100.6 (SD 1.34) compared to those with mild DKA (adjusted mean IQ score of 101.8, SD 1.14) and those with no DKA history (adjusted mean IQ score of 103.0, SD 1.46). Additionally, patients with mild DKA had a lower adjusted mean forward digit span recall score of 8.3 (SD 0.14) compared to those with no DKA history (adjusted mean forward digit span recall score of 8.5, SD 0.20). Furthermore, patients with moderate/severe DKA had a lower adjusted mean forward digit span recall score of 8.0

						(SD 0.17) than those without DKA history.
Kirchhoff et al. (2016)	United States of America	A longitudinal investigation of cognitive function in children and adolescents with type 1 diabetes mellitus	Prospective cohort	One hundred nineteen children aged 4-16 years with type 1 diabetes mellitus and 59 controls. The distance between the first and second data collection was 2 years, and between the second and third data collection was 3 years.	IQ (Wechsler Intelligence Scale Children-III), visual-spatial ability (Woodcock-Johnson III), and memory (Delayed Recall Trial of the Word Lists, which is a subtest of the Children Memory Scale). Reaction speed: Go-No-Go	Spatial relations: scores were 2.95 lower than controls (p = 0.006). Spatial Delayed Response (SDR): 4.42 mm less accurate than control (p=0.046). IQ data not shown. Reaction speed: 5.38 milliseconds slower (p=0.037)
Lin et al. (2014).	Australia	Risk Factor for Decline in IQ in Youth With Type 1 Diabetes Over the 12 Years From Diagnosis/Illness Onset	Prospective cohort	One hundred thirty-three children with type 1 diabetes and 126 controls. Twelve years later, the population size was 106 patients and 75 controls (HC).	IQ was assessed using the Wechsler Preschool and Primary Scale of Intelligence Revised (WPPSI-R) and Wechsler Intelligence Scale for Children-Revised (WISC-R) and at follow-up using the Wechsler Abbreviated Scale of Intelligence (WASI).	VIQ baseline (107.06 HC; 103.65 patients), VIQ follow-up (100.60 HC; 95.81 patients, p=0.01), FSIQ baseline (110.76 HC; 107.05 patients), FSIQ follow-up (105.18 HC; 100.94 patients, p=0.02).
Hershey et al. (1999).	United States of America	Conventional Versus Intensive Diabetes Therapy in Children With Type 1 Diabetes	RCT	Sixteen non-diabetic children and 25 children with DM 1 with an age range of 9-18 years. Taken from St.Louis Children's Hospital. Divided into 3 groups: control group, CT group: Conventional diabetic, and IT group: Intensive diabetic	To compare the memory of non-diabetic children and children who received conventional and intensive therapy in this study, a single-trained experimenter assessed it, including a memory test, Delayed Match to Sample List. Presentation task. Word recognition task, paragraph recall task, spatial and memory object task, grooved pegboard task, response inhibition task, vocabulary and block design task,	Memory: Spatial Delayed Response significant difference between IT and CT against control with 60 seconds delay (p=0.05). Accuracy is not significant. Median response time of task: IT had a delay compared to CT and control (p=0.03) Paragraph recall task: The recall performance of each subject was slowed down, there was no significance. Spatial and Object Memory task: immediate response slowed in all subjects, no significance Motor Speed and Inhibition: There is a significant difference between CT and IT against the non-diabetic group using the right hand where there is a delay (P=0.03). Inhibitory response (accuracy task): no significant difference between the 3 groups, but more accurate in the non-diabetic group. Inhibition response (Median Reaction Time Ask): no significant difference, all subjects experienced slowing down. Vocabulary and Block Design task: no difference from control, CT, and IT groups. For tests that did not produce significant results in all three groups with (P<0.001)

### 3.1. Diabetes and risk of IQ reduction

From the evidence we have gathered that there is a risk of IQ reduction in one of the few studies conducted using children aged 3 to 5 years from various races and ethnicities, it was found that children with moderate to severe diabetes mellitus had significantly lower IQ scores than children with mild diabetes mellitus and without a history of diabetes, which was about 5-10 points from children who were not affected by diabetes (P=0.03). In addition, the study also included ethnicity but did not significantly affect the development of children's IQ. Diabetes mellitus and ketoacidosis are indeed related and affect IQ in children, especially if they have a history and have been

affected in the toddler age. In this study, family economic status also influenced the worsening of diabetes in children ( $p=0.01$ ) (Ghetti et al., 2023).

The risk of decreased IQ and FISQ was also found in a study by Lin et al. (2014). The comparison between FISQ of diabetic and non-diabetic children was significantly different when followed up to see the second result. The examination in the study used the *Wechsler Preschool and Primary Scale of Intelligence Revised* (WPPSI-R) and the *Wechsler Intelligence Scale for Children-Revised* (WISC-R), where the scale was considered valid to determine the IQ level of a child (Lin et al., 2015).

### 3.2. Diabetes and other risks of reduced cognitive function

A study by Hershey et al. (1999) found other evidence of decreased cognitive function, including counting, memorization, and writing skills involving 41 children aged 9-18. In addition, these subjects also received conventional and intensive therapy. The results showed that in some tests, diabetic children were delayed in deciding something or finding answers; in this case, there was a significant delay of 40-60 seconds ( $P = 0.03$ ). However, some tests do not show significance in the delay between the non-diabetes group and the IT and CT groups (95% CI  $P = <0.001$ ) (Hershey et al., 1999).

Another study showed a significant change in IQ scores in patients with type 1 diabetes who experienced DKA. In patients with new-onset diabetes, the difference in IQ score was -0.08 (95% CI -0.16, -0.00). Also, in this study, the change in IQ score in patients without DKA was 0.08 (95% CI -0.16, -0.00). Based on the data provided, the change in FSIQ score was -6.11 (1.76) in *mean* (sd), and from the data provided, the change in FSIQ score was -5.58 (1.76) in *mean* (sd) (Ghetti et al., 2020).

## 4. Discussion

Type 1 diabetes mellitus (T1DM) is an autoimmune disease in which the body's immune system destroys the pancreatic beta cells that produce insulin. A wide range of metabolic, genetic, and immunogenetic characteristics of T1DM and age-related differences require a tailored approach for each individual (Speight & Pouwer, 2023). This insulin deficit can increase glucose levels, which can harm the body. Excessive glucose levels should be treated with exogenous insulin injections several times a day (Kahanovitz et al., 2017a)

The brain is the most complex and command center of the human body. This three-pound organ serves as the seat of intelligence, translator of senses, originator of movement, and regulator of behavior (*Brain Basics: Know Your Brain* | National Institute of Neurological Disorders and Stroke, n.d.) (CDC, 2022). During childhood, the human brain undergoes dynamic and unique structural and functional changes, requiring continuous glucose feeding for brain growth and function.

Children with T1DM are at risk of neurocognitive function deficits compared to their non-diabetic peers, particularly in memory skills, learning, and executive function (e.g., working memory, distraction, and response inhibition) (Broadley et al., 2017; Jaser & Jordan, 2021). T1DM has been associated with reduced amounts of total brain matter (gray and white matter), particularly in the parieto-occipital and temporal regions. Differences in affected brain regions depend on severe hypoglycemia, greater HbA1c, disease duration, and severity of microangiopathy (Ferguson et al., 2005; Mauras et al., 2021; Musen et al., 2006; Wessels et al., 2006).

In children, the number of T1DM cases with diabetic ketoacidosis (DKA) is high, with 71% in Indonesia in 2017 (Speight & Pouwer, 2023). DKA is a complication of T1DM caused by insulin deficiency and is a significant cause of morbidity and mortality in children (Kahanovitz et al., 2017b).

Several studies were conducted to look at the relationship between cognitive type 1 diabetes in children. Research conducted by Lin et al. It was found that at the beginning of the study, the IQ of children with type 1 diabetes was the same as that of controls, but when a follow-up examination was carried out, children with type 1 diabetes had

lower VIQ and FSIQ scores than controls. Younger age at diagnosis and more frequent hypoglycemic seizures showed a significant decrease in PIQ and FSIQ in children with type 1 diabetes.

Another study conducted by Kirchoff et al. found that exposure to hyperglycemic and hypoglycemic conditions, as well as early onset of type 1 diabetes, was associated with decreased intelligence, visual-spatial ability, memory performance, and information processing speed in children with type 1 diabetes.

In children, the number of T1DM cases with diabetic ketoacidosis (DKA) is high, with 71% in Indonesia in 2017 (Pulungan et al., 2021). DKA is a complication of T1DM caused by insulin deficiency and is a significant cause of morbidity and mortality in children (Hadgu et al., 2019; Hanifah et al., 2022; Tonoli, 2013).

Children, especially young ones, have body systems that are still developing, including their central nervous system (Handryastuti et al., 2022; Hanifah et al., 2022). As such, the impact of a severe medical condition such as DKA can have more significant consequences on their cognitive function. The decline in cognitive function associated with DKA can have substantial long-term implications on children's cognitive development (Kostopoulou et al., 2023).

Studies show that children with DKA, regardless of severity, have lower IQ scores compared to children without DKA. This is evident from the statistical test results of Ghetti et al. 2023, which showed that children with DKA had significantly lower IQ scores than children without DKA. This effect remained even after considering socioeconomic and ethnic factors. From the results of this study, it can be concluded that a single episode of DKA is associated with a decrease in IQ scores in children that occurs within a short period after exposure to DKA (Ghetti et al., 2023).

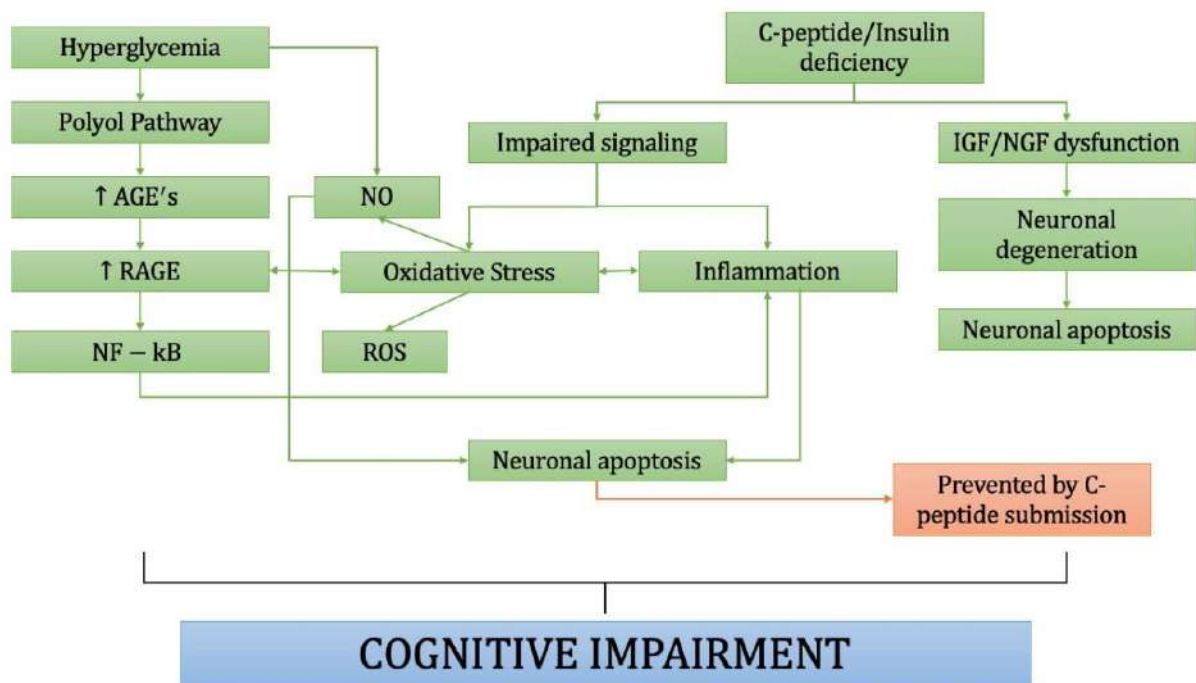


Figure 2: Mechanism of *cognitive decline* in T1DM

Severe hypoglycemia and the age of onset of type 1 diabetes are two of the most frequently studied variables associated with cognitive impairment (Chaytor, 2016). Severe hypoglycemia in children may impair cognitive abilities related to medial temporal functions, such as explicitly recalling past events (delayed declarative memory). The Hershey et al. study showed that severe hypoglycemia in children can impair cognitive abilities related to medial temporal function, such as explicitly recalling past events (delayed declarative memory) (Pourabbasi et al., 2016; Pulungan et al., 2021). In addition, caution should be exercised in imposing strict glucose control standards in pediatric patients with type 1 diabetes due to the higher risk of hypoglycemia associated with

intensive diabetes therapy (IT) (Hershey et al., 1999). Patients with type 1 diabetes have milder to moderate cognitive deficits on various neuropsychological tests compared to control subjects without diabetes. These cognitive deficits mainly relate to mental processing speed, executive function, and memory (Shalimova et al., 2019). Please have a look at Figure 2.

## 5. Conclusions

Type 1 diabetes mellitus in children, both those without DKA complications and those with DKA complications, can reduce children's cognition. Some of the influencing factors are the age at diagnosis of DKA, severe hypoglycemic and hyperglycemic conditions, and high HbA1c results. These factors can worsen the child's cognition as assessed by IQ, decreased intelligence, visual-spatial ability, memory performance, and information processing speed. Therefore, early diagnosis and appropriate management are necessary to reduce cognitive decline in children.

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# Ethanol Extract of Pomelo Peel to Prevent Dental Caries in Extracted Teeth *In-Vitro*

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## Abstract

Dental caries is caused by the bacteria *Streptococcus mutans*. It is said that *S. mutans* can be reduced by the action of toothbrushing with mouthwashes. However, chemical mouthwashes bring adverse effect on the teeth such as tooth staining, microbiota ecology changes, and mucosa lesions. Natural mouthwashes have become the alternative solution. For instance, the ability of ethanol extract from Pomelo peel to inhibit the growth of *S. mutans* bacteria can be used to prevent dental caries. This study aims to determine the effectiveness of ethanol extract of Pomelo peel in preventing dental caries in extracted teeth in vitro. The research design was quasi-experimental with a number of samples is 30. Six treatments were carried out, each treatment consisted of five samples consisting of bacterial culture, ethanol extract of Pomelo peel 20%, 50%, 75%, negative control, and positive control plus teeth and substrate. Observations were recorded and analyzed using Univariate Multi-Way Analysis of Variance (ANOVA). The results of the study showed that the occurrence of dental caries after receiving ethanol extract treatment from Pomelo peel is at least in the 75% concentration group, namely 0 teeth (0%), at the 25% concentration, all teeth experienced caries (100%), and in the 50% concentration group, dental caries occurred 67%. Statistically, grapefruit peel extract with a concentration of 75% significantly inhibits the process of tooth decay in conditions of white spots, black spots and holes. In conclusion, 75% concentration of Pomelo peel ethanol extract is effective in preventing dental caries in extracted teeth in-vitro.

**Keywords:** Caries Teeth, Citrus Maxima, In Vitro Extracted Teeth, Pomelo Peel Extract, *S. Mutans*

## 1. Introduction

Diseases of hard tooth tissue, also known as enamel, dentin, and cementum are caused by the activity of microorganisms contained in a fermented carbohydrate called dental caries. Dental caries is caused by the bacteria named *Streptococcus mutans* (Ozdemir, 2013). The combination of *S. mutans* with other factors such as substrate, host, and time causes the acceleration of dental caries. The process of dental caries commences with white spots, black spots, or lines and subsequently continues to create holes in the teeth (Warreth, 2023). The prevalence of dental caries in the world is quite high, between 49% - 83% and in Indonesia, dental caries is the most common



dental problem cases in Indonesia, namely 45.3%. Dental caries is most common in the age group 55-64 years (96.8%) followed by those aged 65 (95%), 45-54 (94.5%), and 35-44 (92.2%) (Kementerian Kesehatan RI, 2018). The occurrence of dental caries can be inhibited mechanically, chemically, or both, namely by reducing the attachment, proliferation, and aggregation of *S. mutans* bacteria. The plaque removal action through toothbrushing is recognized as the solution to prevent caries. Twice-daily toothbrushing at night and in the morning can remove the leftover residues during meals. The residues can provide the ideal substrate for *S. mutans* to create demineralizing acids. It is generally known and agreed that night toothbrushing is a must in daily routine to do. The study by (Sahoo et al., 2022) shows that the study of dental nursing students who were divided into groups and instructed to follow tooth brushing in pre-breakfast and post-breakfast with rinsing and without rinsing revealed the statement that the action of tooth brushing after breakfast with rinsing and without rinsing shows significant reduction of *S. mutans* colony-forming unit (CFU) in 38% and 29%. The habit of toothbrushing was evaluated in 5 years old children regarding daily tooth brushing and its significant effect on caries shows the number of relative risk for caries is significant with  $p < 0.05$ . This information shows that less than twice toothbrushing commenced in the child stage can bring the potential caries (Boustedt et al., 2020). However, the mechanical action of toothbrushing is not sufficient to prevent the occurrence of dental caries. Therefore, a combination with mouthwash is needed. The study shows that the active ingredients in the mouthwashes are cetyl pyridinium chloride, essential oils, chlorhexidine, triclosan, fluorides, delmopinol, and other substances (Tartaglia et al., 2019). The short duration use of less than 6 months of mouthwash can bring adverse effects such as local morphological (oral mucosa and dental-crown staining, mucosal lesions) and the functional effect comprises taste modifications and abnormal oral sensation. Besides, tooth staining was reported as the most listed adverse effect (Poppolo Deus & Ouanounou, 2022). The exposure of oral biofilms to mouthwash is correlated to adverse reactions such as residual structure, pathogenicity enhancement, and microbiota ecology changes (Takenaka et al., 2022). Long-term use of chemical mouthwash can cause various side effects such as extrinsic staining of the teeth as proven by (Erturk-Avunduk et al., 2021) who investigated the commercial mouthwashes effect on the discoloration of the tooth using a spectrophotometer. The color change was evaluated and shows that the commercial mouthwashes show unacceptable discoloration. Therefore, natural antibacterial ingredients are necessary, as those have fewer side effects from their use.

Pomelo (*Citrus maxima*) is a natural ingredient known for its antibacterial effects. The antibacterial effect of pomelo lies largely in the peel. The initial research showed that the ethanol extract of pomelo peel is positive for containing flavonoids of  $102.92 \pm 1.96$  mg/100g QE, tannins of  $6,867.61 \pm 167.95$  mg/100g TAE, phenols of  $4,865.65 \pm 106.83$  mg/100g GAE. The results of the 25% concentration inhibition test are 6.7517, 50% resulted in 7.2583, and 75% resulted in 7.7550. The results of statistical analysis by Anova show a significant effect ( $\text{sig} < 0.05$ ) on the diameter of the inhibition zone in *S. mutans* bacteria. Other research also found that pomelo contains phenols, tannins, flavonoids, and vitamin C. Pomelo peel contains antibacterial compounds. However, few studies explore the effectiveness of pomelo peel extract in preventing dental caries in extracted teeth. The objective of this research is to determine the effectiveness of ethanol of pomelo peel extract in preventing dental caries of the extracted tooth. The study was conducted by a test of the inhibitory power of ethanol extract of pomelo peel on the growth of *Streptococcus mutans* bacteria.

## 2. Method

This research uses a quasi-experimental research design in the form of a post-test-only control group design.

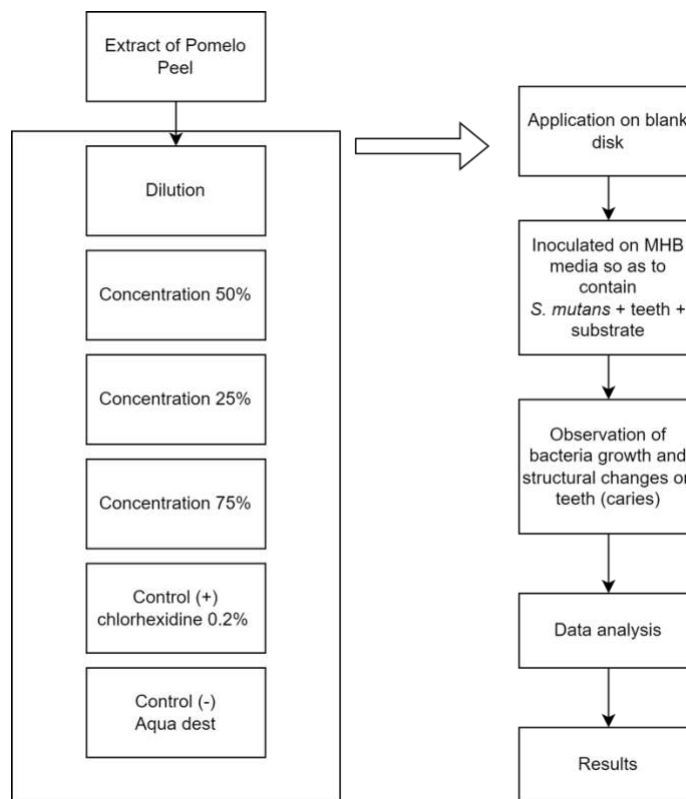


Figure 1: Steps of Extracting Pomelo Peel

The research procedure in this study was that teeth that had been coated with substrate and irradiated with bacterial suspension were placed on each blank disc containing saturated Mueller Hinton Blood (MHB) in a petri dish. Next, extracts of 25%, 50%, and 75% concentration were added to each medium, chlorhexidine as a positive control and distilled water as a negative control, then incubated at a temperature of 37°C during the observation period on days 0, 7, 28, and 42<sup>nd</sup>, 56<sup>th</sup> and 70<sup>th</sup>. Observation results were recorded. The data obtained was entered into a master table and then processed using SPSS 25 program. The results of data processing are presented in the form of tables, narratives, and/or images. Data on the effect activity of Pomelo peel ethanol extract were analyzed using Univariate Multi-way Analysis of Variance (ANOVA). This study was carried out under the Ethical Approval No. LB.02.03/EA/KEPK/0264/2022.

### 3. Results

#### 3.1 Observation of Research Subject

The results of the observation of the research subject regarding the inhibitory power of Pomelo peel ethanol extract with concentrations of 25%, 50%, and 75% on the growth of *S. mutans* in-vitro are shown in Table 1.

Table 1: Average Value of Inhibition Zone Diameter of Pomelo Peel Ethanol Extract

Treatment	Inhibitory Diameter (mm)
Concentration 25%	0.000 c
Concentration 50%	6.688 b
Concentration 75%	7.316 b
Positive control	10.098 a
Negative control	0.000 c

Note: The average value followed by the same letter in the same column indicates that the difference is not significant at the 5% level Duncan test.

Table 1 shows that a concentration of 75% Pomelo peel ethanol extract produces an inhibitory zone diameter that is higher than other concentrations, namely 7,316 mm. However, an extract concentration of 75% resulted in a smaller inhibition zone diameter compared to the positive control. Meanwhile, the lowest is at a concentration of 25% and negative control. The average value of the inhibitory zone diameter of Pomelo peel extract with different concentration variants 2 shows that Pomelo peel extract has the highest antibacterial activity at a concentration of 75%.

The frequency of caries in extracted teeth is based on the inhibitory power of ethanol extract of Pomelo peel with concentrations of 25%, 50%, and 75% on the growth of *S. mutans* in-vitro as shown in Table 2.

Table 2: Treatment in The Teeth

Treatment	Looping	Healthy teeth (0)		White spotted teeth (1)		Black spotted teeth (2)		Cavities (3)		Caries	
		f	%	f	%	f	%	f	%	f	%
Concentration 25%	6	0	0	6	100	6	100	5	83	6	100
Concentration 50%	6	0	0	6	67	4	67	4	67	4	67
Concentration 75%	6	6	100	0	0	0	0	0	0	0	0
Positive control	6	6	100	0	0	0	0	0	0	0	0
Negative control	6	0	0	6	100	6	100	6	100	6	100
Total	30										

Table 2 shows that the occurrence of dental caries after receiving treatment with ethanol extract of grapefruit peel was at least in the 75% concentration group, namely 0 teeth (0%), at the 25% concentration all teeth experienced caries (100%), in the 50% concentration group caries occurred. teeth 67%. Compared with the control group, the positive control had 0 teeth (0%) and the negative control had all teeth caries (100%).

### 3.2 Statistics Results

The results of the Anova test for the inhibitory power of grapefruit peel (*Citrus maxima*) ethanol extract with concentrations of 25%, 50% and 75% on the growth of *S. mutans* are shown in Table 3.

Table 3: ANOVA Test Results on The Zone of Inhibitory Diameter *S. mutans*

Inhibitory Zone	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	504.298	4	126.074	260.547	.000
Within Groups	12.097	25	.484		
Total	516.395	29			

Table 3 shows that the concentration of Pomelo peel extract has a significant effect ( $\text{sig} < 0.005$ ) on the zone of inhibitory diameter against *S. mutans* bacteria.

The results of the analysis of the formation of dental caries can be seen in the ANOVA test results as presented in Table 4.

Table 4: ANOVA Test on Caries Occurrence

		Sum of Squares	df	Mean Square	F	Sig.
White spot	Between Groups	400.000	4	100.000	1.000	.003
	Within Groups	2000.000	20	100.000		
	Total	2400.000	24			
Black spot	Between Groups	3855.600	4	963.900	.590	.004
	Within Groups	32700.400	20	1635.020		
	Total	36556.000	24			
Cavity	Between Groups	3311.200	4	827.800	10.901	.000
	Within Groups	1518.800	20	75.940		
	Total	4830.000	24			

Table 4 shows that the concentration treatment of Pomelo peel has a significant effect on the formation of white spots, and black spots on the teeth and the formation of cavities.

#### 4. Discussion

The initial research of this study investigated the compounds of Pomelo peel such as flavonoids, phenols, and tannins. Flavonoid levels were  $102.92 \pm 1.96$  mg/100 g QE, phenols were  $4,865.65 \pm 106.83$  mg/100g and tannins were  $6,867.61 \pm 167.95$  mg/100g TAE. Subsequently, the inhibitory power analysis of Pomelo peel was performed, and investigated the effectiveness of dental caries prevention was by applying the ethanol extract of Pomelo peel at concentrations of 25%, 50%, 75%, positive control (chlorhexidine 0.2%) and negative control (aqua dest) on the activity of the caries-causing *S. mutans* bacteria to the extracted teeth in vitro. The results in Table 1 show that a concentration of 75%, produces an inhibitory zone diameter that is higher than other concentrations specifically in 7.316 mm. However, an extract concentration of 75% resulted in a smaller inhibition zone diameter compared to the positive control. The lowest was at a concentration of 25% and negative control. The higher the concentration produces a larger inhibitory zone diameter as in Table 1. The results of the ANOVA test (Table 4) show the concentration of the ethanol peel extract of Pomelo has a significant effect ( $\text{sig} < 0.005$ ) on the diameter of the inhibition zone for *S. mutans* bacteria. This is because the ethanol extract of Pomelo peel contains flavonoids, phenols, and tannins. Flavonoid compounds function to exhibit antimicrobial properties, several phenolic groups such as flavonoids, tannins, and other phenolic compounds function as a defense tool for plants against pathogenic microorganisms so that they can act as antibacterial/antimicrobial compounds (Tamsin et al., 2023; Tungmunnithum et al., 2018).

The results of this study also show that an extract concentration of 75% produces a smaller diameter of the inhibition zone compared to the positive control. This is because the positive control used was mouthwash containing 0.2% chlorhexidine. Chlorhexidine is not an antibiotic, not a herbal ingredient but an antiseptic and antibacterial agent. Chlorhexidine belongs to the biguanide antimicrobial group, which has a broad spectrum and works by damaging the integrity of the cell wall and cytoplasm of microorganisms (Ampawong & Aramwit, 2017; Cieplik et al., 2019; Hoang et al., 2021; Vitt et al., 2015).

The results of research on the effectiveness of Pomelo peel ethanol extract in preventing dental caries in extracted teeth in vitro show that the occurrence of dental caries after applied Pomelo peel ethanol extract treatment is at least in the 75% concentration group, namely 0 teeth (0%), concentration 25% of all teeth experienced caries (100%), in the 50% concentration group 67% of dental caries occurred. Compared with the control group, the positive controls experienced dental caries (0%) and the negative controls had all teeth experiencing caries (100%) as shown in Table 2. The results of the ANOVA test show that the concentration of Pomelo peel treatment has a significant effect on the formation of white spots, and black spots on teeth, and the formation of cavities. This is due to the inhibitory power of ethanol extract from Pomelo peel on the activity of the *S. mutans* bacteria which

causes dental caries. This is in accordance with the opinion (Ozdemir, 2013) that dental caries is a disease of the hard tissue of the teeth, namely enamel, dentin, and cementum, which is caused by the activity of microorganisms contained in fermented carbohydrates. Dental caries is caused by the activity of bacteria present in fermented carbohydrates. One of the bacteria that causes dental caries is *S. mutans* (Dianawati et al., 2020; Lemos et al., 2019). The ability of Pomelo peel extract to inhibit the growth of *S. mutans* bacteria can be used to prevent dental caries. The results of this study are in accordance with (Shehata et al., 2021) who stated that Pomelo peel extract contains various phytochemical compounds that function as antibacterial. Pomelo peel extract contains various phytochemical compounds including tannins, terpenoids, flavonoids, saponins, alkaloids, cardiac glycosides, phenol, and ascorbic acid (Lee et al., 2022). Phytochemical compounds known to have antibacterial properties are saponins, flavonoids, tannins, and phenols. Saponin is a class of terpenoid compounds that can inhibit the growth or kill bacteria by interfering with the process of cell wall formation, where the cell wall is not formed or is formed imperfectly (Huang et al., 2022; Rahayu et al., 2019). Flavonoids can create damage to the bacterial cell walls, microsomes, and lysosomes which lead to the interaction of flavonoids and bacterial DNA (Hidanah et al., 2022; Rifa'i et al., 2023). The lipophilic properties of flavonoids cause these compounds to damage bacterial cell membranes. Then, apart from that, the antibacterial activity of tannin compounds is related to its ability to inactivate microbial adhesins, enzymes, and transport proteins on cell membranes (Ngajow et al., 2013; Nirwana et al., 2018). Furthermore, other compounds, namely phenol, can kill bacterial cells, namely by denaturing bacterial cell proteins (Purwantiningsih et al., 2014).

This study has investigated the inhibitory power of Pomelo peel (*Citrus maxima*) ethanol extract on the growth of *S. mutans* and the effectiveness of preventing dental caries in teeth that have been extracted in vitro. The concentration of Pomelo peel extract showed a significant effect on the diameter of the inhibitory zone of *S. mutans* bacteria. A concentration of 75% grapefruit peel ethanol extract produced the highest inhibitory zone diameter compared to concentrations of 25%, and 50%. Giving orange peel extract is 75% effective in preventing dental caries in vitro.

#### **Author Contributions:**

Conceptualization, IMBA.; Methodology, IMBA.; Software, IGSK.; Validation, IMBA.; Formal Analysis, IGSK, ING.; Investigation, IMBA.; Resources, ING.; Data Curation, IMBA.; Writing – Original Draft Preparation, IMBA.; Writing – Review & Editing, IMBA.; Visualization, IMBA.; Supervision, IMBA.; Project Administration, ING.; Funding Acquisition, IMBA.

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**Conflicts of Interest:** The authors declare no conflict of interest.

#### **Informed Consent Statement/Ethics approval:**

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Poltekkes Kemenkes Denpasar No. LB.02.03/EA/KEPK/0264/2022.

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# Content and Antimicrobial Potential of Cambodia Flower (*Plumeria sp.*) Extract

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## Abstract

The case of infectious disease is caused by *Streptococcus aureus* bacteria. The handling of the disease is performed by antibiotics. However, antibiotics can cause drug resistance to the bacteria. Natural ingredients with antimicrobial plant medicine have potential for the safe, and more effective disease handling. Cambodia flowers (*Frangipani P. alba*) are expected to contain a variety of chemical compounds with antimicrobial potential. This research may also contribute to the development of new drugs or natural supplements for infection control. The aim of this study is to identify quantitatively antibacterial phytochemical contents and qualitatively test the antimicrobial potential of Cambodia flower extract. The research was conducted using a true-experimental design of a posttest-only-control design with intervention in the treatment group and control for external factors that may potentially affect the research. The data were analyzed using the Kruskal-Wallis test. The results show that Cambodia flower extract contains phenols, tannins, flavonoids, and saponins, and the extract contains 5.95% phenols, 4.85% tannins, and 3.51% flavonoids. There is a difference in antimicrobial potency at various concentrations (55%, 70%, 85%, and 100%) of Cambodia flower extract in inhibiting the growth of *S. aureus* with a significance value of 0.000. In the in-vitro test, antimicrobial potential is found in the resistant group (with inhibition zone diameter  $\leq 15$  mm) in accordance with NCCLS standards. In conclusion, Cambodia flower is expected to provide a beneficial alternative solution for the community in preventing skin infections caused by *S. aureus* bacteria.

**Keywords:** Antimicrobial, Cambodia, Phytochemical, *Plumeria*, *Staphylococcus Aureus*

## 1. Introduction

Infectious disease is the second most dangerous cause of human death in the world. *Staphylococcus aureus* is known as the cause of various clinical disease infections. It normally does not cause infection on healthy skin. Nevertheless, once it enters the internal tissues or bloodstream, the potential serious infection is unavoidable. This bacterium can also cause scale skin syndrome in young children and is highly contagious. *S. aureus* can cause bacteremia and infective endocarditis, osteoarticular, pleuropulmonary, and device-related infections. It is known



that age is the powerful determinant of *S. Aureus* bacteremia (SAB) in which the occurrence of SAB increases gradually associated with age. Besides, the male gender is associated with SAB incidence with a ratio of ~1.5 compared to females (Laupland et al., 2013; S. Y. C. Tong et al., 2015). Antibiotics have been used against *S. aureus* such as linezolid (100%), trimethoprim-sulfamethoxazole (95%), and tetracyclines (94%). Besides, cephalosporins were agreed appropriate choice for *S. aureus* infections. However, the use of antibiotics and the evolution of bacteria has caused the drug resistance of *S. aureus* to increase gradually (Guo et al., 2020). The development of alternative solutions to prevent *S. aureus* growth is inevitable, and medicine of an antimicrobial nature is needed (Theos et al., 2019).

The use of Indonesian medicinal plants can be used as an alternative to overcome the resistance of microorganisms to antibiotics, considering that Indonesia has various types of plants that have the potential to be used as medicinal ingredients. One of which is Plumeria. Plumeria generally known in Indonesia as frangipani or Cambodia flower, is an ornamental plant popular in Indonesia because of the beauty and distinctive aroma of its flowers. Taxonomically, frangipani belongs to the *Apocynaceae* family which originates from Central America and the Caribbean and has been introduced to Southeast Asia, including Indonesia, especially in Bali where it is used as an ornamental plant (Ayu Fatkhurrohmah Wiyono & Muhtadi, 2020; Gde Sri Adyani Suari et al., 2020). Apart from being an ornamental plant, frangipani is also known to be used as a traditional medicine to treat several diseases, especially the type of *Frangipani P. alba* (Sura et al., 2018). Various bioactive constituents with strong antimicrobial, anti-inflammatory, anthelmintic, antipyretic, and antirheumatic properties have been extracted from the bark, leaves and flowers of *P. alba* (Kaur et al., 2022). The stems and leaves of *P. alba* have been reported to be used to treat skin diseases (R et al., 2014).

One interesting aspect to study is the antimicrobial potential of frangipani flower extract. The ability to inhibit the growth or kill pathogenic microorganisms such as bacteria and fungi is a highly desirable property in the health and medical fields, especially in the context of infection control. In addition, with the increasing resistance of microorganisms to conventional antibiotics (Suganya et al., 2022). Research related to the antimicrobial potential of natural medicinal plants is becoming increasingly important (El-Saadony et al., 2023; Mancuso et al., 2021). By understanding the chemical content of frangipani flower extract and testing its antimicrobial activity, the potential for developing new drugs or herbal supplements to treat infections can be understood. Herbal supplements have been proposed as a potential treatment option for infectious diseases (Mancuso et al., 2021). This study aimed at determining the antibacterial phytochemical content qualitatively and quantitatively as well as determining the antimicrobial potential of frangipani flower extracts in vitro. It is expected that the results of this research can provide an important contribution to the development of natural resources that have the potential new, safer, and more effective antimicrobial agents.

## 2. Method

This study was carried out by making frangipani flower extract and qualitative testing of phytochemical content. The testing was carried out in the Applied Chemistry Laboratory, Department of Medical Laboratory Technology, Poltekkes Kemenkes Denpasar. Quantitative testing of the phytochemical content of Cambodia flower extract was carried out at the Integrated Analytical Laboratory, Udayana University. The antimicrobial potential test of frangipani flower extract was carried out at the Microbiology Laboratory, Faculty of Medicine, Warmadewa University.

The sample of Cambodia flowers was collected from various areas in 8 districts and 1 city in Bali. The process of extracting Cambodia flowers started from performing air-dried the flowers until 5 kg were obtained as shown in Figure 1. A total of 5 kg of dried Cambodia flowers were oven-dried until dry. This sample was then extracted using the maceration method with a TLC spectrophotodensitometer. The anti-bacterial testing was carried out using a true experimental with a posttest-only-control design. The treatment groups were designed with Cambodia flower extract concentrations of 55%, 70%, 85%, and 100%, with repetition carried out 3 times with 4 multiplications for a total of 48 samples. The positive control used the antibiotic Ciprofloxacin 30 g and the negative control was a sterile 96% ethanol solution. The diffusion (disc) method was used to test anti-microbial potential in vitro using *S. aureus* bacteria grown on Mueller Hinton agar media. The research data were analyzed

using the Kolmogorov-Smirnov test followed by the Kruskal Walis test to determine differences in antimicrobial potential for the growth of *S. aureus* with a confidence level of 95% ( $\alpha = 0.05$ ) followed by the Least Significant Difference (LSD) test.



Figure 1: Steps of Extracting Pomelo Peel

### 3. Results

#### 3.1 Cambodia Flower Water Content

The process of making the test substance was started by preparing a 5 kg Cambodia flower. After being baked, the water content was weighed again to determine the quality of the flowers produced. The results of water content measurements were obtained at 10 %.

#### 3.2 Content of Phytochemical Compounds in Cambodia Flower Extract

The results of qualitative tests with phytochemical screening on the antibacterial compound content of Cambodia flower extract showed four phytochemical compounds found i.e. phenols, tannins, flavonoids, and saponins as shown in Table 1.

Table 1: The Phytochemical Content of Cambodia Flower Extract

No.	Test	Start	End	Result
1	Phenol	Clear green	Blue	Positive (+)
2	Tannins	Clear brown	Blue	Positive (+)
3	Flavonoids	Clear yellow	Orange-red	Positive (+)
4	Saponins	Clear green	Light green cloudy, foamy	Positive (+)

Meanwhile, the results of quantitative tests on flavonoid, tannin, and phenol compounds showed varying results from 3.51% to 5.95% as shown in Table 2.

Table 2: Quantitative Phytochemical Cambodia Flower Extract

No.	Parameter	Method	Result (%)
1	Flavonoids	Spectrophotometry	3.51
2	Tannins	Spectrophotometry	4.85
3	Phenol	Spectrophotometry	5.95

### 3.3 Bacterial Inhibition Test

The positive control, discs soaked in the antibiotic Ciprofloxacin 30 g, showed the presence of an inhibition zone starting from repetition groups I to III. The positive control inhibition zone diameter values obtained varied in each repetition group, ranging from 16.250 mm to 16.375 mm as shown in Table 3. Meanwhile, the negative control, discs soaked in 96% ethanol, did not produce an inhibition zone.

Table 3: Inhibition Zone of *S. aureus* in Positive and Negative Control

Repetition	Inhibition Zone Diameter (mm)	
	Positive Control	Negative Control
I	16.25	0
II	16.375	0
III	16.25	0
Average	16.29	0

The growth inhibition zone of *S. aureus* at various concentrations of Cambodia flower extract (55%, 70%, 85%, and 100%) in replication groups I to III from replications I to IV showed the existence of an inhibition zone that varied from 7.75 mm up to 9.5 mm as shown in Table 4. Compared with the diameter of the inhibition zone for the antibiotic Ciprofloxacin in the National Committee for Clinical Laboratory Standards (NCCLS) table, it is in the resistant category ( $\leq 15$ mm).

Table 4: Inhibition Zone for The Growth of *S. aureus* at Various Concentrations

Extract Concentration	Inhibition Zone Diameter (mm)			
	Replication I	Replication II	Replication III	Replication IV
<b>Replication I</b>				
Negative control	0			
55%	8.5	8.5	7.75	8.375
70%	8.75	8.625	8.25	8.625
85%	9.25	9.375	9.25	9.125
100%	9.5	9.5	9.375	9.375
Positive control	16.25			
<b>Replication II</b>				
Negative control	0			
55%	7.75	8.25	8.25	8.5
70%	8.625	8.5	8.75	8.75
85%	9.25	9.125	9.125	9.375
100%	9.375	9.5	9.5	9.5
Positive control	16.375			
<b>Replication III</b>				
Negative control	0			
55%	7.625	7.875	8.25	8.5
70%	8.75	8.375	8.75	8.625
85%	9.25	9.25	9.125	9.125
100%	9.375	9.5	9.5	9.625
Positive control	16.25			

### 3.4 Statistical Analysis

The Kolmogorov Smirnov statistics applied to the data shows that the Asymp sig value obtained is  $0.000 < 0.05$ , which means the data is not normally distributed. Hence, the Kruskal Wallis test was carried out at a confidence level of 95% ( $\alpha = 0.05$ ). The results of the Kruskal Wallis test obtained a significance value of (0.000). The value obtained is less than the  $\alpha$  value (0.05), indicating that there is a difference in the antimicrobial potential of

Cambodia flower extract in inhibiting the growth of *S. aureus*. The LSD test results showed that there were differences in antimicrobial potential at various concentrations (55%, 70%, 85% and 100%) of Cambodia flower extract. This can be seen from the significance value of each concentration with control, namely  $0.00 < 0.05$ .

#### 4. Discussion

The Cambodia flower extract in this study had a water content of 10%. Other studies that dried plant leaves reported that the water content of the extracted leaf powder is in the range of 3 to 5% (Wulandari et al., 2020). Based on this, the water content of Cambodia flower extract in this study is still quite high compared to the research results of Wulandari et al. (2020). Lower water content can maintain the stability of the extract powder with a longer shelf life. This is due to extract powder with low water content will prevent microbial growth, minimize oxidation, maintain physical properties, and prevent unwanted chemical reactions.

The results of qualitative tests on several parameters show that there are phenolic, tannin, flavonoid, and saponin compounds in Cambodia flower extract. Quantitatively, Cambodia flower extract shows a phenolic compound content of 5.95% (595 mg/100g), flavonoids 3.51% (351 mg/100g), and tannins 485% (485 mg/100g). Research by Fathoni et al. (2019) also found phenol, tannin, flavonoid, and saponin compounds in yellow Cambodia flowers (*Plumeria alba*), as well as alkaloids, terpenoids, steroids, hydroquinone, and polyphenols (Fathoni et al., 2019). Flavonoids are a secondary metabolite whose production is influenced by the photosynthesis process (Dave Mehta et al., 2023; Kumar et al., 2018; Mipeshwaree Devi et al., 2023). Flavonoids are widely distributed in plants and are responsible for the pigments that color most flowers, fruits, and seeds (Falcone Ferreyra et al., 2012). Flavonoids are natural compounds from the phenolic group and are valuable to human beings for their contribution to impart color and physiologically active members (Mutha et al., 2021).

Flavonoids are reported to have good antioxidant activity and estrogenic, antiviral, antibacterial and anticancer activity (Panche et al., 2016; Ullah et al., 2020). The benefits of flavonoids in the human body are as antioxidants so they are very good for preventing cancer, protecting cell structure, increasing the effectiveness of vitamin C, anti-inflammatory, preventing bone loss, and as antibiotics. In most cases, flavonoids can act directly as antibiotics by interfering with the function of organisms such as bacteria or viruses. The benefits of flavonoids are known to function as phytoalexin, namely as an antimicrobial for bacteria and fungi, thus helping to inhibit the spread of pathogens in the plant body.

Apart from flavonoids, tannin compounds in plants have also been used as medicine. Tannins are a class of polyphenolic compounds that are widely distributed in plant tissues and have various medical and pharmacological applications (Pizzi, 2021). Tannins are astringents, and polyphenols, have a bitter taste, can bind and precipitate proteins, and are soluble in water (especially hot water). Generally, tannin is used to treat skin diseases and as an antibacterial, but tannin is also widely used to treat diarrhea, hemostasis (stops bleeding), and hemorrhoids (Marcinińczyk et al., 2022; Sun et al., 2022). Tannins have been proven to have anti-cancer properties and can inhibit the growth of cancer cells (Pizzi, 2021), antioxidants that help protect cells from oxidative damage (Z. Tong et al., 2022), antimicrobials that inhibit the growth of fungi and bacteria, and antidiabetic properties and helps regulate blood sugar levels (Pizzi, 2021).

With respect to the results of research in the laboratory, the concentration of Cambodia flower extract shows that it has in-vitro antimicrobial potential with a category of resistance to the growth of *S. aureus* compared to the NCCLS table). The diameter of the inhibitory zone formed at various concentrations of Cambodia flower extract tested was classified into the resistant category ( $\leq 15$ mm) with a growth inhibition power of 7.75 mm to 9.5 mm. This shows that the ability to inhibit bacterial growth is not optimal for *S. aureus* bacteria sensitively in the minimum range of 21 mm. Something slightly different was found in the research of (Rupiniasih et al., 2019) who obtained a wider diameter of the inhibition zone of *S. aureus* using Cambodia/frangipani (*P. alba*) flower extract, namely 20.89 mm (versus 7.75–9.5 mm in this study). The size of the inhibition zone formed by an extract determines its antibacterial strength, which is categorized as very strong, strong, medium, or weak. The extract is considered to have a very strong inhibitory effect if the diameter of the resulting inhibition zone is more than 20 mm. If the diameter is between 10 mm and 20 mm, it is classified as having a strong inhibitory effect. A moderate

inhibitory effect was observed when the inhibitory potential of the extract ranged from 5 mm to 10 mm. An extract is considered weak in its inhibitory strength if the diameter of the inhibition zone produced is less than 5 mm (Sinaga & Jaya, 2022). Based on the classification of antibacterial strength, the Cambodia flower extract in this study showed a moderate inhibitory effect on *S. aureus* bacteria. The anti-microbial potential of Cambodia flower extract is not optimal in inhibiting the growth of *S. aureus* bacteria, which is thought to be caused by the antibacterial phytochemical content in the form of phenol (5.95%), tannin (4.85%) and flavonoids (3.51%) which is still relatively low.

#### Author Contributions:

Conceptualization, INJ.; Methodology, INJ.; Software, IGS.; Validation, IAMSA.; Formal Analysis, IAMSA, CDWHS, INP.; Investigation, INP.; Resources, INP, NM.; Data Curation, INJ.; Writing – Original Draft Preparation, INGS.; Writing – Review & Editing, INGS.; Visualization, INGS.; Supervision, INJ.; Project Administration, NM.; Funding Acquisition, INJ.

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#### Informed Consent Statement/Ethics approval:

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Poltekkes Kemenkes Denpasar for the research Simlitabkes 2023.

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# Analysis of Knowledge and Attitude regarding First Aid and CPR among Myanmar Seafarers

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## Abstract

Addressing a critical knowledge deficit within the maritime workforce, this study investigates the level of preparedness exhibited by Myanmar seafarers in regard to administering first aid and cardiopulmonary resuscitation (CPR). The research underscores the significance of customised training programmes for the maritime environment, as evidenced by the gender disparity and broad age distribution. Although the participants demonstrate noteworthy skills in burns care and CPR, they lack proficiency in specific areas such as managing haemorrhage, attending to unresponsive patients, and understanding the chain of survival. The study highlights the necessity of incorporating practical situations and a collaborative approach from various academic disciplines in order to enhance first aid training and ultimately enhance marine safety. In support of experiential learning in emergency response, the correlation study establishes a positive relationship between first aid knowledge and seafarer experience. Although the research conducted yielded valuable insights, a significant drawback was the lack of a skills assessment element; this underscores the critical need for future studies to incorporate objective measures. This study concludes by contributing to the collective comprehension of seafarers' proficiency in emergency procedures and acting as a catalyst for targeted interventions, policies, and best practises in the maritime industry. Despite the constraints, this research establishes a foundation for future research into maritime safety. It underscores the criticality of rectifying divergent levels of assurance in order to improve emergency medical readiness in the maritime domain as a whole.

**Keywords:** First Aid, CPR, Seafarer, Knowledge, Attitude, Myanmar

## 1. Introduction

In the marine sector, seafarers play a crucial role in maintaining the safe and efficient navigation of ships throughout the world's oceans and waterways. Their demanding profession exposes them to a variety of risks, including accidents and medical emergencies, in which timely and effective first aid and cardiopulmonary resuscitation (CPR) skills can make a significant impact in saving lives. It is indicated that while the number of ship casualties in 2021 was 57% lower than a decade prior, 3000 ship incidents occurred in the year according to

the Allianz global annual report 2022 (Cao et al., 2023). Despite the fact that various associations and organisations report accidents and incidents in maritime industry, incomplete or underreporting of data (Psarros et al., 2010) is still observed in the health-related space. In the context of medical emergency preparedness, research on the knowledge and attitudes of seafarers regarding first aid and cardiopulmonary resuscitation (CPR) remains limited, especially in the context of Myanmar's maritime workforce.

The maritime environment is typically challenging, with limited resources and time, especially in the event of a medical emergency; therefore, seafarers are required to have critical first aid skills. The onboard marine officers are required to undergo medical first aid training in order to respond to medical and health emergencies in accordance with the Maritime Administration Guidance (D'agostini, 2017). The maritime training providers are also regulated by the Myanmar Maritime Administration Department (DMA), which also governs the framework and structure of the first aid examination and certification (DMA, 2016).

Through its strategic location and rich maritime history, Myanmar relies heavily on a competent and committed marine crew for its contribution to its economy and international trade (D'agostini, 2017). Despite the critical significance of seafarers' ability to handle medical emergencies, few studies have examined their readiness and knowledge of first aid and CPR. Recognising the present state of knowledge and attitudes among Myanmar seafarers is essential for identifying potential knowledge gaps and developing targeted interventions to improve their capacity to respond effectively to medical emergencies at sea.

This study aims to address the current knowledge gaps by conducting an evaluation of Myanmar seafarers' knowledge and attitudes regarding first aid and CPR. By investigating this topic, it is intended to describe on the current state of preparedness among this essential group of maritime professionals and provide critical insights that can inform training programmes, policies, and best practises in the maritime industry.

## **2. Method**

The study includes the seafarers working within the maritime industry in Yangon Myanmar. There are two OPITO (Offshore Petroleum Industry Training Organisation)-approved offshore and maritime training centres in Yangon, Myanmar, and the sample seafarer population was selected from one of these training centres.

### *2.1 Inclusion and exclusion criteria*

*Inclusion Criteria:* the seafarers who are above 18 years of age and who have previously received first aid training.  
*Exclusion Criteria:* new seafarers who haven't received first aid training before or who are the new seafarer trainees.

### *2.2 Sample Size*

Approximately 100 seafarer refresher trainees are expected to be trained in the training centre within three months. Sample size is calculated based on the sample size power calculator. 49 samples are needed to have a confidence level of 95% with  $\pm 5\%$  of the margin of error.

### *2.3 Sampling Procedure*

An email consent was obtained from the training centre manager to conduct the study whereas the random sampling method was utilised as the sampling procedure. The online questionnaire including the information of the study and online consent form were distributed to the randomly selected participants via the training centre manager.

#### **2.3.2 Questionnaire and Data Collection**



A Microsoft online form was used to collect demographic information, first aid and CPR knowledge, and attitudes. First aid and CPR questions was created using the American Heart Association's 2020 First Aid Guidelines (Singletary et al., 2020) as a guide. The questions on injury and trauma management, CPR, giving breaths, burns and choking are added in the questionnaire. The data was collected from August-October 2023.

### 2.3.3 Data Analysis

Data analysis was performed using JASP Version 0.17.3 for Windows (JASP Team, 2023). A cross sectional descriptive statistic and correlational analysis were generated for the seafarers' knowledge and attitude about first aid variables.

## 3. Results

The survey was completed by a total of 58 seafarer respondents from the training centres after following the application of data cleaning and exclusion criteria.

### 3.1 Demographics

The survey findings indicate a notable disparity in gender representation within the seafaring community in Myanmar, since all participants self-identified as male. The lack of female participants implies a predominantly male-dominated composition within the marine sector in Myanmar.

The survey reveals a heterogeneous population of people in terms of age, comprising sailors from various age groups. It is worth noting that the survey participants do not include those under the age of 20, with the bulk of respondents falling between the age range of 30 to 59. The age categories of 30-39 and 40-49 have the greatest levels of representation, accounting for 33% each.

The study aims to gather data on the experience levels of seafarers, with the objective of gaining valuable insights about their professional tenure. The vast majority of participants in the survey possess professional experience ranging from 1 to 15 years. The category with the biggest proportion of responders is the 1-5 years' category, which accounts for 43% of the total. This observation implies the presence of a considerable proportion of individuals who have just joined the marine industry. The distribution of the participant demographic is shown as per Table 1.

Table 1: The distribution of the participant demographics

Name	Categories	n	Percentage
<b>Gender</b>	Male	58	100
	Female	0	0
<b>Age</b>	<20	0	0
	20-29	14	24
	30-39	19	33
	40-49	19	33
	50-59	6	10
<b>Years of Experience</b>	1-5	25	43
	6-10	9	16
	11-15	13	22
	16-20	7	13
	21-25	4	6

### 3.2 First Aid and CPR Knowledge among the Seafarers

The examination of the outcomes from the evaluation of first aid knowledge provides a comprehensive comprehension of the participants' competence in fundamental skills related to emergency medical response. Significantly, the participants exhibited excellent proficiency in burns care, with 81% demonstrating expertise in

this domain. Additionally, all participants shown a comprehensive comprehension of CPR (100%), indicating a strong grasp of this vital subject matter.

Nevertheless, it was observed that there were areas of modest proficiency in the care of bleeding (60%), handling unresponsive casualties (64%), and understanding the chain of survival (60%). The research indicates that there may be gaps in knowledge about the first evaluation of casualties' breathing (53%) and the management of choking incidents (59%). These findings highlight the need for targeted training interventions to address these areas of concern. The study found that traumatic airway management and rescue breathing with a pocket mask yielded the outcomes, with success rates of 67% and 79% respectively. The detail distribution of the knowledge assessment findings is shown in Table 2.

Table 2: the distribution of the percentage of the participants achieving a pass in each first aid knowledge element.

<b>First Aid Knowledge Element</b>	<b>Percentage of participants achieving a pass in each knowledge element</b>
<b>Bleeding Management</b>	60
<b>Burns Management</b>	81
<b>Traumatic Airway Management</b>	67
<b>Unresponsive Casualty Management</b>	64
<b>Initial Casualty Breathing Assessment</b>	53
<b>Rescue Breathing with Pocket Mask</b>	79
<b>Choking Management</b>	59
<b>CPR</b>	100
<b>Characteristics of CPR</b>	74
<b>Chain of Survival</b>	60

The first aid knowledge questions were analysed, compiled and the correlation analysis was performed between total first aid knowledge scores and the years of seafarer experience. According to the analysis, the correlation to assess the total first aid knowledge score and the years of seafarer experience is highly, significantly positively related with a small effect size,  $r=0.580$ , 95% CI [0.729, 0.378],  $p<0.001$  as shown in Table 3 and Figure 1.

Table 3: The correlates of First Aid Knowledge Total Score and Years of Seafarer Experience

<b>Variable</b>	<b>Years of Experience</b>
<b>First Aid Knowledge Total Score</b>	N
	58
	Pearson's r- Value
	0.580
	Upper 95% CI
	0.729
	Lower 95% CI
	0.378
	p-value
	<0.001

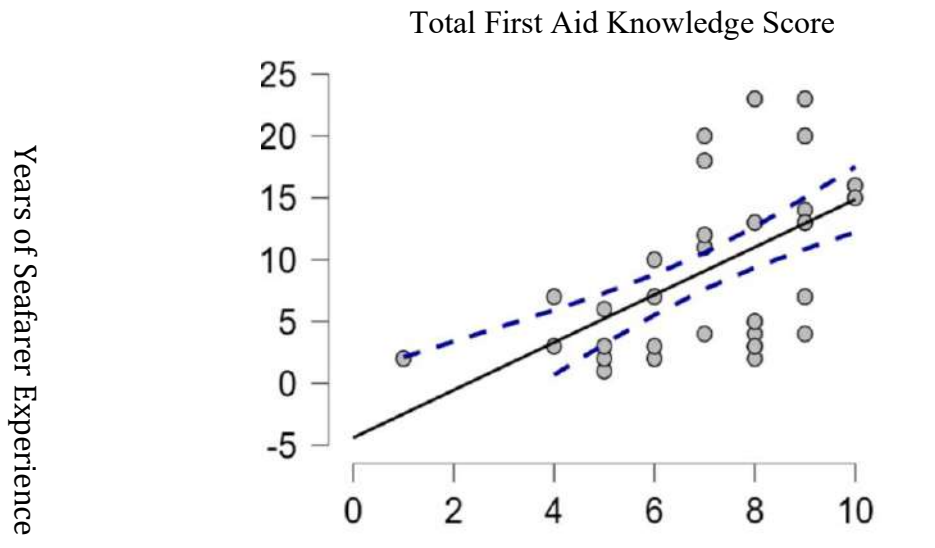


Figure 1: The Scatterplot correlates of first aid knowledge total scoring and the years of seafarer experience

### 3.3 Participants' Attitude towards the Confidence Level in First Aid and CPR Administration

The distribution of participant responses to the question "I am confident in my ability to administer first aid and CPR based on my current knowledge" is presented in Table 4. The responses were measured using a 5-point scale. The findings demonstrate that the participants exhibited different levels of confidence, providing insights into their subjective assessment of their readiness for emergency medical procedures.

A total of 20% of the participants responded 3 out of 5, signifying a moderate degree of confidence and suggesting a possible requirement for more reinforcement or practical training. The largest proportion, accounting for 55.2% of the participants, responded 4 out of 5, indicating a significant level of self-assurance in their competence to provide first aid and CPR. This implies a generally favourable evaluation of their level of expertise and preparedness in the context of emergency response. Moreover, it was found that 22.4% of the participants exhibited a substantial degree of confidence, 5 out of 5 which is indicative of persons possessing advanced expertise or undergoing comprehensive training. It is worth noting that a non-response rate of 1.7% was observed in the study.

Table 4: The distribution of the participant responses on the question "I am confident in my ability to administer first aid and CPR based on my current knowledge" in a 5-point scale.

Confidence Level (in a 5-point Likert scale)	Number of responses	Percent
3	12	20.7
4	32	55.2
5	13	22.4
Non responder	1	1.7

## 4. Discussion

The findings of the demographic study revealed a notable gender imbalance, since all respondents identified themselves as male. This observation implies that the marine industry in Myanmar is largely controlled by men. Furthermore, the study revealed a heterogeneous age composition among the participants, encompassing individuals aged 30 to 59 years. Notably, the age groups of 30-39 and 40-49 had the highest representation, suggesting a substantial proportion of seafarers at their peak professional years. A significant section of the participants (43%) had between 1-5 years of experience, suggesting a considerable number of individuals who are relatively new to the marine sector.

The assessment of first aid and CPR knowledge yielded results that were consistent with the latest criteria, highlighting the crucial abilities required for ensuring safety in marine settings. Significantly, the volunteers

demonstrated impressive expertise in burns care (81%) and CPR (100%), in accordance with established benchmarks such as the criteria set by the American Heart Association (Pellegrino et al., 2020). Nevertheless, there were places where the level of competence in bleeding management (60%), treating unresponsive patients (64%), and comprehending the chain of survival (60%) was quite low, suggesting possible deficiencies in knowledge.

According to the European Resuscitation Council First Aid Guideline (Zideman et al., 2021), effective haemorrhage control is essential for treating wounds and reducing the potential for further damage. Managing unresponsive patients necessitates a prompt and precise reaction, since it frequently entails life-preserving treatments. Comprehending the chain of survival is essential for orchestrating a series of acts that can greatly influence the result of a marine emergency. Based on a comprehensive review of marine incidents spanning fifty years (Luo & Shin, 2019), the research highlights that despite significant endeavours to improve maritime safety through technology progress, navigation enhancements, and crew education, human error continues to be the key factor behind the maritime medical emergency accidents. In order to enhance marine safety and reduce human error during emergencies, it is crucial to enhance the quality of first aid training programmes. It is essential to have customised curriculum specifically designed for the marine setting, which include realistic scenarios and employ a multi-disciplinary approach.

Similarly, the correlation study revealed a strong positive association ( $r=0.580$ ) between the overall scores of first aid knowledge and the experience of seafarers, which supports the idea of experiential learning in emergency response (Türkistanlı & Sevgili, 2018). The aforementioned connections highlight the importance of customising training programmes to suit the different levels of expertise among seafarers, while also ensuring that they adhere to the recommended best practises outlined in international recommendations.

An analysis of participants' perceptions regarding their self-assurance in doing first aid and CPR provides useful insights into their subjective evaluations of preparedness for emergency first aid preparedness. Significantly, 20% of participants indicated a moderate level of assurance, assigning themselves a rating of 3 out of 5. This indicates a possible requirement for more reinforcement or hands-on instruction to further strengthen their confidence (Häske et al., 2022). Majority of participants, 55.2%, expressed a high level of confidence with a rating of 4 out of 5, indicating a generally positive evaluation of their competence in first aid and CPR according to established guidelines. Furthermore, an additional 22.4% gave themselves a perfect score of 5 out of 5, suggesting advanced expertise or comprehensive training.

## **5. Limitations and the Future Research**

A significant limitation of the study is the absence of a skills assessment component, which is considered the most essential aspect of first aid training (Forbes, 2020). This is because the study solely relies on self-reported data regarding participants' confidence levels in administering first aid and CPR. The inherent subjectivity of self-assessment may induce response bias (Mazor et al., 2002), which can possibly result in an overestimation or underestimating of true confidence levels. The study's assessment of participants' competency in emergency medical procedures is incomplete due to the absence of a direct examination of their practical abilities. Incorporating objective skills evaluations or simulation exercises in future research endeavours would enhance the evaluation of seafarers' preparation in maritime first aid and CPR administration. This approach would complement self-reported data and result in a more comprehensive and reliable assessment.

## **6. Conclusion**

Overall, this research endeavour that centred on the maritime industry has yielded significant findings regarding the preparedness of seafarers to perform CPR and first aid, placing particular emphasis on the confidence levels of the participants. The results indicate a wide range of perceived confidence levels, although the majority of respondents demonstrated considerable self-assurance in accordance with established protocols. Despite the limitations of the study, the analysis of confidence levels offers a foundation for customised training interventions, highlighting the importance of addressing varying confidence levels to enhance overall emergency medical

preparedness in the maritime context. This research functions as a catalyst for subsequent investigations aimed at enhancing assessments and interventions in maritime safety, thereby augmenting the collective comprehension of seafarers regarding their proficiency in emergency procedures.

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**Conflict of Interest:** The authors declare no conflict of interest.

**Informed Consent:** All participants gave their informed consent for inclusion before they participated in the study.

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# An Experimental Evidence for Antibacterial Activity of Propolis on Bacteria from Lebanese Patients

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## Abstract

Propolis, with its distinctive chemical composition, has been known for therapeutic potential in treating numerous diseases. This study investigated whether propolis has an antibacterial effect on bacteria in Lebanon. Twenty-eight samples of gram-negative and gram-positive bacteria were collected from Raii Hospital and Al-Taakhi Medical Center in Gazieh, South Lebanon. Each sample was streaked on three different Petri dishes with different percentages of propolis under aseptic conditions. The results were recorded visually and confirmed by Gram staining after incubation for 24 h at 37°C. The obtained results show that propolis inhibited the growth of 18% of the total number of collected bacteria. The majority of bacteria on which propolis had an inhibitory effect were gram-positive bacteria, which inhibited 50% of them, whereas it only inhibited the growth of 9% of the gram-negative bacteria. Propolis was also shown to have an antifungal effect.

**Keywords:** Propolis, Anti-Bacterial, Anti-Fungal, Lebanon

## 1. Introduction

Propolis is a natural mixture produced by bees. It is gathered from substances collected from parts of plants, buds and exudates (Burdock, 1998). Honey bees use a combination of bees' wax and saliva to produce propolis (Cornara et al., 2017). The propolis name is derived from Greek origin "Pro" which means in front of and "polis" means community or city (Aminimoghadamfarouj & Nematollahi, 2017) which indicates that propolis is the hive defensive substance (Al-Hariri, 2011; Araujo et al., 2012). Propolis is one of the famous honeybee products used in folk medicine since ancient times for its various health effects (Ahangari et al., 2018).

## 2. Physical properties of Propolis

There are several types of propolis based on the area they originate from and their plant source (Ahmed et al., 2017). Propolis is a lipophilic substance that is also hard, brittle, and very sticky when heated (Hausen et al., 1987). Depending on its source and age, propolis could be a yellow green substance, or a red to dark brown

substance (Marcucci, 1995). The melting point of propolis at which it turns into its liquid state is 60°C to 70°C but for some samples, it may be 100°C (Wagh, 2013).

Propolis is commercially extracted by a suitable solvent, of which ethanol, methanol, water, hexane, acetone, dichloromethane, and chloroform are most common used (Gómez-Caravaca et al., 2006 ; Kumar N. et al., 2008). These solvents should remove the inner materials and reserve the desired compounds (Marcucci, 1995).

### 3. Chemical Composition of Propolis

The Biological activity and quality of propolis are directly related to its chemical constituents (Zhang X. et al., 2014). More than 300 constituents were identified in different propolis samples (De Castro SL., 2001), depending on its place of origin and time of collection (Kujumgiev A. et al., 1999). The main groups of propolis constituents are Plant resins (50%) in addition to other components such as waxes, essential oil, pollens, and other organic substances in different percentages as shown in Figure 1 (Przybyłek, I., & Karpiński, T. M. 2019).

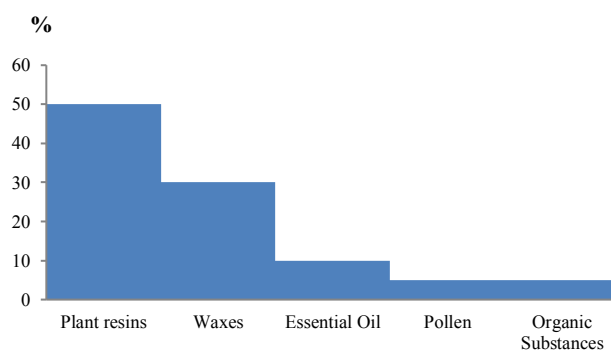


Figure 1: Raw Propolis chemical composition (%).

Propolis has many bioactive properties, such as antioxidant, antimicrobial, anti-inflammatory, wound healing and anti-hyperlipidemic (Ansoerge S. et al., 2003; Pimenta, H. C. et al., 2015; Manso et al., 2021). The main chemical components that are responsible for this activity are phenolic compounds, including flavones and aromatic acids and their esters (Ansoerge S. et al., 2003; Pimenta, H. C. et al., 2015 ; Manso et al., 2021). Several researches ensured that propolis from Asia, Europe and North America is mostly composed of phenolic compounds (Uzel et al., 2005). In a research done by Touzani et al. (2021) in determining the phenolic compounds in propolis samples collected from an African and an Asian region shows that phenolic content was the lowest in Palestinian sample of  $74.71 \pm 0.89$  mg GAE/g while the highest in Moroccan sample of  $148 \pm 1.31$  mg GAE/g. Similarly, flavone and flavonol content were higher in Moroccan sample of  $118 \pm 1.92$  mg QE/g than Palestinian sample  $26.97 \pm 2.44$  mg QE/g. The total antioxidant capacity is positively correlated with the content of phenolic compounds were it is  $90.87 \pm 2.91$  mg AAE/g for Moroccan sample and  $48.01 \pm 0.51$  mg AAE/g for Palestinian sample. Moreover Zeitouna et al. (2019) analyzed the chemical composition of Lebanese propolis and identified twenty-eight different compounds of which two phenolic acids and nine other flavonoids, also ferulic acid, caffeic acids, chrysin, galangin, quercetin, and pinocembrin were specified among the most representative compounds inside the Lebanese propolis.

### 4. Pharmacological Activity of Propolis

Several studies confirmed that Propolis has a therapeutic potential in pharmacology and medicines to treat various diseases due to its various chemical compositions.

#### 4.1. Antibacterial Activity

Propolis is increasingly known for its antibacterial activity. The antibacterial activities depend on the concentration, treatment time, and bacterial mode of action (Clemente J.C. et al., 2012 ; Kim Y-H, 2011). It acts

either by directly interacting with the microbial cell or by stimulating the immune system of the host cells (Bouchelaghem S., 2022). One of the hypothesized mechanisms include the inhibition of bacterial adherence and division, decrease of bacterial mobility, disturbance of membrane potential, and increase in cell membrane permeability (Ristivojević et al., 2018). Phenolic compounds elevate the antibacterial activity of propolis by enhancing their interaction with the cell membrane (Sikkema et al., 1995). In addition to that Kumar N. et al. (2008) emphasized that this antibacterial activity is highly activated against Gram-positive bacteria and less activated against Gram-negative bacteria, unless high concentration of Propolis is used.

#### 4.2. Antifungal Activity

Propolis shows anti-fungal activity against different fungi, such as *Candida albicans*, *C. parapsisolis*, *C. tropicalis*, *Saccharomyces cerevisiae* and *C. krusei* (Ożarowski et al., 2022). Ozcan, (1999) emphasized that different propolis chemical compositions such as, 3-acetylpinobanksin, pinobanksin-3-acetate, pinocembrin, p-coumaric acid and caffeic acid and more compounds enhances propolis antifungal activity. Previously, researches emphasized that propolis antifungal activity occurred by inhibiting the extracellular phospholipase, directing to alleviation of the fungal cell adhesion to epithelium (D'Auria et al., 2003). Recently, researchers spotted that propolis may affect the formation of the cell wall and inhibit the morphological transformation of fungi (Gucwa et al., 2018).

### 5. Methods

#### 5.1. Sample Collection & Identification

A total of twenty-eight samples were collected from Raii Hospital and Al-Taakhi Medical Center- Gazieh. Both of these institutions are located in Ghazieh, a village in the vicinity of Said but receive patients from Saida, Ghazieh and several other villages and towns in South Lebanon. The collected samples that are available in the hospital or the medical center were samples taken from patients submitted to bacterial culturing and antibiogram process to specify the type of the bacteria and the effective drug to be prescribed. The samples were saved in incubators for short time to be taken and test propolis effect on these samples. The samples were including gram-negative and gram-positive bacteria that are randomly selected based on the available samples at the time of collection. The collection process took place over several days separated by two-week duration.

Figure 2 depicts the distribution of the bacterial samples such that the gram-negative bacteria exceed the gram-positive bacteria in number thus, in percentage as well. In total, there were 6 gram-positive bacteria, accounting for 21.4% of the total samples. On the other hand, 22 gram-negative bacteria were available accounting for 78.57% of the total number of samples.

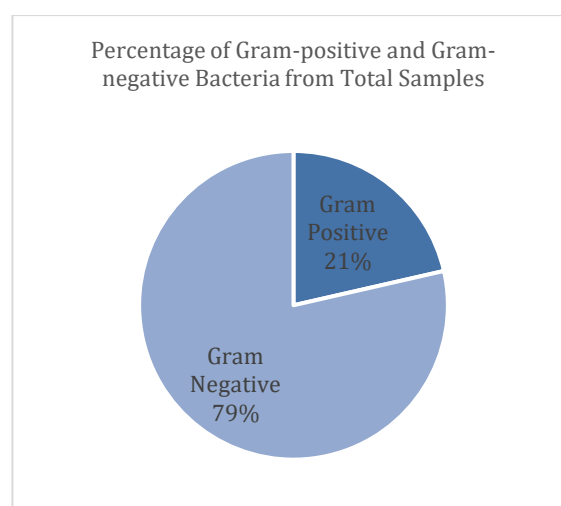


Figure 2: Distribution of Gram-positive and Gram-negative Bacteria Samples According to Percentage



The collected bacteria were diverse including *Staphylococcus aureus*, *E. coli*, *Klebsiella*, *Proteus*, *Streptococcus* and *Klebsiella*. Some of these samples are shown in the figure 3 below.



Figure 3: Examples of the Collected Bacteria Samples

### 5.2. Propolis Agar Preparation

In order to investigate the effect of propolis on the growth of several species of bacteria, a nutritional medium that permits the growth of these bacteria must be chosen so that there wouldn't be any need to change the medium type for each of the corresponding bacteria. For this reason, Mueller Hinton Agar (MHA) was selected. MHA is a non-selective and non-differential medium that allows the growth of a very wide range of bacteria and is often used for antibiotic susceptibility testing. Both of these characteristics make MHA a suitable medium for this study since the study includes different bacterial species and aims to determine the anti-bacterial effect of propolis. Therefore, MHA was used in the "control petri-dishes" for all the collected samples. On the other hand, propolis samples found in Lebanese market were in the form of a liquid state means that propolis dissolved in appropriate solvent. The liquid propolis found in the market were used in the "testing petri-dishes", varying volumes of Propolis were added and infused in the MHA agar medium to find out how different concentrations of Propolis might affect the bacterial growth. Rather than using agar diffusion method that is used by researchers such as (Balouiri et al., 2016; Stepanović et al., 2003; Alhassan Sa-eed et al., 2023) so that the bacteria diffused in the agar and the propolis tested by disk diffusion method. However, in this methods propolis diffused in the agar with different concentrations prepared as follows:

- 1) 0 mL of Propolis and 400 mL of MHA agar were added into petri-dishes as "Control"
- 2) 20 mL of Propolis were added to 380 mL of MHA agar, making a total of 400 mL, added to petri-dishes as "5% Propolis".
- 3) 40 mL of Propolis were added to 360 mL of MHA agar, making a total of 400 mL, added to petri-dishes as "10% Propolis".

### 5.3. Plating Samples on Petri-dish

It is critical in this study to maintain the same concentration of the bacteria sample between the three different petri-dishes. This is essential to ensure that the initial quantity of streaked bacteria doesn't affect the outcome in the 3 petri-dishes after 24 hours. The method used to plate the bacteria on different agar plates (one control, and the others contain propolis) is shown in the sketched diagram below:

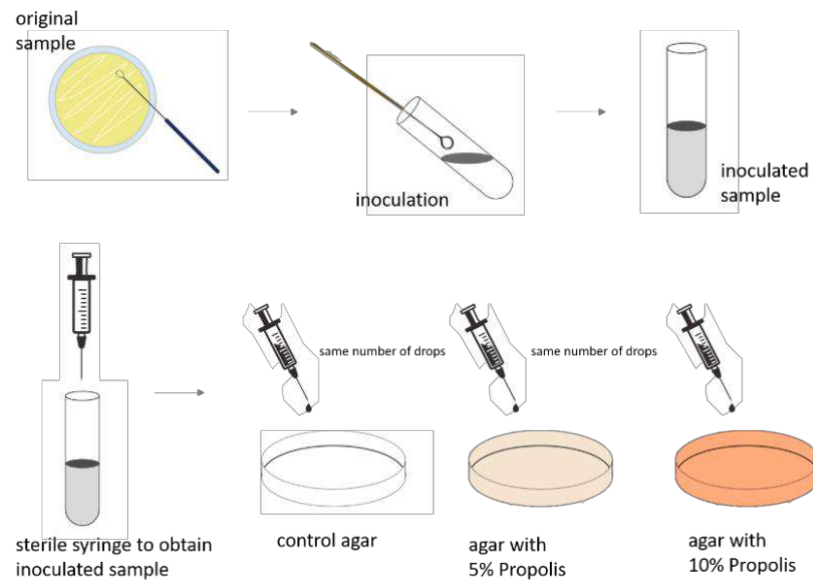


Figure 4: Procedure of Plating the Bacterial Samples in Petri-dishes

Figure 4 explains the detailed process by which the three different petri-dishes were streaked with bacteria. For each of the samples, an inoculum was transferred from the original sample into a sterile test tube with saline water to obtain a homogeneous bacterial suspension. Then, a sterile syringe was used to collect a volume of the prepared suspension and to transfer a limited number of drops into the control agar, the agar with 20 mL Propolis, and the agar with 40 mL Propolis, keeping in mind that the same number of drops is put into each petri-dish. After that, a sterile swab is used to uniformly distribute the drops of the bacterial suspension over the entirety of the petri-dish, and the process is repeated in each petri-dish separately to avoid contamination. The process was performed for each of the twenty eight samples individually. Finally, the plated petri-dishes were incubated at 37°C for 24 hours.

#### 5.4. Gram Staining

The results are viewed after 24 hours of incubation to determine the presence or absence of bacterial growth in each of the petri-dishes. Visual observation was done initially, followed by gram staining to confirm the observed results. Gram staining procedure took place according to the commonly accepted method starting with staining with Crystal Violet, followed by Iodine, Acetone Ethanol, and finally washing with Safranin. After staining, the samples were observed under the microscope.

## 6. Results

The main objective of this study was to investigate whether Propolis, a naturally produced substance, has an actual antimicrobial effect, and more specifically an antibacterial effect. For this reason, a control petri-dish, a 5% Propolis petri-dish and a 10% Propolis petri-dish were used for each of the tested bacterial samples. In order to identify the effect of Propolis on the different bacterial species, the bacterial growth was monitored visually and by gram staining for confirmation.

### 6.1. Growth Identification (visual and staining)

The following table illustrates the type of collected bacterial samples alongside their classification as gram-negative or gram-positive and their respective results in the three different mediums: control, 5% propolis and 10% propolis.

Table 1: The Collected Bacteria Species with Their Respective Results on the Control Agar And Propolis Containing Agar

<i>Bacteria</i>	<i>Gram + /Gram -</i>	<i>Control Agar</i>	<i>Agar with 5% Propolis</i>	<i>Agar with 10% Propolis</i>
<i>Klebsiella</i>	gram -ve	Growth	Growth	Growth
<i>Pseudomona</i>	gram -ve	Growth	Growth	Growth
<i>Klebsiella</i>	gram -ve	Growth	Growth	Growth
<i>E. Coli</i>	gram -ve	Growth	Growth	Growth
<i>S. aureus</i>	gram +ve	Growth	Growth	Growth
<i>E. Coli</i>	gram -ve	Growth	Growth	growth
<i>Streptococcus</i>	gram +ve	Growth	Growth	NO growth
<i>S. aureus</i>	gram +ve	Growth	Growth	NO growth
<i>S. aureus</i>	gram +ve	Growth	Growth	growth
<i>S. aureus</i>	gram +ve	Growth	NO growth	NO growth
<i>E. Coli</i>	gram -ve	Growth	Growth	Growth
<i>E. Coli</i>	gram -ve	Growth	Growth	NO growth
<i>E. Coli</i>	gram -ve	Growth	Growth	Growth
<i>Klebsiella</i>	gram -ve	Growth	Growth	Growth
<i>Proteus</i>	gram -ve	Growth	Growth	Growth
<i>Proteus</i>	gram -ve	Growth	Growth	Growth
<i>E. Coli</i>	gram -ve	Growth	Growth	NO growth
<i>E. Coli</i>	gram -ve	Growth	Growth	Growth
<i>E. Coli</i>	gram -ve	Growth	Growth	Growth
<i>E. Coli</i>	gram -ve	Growth	Growth	Growth
<i>E. Coli</i>	gram -ve	Growth	Growth	Growth
<i>E. Coli</i>	gram -ve	Growth	Growth	Growth
<i>S. aureus</i>	gram +ve	Growth	Growth	Growth
<i>Klebsiella</i>	gram -ve	Growth	Growth	Growth
<i>E. Coli</i>	gram -ve	Growth	Growth	Growth
<i>E. Coli</i>	gram -ve	Growth	Growth	Growth
<i>E. Coli</i>	gram -ve	Growth	Growth	Growth
<i>E. Coli</i>	gram -ve	Growth	Growth	Growth

The table shows that all the samples presented growth in the control agar, as expected. However, only 1 bacteria sample presented no growth in the agar with 5% Propolis (*S. aureus*), and 5 samples presented no growth in the 10% Propolis agar. If the 10% Propolis results were taken into consideration, then 17.85% of the total bacterial samples were affected by Propolis to the extent of complete absence of growth.

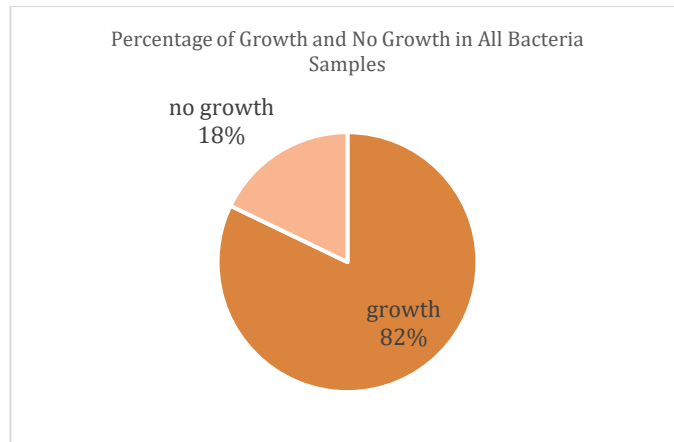


Figure 5: Percentage of Growth and NO Growth in All Bacterial Samples

Additionally, it can be seen from table 2 that three gram-positive bacteria (*S. aureus*) showed no growth in 10% Propolis, and two gram-negative bacteria (*E. coli*) showed no growth in 10% Propolis. In terms of percentages, this means that 50% of the gram-positive bacteria were negatively affected by Propolis, while only 9.09% of the gram-negative bacteria were affected by Propolis.

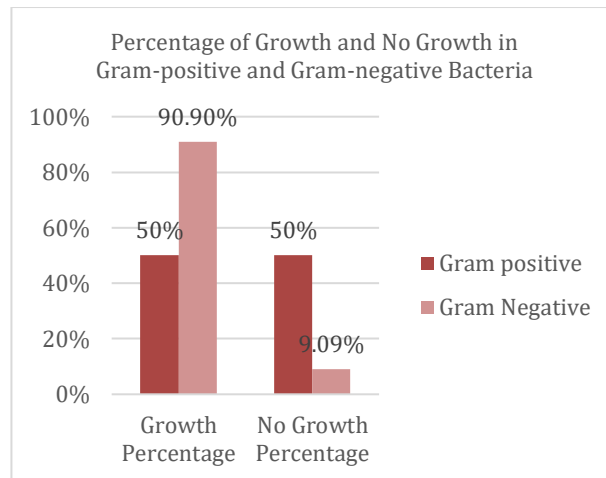


Figure 6: Percentage of Growth and No Growth in Gram-positive and Gram-negative Bacteria

Upon staining, gram-positive bacteria exhibit a purple color and a shape respective to the tested bacteria sample. For instance, grape like purple formation indicate *S. aureus*. On the other hand, a gram-negative bacteria display a pinkish color. For instance, *E. coli* appears as pink rod-shaped formations. Figure 7 shows some of the gram staining results at 5% Propolis through which two negative staining results and one positive staining result are shown.

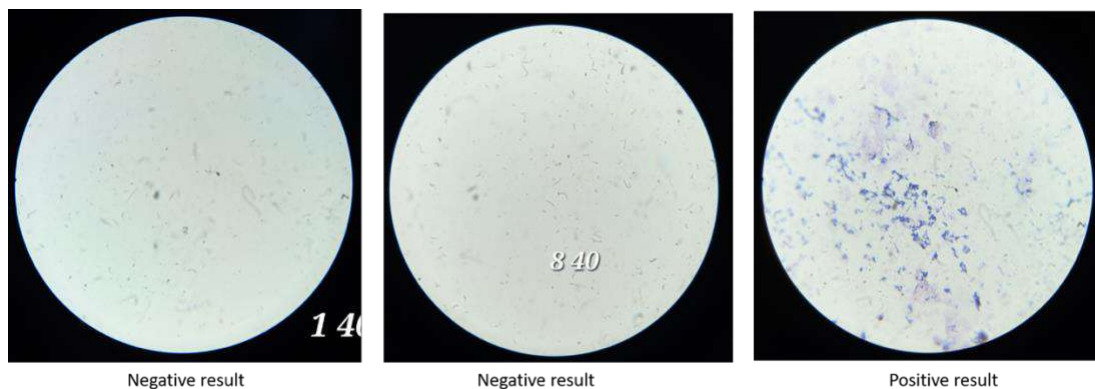


Figure 7: Gram Staining Results of some Bacteria Samples

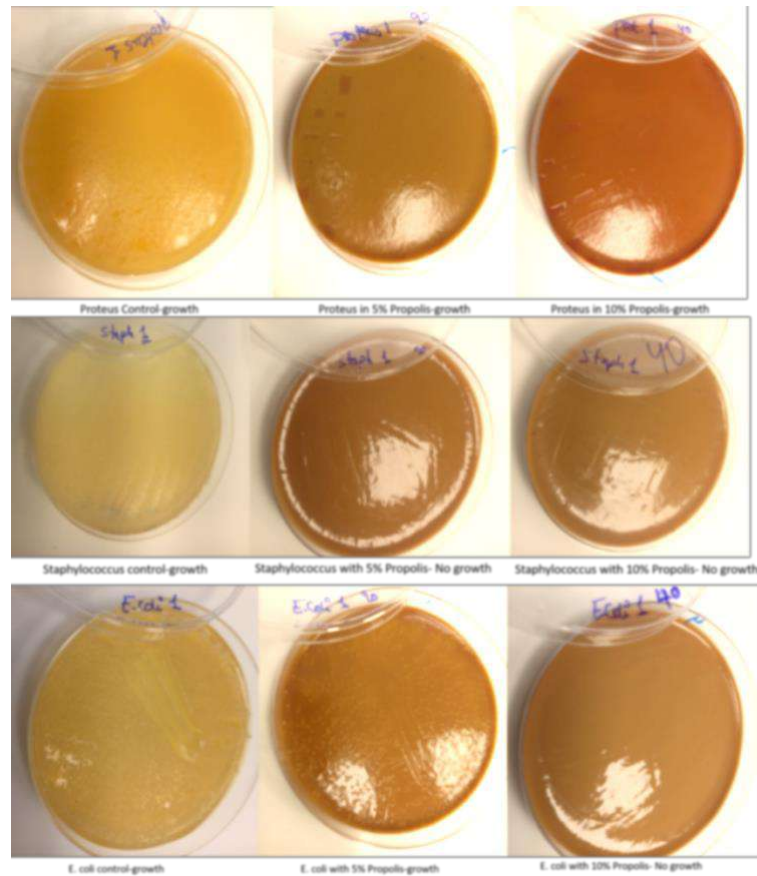


Figure 8: Examples of Growth Results for 3 Different Bacteria Species

From Figure 8, three different bacterial samples are presented where each sample illustrates the results in the control agar, the agar with 5% Propolis, and the agar with 10% Propolis. More specifically, the *Proteus* sample shows growth in all of the three cases: control agar, agar with 5% Propolis, and the agar with 10% Propolis. On the other hand, the *staphylococcus* sample showed growth only in the control agar and no growth in neither of the other cases. As for the *E. coli* sample, it showed growth in both the control agar and the agar with 5% Propolis whereas it showed no growth in the agar with 10% Propolis. These visual results were of course validated through the gram staining procedure.

### 6.2. Anti-fungal effect of Propolis

After leaving the plates for several days, fungi appear on the controlled plates while no appearance for any type on the plates containing Propolis as shown in Figure 9.



Figure 9: Anti-fungal effect of Propolis

## 7. Discussion of Results

The results obtained from the collected data in this study show that first of all, once randomly collected from a hospital or a medical center, the percentage of gram-negative bacteria (79%) exceeds the percentage of gram-positive bacteria (21%) highlighting the predominance of gram-negative bacteria in Lebanese patients. Furthermore, 53% (15 samples) of the total collected bacterial species in this study were *E. coli*. These results are in agreement with several previous studies that illustrated the predominance of gram-negative bacteria in Lebanon. For instance, in their published research, Moustapha Khodor et al., (2022) demonstrated that when monitoring the bacterial co-infection with covid-19 virus in the gram-negative bacteria accounted for 61.7% of the co-infections, whereas gram-positive bacteria accounted for 23.4% only. Among the gram-negative bacteria, *E. coli* was predominant (25.5%). Their study was conducted in Tripoli, Lebanon. Similarly, Kamal Chamoun et al. (2016) performed a nationwide investigation and concluded that from 16 hospitals, the percentage of collected gram-positive bacteria was 27.1% compared to 72.8% of gram-negative bacteria among which 54.7% was *E. coli*. In another study, the percentage of *E. coli* from urinary tract infection patients was 72% compared to only 2% UTI caused by *Staphylococcus aureus* (Hamzé, M. et al., 2017).

As for the experimental results related to the antibacterial effects of Propolis, it was evident that Propolis had a greater effect on the gram-positive species, where it inhibited the growth of 50% of the total gram-positive bacteria. On the other hand, Propolis was able to inhibit the growth of gram-negative bacteria by 9.09%. These results were achieved by combining MHA agar with 10% Propolis preparation. Thus, the results confirm that Propolis is more efficient in inhibiting the growth of gram-positive bacteria than gram-negative bacteria. Studies such as (Przybyłek, I., & Karpiński, T. M. 2019) which tested the Propolis extract on a total of 600 aerobic and anaerobic bacteria showed with minimum inhibition concentration evidence that Propolis has a greater inhibitory effect on gram-positive bacteria. Similarly, Bratko et al. (2020) and Almuhayawi (2020) and Silva-Carvalho et al. (2015) confirmed the gram-positive bacteria susceptibility to Propolis, also confirmed the great inhibitory effect of Propolis on fungi, since 5% Propolis was able to prevent the natural growth of fungal contaminants in comparison to the control agar. These results confirmed the general knowledge of the anti-fungal effect of Propolis (Mutlu Sariguzel, F., 2016).

## 8. Conclusion

Propolis is a natural substance produced from honeybees after being collected from plant sources such as tree buds, sap flows, and botanical exudates. Even though bees use it for practical reasons such as sealing the gaps in their hives, human have used it as a healthy product for centuries after discovering its potential in preventing diseases. Numerous studies have been conducted to investigate the effect of Propolis against different strains and types of bacteria, and recently against antibiotic resistant bacteria as well. These studies concluded that Propolis has an antibacterial effect as well as an anti-fungal and antiviral effect.

In this study, the effect of Propolis was investigated on bacterial samples collected from south Lebanon. The samples included a number of gram-positive bacteria (21%) and gram-negative bacteria (79%). Each of the collected samples was incubated in a control Mueller Hinton Agar, an MHA agar with 5% Propolis preparation, and MHA with 10% Propolis. After a 24-hour incubation, the bacterial growth was investigated visually and confirmed by gram staining. As a result, the 10% Propolis preparation was able to inhibit the growth of 50% of the gram-positive bacteria and 9% of the gram-negative bacteria.

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# Gender Differences in Nutritional Status Among Adolescents Living with Family in Selected Slums of Dhaka, Bangladesh: A Mixed-Method Study

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## Abstract

**Introduction:** Nutritional vulnerability of adolescents living in slums is more compare to general adolescents. Adolescent girls are disproportionately impacted by nutritional deficiency due to gender norms, many adolescent boys are malnourished as well. This study sought to assess gender differences in nutritional status among adolescents living with family in selected slums of Bangladesh. **Methods:** The study used cross-sectional design with mixed method approach. Male and female adolescents between 10 to 19 years living in the Bauniabadh slum and ‘Ta’ Block Jhil Par slum of Dhaka were study population. Quantitative data was collected through pre-tested structured Bangla questionnaire by household survey of 115 adolescents. Qualitative interviews were sought through 12 In-depth interviews. BMI was categorized and 24-hour dietary recall was used to obtain dietary information by dietary diversity score. **Results:** Around 40.0% male adolescents and 46.6% female adolescents were underweight. Approximately 5% male adolescents and 3.4% female adolescents were overweight. Almost 67% male adolescents and 63.8% female adolescents had lowest dietary diversity score. One-fourth of male adolescents and 36.2% female adolescents had medium dietary diversity Score. There is observed association between sex of respondents and eating vegetables, and eating fish ( $p<0.05$ ). Dietary behavior and eating more foods for female adolescents had significant observed association with sex of respondents ( $p<0.05$ ). The qualitative result revealed that females were expected to learn cooking since they had to feed other members of her in laws house. Females made food sacrifices so that other family members could eat more. **Conclusion:** There were gender differences in nutritional status, dietary behaviour and nutritional knowledge among male and female adolescents living with family in selected slums of Dhaka, Bangladesh.

**Keywords:** Adolescents, Bangladesh, Dietary Behaviour, Gender, Nutrition

## 1. Introduction

Adolescence is a transitional period of development from childhood to adulthood characterized by rapid physical, mental and social changes which have an impact on a person's eventual dietary habits and nutritional status (Kahssay *et al.*, 2020). There are about 1.2 billion adolescents in the world among them 19% suffer from major nutritional deficiencies, who resides in developing countries (Kabir *et al.*, 2016). During adolescence nutritional insufficiency leads to poor nutritional status such as underweight, stunting, wasting (Ahmad *et al.*, 2020). Globally, girls continue to be twice as likely to suffer from all types of malnutrition compared to their male peers (Nasreddine, 2020). Adolescent boys also suffer from a high burden of malnutrition particularly thinness while there is inadequate nutritional data on them (GAIN, 2018). Poor nutritional status of adolescents in early life reduces learning abilities, increases reproductive and maternal adverse health effects and reduces productivity (Oniang'o *et al.*, 2020). In South Asia, Adolescent girls have a low social position, and low birth weight children born to undernourished adolescent mothers pass on their malnutrition to the next generation (Sen & Hook, 2012).

Malnutrition is a major public health concern in Bangladesh as the prevalence of malnutrition is higher in female than male (Blum *et al.*, 2019). There are about 36 million adolescents in Bangladesh comprised of 22% of the population (UNICEF, 2018). The prevalence of adolescent's stunting is 36% and low body mass index (BMI) is 50% in Bangladesh (Kabir *et al.*, 2016). There are 13.7 million adolescent girls among them the prevalence of Low BMI is 50% (Ahmed *et al.*, 2020). About 31% of adolescent girls (15–19 years old) are undernourished (BMI<18.5) in Bangladesh (Leroy *et al.*, 2018). Among ever-married adolescent girls, 4% are underweight and around one-in-ten unmarried adolescents are underweight (NIPORT, 2020).

Lack of dietary diversity is particularly an important concern in adolescent nutrition (Kaur *et al.*, 2020). Studies conducted in low income developing countries, revealed girls have lower intakes of nutritious foods such as meats, eggs, milk, pulses, fruits, and vegetables and a greater risk for micronutrient deficiencies compared to boys (Nasreddine, 2020). Adolescent females are at least twice as likely as boys to go to bed hungry, skip meals, and eat smaller meals as a coping strategy during food insecurity (GAIN, 2018).

The nutritional needs of Bangladeshi adolescent girls for physical maturation and menstruation are disproportionately impacted by gendered cultural norms (GAIN, 2018). Due to the parents' preference for sons, there is discrimination against daughters in intra-household food allocation, resulting in undernutrition (Christian & Smith, 2018). Gender norms between female and male (roles and responsibilities) have an impact on food attainment, taking decisions about intrahousehold food distribution, food consumption pattern and differences related to food intake (Blum *et al.*, 2019).

There are very limited studies on gender perspective of adolescent nutrition in Bangladesh. Adolescents of the slum area are nutritionally more vulnerable because of poverty, lack of knowledge about the long-term consequences of adolescent malnutrition, poor housing conditions, and inadequate quality and quantity of food (Alam *et al.*, 2018). Nutritional vulnerability of adolescents living in slum areas is more, compare to general adolescents. Addressing gender dimensions is effective way to tackle malnutrition. The way towards improved nutrition for adolescents should be gender equitable process.

## 2. Method

In order to conduct a thorough study of the slums in Pallabi thana of Mirpur, Dhaka, a cross-sectional mixed method research approach was utilized. Specifically, Bauniabadh and the "Ta" block of Jhil Par were purposely selected as our sample size from the 107 slums under the authority of Dhaka North City Corporation. Bauniabadh slum is located in Pallabi Thana of Dhaka district, ward number 5, DNCC zone 2, and is divided into 5 blocks: A, B, C, D, and E. Meanwhile, 'Ta' Block Jhil par is situated in Pallabi Thana of Dhaka district, ward number 6, DNCC zone 2. Although both impoverished areas are about two kilometers apart, they were both chosen as important study locations. Participants were selected from both slums using a simple random sampling technique and household list. This list was utilized to develop an outline, and participants were chosen by lottery method. Both quantitative and qualitative methods were utilized in order to gather comprehensive data.

The quantitative study enlisted a total of 115 male and female adolescents. Participants were selected based on the age between 10 to 19 years, voluntary participation in the study, parent/guardian's informed written consent and assent. Pre-tested semi-structured Bangla questionnaire was used for data collection. Standard height was measured with measuring tape to the nearest of centimeters and weight was measured on a weighing machine in kilogram. BMI was calculated as a person's weight in kilograms divided by the square of the person's height in meters (kg/m<sup>2</sup>) and BMI was categorized into 4 groups- Underweight (Below 18.5), Normal (18.5-24.9), Overweight (25.0-29.9), Obesity (Above 30) (WHO 2019).

24-hour dietary recall was used to obtain dietary information by dietary diversity score. The score was calculated by using the Guidelines for Measuring Individual Dietary Diversity Score (DDS) for adolescents (Alam, 2018). The DDS was used as a proxy of household dietary diversity, such that the higher the DDS, the higher the dietary diversity. Based on food items consumed in the last 24 hours, respondents were assigned the number of food groups they consumed, ranging from 0 to 9. Dietary Diversity Scores (DDS) were calculated using these 9 food group indicators. The 9 food groups included starchy staples (e.g., rice, etc.), legumes and nuts, dairy, organ meats, eggs, flesh foods (meat, fish, or poultry), vitamin A-rich dark green leafy vegetables, other vitamin A rich fruits and vegetables, and other fruits and vegetables. DDSs were calculated by summing the number of food groups consumed by the respondents on a day. Individual dietary diversity scores were categorized into 3 groups which was based on the distribution of 9 food groups,  $\leq 3$  food groups as lowest dietary diversity, 4-5 food groups as medium dietary diversity and  $\geq 6$  as high dietary diversity.

A database in SPSS version 23 (Chicago, IL, USA) was developed according to the questionnaire. Data regarding all question was entered in the developed data base. Descriptive statistics, bivariate statistics were updated. Data related to Dietary Diversity score was calculated by summing of nine dietary diversity indicators. This score was categorized as per the guideline and presented by frequency distribution, appropriate chart and table. Chi-square test was used to analyze the association. The significance p-value of the associations was analyzed.

For our In-depth interview, we interviewed 3 male adolescents, 3 female adolescents, 3 fathers and 3 mothers. These participants were purposively sampled based on our inclusion criteria. Notes were taken during the interview and interviews were recorded with voice recorders and then transcribed. Data were coded manually. All transcripts were reviewed and themes were developed based on analysis plan and thematic analysis was done.

### 3. Results

#### 3.1. Quantitative results

##### 3.1.1. Sociodemographic characteristics of the participants

Among 115 adolescents, 49.6% are male adolescents and 50.4% are female adolescents. Majority of adolescents (47.0%) were aged between 14-16 years and 33.0% were aged between 10-13 years. Around 70.4% adolescents were in secondary and 16.5% adolescents were in primary level of education. About 29.6% and 40.9% adolescents' fathers and mothers had primary level of education respectively. Approximate 69.6% adolescents' fathers were self-employed and 67.0% adolescents' mothers were housewife. Almost 54.8% respondents had 5-7 family members and 36.5% adolescents had  $\leq 4$  family members.

##### 3.1.2. Nutritional status of the respondents

Table 1 shows that 40.4% male adolescents and 46.6% female adolescents were underweight. About 5.3% male adolescents and 3.4% female adolescents were overweight. Only 1.7% female and no male adolescents were obese.

Table 1: Distribution of BMI category among male and female respondents (n=115)

BMI Category (kg/m <sup>2</sup> )	Male (n=57) n (%)	Female (n=58) n (%)
Underweight (<18.5)	23 (40.4)	27 (46.6)

Normal (18.5-24.9)	31 (54.4)	27 (48.3)
Overweight (25.0-29.9)	3 (5.3)	2 (3.4)
Obesity ( $\geq 30$ )	0 (0)	1 (1.7)

Table 2 shows 66.7% male adolescents and 63.8% female respondents had lowest DDS. About 33.3% male adolescents and 36.2% female adolescents had medium DDS.

Table 2: Distribution of Dietary Diversity Score (DDS) among male and female respondents (n=115)

Dietary Diversity Score	Male (n=57) n (%)	Female (n=58) n (%)
Lowest DDS ( $\leq 3$ food groups)	38 (66.7)	37 (63.8)
Medium DDS (4 and 5 food groups)	19 (33.3)	21 (36.2)

Table 3 shows that 100% male and 100% female adolescents consumed starchy staples. About 73.7% male and 77.6% female adolescents consumed meat and fish, 43.9% male and 36.2% female adolescents consumed other vitamin A rich fruits and vegetables (e.g. tomato, onion, eggplant, wild fruits, locally available vegetables), 57.9% male and 53.4% female adolescents consumed legumes, nuts and seeds, 10.5% male and 13.8% female adolescents consumed dark green leafy vegetables, only 3.4% female and no male adolescents consumed vitamin A rich fruits and vegetables (pumpkin, carrot, squash, or sweet potato that are orange inside, red sweet pepper), 28.1% male and 34.5% female adolescents consumed eggs, 5.3% male and 3.4% female adolescents consumed milk and milk-products.

Table 3: Different food groups consuming in 24 hours by male and female respondents (n=115)

Food groups	Male (n=57) n (%)	Female (n=57) n (%)
Starchy staples	57 (100)	58 (100)
Dark green leafy vegetables	6 (10.5)	8 (13.8)
Vitamin A rich fruits and vegetables	0 (0)	2 (3.4)
Other vitamin A rich fruits and vegetables	25 (43.9)	21 (36.2)
Organ meat	1 (1.8)	0 (0.0)
Meat and fish	42 (73.7)	45 (77.6)
Eggs	16 (28.1)	20 (34.5)
Legumes, nuts and seeds	33 (57.9)	31 (53.4)
Milk and milk products	3 (5.3)	2 (3.4)

Table 4 shows that 67.4% female and 32.6% male adolescents gave their opinion to eat vegetables daily, respectively. 61.5% female and 38.5% male responded to eating fish 3 or 4 times per week. About 22.6%, 38.3%, and 24.3% of the adolescents picked the correct food group to see the knowledge about carbohydrate, protein and fiber rich food. Surprisingly, most of the adolescents didn't know the right food according to carbohydrate (60.0%), protein (47.0%) and fiber rich food (69.9%). Almost 54.2% female and 45.8% male adolescents suggested eating vegetables, fruits, milk for female adolescents. About 61.4% female and 38.6% male adolescents agreed to eat more food for female adolescents. So knowledge level of female respondents is significantly higher

than male adolescents. There is association between sex respondents with eating vegetables and eating fish in a week where the respective p-value is smaller than 0.05 at 5% level of significance. Also, food behavior and eating more food for female adolescents have significant association with sex of the respondents.

Table 4: Nutrition related knowledge among male and female respondents (n=115)

Variables	Male n (%)	Female n (%)	p-value
<b>Minimum fruits intake per week</b>			
≤ 3 days	17(47.2)	19 (52.8)	0.984
≥ 4 days	13 (50.0)	13 (50.0)	
Daily	22 (50.0)	22 (50.0)	
Don't know	5 (55.6)	4 (44.4)	
<b>Minimum vegetables intake per week</b>			
≤ 4 days	28 (68.3)	13 (31.7)	0.004
≥ 5 days	9 (42.9)	12 (57.1)	
Daily	15 (32.6)	31 (67.4)	
Don't know	5 (71.4)	2 (28.6)	
<b>Minimum fish intake per week</b>			
1 or 2 times in a week	28 (68.3)	14 (33.3)	0.015
3 or 4 times in a week	25 (38.5)	40 (61.5)	
Daily	0 (0.0)	1 (100)	
Don't know	4 (57.1)	3 (42.9)	
<b>Carbohydrate rich food</b>			
Rice, bread, potato	14 (53.8)	12 (46.2)	0.462
Fish, meat, egg, pulse	4 (44.4)	5 (55.6)	
Vegetables, fruits	3 (27.3)	8 (72.7)	
Don't know	36 (52.2)	33 (47.8)	
<b>Protein rich food</b>			
Rice, bread, potato	1 (20.0)	4 (80.0)	0.298
Fish, meat, egg, pulse	22 (50.0)	22 (50.0)	
Vegetables, fruits	4 (33.3)	8 (66.7)	
Don't know	30 (55.6)	24 (44.4)	
<b>Fiber rich food</b>			
Rice, bread, potato	0 (0.0)	2 (100)	0.239
Fish, meat, egg, pulse	4 (80.0)	1 (20.0)	
Vegetables, fruits	12 (42.9)	16 (57.1)	
Don't know	41 (51.3)	39 (48.8)	
<b>Foods that male adolescents should eat</b>			
Rice, bread, potato	8 (61.5)	5 (38.5)	0.310
Pulse, meat, egg	9 (69.2)	4 (30.8)	
Vegetables, milk, fruits	38 (44.7)	47 (55.3)	
Don't know	2 (50.0)	2 (50.0)	
<b>Foods that female adolescents should eat</b>			
Rice, bread, potato	6 (54.5)	5 (45.5)	0.004
Pulse, meat, egg	6 (31.6)	13 (68.4)	
Vegetables, milk, fruits	33 (45.8)	39 (54.2)	
Don't know	12 (92.3)	1 (7.7)	
<b>More foods required for female adolescents</b>			
Yes	32 (38.6)	51 (61.4)	0.001
No	20 (76.9)	6 (23.1)	
Don't know	5 (83.3)	1 (16.7)	
<b>More foods required for male adolescents</b>			
Yes	43 (47.8)	47 (52.2)	0.172
No	11 (68.8)	5 (31.3)	
Don't know	3 (33.3)	6 (66.7)	

### 3.2. Qualitative results

This section provides details about in depth interviews (IDIs) of male adolescents, female adolescents, fathers and mothers. Three themes were developed in English (gender norms and nutritional knowledge, gender norms and food management and challenges to healthy diet).

#### 3.2.1. Gender norms and nutritional knowledge

Adolescents and their parents think that nutritious food is food that is healthy for the body, gives energy to the body so that they can complete the activities of everyday life. Vegetables, fish, meat and eggs are considered nutritious foods by them. Vegetables, on the other hand, are known to them as the most nutritious food. They believe that eating more vegetables will improve their health and provide them with more vitamins. Adolescents said that their families' assistance helped to make healthy food choices; parents gave them food recommendations and encouraged them to cook. Foods including fruit, vegetables and dairy products were the subject of parental guidance. Parents also encouraged their children to eat a variety of foods. Family members also emphasized the necessity of eating nutritious, regular meals in order to avoid sickness, and encouraged adolescents to eat foods prepared at home.

*"I learn these things in books. Then my mother claims that eating more of these vegetables at mealtime will improve your health. My bodily structure will be in good shape and everything will be in place. Following my mother's advice, I believe that if I eat these foods, my health will improve and I will be able to maintain a reasonable level of fitness."* (19 years, female adolescent)

*"Nutritious foods are those foods that strengthen the body, improve health and boost immunity. Such as rice, fish, meat, colorful vegetables, pulses, milk, eggs. There are nutrients in the food that you eat in general but you have to change the type of food and eat it."* (35 years, mother)

#### 3.2.2. Gender norms and food management

When there is less food at home, mothers tend to eat later so that their children can get enough food to eat. When evaluating intrahousehold food allocation decisions, gender has proven to be an important criterion. Food insufficiency in the home requires adjustments in meal quality and frequency. Gender norms dictate that women have lower meal portions and make food sacrifices so that other family members can eat more.

*"My mother controls the family. Her family and children are her first priorities. When her children eat, her tummy fills up. When her husband eats, her tummy fills up. In that scenario, my mother makes a sacrifice."* (17 years, male adolescent)

Female adolescents think their fathers need to eat first because their fathers work all day.

*"My father works all day. If he does not eat first, he won't get energy. I stay at home."* (16 years, female adolescent)

Parents believe they need to learn cooking because they will have to feed the members of her in laws house.

*"Why do you need to teach this? In addition to her studies, she should also learn to cook with her mother. She should be able to cook and feed her mother-in-law when we arrange her marriage. So her mother is teaching her"* (42 years, father)

When asked about hurdles to healthy diet, participants indicated a lack of financial resources to purchase food. Parents often cannot provide adequate nutritious food to their children due to financial constraints. Currently, their financial situation has become more fragile due to Covid pandemic.

*"We should eat the same amount of food as our two brothers and sisters. But normally it is not possible for us. Because we are middle-class family. So many things of the middle-class family have to be accepted with a smile. So we can feed my sister but we can't feed ourselves."* (19 years, male adolescent)

*"Dietary pattern was not good at all before pandemic, but it was fine. The condition of nutrition has been a little weak since Corona. We feel poor here, everyone is poor. There is very little middle-class family. Since there is*

*less income in poor areas, where is the food from? Having three meals a day is very difficult. For this reason, she thinks that the issue of nutrition is less than it used to be." (35 years, mother)*

*"Every day I think I will feed them a little bit of nutritious food. My son and daughter will be fine. But I can't do much. I want to, but I can't. " (35 years, mother)*

Parents stated that their children don't want to eat vegetables or milk because they don't like it.

*"They eat meat, eggs. Consumption of milk is less. Eating vegetables is much less, they don't like vegetables. I mean, they don't want to eat even if i cook. " (35 years, mother)*

### 3.2.3. Challenges to healthy diet

When asked about hurdles to healthy diet, participants indicated a lack of financial resources to purchase food. Parents often cannot provide adequate nutritious food to their children due to financial constraints. Currently, their financial situation has become more fragile due to Covid pandemic.

*"We should eat the same amount of food as our two brother and sister. But normally it is not possible by us. Because we are middle class family. So many things of the middle class family have to be accepted with a smile. So we can feed my sister but we can't feed ourselves. " (19 years, male adolescent)*

*"Every day I think I will feed them a little bit of nutritious food. My son and daughter will be fine. But I can't do much. I want to, but I can't. " (35 years, mother)*

Parents say their children don't want to eat vegetables or milk because they don't like it.

*"They eat meat, eggs. Consumption of milk is less. Eating vegetables is much less, they don't like vegetables. I mean, they don't want to eat even if i cook. " (35 years, mother)*

Dietary behaviours are influenced by a family's socioeconomic condition, socio-cultural norms, gender norms and food preferences.

## 4. Discussion

This study observed one of the most notable findings of our study was among 115 respondents 51.3% of respondents had normal BMI, which is highest among surveyed respondents. Almost 43.5% adolescents were underweight, on the other side, 4.3% adolescents were overweight and 0.9% adolescents had obesity. More of the female adolescents (46.6%) were underweight compared to male adolescents (40.4%), but the difference was not significant. In contrast to our study, some other studies showed similar result of nutritional status. An almost similar study (Kabir et al., 2010) was carried out among 82 adolescents found that 39% of adolescents were underweight, 69.8 % were normal and 1.2% were overweight.

A similar study (Verma *et al.*, 2020) was conducted in India among school going male and female adolescents found that majority of adolescents (58.8%) were underweight. There were gender-based differences in the nutritional status among male and female adolescents. More of the female adolescents (63.2%) were underweight compared to male adolescents (53.1%).

In our study, the micronutrient intake adequacy of male and female adolescents was less because the majority (100%) of adolescents ate starchy staples. Starchy staples (mostly white rice), which are deficient in micronutrients (Arsenault et al. 2013). We have seen that the majority of individuals eat rice, that many have poor financial conditions and that many have good financial and educational conditions, but when we ask, many people can reply yes without even consuming that food, thus socially desirable information may arise.

Around 73.7% male and 77.6% female adolescents consumed meat (mainly chicken) and fish. 43.9% male and 36.2% female adolescents consumed other vitamin A rich fruits and vegetables (e.g. tomato, onion, eggplant, wild fruits, locally available vegetables). These findings are similar to Bangladesh Adolescent Health and Well-being Survey 2019-2020 where 24% female adolescents had consumed vitamin A-rich foods in 24 hours preceding the survey. The proportion was slightly higher (29%) among the male adolescents. 57.9% male and 53.4% female adolescents consumed legumes, nuts and seeds, 10.5% male and 13.8% female adolescents consumed dark green leafy vegetables, only 3.4% female and no male adolescents consumed vitamin A rich fruits and vegetables

(pumpkin, carrot, squash, or sweet potato that are orange inside, red sweet pepper), 28.1% male and 34.5% female respondents consumed eggs, 5.3% male and 3.4% female adolescents consumed milk and milk-products. Only 1.8% male and no female adolescent consumed organ meat. Poor dietary diversity has been associated with low food expenditures, particularly non-starchy foods that are nutrient-dense but expensive, such as organ meat, eggs, and dairy products (Thorne-lyman *et al.* 2010).

In our qualitative study we have observed that when there is less food at home, mothers tend to eat later so that their children can get enough food to eat. Gender has been shown to be an essential factor in assessing intrahousehold food allocation decisions. According to gender stereotypes, women serve themselves smaller quantities at meals and give up certain foods so that their male family members can eat more. Another similar study conducted among female adolescents in some slums of Dhaka and some rural areas of Bangladesh by Blum *et al.*, 2019 showed that how gender norms impact male and female roles, which in turn influence food acquisition, intrahousehold food allocation decisions, consumption habits and differences in actual food intake. Gender-based eating differences are enforced by cultural norms, which explain why females are expected to serve more and special meals to male family members and are expected to consume less during food shortages and financial struggles. In our study female adolescents think that their fathers need to eat first because their fathers work all day. A similar study conducted among female adolescents in some slums of Dhaka and some rural areas of Bangladesh by Blum *et al.*, 2019 showed that men and adolescent males were reported to be given both greater amounts and better-quality foods due to their economic roles, larger physiques and perceptions that males are more active, with boys also being preferred because they are expected to provide money and care for their parents in old age.

## 5. Conclusion

There are gender differences where female adolescents were more underweight than male adolescents though female had better dietary behaviour than male adolescents. Lack of dietary diversity was also prevailing in both sexes. Lowest dietary diversity is higher among male than female adolescents. There was significant association between sex with eating vegetables and eating fish. Dietary behavior and eating more foods for female adolescents had significant association with sex of the respondents. So, proper knowledge on nutrition can improve the dietary behaviour. Adolescents gathered nutritional knowledge from books and their mothers. Female adolescents are not allowed to go to the market since it is not a safe place. Female made sacrifices in food consumption so that other family members could eat more and they were expected to learn cooking since they had to feed other members of her in laws house. About challenges to healthy diet, participants indicated a lack of financial resources to purchase nutritious food.

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**Ethical approval and consent to participate:** The Institutional Review Board of Bangabandhu Sheikh Mujib Medical University officially approved this study (Reference No. BSMMU/2021/8653) and it was conducted in accordance with the Declaration of Helsinki. Each participant signed a written informed consent form that included all the information about the research, their participation rights, and the right to withdraw from the study at any time. Adolescents under the age of 18 years were requested to provide written assent, which was supported by obtaining written informed consent from the adolescent's parents and guardians.



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# “Yummy” Snakehead Sausage: Analysis of Nutrient Content and Acceptability of Fish Sausage in Lake Sentani Jayapura

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## Abstract

Sausages are processed meals with two changes based on the composition and the formulation. The trend of consuming sausage increases annually both at national and international levels. The most common ingredients of sausages are beef and chicken. On the other hand, fish and snails could also become the ingredients as found in Japanese practices. This research determined the influence of the fish type on the nutrition contents, such as the water, ash, protein, fat, and carbohydrate; and the acceptability of fish sausage. The researchers carried out the research at the Food Laboratory of the Nutritional Department, the Integrated Laboratory of Polytechnic of Health Ministry of Jayapura, and the Mathematics and Science Laboratory of Universitas Cenderawasih. This complete random research design applied some factors to investigate, such as the formulation of the fish. The applied formulations were: F1 with 90% fish meat and 10% flour; F2 with 80% fish meat and 20% flour; and F3 with 70% fish meat and 30% flour. The researchers used some meats from Nile tilapia, snakehead, and flower horn cichlid fish. The researchers analyzed the nutrition content and found differences among the carbohydrate, water, and ash contents from all the fish. On the other hand, the protein and fat content of each fish were not significantly different. The organoleptic test found that the F3 category was the most preferable fish meat. The acceptability test found that 95.6% of respondents consumed all given samples. The researchers concluded that the fish sausage from snakehead fish, with a ratio of 70% fish meat and 30% flour, had the best organoleptic feature, excellent acceptability, and all the nutrition requirements suggested by Indonesia's National Standard of Fish Sausage.

**Keywords:** Fish Sausage, Nutrition Content, Organoleptic, Acceptability

## 1. Introduction

Sausages are processed meals with two changes: the composition and the formulation (Rosmawati et al., 2023). Sausage sales experience an increased trend annually (NasDaq, 2021; Pellegrini, 2022). The same trend is also observable in the United States of America (NHDSC, 2023; Statistika, 2023). The outcomes of sausage consumption in the United States of America reached 5.3 million dollars in 2022 (NHDSC, 2023). In Indonesia, the related data about consuming sausages are inaccessible. However, the researchers assume that sausage

consumption increases. PT. Charoen Pokphand Indonesia Tbk (CPI) also found increased sales from 2020 to 2022 with a percentage of 10.2% (PT. Charoen Pokphand Indonesia, 2023). CPI is the largest sausage manufacturer in Indonesia. The trend of consuming sausage increases because this food is familiar to all age communities (Nasdaq, 2021; NHDSC, 2023; Statistika, 2023).

Sausage ingredients are usually beef or chicken (Farida, 2018). However, some ingredients may be also from seafood and fish (Tanikawa, 1963; Chuapoehek, Raksakulthai, & Worawattanamateekul, 2001; Oliveira et al, 2014; Kazemzadeh, 2022). Japanese people have been familiar with fish sausage for centuries. Tanikawa (1963) also explains that sausages in Japan are usually made from tuna, marlin, skipjack, bonito, salmon, and whale. The ingredients for producing sausages are developing (Sali & Rahmawati, 2023). This development includes the implementation of snakehead as the ingredient with frequent investigations. One of the investigations identifies the implementation of snakehead meat as the traditional and modern medication (Shafri & Manan, 2012). Therefore, snakehead sausage is more popular. Moreover, this ingredient also has high nutrition content (Lestari & Nanisa, 2014; Chaerunnimah et al, 2021). Studies also find snakehead meats have collagen as medication (Issains et al., 2019).

Many researchers studied snakeheads (Truc et al, 2017; Zakaria & Sarbon, 2018; Marlinda, 2020; Putri, 2022; Tawali et al, 2023). Many researchers used the snakehead as the ingredient to produce gelatin to preserve beef sausage (Tawali et al, 2023). Other studies cultivated snakehead as the ingredient to produce sausages (Truc et al, 2017). Some researchers also examined the organoleptic quality and protein levels of the pulps made from snakeheads (Marlinda, 2020). A study also examined the acceptability of the snakehead sausage with moringa leaf powder (Putri, 2022). Research also examined the benefits of snakeheads in preventing stunting (Chaerunnimah et al, 2021). Therefore, the researchers did not find any studies comparing the nutritional content and the acceptability of snakehead fish as the sausage ingredients. The researchers also did not find related research with fish from Sentani Lake in Jayapura.

The researchers analyzed the acceptability of Nile tilapia, snakehead, and flower horn cichlid fish. The researchers involved primary school learners as the respondents. The underlying reason is - primary school learners tend to consume sausages since sausages are a popular food among Indonesian learners (Arifin & Setyaningrum, 2022).

## 2. Research Methodology

This complete randomized research took three types of fish and three formulations. See Table 1 to understand the formulations.

Table 1: The Matrices and the codes of research treatments

The fish types	The first formula (F1)	The second formula (F2)	The third formula (F3)
	10% flour: 90% fish meat	20 % flour: 80% fish meant	30 % flour: 70 % fish meat
Snakehead fish	GF1	GF2	GF3
Nile fish	NF1	NF2	NF3
Flowerhorn fish	LF1	LF2	LF3

The researchers conducted the research at the Food Laboratory of Nutritional Development at the Polytechnic of the Health Ministry of Jayapura to produce the sausages and promote the organoleptic test. On the other hand, the researchers conducted the chemical test, proximate, at the Mathematics and Science Laboratory of Universitas Cenderawasih. Then, the researchers conducted the acceptability test at Public Primary School 3 Abepura from May to October 2022.

The other applicable ingredients include Chicken eggs, cornstarch, sugar, garlic, pepper, cooking oil, water, ice, thread, and food-grade sausage plastic. Then, the researchers analyzed the nutrition content with  $H_2SO_4$ ,  $Na_2SO_4$ ,

Aquades, HCl, and Petroleum Ether. The sensory test or the hedonic test used: Sausage, drinking water, an organoleptic assessment form, and a comstock form.

The applied instruments to produce sausages included: a food scale, a container, a blender, a measuring cup, a stove, a pan, and a sausage maker. The sensory test instruments were: stationary and small plates. The analysis of the nutritional content used: A distiller+ an Erlenmeyer, a soxhlet, an oven, a furnace, a desiccator, a Waring blender, a volume pipet, and a scale + scaling bottle.

## 2.1. The Research Procedure

### 2.1.1. Producing the Fish Sausage

The researchers washed, filleted, and chopped the fish. Then, the researchers mixed the fish with salt and sugar. After that, the researchers stirred and left the mixture at a temperature between 3 and 4°C for 48 hours. The researchers then put the chopped fish and flour based on the ratio. After that, the researchers put all the ingredients, seasoning, and ice cubes into the mixed fish and flour. Then, the researchers ground the ingredients with a blender or a chopper.

The researchers put the mixtures into the sausage plastics with a sausage maker. The length of the sausage was 10 cm for each sausage. Then, the researchers tied the tips of the sausages. Then, the researchers boiled the sausages at a temperature between 50 and 60°C for 30 minutes. The researchers took out the boiled sausages and dipped them into ice liquid to cool the temperature down. Then, the researchers took the cooled sausages and the sausages were ready to serve.

## 2.2. The analysis procedure

### 2.2.1. The water content

The researchers took the samples for 2 grams to scale in a container. In this process, the researchers determined the weight of the bottle container so that the container weight was constant. Then, the researchers dried the ingredients inside the container in an oven at the temperature of 100°C for 5 hours. After that, the researchers took the ingredients and cooled them inside a desiccator before scaling. The researchers heated the ingredients for 30 minutes and cooled them again before re-scaling the ingredients. The researchers repeated this treatment to reach the constant weight (the gap between the consecutive scaling process is 0.02 grams). Then, the researchers calculated the water content with the following equation.

(Normilawati et al, 2019):

$$\text{The water content} = \frac{\text{the initial weight} - \text{the final weight}}{\text{The initial weight}} \times 100$$

### 2.2.2. The ash content

The researchers measured the ingredients carefully for at least 20 grams within the dried porcelain with the given weight. The researchers lit the muffle to obtain the whitish ashes. Then, the researchers put the porcelain and the ashes into an exicator. After that, the researchers measured the weight of the ashes once they were cooled.

$$\text{The content of the ash} = \frac{A-B}{A} \times 100$$

Remarks:

- A. The initial weights of the porcelain and the ingredients
- B. The final weights of the porcelain and the ingredients

### 2.2.3. Determining the Protein Content with the Kjeldahl Method

The researchers applied these steps: measuring 0.51 grams of the sample to put into the 100ml kjeldhal flask; adding 2 grams of the selen mixture and 25 ml of thick H<sub>2</sub>SO<sub>4</sub>; heating or boiling up on electric heater to make the liquid clear and greenish (approximately 2 hours at the temperature of 420°C); letting the liquid cool; diluting the liquid; and putting the liquid into a 100ml flask with a marked scale; adding 5 ml of the liquid and putting the liquid into a distillation; adding 5 ml NaoH 30%; adding some drops of PP indicator; distilling the liquid for 10 minutes; administering 10 ml boric acid 2% that previously mixed with the indicators; washing the tip of the coolant with the distilled water; and applying the HCL 0.01 N (4,5).

$$\% \text{ Protein} = \frac{(V1-V2) \times N \times 0,014 \times f.k \times f.p}{W}$$

Remarks:

W = the weight of the sample

V1 = the volume of HCL 0,01 N for sample penitentiary purposes

V2 = the volume of HCl for penitentiary purposes of the form

N = The normality of HCL

f.k = the common protein content of meals, 6.25

f.p = the distillation factor

### 2.2.4. The Fat Content Analysis with Soxhlet Method

The researchers grinded the samples, 2 grams. Then, the researchers put the samples into paper shells with the base covered by cotton. The researchers sealed the shells with cotton and dried them in an oven. The temperature was not higher than 80°C for an hour. Then, the researchers put the samples into the soxhlet. In the previous step, the researchers put the dried-boiled stones into the fat flask. In this process, the researchers were aware of the stone weights. Then, the researchers extracted the fat with fat solvent or hexane for 6 hours. Then, the researchers distilled and dried the fat extract in a dryer oven at the temperature of 105°C. Then, the researchers cooled the extract in an exicator for further scaling process. After that, the researchers re-conducted the process to reach the constant weight (6).

$$\% \text{ fat} = \frac{W - W1}{W2} \times 100$$

Remarks:

W = the weight of the sample (g)

W1 = the weight of the fat flask before the extraction (g)

W2 = the weight of the fat flask before the extraction (g)

### 2.2.5. The carbohydrate content (by the difference)

The researchers determined the carbohydrate contents with the by-difference method. This method calculates the contents of the water, ash, protein, and fat. Here is the equation to measure the carbohydrate content with the by-difference method (7).

$$\text{The carbohydrate content (\%)} = 100\% - (\% \text{ water content} + \% \text{ ash content} + \% \text{ protein content} + \% \text{ fat content})$$

### 2.2.6. The organoleptic test

The researchers applied the organoleptic test with the hedonic method. This method measures the preferences toward the textures, tastes, colors, and smells of the fish sausages. Then, the researchers served the sausages to 25 respondents. Every respondent assessed the produced sausages twice at different times. Then, the researchers asked the respondents to assess by selecting specific criteria. Then, the respondents scored each criterion. Here is the

scale (8): Very like: score of 5; averagely like: score of 4; neutral: score of 3; dislike: score of 2; extremely dislike: score of 1

### 2.2.7. The acceptability

The researchers applied the Comstock test to examine the acceptability of 45 child respondents. The researchers served the fish sausage for the respondents to consume. If the respondents consumed all fish sausages, the researchers considered the respondents liked the fish sausages.

## 3. Results

### 3.1. The Nutrition Content of the Sausage

The nutrition of the sausages included protein, fat, water, and ash. The researchers analyzed the content proximately with the Indonesian National Standard Number 7755;2013. On the other hand, the researchers calculated the carbohydrate content with mathematics calculation by the difference. The researchers analyzed repeatedly, three times, for each sample. Table 2 shows the mean.

Table 2: The mean nutritional content of the fish sausage

Nutritional substances	Types of sausages									F	p-value
	Nile fish			Snakehead fish			Flowerhorn fish				
	F1	F2	F3	F1	F2	F3	F1	F2	F3		
Protein	13,66	11,98	8,12	16,12	14,75	11,25	10,29	8,54	6,34	3,926	0,081
Fat	5,44	4,32	3,53	6,56	5,46	5,01	4,26	4,05	3,68	4,167	0,073
Carbohydrate	9,59	13,67	19,39	5,31	9,83	15,35	20,66	23,17	26,27	7,245	0,025
Ash	1,07	0,94	0,89	0,78	0,63	0,57	1,12	1,11	1,04	19,845	0,002
Water	70,24	69,09	68,07	71,23	69,33	67,67	63,67	63,13	62,67	26,612	0,002

Source: the primary data

The researchers found the nutrition of the fish sausage. The highest one was the protein of the GF1 formula with a percentage of 16.12%. The same result was also observable in the fat content. The GF1 had the highest fat with a percentage of 6.56%. On the other hand, the highest carbohydrate was observable on LF3 with a percentage of 26.71%. The highest ash content was observable on NF1 with a percentage of 1.07%. The last one, the highest water content, was observable on GF1 with a percentage of 71.23%. The ANOVA analysis found the protein content of the fish sausage was 8.1%, while the fat was 7.3%. The result showed significant differences in each formula in terms of the carbohydrate content with a p-value of 0.025, the ash content with an ap-value of 0.002, and the water content with a p-value of 0.002. On the other hand, the researchers found no differences in terms of protein and fat content.

### 3.2. The organoleptic test

The researchers applied the hedonic test for the organoleptic test with a scale of 5. Then, the researchers determined the mean of the respondent acceptability with the scoring system. A score of 5 for the very like option, 4 scores for the 'like' option, a score of 3 for the 'average' option, a score of 2 for the 'dislike' option, and a score of 1 for 'the extremely disliked' option. The excellent acceptability of the respondents is represented by the high score. The researchers involved 25 respondents in this organoleptic test. All respondents were trained. Table 3 shows the results.

Table 3: The organoleptic mean score of the fish sausage

The feature of the organoleptic	Nile fish			Snakehead fish			Flowerhorn fish		
	F1	F2	F3	F1	F2	F3	F1	F2	F3
Flavor	3,36	3,56	3,84	3,24	3,76	3,84	3,64	3,76	3,72
Color	3,6	3,96	3,52	4,04	3,84	3,56	2,3	2,8	3,44
Aroma	3,36	3,72	3,4	3,56	3,4	3,88	2,84	3,68	3,32
Textures	3,2	2,48	4,04	3,92	3,96	3,92	2,92	3,6	3,92

<b>Sum</b>	<b>13,52</b>	<b>14,72</b>	<b>14,8</b>	<b>14,76</b>	<b>14,96</b>	<b>15,2</b>	<b>11,72</b>	<b>13,84</b>	<b>14,4</b>
<b>Mean</b>	<b>2,38</b>	<b>3,68</b>	<b>3,7</b>	<b>3,69</b>	<b>3,74</b>	<b>3,8</b>	<b>2,93</b>	<b>2,46</b>	<b>2,6</b>

Source: the primary data

Table 3 shows that the flavor of the fish sausage, the Nf3, has the highest score with 3.84 (ranging from neutral or average until very like). The GF3, the snakehead fish with the third formulation, is the most preferable flavor with a score of 3.84 (neutral or average until very like). For the flower horn fish, the most preferable flavor is LF2 (neutral until very like option).

### 3.3. The best formulation and the advanced organoleptic test

The researchers had to calculate the mean scores of the three fish sausage types and the three formulas to determine the mean score of each fish sausage type. The researchers compared the highest mean scores with other fish sausage types to determine the highest acceptability. Here is the assessment.

The data analysis results of the organoleptic features of all fish sausages, starting from the Nile, snakehead, and flowerhorn types, showed that F3 was higher than F1 and F2. Thus, the researchers conducted the advanced organoleptic for F3. The test found the most preferable fish sausage. Table 4 shows the advanced test explanation.

Table 4: The organoleptic test mean of the fish sausage

<b>The organoleptic feature</b>	<b>Nile fish</b>	<b>Snakehead fish</b>	<b>Flowerhorn fish</b>
Color	3,44	3,48	3,44
Flavor	3,56	3,36	3
Aroma	3,48	3,52	2,72
Textures	3,32	3,72	3,2
<b>Sum</b>	<b>13,8</b>	<b>14,08</b>	<b>12,36</b>
<b>Mean</b>	<b>3,45</b>	<b>3,52</b>	<b>3,09</b>

Source: The primary data

The organoleptic of snakehead fish has the highest mean score (3.52) than the other types of fish sausages. Thus, the researchers examined the snakehead sausage to determine the acceptability of the respondents.

### 3.4. The Acceptability Test

The researchers examined the acceptability of the primary school learners as the respondents, 45 respondents. They were the fifth and the sixth graders. The researchers conducted the test at 10 in the morning in the classroom of the learners. The research site was at Public Primary School 3 Jayapura. The researchers examined the acceptability of the Comsok assessment form. Table 5 shows the acceptability of the sausage.

Table 5: The acceptability of the primary school learner respondents

<b>Percentage (%) of the consumed samples</b>	<b>N</b>	<b>%</b>
0 (not being consumed)	0	0
25 (being consumed for a fourth portion)	1	2,2
50 (being consumed for a half portion)	0	0
75 (being consumed for three-fourths portion)	1	2,2
100 (100% consumed)	43	95,6
<b>Sum</b>	<b>45</b>	<b>100</b>

Source: The primary data

Table 5 shows the test of acceptability. Most respondents, 43 respondents or 95.6% of primary school learners consumed all the given samples. On the other hand, only two respondents, 4.4%, did not consume the given samples.



## 4. Discussion

### 4.1. *The nutritional content of the fish sausage*

The researchers found the contents of protein, fat, and water in the GF1 were higher than the NF3 and LF3. The researchers also found the highest ash content in the first formula of the Nile fish, NF1. The results showed that snakehead fish was superior to Nile and flowerhorn fish as the ingredients to make sausages. The results also confirm the previous research's findings. Snakehead fish has a higher protein level than other freshwater fish (Truc et al, 2017; Marlinda, 2020; Chaerunnimah et al, 2021; Gobel et al, 2022).

On the other hand, the high meat content of fish also has high protein and fat content. On the other hand, high carbohydrate leads to low ash content. Zakarian & Sarbon (2018) also found that with every added content of 0 - 3%, of the snakehead fish, the protein of the sausage would increase by 18.83–19.59% while the fat with the increment between 7,91–9,07%. Zakaria & Sarbon (2018) explain that snakehead fish have the highest protein and fat content than Nile, flowercorn, and other freshwater fish.

The ANOVA results also showed the carbohydrate, water, and ash contents. Iqbal, Supriadi, and Nopianti (2015) also found that high ash content indicated the fish meat had mineral resources. Thus, the ash content could represent the total mineral of an ingredient. Other minerals in an ingredient consists of two salt types: the organic and the inorganic salts. Most ingredients consist of 96% organic substances and water. The remaining percentage is full of mineral elements. High ash content indicates high inorganic materials in a product.

### 4.2. *The organoleptic test*

The organoleptic test found that snakehead fish was most dominant with a mean score of 3.74 on all formulations. This finding showed that snakehead fish was preferable by the respondents based on flavor, color, and aroma. However, the textures were still under average compared to Nile sausages. The results showed that the snakehead fish had better nutrition content, such as protein, fat, and water. The fish could also become the potential alternative for children to improve their protein and fat so they could grow up better (Lestari & Nanisa, 2014; Truc et al, 2017; Zakaria, & Sarbon, 2018; Chaerunnimah et al, 2021; Gobel et al, 2022). Snakehead fish is also useful for medication because of its high collagen content (Shafri & Manan, 2012; Issains, et al, 2019). Snakehead fish is also useful as an additive ingredient to produce sausages with different main ingredients (Roemawati et al, 2023). Zakaria & Sarbon (2018) also found that the addition of hydrolyzate protein content from snakehead fish to produce sausages could improve the hardness, cohesiveness, and springiness of the sausages.

### 4.3. *The Acceptability*

Table 5 shows the acceptability results of the snakehead sausage. Most respondents, 43 (95.6%), consumed the given samples while only 2 respondents, 4.4%, did not. The findings showed that the respondents liked the sausages although the sausages were harder than Nile and Flowercorn fish. The result proved that the hardness was below the tolerance of the meal. Marlinda, Y. (2020) found that sausages from snakehead pulps also had excellent acceptability than other freshwater fish.

## 5. Conclusion

The snakehead fish sausage has excellent nutrition and is preferred by most primary school learners. The most preferable formula for the snakehead fish sausage is - 70% of snakehead fish meats and 30% flour. This formulation has the best organoleptic feature and acceptability. The results found a percentage of 95.7% of primary school learners consumed all given samples. The nutrition content of the sausage also met Indonesia's National Standard of Fish Sausage.

## 6. Suggestion

This research does not consider the influence of packaging on the storability of the product. The efforts of taking the benefits from sausages as healthy snacks for children could be an alternative to manage stunting problems and other nutritional problems of school-aged learners.

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# Minimally Invasive Thoracoscopic Surgery of Lung Adenocarcinoma in Old Age People

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## Abstract

Background: Lung cancer is the most frequent human malignancy and the principal cause of cancer-related death worldwide. Adenocarcinoma is now the main histologic type, accounting for almost half of all the cases. Lung cancer is the leading cause of cancer-related death in most developed countries. Over the last 50 years, the prevalence of adenocarcinoma has been increasing comparative to other lung cancer subtypes. Objective: To determine Minimally invasive thoracoscopic surgery of lung adenocarcinoma in old age. Methods: A cross-sectional study was conducted at Shifa International hospital Islamabad Pakistan, which was performed between April 2020 and January 2022. The total number of patients in our study was 152. The number of Male patients was 62 and female were 90. In 152 consecutive patients who underwent for CT guided biopsy, the needle was used 18 Gauge. We diagnosed the Lung adenocarcinoma of all patients on CT scan. The age of all patients was more than 40 years. We took in our study stage (1A) of lung adenocarcinoma, which has further 3 subtypes 1A1, 1A2 and 1A3. The size of Stage 1A1 up to 1 cm, Stage 1A2 >1 cm <2cm and stage 1A3 >2cm <3cm. We did for all patients Video-assisted thoracoscopic surgery. The surgeon makes one to five small incisions, each one an about 1 inch in between two ribs. Data was tabulated and analyzed by SPSS. Results: The stage of lung adenocarcinoma 1A1 in male patients were 17 and female were 31. The stage of lung adenocarcinoma 1A2 in male patients were 29 and female were 37. The stage of lung adenocarcinoma 1A3 in male patients were 16 and female were 22. Total male patients were 62 and females were 90. P-value of stages of lung adenocarcinoma in gender was 0.64. The stage of lung adenocarcinoma in the age group of 40-50 years 1A1 were 8, 1A2 were 7 and 1A3 were 2. The total patients with age 40-50 years were 17. The stage of lung adenocarcinoma in the age group of 51-65 years 1A1 were 34, 1A2 were 48 and 1A3 were 19. The total patients with age 51-65 years were 101. The stage of lung adenocarcinoma in the age group of >66 years 1A1 was 6, 1A2 was 11 and 1A3 was 17. The total patients with age >66 years was 34. P-value of stages of lung adenocarcinoma in age group was 0.003. The minimum patient recovery time was 3 weeks and the maximum patient recovery time was 5 weeks. The minimum age group of patient was 43 and the maximum age group of patients was 77. MEAN±SD of age was 59.67±7.85. Conclusion: Video-assisted thoracoscopic surgery (VATS) is a reliable and safe approach for the diagnosis and treatment of lung adenocarcinoma with a low complication rate. Minimally invasive techniques are even more advantageous among the elderly. The patient recovery time from 3 weeks to 5 weeks. The frequency of lung adenocarcinoma is more common in the upper lobe as compare to other lobes. In our study, the prognosis of VATS was better than Open Surgery because the patient's recovery time was less than the open surgery procedure.

**Keywords:** Video-Assisted Thoracoscopic Surgery (VATS), Lung Adenocarcinoma and Minimally Invasive Surgery

## 1. Introduction

Lung cancer is the most common human malignancy and the principal cause of cancer-related death worldwide. Adenocarcinoma the main histologic type nowadays, accounting for almost half of all the cases (Kuhn et al., 2018). In most developed countries lung cancer is the leading cause of cancer-related death (Nakamura et al., 2014). Comparative to other lung cancer subtypes, the prevalence of adenocarcinoma has been increasing Over the last 50 years (McLean et al., 2018). The mortality and prevalence, of lung cancer in Pakistan are not known, due to consistent statistics on the incidence, the absence of a population-based cancer registry (Sheikh et al., 2022). Many factors have been linked to this change, such as: a) the development of filtered cigarettes with less tar, which permit deeper inhaling and greater peripheral dispersion of cigarette smoke; b) rising air pollution; and c) smoking cessation at an earlier age. In comparison to other histologic subtypes of lung cancer, the proportion of adenocarcinomas has grown due to improved attitudes on the hazards associated with smoking cigarettes (Hutchinson et al., 2019). A significant portion of patients with lung cancer experience severe symptoms, including dyspnea, hemoptysis, tiredness, appetite loss, and weight loss (Lemjabbar-Alaoui et al., 2015). Low-dose CT (LDCT) is now the gold standard for screening for lung cancer. Furthermore, compared to no screening, this particular screening has a 99% specificity and an 85% selectivity, according to a study (NELSON). Lung cancer kills people because it is frequently discovered when the disease has progressed to an advanced stage. Effective early identification, a thorough etiology, and the right medications all contribute to lung cancer treatment (Nooreldeen et al., 2021). Tobacco use is the primary risk factor for all forms of lung cancer, including adenocarcinoma. Because tobacco smoke frequently contains carcinogens, the risk increases with exposure, whether primary or secondary (Myers et al., 2023).

Surgical methods, such as lobectomy or segmentectomy, are the mainstay of treatment for individuals with early-stage lung cancer (Ogawa et al., 2015). Numerous significant prognostic markers, including gender, age, performance status, tumour-node-metastasis (TNM) stage, and histology, have been identified (Sakurai et al., 2014). Men's rates were 40.30 per 100,000 while women's rates were 17.13 per 100,000. Both men's and women's age-standardized mortality rates (ASMR) increased in rural regions. because to changes in the cancer spectrum and the aging population (Cao et al., 2019). The size of the main tumor in the long axis as evaluated by multiplanar reconstruction, as well as its connection with the surrounding structure, determine the tumor stage. Stage 1A1 is up to 1 centimeter, Stage 1A2 is between 1 and 2 cm, and Stage 1A3 is between 2 and 3 cm (Lim et al., 2018). For patients with stage I non-small cell lung cancer (NSCLC), VATS surgery is a safe and feasible option that allows for timely surgical therapy while maintaining the same level of medical care (Jiang et al., 2021). When it comes to postoperative results, the minimally invasive pulmonary resection technique is thought to be the best surgical method for treating early-stage non-small cell lung cancer (NSCLC). It has significant benefits over standard open surgery (Gonfiotti et al., 2018). One of VATS's main advantages is that it causes less discomfort after surgery (Dziedzic et al., 2015). Making 1.5–2 cm access incisions for two to four thoracoscopic ports and 2.6–6 cm access incisions in the frontal region of the thorax for a mini-thoracotomy (utility incision) are the fundamental presumptions of VATS lobectomy. The number of ports (with 1, 2, or 3) that are used to introduce surgical tools varies and is determined by the surgeon's level of skill (Dziedzic et al., 2015). Recently, minimally invasive thoracic surgery (MITS) has been added to the toolkit of thoracic surgeons. It can be used in both therapeutic and diagnostic processes (Hsin et al., 2010). For the diagnosis and treatment of pulmonary disorders, video-assisted thoracoscopic surgery (VATS) is a trustworthy and safe method with a low complication rate (less than 10%) and a mortality rate of less than 1-2 percent (Imperatori et al., 2008). A safe and effective sequential procedure for VATS has been developed, integrating thoracoscopic surgery and intraoperative C-arm CT scanning in a hybrid operating room (Gill et al., 2015). If patients agree to a 23-hour accelerated recovery pathway following a VATS lobectomy, a sizable percentage of them can be safely released (Dumitra et al., 2020). Reductions in blood loss, drainage time, surgical discomfort, and hospital stay were found to be very beneficial (Abouarab et al., 2018). Even more beneficial are less invasive procedures for the elderly and individuals with impaired lung function (Klapper et al., 2015).

## 2. Materials and Methods

A cross-sectional study was conducted at Shifa International hospital Islamabad Pakistan, which was performed between April 2020 and January 2022. The total number of patients in our study was 152. The number of Male patients was 62 and female were 90. In 152 consecutive patients who underwent for CT guided biopsy, the needle was used 18 Gauge. We diagnosed the Lung adenocarcinoma of all patients on CT scan. The age of all patients were more than 40 years. We took in our study stage (1A) of lung adenocarcinoma, which has further 3 subtypes 1A1, 1A2 and 1A3. The size of Stage 1A1 up to 1 cm, Stage 1A2 >1 cm <2cm and stage 1A3 >2cm <3cm. We did for all patients Video-assisted thoracoscopic surgery. The surgeon makes one to five small incisions, each one an about 1 inch in between two ribs. Data was tabulated and analyzed by SPSS.

### 2.1. Clinical and laboratory examination

Weight, sex, and age were noted. For all patients, we did CT guided biopsy to confirm Lung adenocarcinoma.

## 3. Results

Table 1: Patient characteristics of enrolled patients (n=152)

<b>Variables</b>		
<b>Gender</b>	Frequency	Percentage
Male	62	40.8
Female	90	59.2
<b>Age Group</b>		
40-50 years	17	11.2
51-65 years	101	66.4
>66 years	34	22.4
<b>Laterality Lung</b>		
Right lung	95	62.5
Left lung	57	37.5
<b>Stage of Lung Adenocarcinoma</b>		
1A1	48	31.6
1A2	66	43.4
1A3	38	25.0
<b>Smoking</b>		
Yes	49	32.2
No	103	67.8
<b>Cough</b>		
Yes	101	66.4
No	51	33.6
<b>Weight Loss</b>		
Yes	94	61.8
No	58	38.2
<b>Major Complication</b>	0.0	0.0
<b>Cancer spread to mediastinal Lymph nodes or other organs</b>	0.0	0.0
<b>Lung Lobe</b>		
Upper Lobe	107	70.4
Middle Lobe	35	23.0
Lower Lobe	10	6.6

The current study included a total of 152 patients with Lung adenocarcinoma whose characteristics are summarized in Table 2. The frequency of male patients in our study was 62 and their percentage was 40.8. The frequency of female patients in our study was 90 and their percentage was 59.2. The frequency of age group 40-50 years patients

was 17 and their percentage was 11.2. The frequency of age group 51-65 years patients was 101 and their percentage was 66.4. The frequency of age group >66 years patients were 34 and their percentage was 22.4. The frequency of the right lung was 95 and their Percentage was 62.5. The frequency of the left lung was 57 and their Percentage was 37.5. The frequency of the Stage of lung adenocarcinoma in stage 1A1 was 48 and their percentage was 31.6. The frequency of the Stage of lung adenocarcinoma in stage 1A2 was 66 and their percentage was 43.4. The frequency of the Stage of lung adenocarcinoma in stage 1A3 was 38 and their percentage was 25.0. The frequency of smoker in our study were 49 and their frequency was 32.2. The frequency of non-smoker in our study were 103 and their frequency was 67.8. The frequency of cough was 101 and their percentage was 66.4. The frequency of non-cough patients was 51 and their percentage was 33.6. The frequency of weight loss was 94 and their percentage was 61.8. The frequency of patients whose don't lose weight was 58 and their percentage was 38.2. The frequency of cancer spread to mediastinal lymph node or other organs were 0.0 and their percentage was same 0.0. The frequency of the upper lobe of the lung was 107 and their percentage was 70.4. The frequency of the middle lobe of the lung was 35 and their percentage was 23.0. The frequency of the lower lobe of the lung was 10 and their percentage was 6.6.

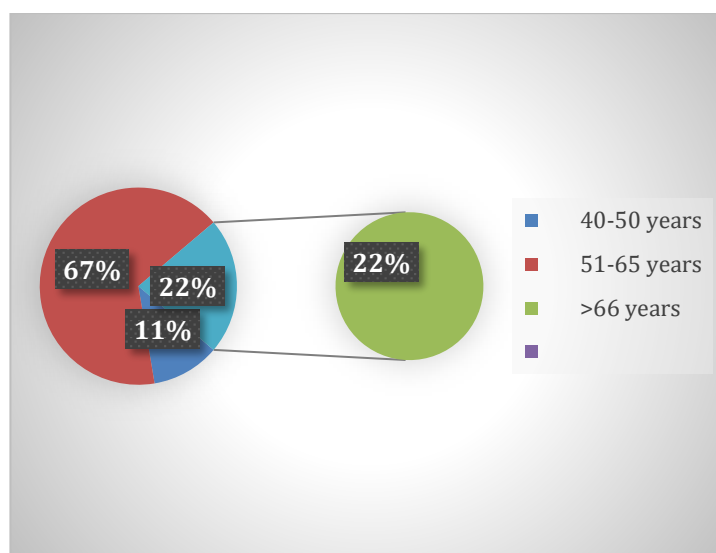


Figure 2: graph showing stages of Lung Adenocarcinoma

Figure 2: The above figure shows lung adenocarcinoma 67% in the age group of 51-65 years. Lung adenocarcinoma 22 % in the age group of >66 years. Lung adenocarcinoma 11% in the age group of 40-50 years.

Table 2: different characteristics of all the enrolled patients ( $n=152$ )

Variables	Minimum	Maximum	Mean $\pm$ SD
Age (Years)	43	77	59.67 $\pm$ 7.85
Patient Recovery Time (Weeks)	3	5	3.69 $\pm$ 0.47
Size of Lung Adenocarcinoma (cm)	---	---	1.418 $\pm$ 0.62

According to our study today patients were 152, The minimum age group of patients was 43 and the maximum age group of patients was 77. MEAN $\pm$ SD of age was 59.67 $\pm$ 7.85. The minimum patient recovery time was 3 weeks and the maximum patient recovery time was 5 weeks. MEAN $\pm$ SD of patient recovery time was 3.69 $\pm$ 0.47. Mean $\pm$ SD of the Size of lung adenocarcinoma was 1.418 $\pm$ 0.62.

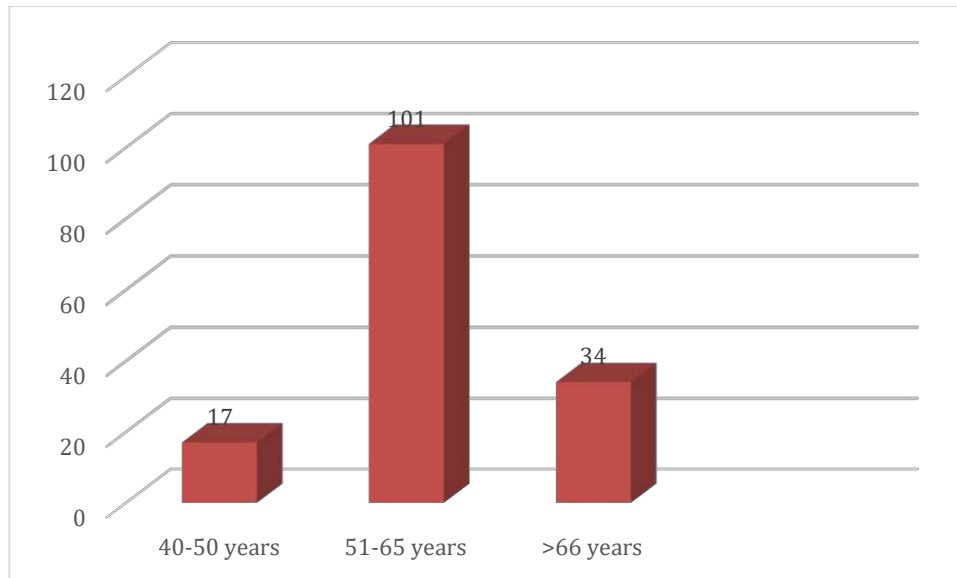


Figure 3: Patients distribution on the basis of Lung Lobe

Figure 3: The above figure shows patients distribution on the basis of Lung Lobe. The number of patients have lung adenocarcinoma in the upper lobe was 101, middle lobe was 34 and lower lobe was 17.

Table 3: stratification of Stage of Lung Adenocarcinoma on the basis of gender and age group ( $n=152$ )

	Stage of Lung Adenocarcinoma			Total	P-value
	1A1	1A2	1A3		
<b>Gender</b>					0.64
Male	17	29	16	62	
Female	31	37	22	90	
<b>Age Groups</b>					0.003
40-50 years	8	7	2	17	
51-65 years	34	48	19	101	
>66 years	6	11	17	34	

The stage of lung adenocarcinoma 1A1 in male patients were 17 and female were 31. The stage of lung adenocarcinoma 1A2 in male patients were 29 and female were 37. The stage of lung adenocarcinoma 1A3 in male patients were 16 and female were 22. Total male patients were 62 and females was 90.

P-value of stages of lung adenocarcinoma in gender was 0.64.

The stage of lung adenocarcinoma in the age group of 40-50 years 1A1 were 8, 1A2 were 7 and 1A3 were 2. The total patients with age 40-50 years were 17. The stage of lung adenocarcinoma in the age group of 51-65 years 1A1 were 34, 1A2 were 48 and 1A3 were 19. The total patients with age 51-65 years were 101. The stage of lung adenocarcinoma in the age group of >66 years 1A1 was 6, 1A2 was 11 and 1A3 was 17. The total patients with age >66 years was 34.

P-value of stages of lung adenocarcinoma in age group was 0.003



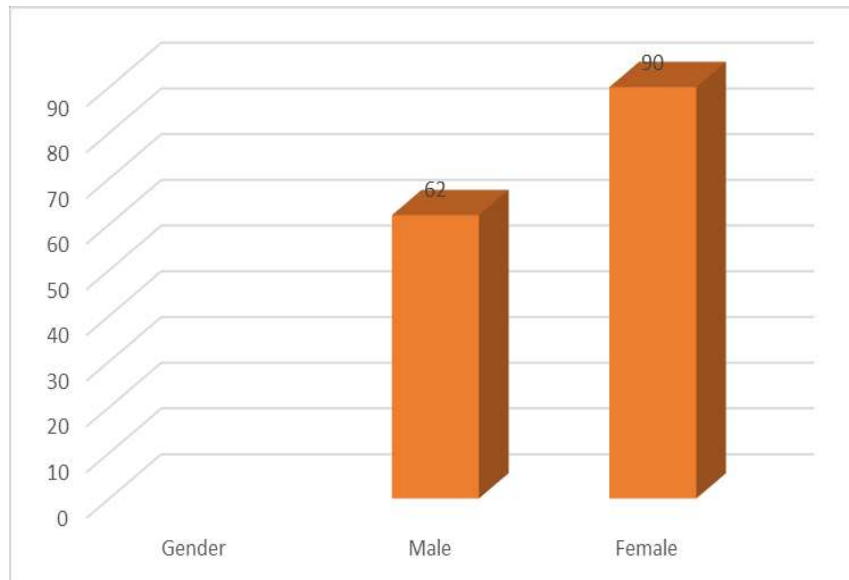


Figure 1: Bar graph showing gender distribution ( $n=152$ ).

In the above bar graph gender distribution the total number of patients was ( $n=152$ ). The number of male patients in this study was 62 and the number of female patients was 90.

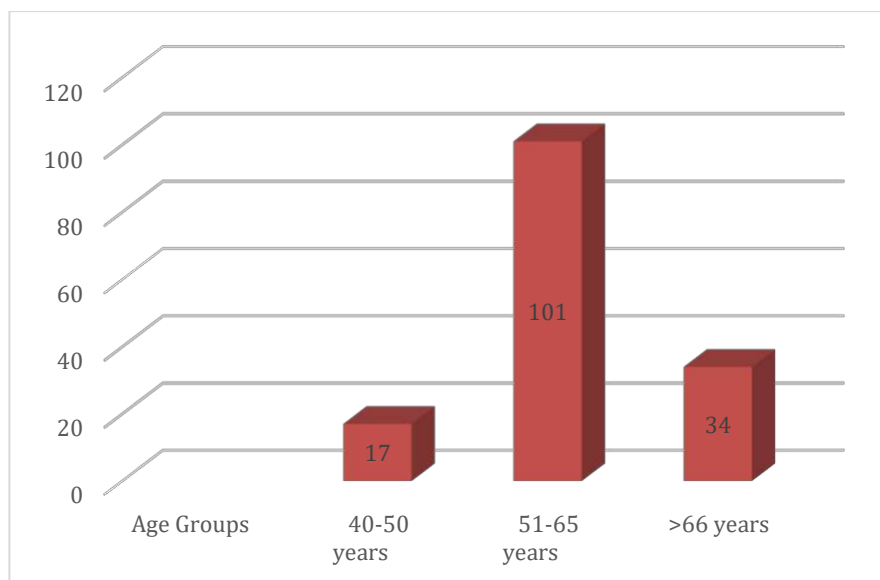


Figure 4: Patients distribution on the basis of Age groups

Figure 4: The above figure shows patients distribution on the basis of age group. Age group of 51-65 years patients was more 101. Age group of >66 years patients was 34. Age group of 40-50 years patients was 17.

#### 4. Discussion

The NCCN guidelines have recommended Video-assisted thoracoscopic surgery (VATS) lobectomy as the preferred surgical procedure for non-small cell lung cancer (NSCLC). Since its inception twenty years ago, it has become more well-established worldwide for the treatment of lung cancer, particularly in the early stages of non-small cell lung cancer. When compared to open thoracotomy, VATS lobectomy presents a number of potential advantages, including a shorter hospital stay, less discomfort following surgery, a lower inflammatory response, expedited access to adjuvant chemotherapy, and accelerated recuperation. Many facilities now treat early-stage lung cancer with VATS lobectomy with lymph node dissection as the standard of care because of the favorable short- and perioperative outcomes it provides, such as shorter hospital stays, shorter chest drain times, and less

intraoperative blood loss (Augustin et al., 2016). There are three types of VATS resections for lung cancer: standard, limited, or sub-lobar, and extended. A VATS lobectomy combined with a lymphadenectomy constitute a standard resection. In most facilities, it is now the norm for treatment, and long-term survival rates are comparable to those of traditional thoracotomies. It is limited to early-stage peripheral lung malignancies when endostaplers can be used to separate the bronchial and lobar vascular systems with fissures (Augustin et al., 2013).

## 5. Conclusion

Video-assisted thoracoscopic surgery (VATS) is a reliable and safe approach for the diagnosis and treatment of lung adenocarcinoma with a low complication rate. Minimally invasive techniques are even more advantageous among the elderly and those with limited pulmonary function. Lung adenocarcinoma is more in females as compare to males. After Video-assisted thoracoscopic surgery (VATS) the patient recovery time from 3 weeks to 5 weeks. The frequency of lung adenocarcinoma is more common in the upper lobe as compared to other lobes. The patient's weight is slightly reduced. In our study, the prognosis of VATS was better than Open Surgery because the patient's recovery time was less than the open surgery procedure.

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**Conflict of Interest:** The authors declare no conflict of interest.

**Informed Consent Statement/Ethics Approval:** Not applicable.

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# Gangs, Low Detection Rates, and Educational Achievement: Major Drivers of Violence

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## Abstract

This study analyses violent crimes (murder, kidnapping, incest, sexual offences, rape, and suicide), their drivers, and associated factors. This descriptive study employs secondary violent crime data from Trinidad and Tobago over at least two decades. The data were collected from multiple search engines and websites and included the socio-demographics of perpetrators, gang and gun-related violence, crime detection levels, and socio-economic factors. A descriptive analysis was used to determine associations between these factors and crime rates. Overall, major crimes rose by 790% between 1990 and 2022, rising from 7.94 per 100,000 people in 1990 to 70.63 in 2022. The number of crime victims cumulatively increased from 7541 in 2013 to 68 322 in 2022, surging by 806%. Moreover, the number of people indirectly affected (family, friends, and members of the community) are estimated (using 10 per victim) to be at least 600 000 or half the population. The analysis shows no association between violent crimes and employment level, income, or national security and social welfare budgets. However, school performance/educational status, gang numbers, and detection rates are correlated with violent crime, suggesting that these factors are the driving forces behind violent crimes.

**Keywords:** crime burden, Republic of Trinidad and Tobago, crime, gang violence, crime detection levels

## 1. Introduction

Crime is ‘the intentional commission of an act usually deemed socially harmful or dangerous and specifically defined, prohibited, and punishable under criminal law’ (‘Crime | Definition,’ 2023). It is ‘a gross violation of law’ (‘Crime Definition & Meaning,’ n.d.) and is punishable by the State (Citizensinformation.ie., n.d.). Crime is quite prevalent across the world, with levels varying between a crime index of 83.76 in Venezuela and 1.107 in Iceland (‘Crime Rate by Country,’ 2023). Caribbean countries are particularly affected, with the Republic of Trinidad and Tobago ranking sixth-highest worldwide in crime/murder after Venezuela, Papua New Guinea, South Africa, Afghanistan, and Honduras (‘Crime Rate by Country,’ 2023). High crime rates in the Caribbean have ‘posed a clear and present danger’ for some time (Griffith, 2023), stunting growth and creating a vicious cycle of problems (Wong & Department, 2017). Besides criminal activity’s mental (Kiener-Manu, 2019), social (Taylor, 1995), economic (Shenk et al., 1984), and physical (World Health Organization, 2014) effects on victims, it reduces

leisure (Rees-Punia et al., 2018) and productive hours (Corso et al., 2007), increases disease burden, and reduces quality of life in later years (Koepfel & Bouffard, 2012). The genesis of crime is multifaceted—biological, sociological, psychological, geographical, and economical ('Strategic Policy Brief - Theories,' 2009)—and can be considered 'a public health issue' (Middleton, 1998).

This study explores violent crimes and their relationship with selected variables: gang and gun-related violence, crime detection levels, public health variables, national security, and welfare budgets. According to Crime and Problem Analysis (CAPA), crimes are classified as major and minor (Citizensinformation.ie, n.d.). Major violent crimes include murder, incest, rape, sexual offences, kidnapping, and suicide. This study's specific objectives include determining the: (1) crime burden and detection rates (intelligence and non-intelligence); (2) association between violent crimes and selected factors (public health issues, national security and social welfare budgets, gang, and gun-related violence); and (3) population affected by crime.

The Republic of Trinidad and Tobago has an area of 1864 square miles; its 2023 population was 1.53 million people (Kemp, 2023), predominantly Indo-Trinidadian (35.4%; 2011) and Afro-Trinidadian (34.2%; 2011) ('Trinidad and Tobago—Caribbean,' n.d.). It is the southernmost Caribbean Island and has links to South America and the United States. While there have been a small number of migrants from Venezuela over the decades, this has increased to an estimated 30,000 Venezuelan migrants within the last two years, putting additional strain on the country's financial, social, and security systems.

Investments in crime have always been a top priority; however, a multitude of additional crimes or interventions have been instituted by the government to curb this crime epidemic, including recent increases in policing (Bruzual, 2022) and laws. Additional officers have been recruited from retirees, special reserves, and the army, and the number of police officers grew from 2300 in 2019 (Kissoon, 2019) to over 6500 in 2021 ('About TTPS,' n.d.). Moreover, special units have been created, such as the anti-kidnapping squad, child protection unit, domestic violence unit, and Special Weapons and Tactics (SWAT) unit. Financial investments in the Ministry of National Security increased from 4.762 billion in 2011 to 6.497 billion in 2014 but then decreased to 5.664 billion in 2022 ('Budget Statements,' n.d.). These investments are reflected in the increasing number of physical structures, such as police stations, which grew to 77 in 2019 (Kissoon, 2019). Other changes were made to the police administration with the enactment of the Police Authority Bill ('The Supplemental Police,' 2022) and a new method of appointing a Commissioner of Police ('The Judiciary of Trinidad and Tobago,' 2021). The country also benefitted from a high gross domestic product (GDP), increasing employment, high education levels (nearly universal primary and secondary school enrolment), and other sectorial improvements (water, communication, electricity). Despite this, in keeping with the 'inverse care law,' which states that those who need services the most receive the least, many communities with high crime levels are deprived of these very facilities (Cookson et al., 2021).

## 2. Methods

This is a retrospective, observational study using secondary data obtained from multiple recognised websites such as the Pan American Health Organization (PAHO), Central Statistical Office (CSO), World Health Organization (WHO), Ministries of National Security and Health; Centre for Arms Control and Non-Proliferation, Crime and Problem Analysis (CAPA), World Databank, and Central Intelligence Agency (CIA) fact book from 1990 to 2022. The search words used were crime, public health, surveillance, violence, health, and Trinidad and Tobago. Additionally, a review of the literature included searches in PubMed, EBSCOHOST, and Google. The data were collected by research assistants who were university students. Secondary data on crime statistics, public health statistics (poverty, unemployment, internet users, SEA (Secondary Entrance Assessment) candidates scoring  $\leq 30\%$ , social service grants), national security, social welfare budgets, and firearm availability were collected, documented, and analysed. Crime data included woundings and shootings, burglaries and break-ins, murders, kidnappings, kidnappings for ransom, rapes, incest and sexual offences, robberies, possession of firearms and ammunition, and domestic violence between 1990 and 2022. Gang sizes and detection rates from 2013 to 2022 were also collected. These were examined to determine links between violent crimes and socio-economic and criminal justice issues (detection rates, gang, and gun-related crimes). A descriptive analysis was conducted, and

the results were documented in graphs and tables. Crime rates are defined as the total number of crimes per 100,000 or total number of reported crimes of any kind divided by the total population, multiplied by 100,000 ('Crime Rate by Country,' 2023).

### 3. Results

#### 3.1. Section A

##### 3.1.1 Violent crime and associations

Although there are yearly fluctuations in criminal activities, there was a general increase in crime up to 2006, which was followed by peaks and troughs. However, there was a decrease in 2022 compared to earlier years (Figure 1). Over the last two decades, minor crimes such as burglaries and break-ins, robberies, and fraud offences decreased, while serious/major crimes, particularly murder, increased (Figure 1). Murder rates increased from 0.007% (1990) to 0.009% (2000) to 0.032% (2021); the incest, sexual offences, and rape rate increased from 0.023% (1993) to 0.052% (2010) and then decreased in later years from 0.027% (2020) to 0.026% (2021). Over the last two decades, there has been an increase in kidnappings from 0.001% (1990) to 0.012% (2000), and then a decrease to 0.005% in 2021. However, suicide rates decreased from 0.016% (2000) to 0.009% (2019).

Overall, there has been an increase in major crimes from 7.94 in 1990 to 70.63 in 2022 (an increase of 790%)

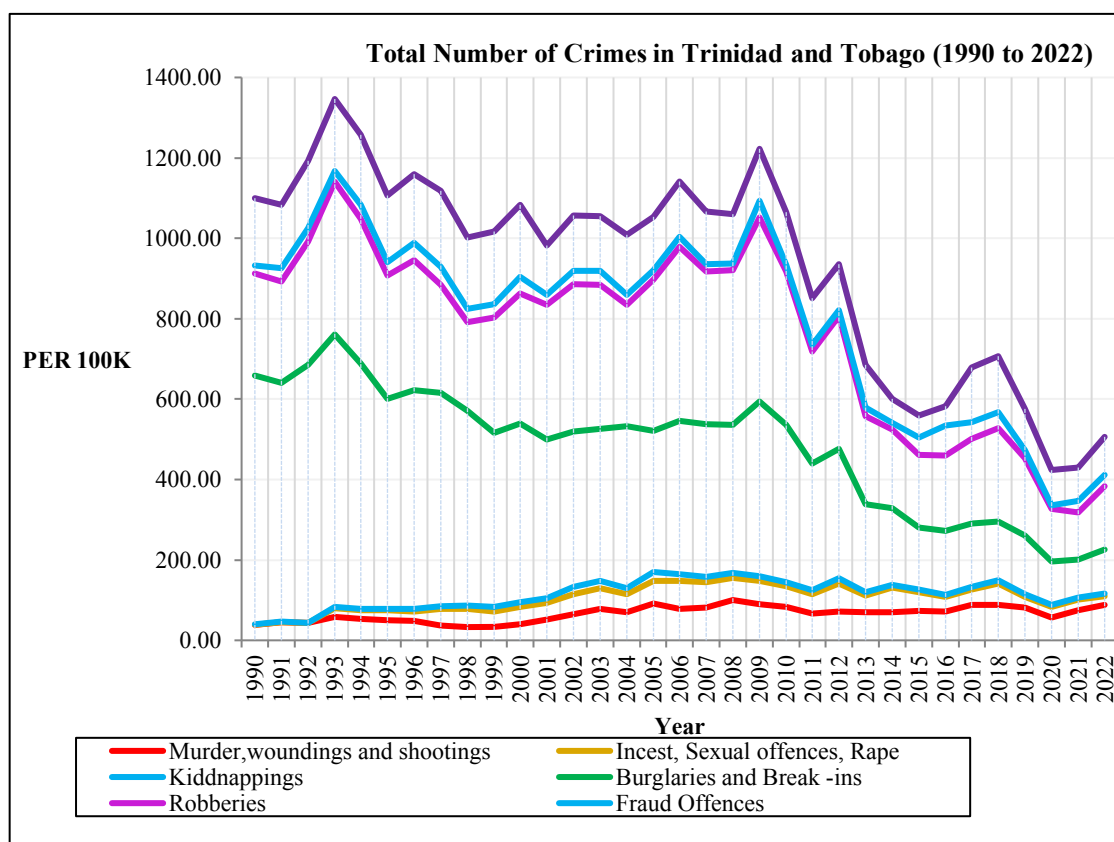


Figure 1: Total Number of Crimes in Trinidad and Tobago per 100 000 population (1990-2022)

Sources: *Crime Totals by Month*. (n.d.). Retrieved November 26, 2023, from <https://www.ttps.gov.tt/Stats/Crime-Totals-By-Month>;

Seepersad, R. (2016). *Crime and Violence in Trinidad and Tobago: IDB Series on Crime and Violence in the Caribbean*.

<https://publications.iadb.org/en/crime-and-violence-trinidad-and-tobago-idb-series-crime-and-violence-caribbean>

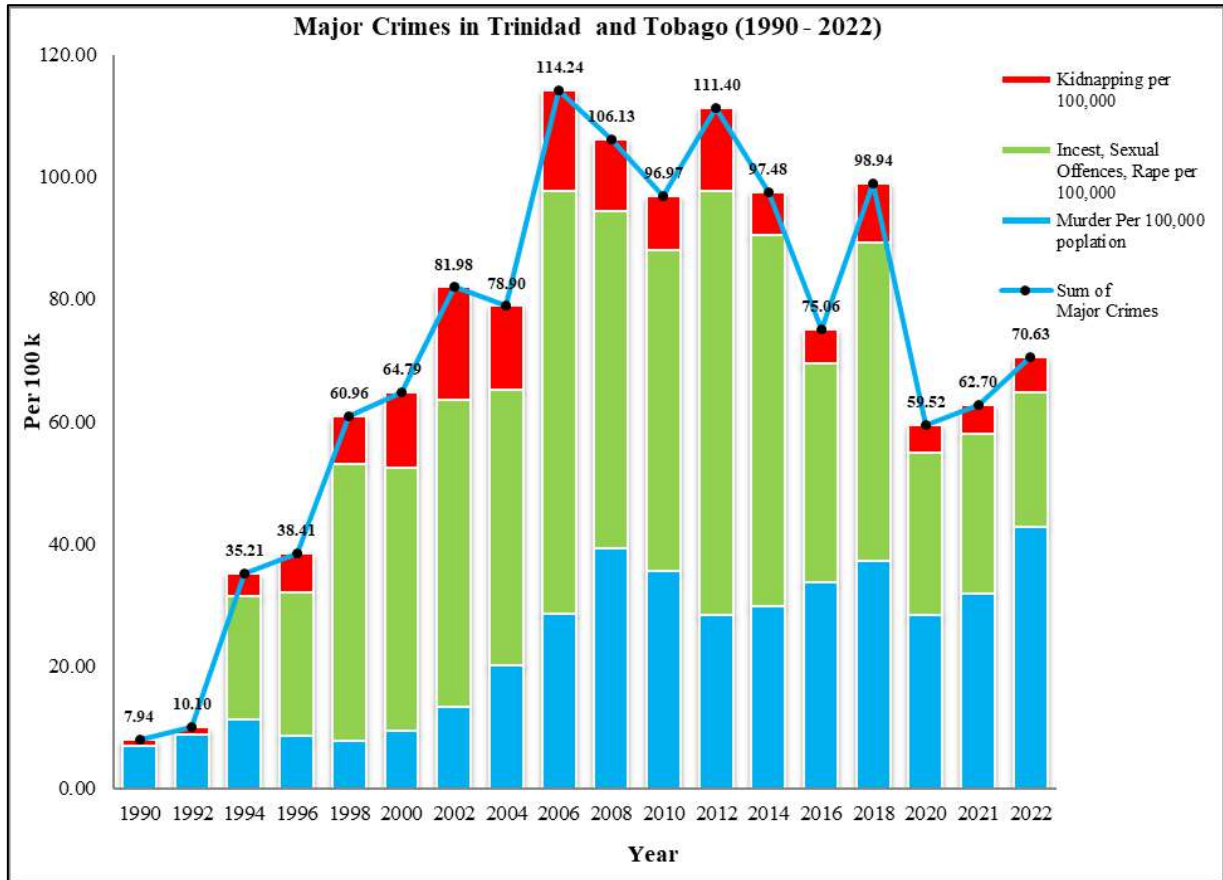


Figure 2: Total Major Crimes (Murder, Kidnapping, Incest, Sexual Offences, Rape) per 100 000 population (1990-2022)

Sources: *Crime Totals by Month*. (n.d.). Retrieved November 26, 2023, from <https://www.ttps.gov.tt/Stats/Crime-Totals-By-Month>; Seepersad, R. (2016). *Crime and Violence in Trinidad and Tobago: IDB Series on Crime and Violence in the Caribbean*. <https://publications.iadb.org/en/crime-and-violence-trinidad-and-tobago-idb-series-crime-and-violence-caribbean>

Note 1: Major Crimes–Murder, woundings and shootings, kidnappings, incest, sexual offences, and rape.

### 3.1.2 Crime, gang, and gun-related violence

There appears to be a correlation between the number of gangs and guns seized and the prevalence of violent crime (Figure 3).

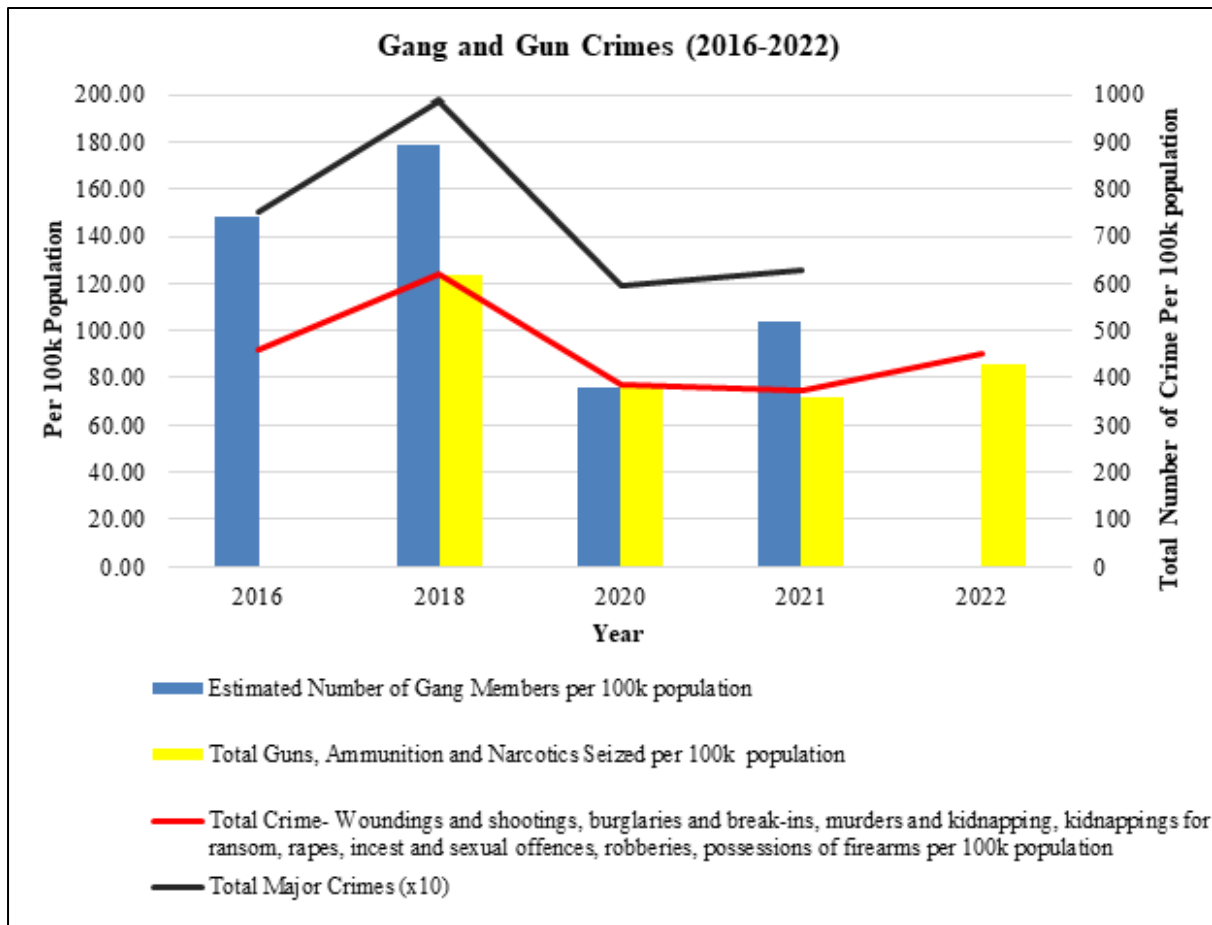


Figure 3: Gang and Gun Crimes, in Relation to Total Number of Crimes and Total Major Crimes (2016-2022)  
 Note 1:

- Total Major Crimes are multiplied by a factor of 10 to create a clearer display of the crime trends.
- Major Crimes–Murder, woundings and shootings, kidnappings, incest, sexual offences, and rape.

Crime detection levels: Overall crime detection levels are very low at approximately 20 to 30%. However, upon dis-aggregation, the rate of intelligence-driven detection was even lower in 2014 at 14.04% and then decreased to 13.66% in 2022. In contrast, non-intelligence-driven detection saw an overall rise from 2016 to 2022, where it stabilised at approximately 50% to 60% (Figure 4). The low detection of intelligence-driven crimes is unlikely to deter the high level of crimes. Paradoxically, but not surprisingly, the relatively higher detection levels of non-intelligence-driven crime have also not curtailed violent crime. This may be because although the detection levels for non-intelligence crimes are higher, they are still quite low.



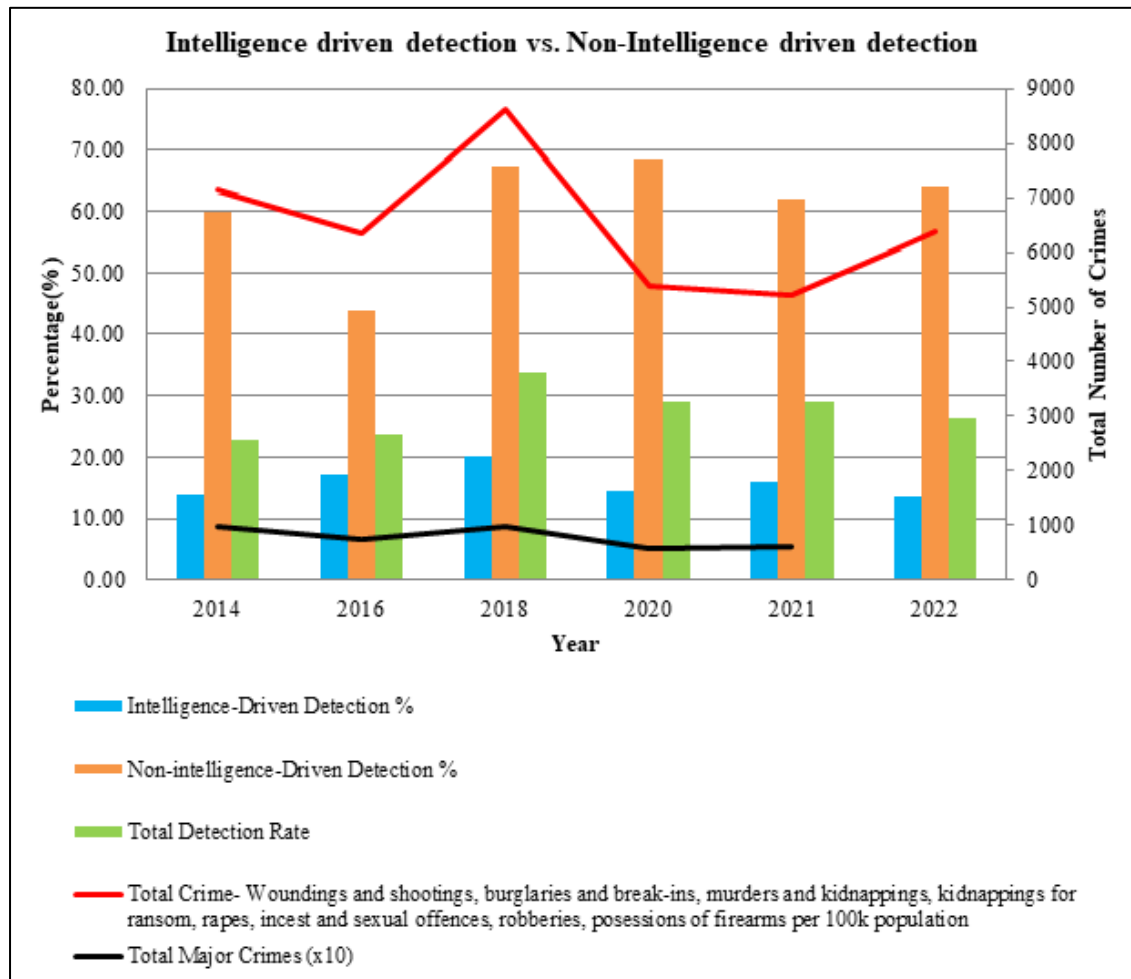


Figure 4: Detection Levels of Intelligence-driven and Non-intelligence Driven

Source: *Crime Totals by Month*. (n.d.). Retrieved November 26, 2023, from <https://www.ttps.gov.tt/Stats/Crime-Totals-By-Month>

**Note 1:**

- **Intelligence-driven detection**—Woundings and shootings, robberies, burglaries and break-ins, larceny-motor vehicles, larceny-dwellings, houses, murders, kidnappings, and general larceny.
- **Non-intelligence-driven detection**—Fraud offences, serious indecency, kidnappings for ransom, narcotics, other, rapes, incest, sexual offences, possession of firearms and ammunition.
- **Total detection rate**—Intelligence-driven and non-intelligence-driven, combined.
- **Total major crimes** are multiplied by a factor of 10 to create a clearer display of crime trends.

Over the last decade, unemployment has varied between 2 and 6% ('Trinidad and Tobago Unemployment,' n.d.), and poverty has remained at approximately 20% ('Trinidad and Tobago Poverty, n.d.). There was no significant association between overall violent crimes and the variables studied except SEA performance. Student performance on the SEA exam (students scoring  $\leq 30\%$ ) increased specifically during the pandemic years (Figure 5). Poor performance on the SEA appears to be correlated with the crime rate. SEA performance may reflect society's educational status.

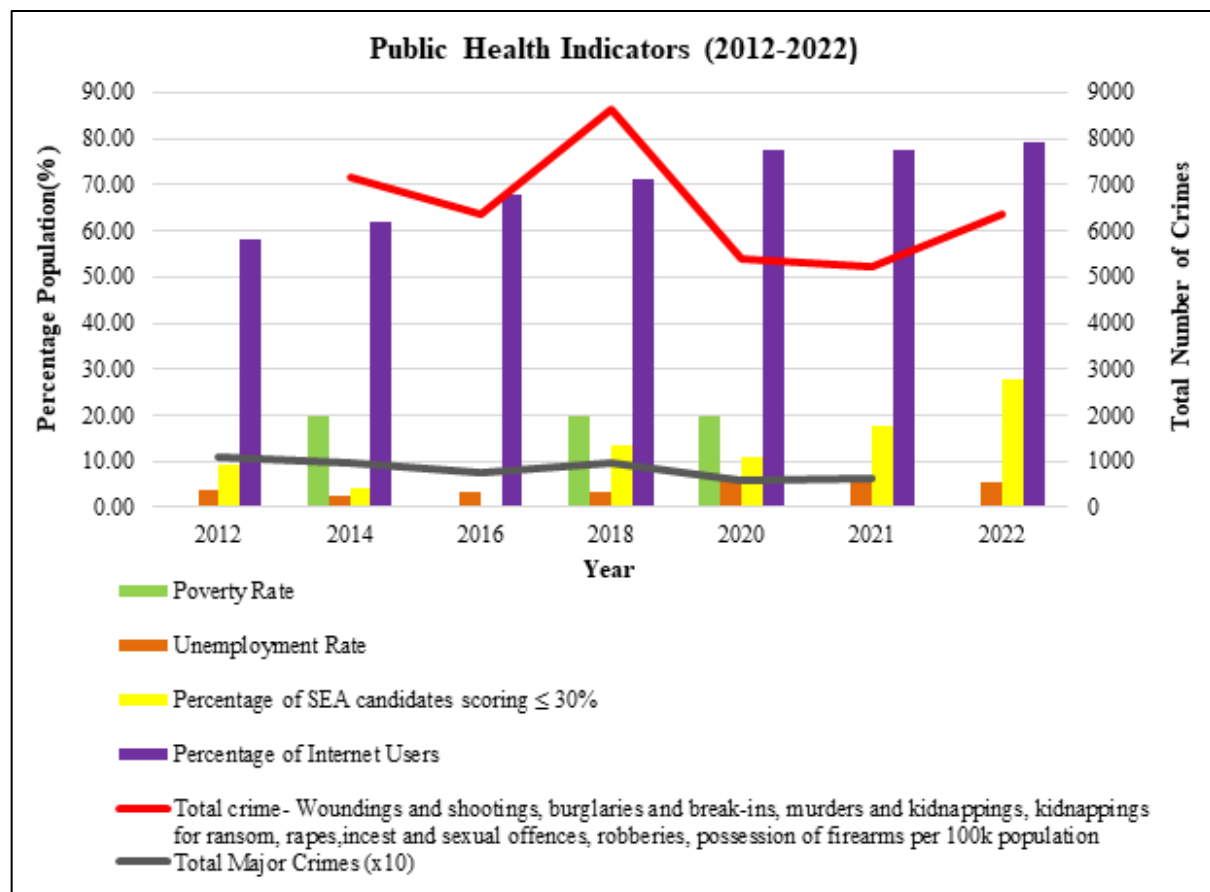


Figure 5: Total Crime and Public Health Indicators

Sources: *Crime Totals by Month*. (n.d.). Retrieved November 26, 2023, from <https://www.ttps.gov.tt/Stats/Crime-Totals-By-Month>;  
 Seepersad, R. (2016). *Crime and Violence in Trinidad and Tobago: IDB Series on Crime and Violence in the Caribbean*. <https://publications.iadb.org/en/crime-and-violence-trinidad-and-tobago-idb-series-crime-and-violence-caribbean>; Doodnath, A. (2021, September 14). "Concerning" SEA statistics: Education Minister takes action | Loop Trinidad & Tobago. <https://tt.loopnews.com/content/concerning-sea-statistics-ministry-take-action>; Ministry of Education's Press Conference On SEA 2022 – TTT News. (2022, July 1). <https://news.ttlimited.com/ministry-of-educations-press-conference-on-sea-2022/>; Kemp, S. (2023, February 14). *Digital 2023: Trinidad and Tobago. DataReportal – Global Digital Insights*. <https://datareportal.com/reports/digital-2023-trinidad-and-tobago>; Kemp, S. (2022, February 16). *Digital 2022: Trinidad and Tobago. DataReportal – Global Digital Insights*. <https://datareportal.com/reports/digital-2022-trinidad-and-tobago>; Kemp, S. (2021, February 12). *Digital in Trinidad and Tobago: All the Statistics You Need in 2021. DataReportal – Global Digital Insights*. <https://datareportal.com/reports/digital-2021-trinidad-and-tobago>; Trinidad and Tobago Unemployment Rate 2023 & Employment Data | Take-profit.org. (n.d.). Take-Profit. Retrieved November 26, 2023, from <https://take-profit.org/en/statistics/unemployment-rate/trinidad-and-tobago/>

Note 1;

- Total Major Crimes are multiplied by a factor of 10 to create a clearer display of crime trends.
- Major Crimes–Murder, woundings and shootings, kidnappings, incest, sexual offences, and rape.

Financial support: The budgetary allocations to national security and social welfare ministries have remained fairly constant and show no association with the number of crimes (Figure 6).

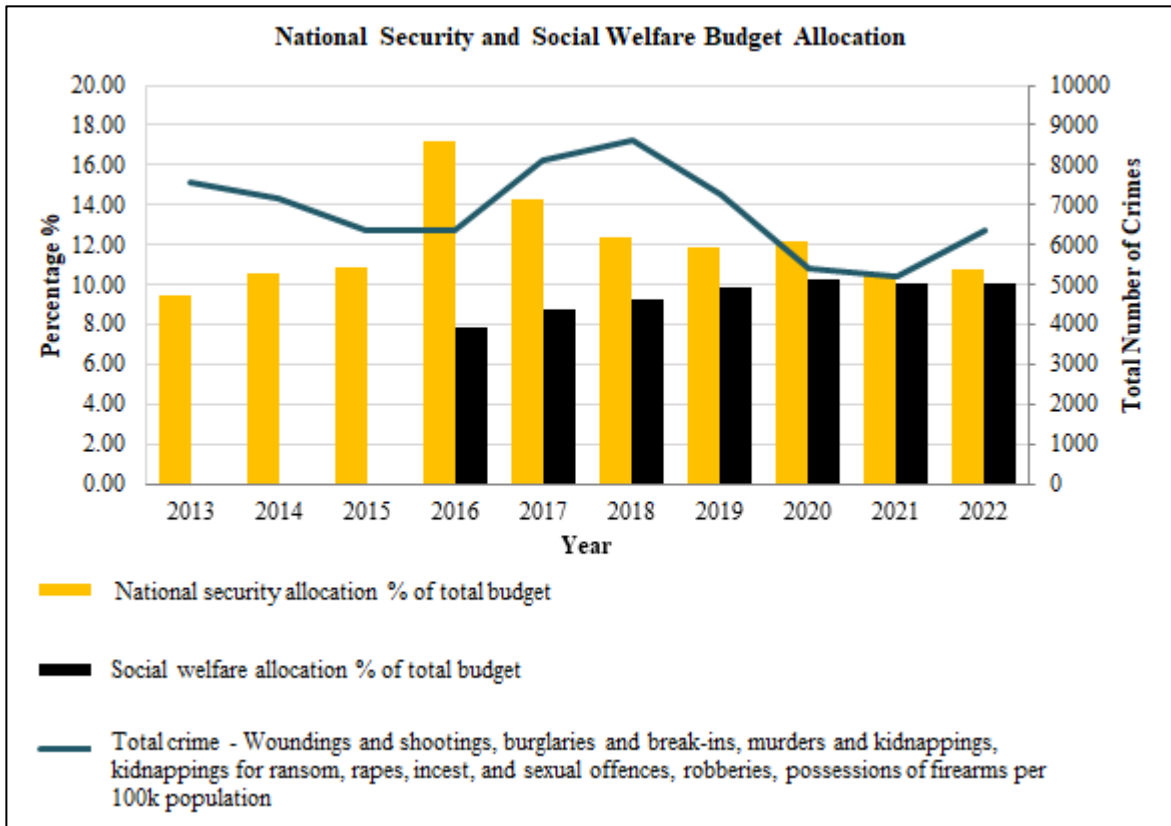


Figure 6: Total Crime and Budget Allocation of National Security and Social Welfare

Sources: Summary of the Ministry's Expenditure, Divisions and Projects. Second Sessions of the 12<sup>th</sup> Parliament. (n.d). <https://www.tparliament.org/wp-content/uploads/2021/10/Budget-Summary-2022-Ministry-of-Social-Development-and-Family-Services.pdf>; Budget Statements – Ministry of Finance. (n.d.). Retrieved November 29, 2023, from <https://www.finance.gov.tt/publications/national-budget/budget-statements/>

### 3.2 Section B

#### 3.2.1 Crime: human impact

The human impact of crime is reflected in the number and types of perpetrators (detected or overt, undetected or covert) and victims (directly and indirectly affected) of crimes. Using 2013 as a baseline, a total of 7541 crimes were reported in 2013. Assuming at least one perpetrator per victim and 10 people indirectly affected, over a 10-year period, the total numbers of people directly and indirectly affected are 68 322 and 683 220, respectively (i.e. at least 50% of Trinidad and Tobago's population). While crimes spread, the number of potential victims who are 'presumably unaffected' decreased from 1 301 967 in 2013 to 511 814 in 2022, which is an overall 61% decrease in unaffected people (Figure 7).

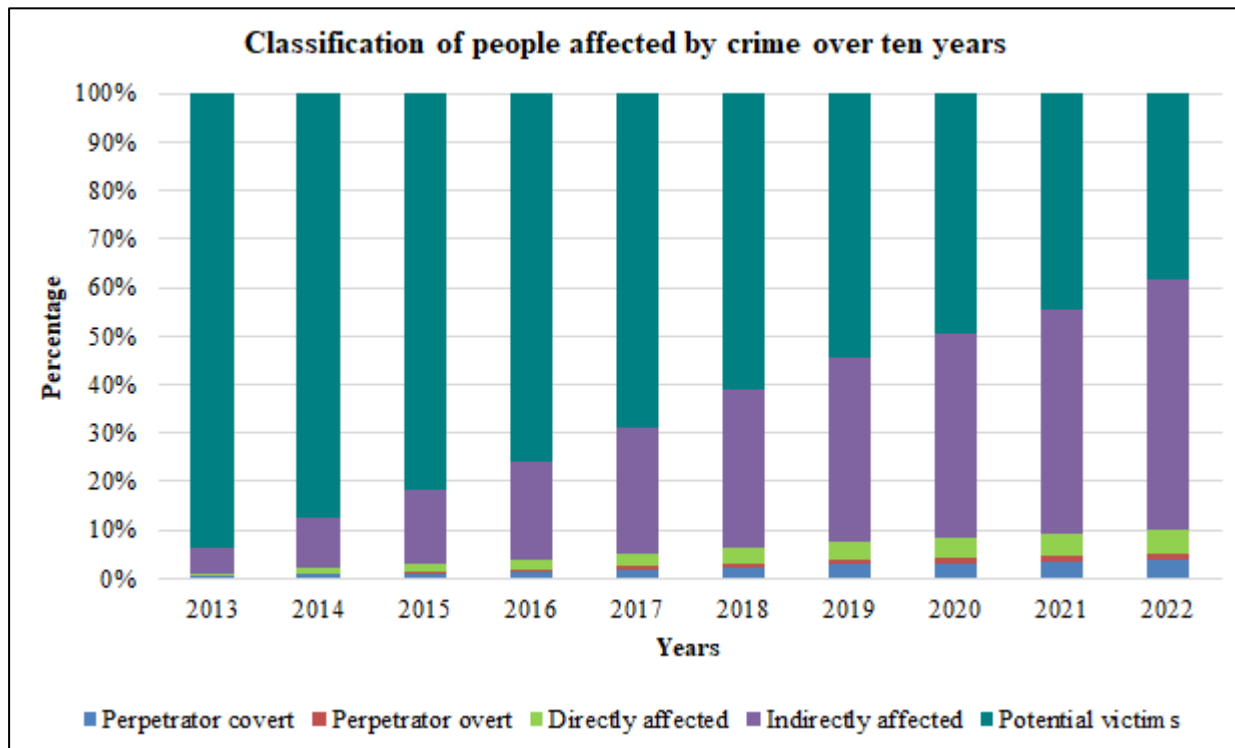


Figure 7: Classification of people affected by crime from 2013 to 2022 with 2013 as baseline

Source: *Crime Totals by Month*. (n.d.). Retrieved November 26, 2023, from <https://www.ttps.gov.tt/Stats/Crime-Totals-By-Month>

Note 1:

- True/Cumulative 2022 is the successive addition of affected people every year through 2022 with 2013 as a baseline.
- Baseline population for all years = 1.4 million persons

## 4. Discussion

### 4.1 Section A

#### 4.1.1. General

With a crime level of **2 243.3 per 100 000 in 2022** ('Crime Statistics,' 2021), the Republic of Trinidad and Tobago is ranked sixth among the countries worldwide with the highest crime rates ('Crime Rate by Country,' 2023). Comparisons among some Caribbean and other countries reveal wide variations in murder rates, with Trinidad and Tobago faring worse and Denmark ranking the lowest worldwide (Figure 8). A comparative ratio of murder rates for Jamaica, Trinidad and Tobago, Barbados, the United States, Canada, and Denmark is 8:6:5:4:3:1, respectively. Iceland's crime rate of 1.107 is one of the lowest crime rates in the world ('Crime Rate by Country,' 2023).

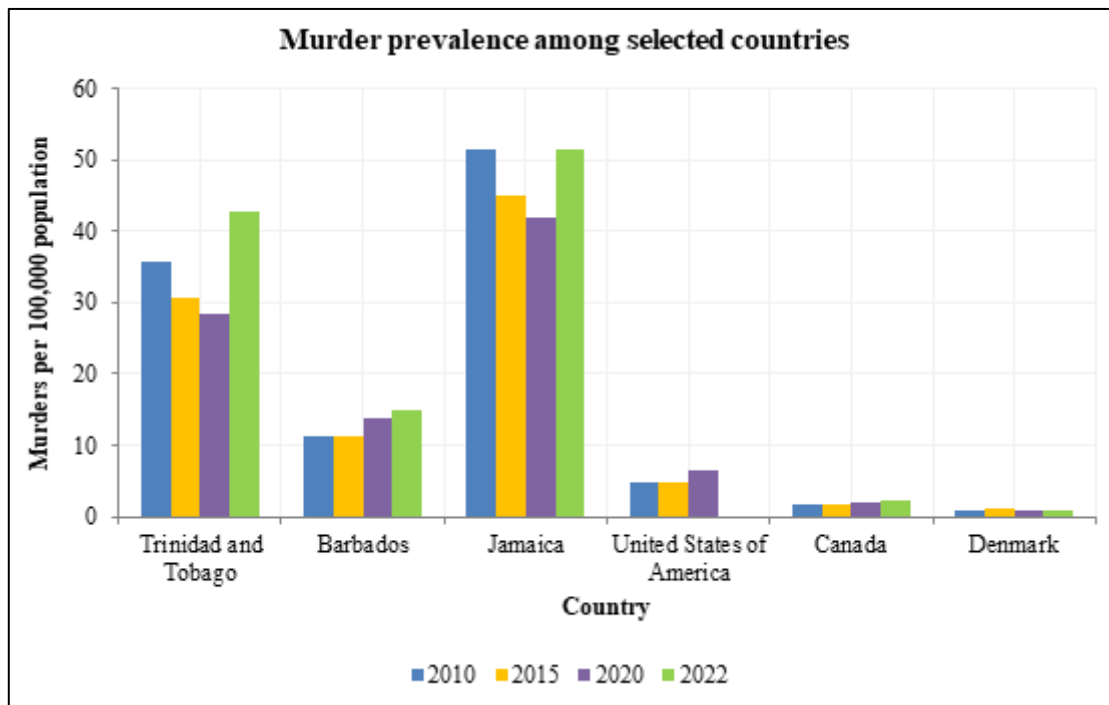


Figure 8: Murder prevalence per 100k population among selected countries (Trinidad and Tobago, Barbados, Jamaica, the United States, Canada, Denmark) 2010 to 2022.

Sources: *Crime Totals by Month*. (n.d.). Retrieved November 26, 2023, from <https://www.tps.gov.tt/Stats/Crime-Totals-By-Month>; *Barbados Murder Data and Statistics*. (n.d.). Retrieved November 26, 2023, from <https://murders.opendatabarbad.org/>; *Jamaica Murder/Homicide Rate 1990-2023* | MacroTrends. (n.d.). Retrieved November 26, 2023, from <https://www.macrotrends.net/countries/JAM/jamaica/murder-homicide-rate>; *Jamaica recorded 1,498 murders in 2022* | News | Jamaica Gleaner. (n.d.). Retrieved November 26, 2023, from <https://jamaica-gleaner.com/article/news/20230103/jamaica-recorded-1498-murders-2022>; *Jamaica population (2023) live—Countrymeters*. (n.d.). Retrieved November 26, 2023, from [https://countrymeters.info/en/Jamaica#population\\_2023](https://countrymeters.info/en/Jamaica#population_2023); *U.S. Murder/Homicide Rate 1990-2023* | MacroTrends. (n.d.). Retrieved November 26, 2023, from <https://www.macrotrends.net/countries/USA/united-states/murder-homicide-rate>; *Government of Canada, S. C. (2021, April 13). Number, rate, and percentage changes in rates of homicide victims*. <https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=3510006801>; *Denmark Murder/Homicide Rate 1990-2023*. (n.d.). Retrieved November 26, 2023, from <https://www.macrotrends.net/countries/DNK/denmark/murder-homicide-rate>; *Denmark: Number of homicides 2022*. (n.d.). Statista. Retrieved November 27, 2023, from <https://www.statista.com/statistics/576114/number-of-homicides-in-denmark/>

Overall, violent crimes are increasing. However, major crimes such as incest, sexual offences, and rape had minimal decreases or only marginal increases in some years. *Using a decade of data from 2013 to 2022, an additional 60,781 persons or 806% more victims are directly affected. However, total perpetrators between 2013 to 2022 increased by 16,598 persons (a 1223% increase).* While public health issues and crimes of necessity (crimes committed to attain basic needs) are important, the big drivers of violent crimes are an increase in gangs, low detection levels, and poor educational performance.

#### 4.1.2. Crime rate drivers

**Gang and gun-related violence:** The number of gangs seems to be related to the number of violent crimes (Figure 3), which has increased from 75.46 to 104.18 per 100k of population between 2020 and 2021. The reported number of crimes increased from 384.57 to 450 per 100k of population between 2020 and 2022. Gangs represent 'a group of lawbreakers who are primarily organized around violence and other illegal activities' (Haskell & Yablonsky, 1982, as cited in Yearwood & Hayes, 2000). In our context, guns and gangs are major driving forces of violent crimes, a finding supported by other studies (Seepersad, 2013; 'Youth Gangs and Violence,' 1998). In the last decade, 'gun-related homicides in Trinidad and Tobago (T & T) have risen about 1,000 per cent' (Townsend, 2009). Gangs have been reported as contagious in many countries (Patel et al., 2013). In fact, certain areas, such as the eastern districts of the Port of Spain, are among the most dangerous places on the planet and 'the murder rate for (the) Port of Spain is comparable to that of Baghdad' (Kukis, 2009, as cited in Townsend, 2009). Strand

(2014) states that persons may join gangs for a sense of belonging, family situations, poverty, peer pressure, protection, and a lack of social structure and support.

Crime detection rate: Detection levels of overall crimes range between 22.94 to 33.80%. However, when disaggregated into intelligence- and non-intelligence-driven crime, intelligence-driven crimes had much lower detection levels, ranging between 14.04 to 20.01%. This compares poorly with other countries like Finland, which had a detection rate of 59.36% in 2022 ('Finland: Criminal Offenses,' 2023) and a low crime level (2.71 in 2023) ('Criminality in Finland,' n.d.). Detection levels are one of the major drivers of crime as demonstrated in many studies (Abramovaite et al., 2023; Drake & Simper, 2005). Bun et al. (2020) reveal that high detection and high conviction rates can serve as deterrents to crime. Furthermore, 'low detection rates produce a criminal multiplier effect' (Deosaran, 2022). Low levels of crime detection imply that a substantial number of perpetrators freely roam the streets with the potential for more crime.

Public health issues: The percentage of SEA candidates that score  $\leq 30\%$  seems to be related to the extent of violent crime. School systems are microcosms of a larger society. The underperformance of SEA students may reflect the educational attainment of society at large, as reported in other studies ('The Impact of Local Crime,' 2019). There is no conclusive evidence that the other public health issues (poverty level, unemployment, Internet users) analysed are related to violent crimes (Figure 5). This contrasts with other studies, which reveal that crime is linked to public health indicators such as unemployment (Janko & Popli, 2015), poverty (Johnstone, n.d.), air pollution (Plain, 2019), education (Hjalmarsson & Lochner, 2012), and property prices (Braakmann, 2017).

Social and physical determinants ('Social Determinants of Health,' n.d.) form the basis for a healthy and nurturing environment. Crime is a social and cultural issue that originates within communities and is the result of a combination of numerous social factors. When crime risks are not identified and treated, significant increases occur in societal crime rates, leading to 'a society in disorder and chaos and unsafe for residents' (Onyeneke & Karam, 2022). According to the social disorganisation theory, 'a person's physical and social environments are primarily responsible for the behavioural choices that a person makes' (Bond, 2015). Poverty (Fafchamps & Minten, 2002), education (Lochner & Moretti, 2004), socialisation (McCord, 1991), and belief systems ('Religion and Crime,' n.d.) are some of the social factors that cause crime. In this study, the lack of an association between violent crime rates and national security and social welfare budgets contrasts with the findings of other studies. Foley (2011) reports the opposite and states that crime increases as welfare increases. However, Rudolph and Starke (2020) demonstrate that social welfare helps decrease crime. According to Halpert (2022) from Forbes, removing such benefits from young adults will more likely cause them 'to be charged with an illicit crime than they were to find and maintain steady employment'.

## 4.2 Section B

### 4.2.1 Crime solution

Gang violence and low detection levels must be addressed upfront through the criminal justice system. The educational system must be revamped to allow achievement and holistic development for everyone, not necessarily through the traditional methods (a classroom and student-teacher relationship) but perhaps through alternative means (e.g. out-of-classroom training). The governance structure must address the challenges of corruption, lack of transparency, and accountability. In general, a more holistic approach is required. This includes decreasing risks, increasing protective factors, minimising corruption, and ensuring transparency and accountability. (Figure 9)

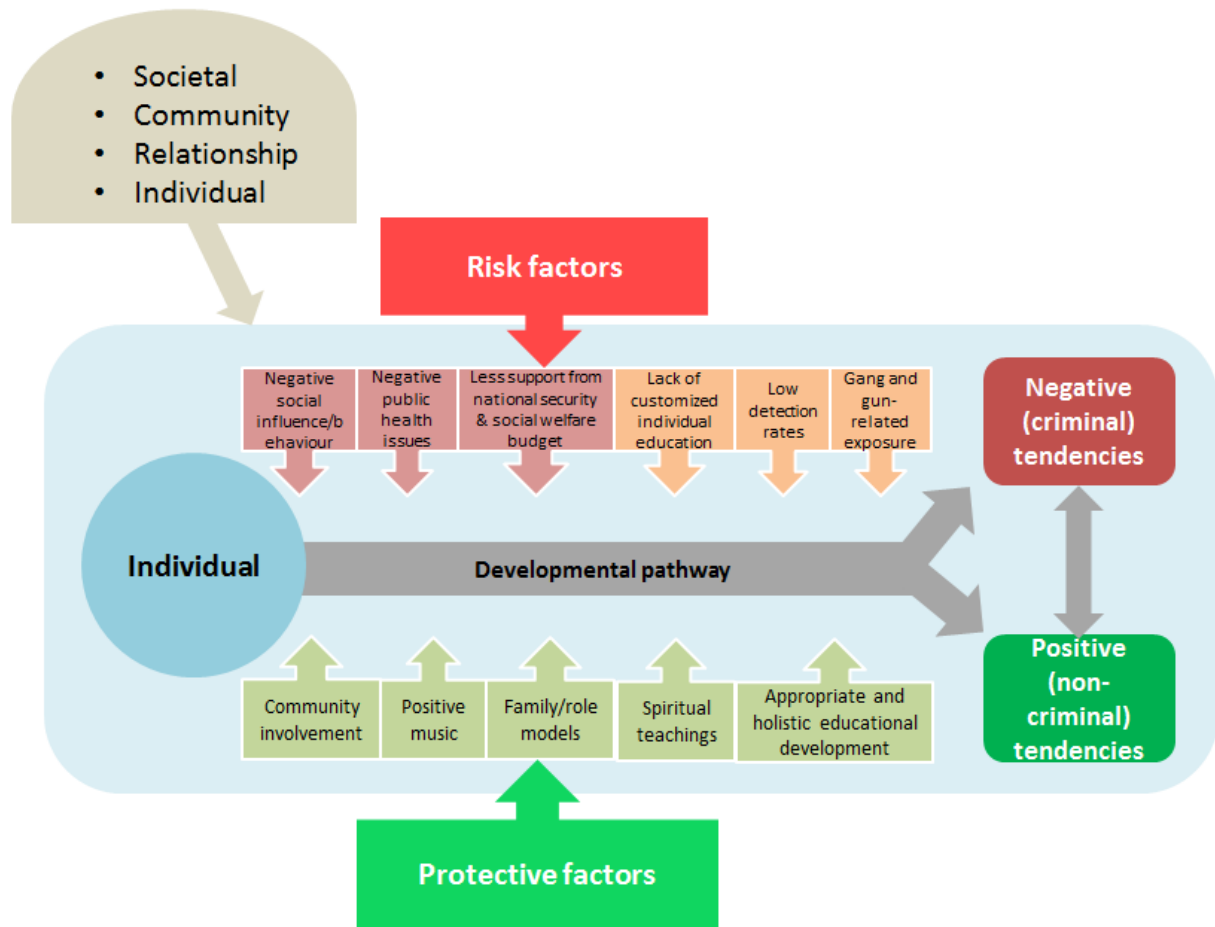


Figure 9: Criminal Tendency Development - Force Field Model

Note 1:

- Public health issues include poverty, unemployment, percentage of internet users, and SEA students scoring  $\leq 30\%$ .
- Negative social influences/ behaviours include alcohol consumption, delinquent peers and behaviours, and drug use.
- Community involvement helps develop social skills, and emotional maturity, amongst others.

*Risks for criminal or deviant behaviour: low literacy, presence of neighbourhood crime, anti-social behaviour, low self-esteem, poverty etc. ('Risk and Protective Factors,' 2018) and anxiety and stress, poor supervision by parents, few friends etc. ('Strategic Policy Brief - Risk Factors,' 2009).*

*Protective behaviour: Parental supervision, availability of services, community engagement, steady employment, and positive attitudes, amongst others ('Risk and Protective Factors,' 2018), and self-control and good academics. ('Strategic Policy Brief - Risk Factors,' 2009).*

#### 4.3 Limitations

Data from government agencies are difficult to access, resulting in a lack of detail regarding at-risk individuals and communities.

## 5. Conclusion

Although crime is a universal phenomenon, the crime problem in the Republic of Trinidad and Tobago is predominantly observed in unhealthy environments and communities characterised by a self-sustaining gang culture and low levels of crime detection and educational attainment. While the public health system may play a significant role, the immediate needs require an efficient and results-oriented criminal justice system and a non-traditional educational approach.

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**Ethics approval and consent to participate:** Not applicable.

**Data Availability Statement:** The data supporting the findings of this study shall be made available from the corresponding author upon reasonable request.

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# Evaluating Heterogeneity in Meta-Analyses: A Review

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## Abstract

Meta-analysis, as a fundamental aspect of evidence-based practice, synthesizes findings from multiple studies to draw comprehensive conclusions. A critical element of this synthesis is heterogeneity - the variability in outcomes, methodologies, and characteristics across studies. This review provides an in-depth exploration of heterogeneity in meta-analyses, highlighting its types, impact, and evolution over time. It emphasizes the significance of methodological rigor in detecting and managing heterogeneity, which is crucial for the credibility and utility of meta-analytic results. We delve into the methods for evaluating heterogeneity, including statistical tests like Cochran's Q test and the  $I^2$  statistic, and visual methods such as forest plots and funnel plots. The paper also discusses strategies for managing identified heterogeneity, such as subgroup analysis, meta-regression, and sensitivity analysis, and the importance of choosing the appropriate statistical model. Advanced developments in heterogeneity evaluation, driven by statistical, technological, and methodological innovations, are also examined. This includes Bayesian approaches, individual participant data (IPD) meta-analysis, and automated tools for literature search and data extraction. The review includes case studies to demonstrate the application of these methods in various research contexts, underscoring the complexity and necessity of continuous advancements in handling heterogeneity. This paper serves as a comprehensive guide for researchers, contributing to the enhancement of meta-analytic practices and the quality of research findings across disciplines.

**Keywords:** Meta-Analysis, Heterogeneity, Statistical Methods, Research Synthesis, Methodological Rigor

## 1. Introduction

### 1.1 Heterogeneity: Definition and Significance

Meta-analysis, a cornerstone of evidence-based practice, amalgamates findings from multiple studies to arrive at comprehensive conclusions. Central to this process is the concept of heterogeneity - the variability or differences in study outcomes, methodologies, and characteristics. Heterogeneity is not merely a statistical nuance; it fundamentally impacts the interpretation and validity of meta-analytic results (Rokhshad et al., 2023). Understanding and appropriately addressing this heterogeneity is vital for ensuring that meta-analyses provide accurate and meaningful insights into the research questions they aim to answer.

### *1.2 Challenges Posed by Heterogeneity*

The presence of heterogeneity in meta-analyses presents unique challenges. It can stem from various sources, such as differences in study populations, interventions, outcomes measured, or study designs. When unacknowledged or improperly managed, heterogeneity can lead to misleading conclusions, either overstating the consistency of findings across studies or obscuring meaningful patterns and relationships. The challenge for researchers lies in identifying the extent of heterogeneity, understanding its sources, and determining how to integrate diverse study results into a coherent and reliable conclusion.

### *1.3 Purpose and Scope of the Review*

This review aims to elucidate the concept of heterogeneity in meta-analyses, its implications, and the methodologies for its evaluation and management. By delving into statistical tests and measures designed to detect and quantify heterogeneity, we provide a comprehensive overview of the current best practices in the field. Additionally, we aim to bridge the gap between statistical heterogeneity and its practical implications, offering insights into how researchers can interpret and address variability in meta-analysis to enhance the reliability and applicability of their findings.

In doing so, this review serves as a vital resource for researchers engaged in conducting meta-analyses, contributing to the refinement of methods and the advancement of knowledge in various scientific disciplines. It underscores the nuanced understanding required to navigate the complexities of combining disparate studies and highlights the continuous evolution of methodologies in this ever-expanding field.

### *1.4 Background and Evolution of Heterogeneity in Meta-Analyses*

The concept of heterogeneity has evolved significantly since the inception of meta-analytic techniques. Initially, the focus was predominantly on quantifying and mitigating statistical variance among study results. However, as the field of meta-analysis has matured, there is an increasing recognition of the multifaceted nature of heterogeneity. It encompasses not just statistical discrepancies, but also clinical and methodological diversity. This broader understanding acknowledges that heterogeneity is an inherent and sometimes valuable aspect of meta-analysis, reflecting the real-world diversity of populations, settings, and interventions.

### *1.5 The Importance of Methodological Rigor*

The credibility of a meta-analysis largely hinges on how well it addresses heterogeneity. Methodological rigor in detecting and managing heterogeneity not only strengthens the validity of the findings but also enhances the utility of the meta-analysis for informing policy, practice, and future research. Given the expanding role of meta-analyses in guiding decision-making in various fields, including healthcare, education, and public policy, the need for robust methodologies in evaluating heterogeneity has never been more critical.

### *1.6 Objectives and Structure of the Review*

This review aims to provide a thorough exploration of the methodologies used to evaluate heterogeneity in meta-analyses. We will discuss statistical tests such as Cochran's Q test and the  $I^2$  statistic, delve into visual methods like forest plots, and consider advanced techniques like meta-regression. Furthermore, we will examine the challenges and debates surrounding the interpretation of these methods, offering insights into both their strengths and limitations.

The subsequent sections of this review are structured to offer a comprehensive understanding of heterogeneity in meta-analyses. We begin with a detailed background of heterogeneity, followed by an exploration of the various methods for its evaluation. We then discuss strategies for addressing heterogeneity, including statistical models and sensitivity analyses. Case studies are presented to illustrate these concepts in practice, followed by a discussion

of recent advances and ongoing challenges in the field. The review concludes with a summary of key findings and recommendations for future research.

In sum, this review endeavors to provide a holistic view of heterogeneity in meta-analyses, equipping researchers with the knowledge and tools to navigate this complex but crucial aspect of research synthesis. Through this exploration, we aim to contribute to the enhancement of meta-analytic practices, ultimately improving the quality and impact of research findings across various disciplines.

## 2. Background

In the realm of meta-analysis, heterogeneity stands as a pivotal concept, encompassing the variability or differences observed across individual studies. This variability manifests in various forms: clinical, methodological, and statistical heterogeneity (Smela et al., 2023). Clinical heterogeneity arises from differences in participant characteristics, interventions, or outcomes, reflecting the diverse nature of research settings and populations. Methodological heterogeneity, on the other hand, stems from variations in study design, measurement tools, and risk of bias, critically influencing the meta-analysis's validity. Finally, statistical heterogeneity refers to the degree of variation in effect sizes reported in different studies that extends beyond chance, a quantifiable aspect crucial for assessing the consistency of study findings.

The impact of heterogeneity on meta-analysis outcomes is profound. It can significantly influence the results and conclusions, potentially leading to an overestimation or underestimation of the true effect size. High levels of heterogeneity might indicate that pooling data from the studies is inappropriate, necessitating a cautious interpretation of the meta-analysis results. However, heterogeneity is not solely a challenge to be mitigated; it can also offer valuable insights into the variability of effects in different contexts or subgroups, reflecting real-world diversity and aiding in the application of findings.

Historically, the treatment and perception of heterogeneity in meta-analyses have undergone a significant evolution. Initially regarded as a nuisance, heterogeneity is now acknowledged as an integral and informative component of meta-analysis. This shift is supported by methodological advancements that have improved the detection and quantification of heterogeneity, enabling a more nuanced interpretation and understanding of its implications. There are several good examples of assessing the heterogeneity, e.g., (Alhasan et al., 2023; Bhattacharjee & Khan, 2023; Chen et al., 2023; Cormier et al., 2023; Dong et al., 2023; Huang et al., 2023; Li et al., 2023; Mokhtari-Ardekani, 2023; Pereira et al., 2023; Rahmani, Fayyazishishavan, et al., 2023; Salazar de Pablo et al., 2023; Varhlunchungi et al., 2023; Zhang et al., 2023).

Heterogeneity also plays a critical role in guiding meta-analytic decision-making. The presence and extent of heterogeneity influence the choice of statistical models, such as fixed-effect or random-effects models, and shape the interpretation of results and formulation of conclusions. It is also integral to conducting meaningful subgroup analyses and meta-regression, which can explore the sources of variability and provide tailored insights for specific populations or contexts (Soleimani et al., 2023).

In essence, heterogeneity in meta-analysis is a multifaceted and dynamic element, the understanding of which is essential for ensuring the reliability and relevance of meta-analytic findings. The appropriate evaluation and interpretation of heterogeneity are key to advancing the field and enhancing the impact of research synthesis.

## 2. Methods for Evaluating Heterogeneity

The evaluation of heterogeneity in meta-analysis involves several statistical methods and measures, each offering unique insights into the degree and implications of variability among studies. Understanding and correctly applying these methods is crucial for a valid interpretation of meta-analytic results.

### 2.1 Statistical Tests for Detecting Heterogeneity

1. Cochran's Q Test: This is a widely used statistical test for detecting heterogeneity. The test is based on the principle that, under the null hypothesis of no heterogeneity, the weighted sum of squared deviations of individual study estimates from the overall estimate follows a chi-square distribution. The formula for Cochran's Q is:

$$Q = \sum_{i=1}^k w_i (x_i - \bar{x})^2 \quad (1)$$

where  $x_i$  is the effect estimate from the  $i$ -th study,  $w_i$  is the weight given to the  $i$ -th study (usually the inverse of the variance), and  $\bar{x}$  is the weighted mean of the effect estimates.

2. Significance of Q: A significant Q (p-value < 0.10 is often used due to low power of the test) suggests the presence of heterogeneity. However, it's important to note that the test has limitations, particularly in terms of its power to detect heterogeneity in meta-analyses with a small number of studies or with studies of varying sizes.

## 2.2 Measures of Heterogeneity

1. I<sup>2</sup> Statistic: The I<sup>2</sup> statistic quantifies the proportion of total variation across studies that is due to heterogeneity rather than chance. It is calculated as:

$$I^2 = \frac{Q - (k-1)}{Q} \times 100\% \quad (2)$$

where Q is Cochran's Q and k is the number of studies. I<sup>2</sup> values of 25%, 50%, and 75% are typically considered to represent low, moderate, and high heterogeneity, respectively (Taşçı et al., 2023).

2. Tau<sup>2</sup> (Tau Squared): This is an estimate of the between-study variance in a random-effects meta-analysis. It gives an idea of the absolute amount of variability between studies. There is no direct formula for Tau<sup>2</sup>; it is usually estimated using iterative statistical methods (Sharma et al., 2023).

## 2.3 Visual Methods

1. Forest Plots: These plots visually represent the results of individual studies and the overall meta-analysis estimate. The degree of heterogeneity can be visually assessed by observing the spread and overlap of the confidence intervals of the individual studies.
2. Funnel Plots: Used primarily for assessing publication bias, funnel plots can also provide insights into heterogeneity. Asymmetry in the plot may suggest heterogeneity, although this interpretation should be made cautiously.

Each of these methods contributes to a comprehensive understanding of heterogeneity in meta-analyses. While statistical tests and measures provide quantifiable evidence of variability, visual methods offer an intuitive understanding of the spread and impact of this variability. It's crucial for researchers to use a combination of these methods to fully grasp the extent and implications of heterogeneity in their meta-analytic work.

## 3. Addressing Heterogeneity in Meta-Analyses

Successfully addressing heterogeneity is a critical step in ensuring the reliability and validity of meta-analytic results (Ji et al., 2023). Once heterogeneity has been identified and quantified, researchers must employ various strategies to manage and interpret it appropriately.

### 3.1 Strategies for Managing Identified Heterogeneity

1. Subgroup Analysis: This involves breaking down the overall set of studies into smaller, more homogenous groups based on shared characteristics (Oliva Morgado Ferreira et al., 2023). By comparing these subgroups, researchers can explore potential sources of heterogeneity, such as differences in study populations, interventions, or outcomes. Subgroup analysis helps in understanding whether and how the effect size varies across different categories.
2. Meta-Regression: Meta-regression extends the idea of subgroup analysis by examining the impact of continuous or categorical study-level variables on the effect size. It allows for a more nuanced exploration

of how and why results vary across studies, providing insights into potential moderators of the effect.

3. Sensitivity Analysis: This method involves repeating the meta-analysis while varying certain methodological decisions, like inclusion/exclusion criteria, effect measure, or statistical model. Sensitivity analyses can reveal the robustness of the overall findings to these changes and help identify if specific studies or methodological choices are driving the heterogeneity.

### 3.2 Choosing the Appropriate Statistical Model

1. Fixed-Effect vs. Random-Effects Models: The choice of model is pivotal in the context of heterogeneity.
  - Fixed-Effect Model: Assumes that all studies estimate the same underlying effect and that observed differences are due to sampling error. This model is appropriate when studies are sufficiently homogenous.
  - Random-Effects Model: Assumes that study effect sizes follow a distribution, considering both within-study and between-study variability. This model is more suitable in the presence of heterogeneity, as it allows for variability between studies.
2. Interpreting Results from Different Models: Understanding the implications of model choice on the results is crucial. A random-effects model, while it provides a more generalizable estimate, may also introduce more uncertainty into the meta-analysis results.

### 3.3 Limitations and Challenges

Addressing heterogeneity in meta-analysis is not without its challenges (Zhao et al., 2023). Subgroup analyses and meta-regression require sufficient data and can be limited by the availability and quality of reported variables. Overinterpretation of subgroup differences can lead to spurious conclusions (Oliva Morgado Ferreira et al., 2023). Similarly, sensitivity analyses are only as informative as the range of variations tested. The choice of model also comes with trade-offs in terms of interpretability and applicability of results.

### 3.4 Best Practices

To address heterogeneity effectively, researchers should:

- Clearly justify the choice of statistical model based on the level of heterogeneity.
- Use subgroup analyses and meta-regression to explore potential sources of heterogeneity, while being cautious of overinterpretation.
- Conduct sensitivity analyses to assess the robustness of the results.
- Interpret the findings in the context of identified heterogeneity, acknowledging limitations and implications for generalizability.

In summary, addressing heterogeneity is an integral part of conducting a meta-analysis. Through careful consideration of the sources of heterogeneity and the application of appropriate statistical methods and models, researchers can provide more accurate and meaningful interpretations of the combined study results.

## 4. Advances and Innovations

The field of heterogeneity evaluation in meta-analyses has witnessed significant advancements and innovations, particularly in recent years (Varhlunchungi et al., 2023). These developments not only enhance our understanding of heterogeneity but also improve the accuracy and efficiency of meta-analytic practices.

### 4.1 Recent Developments in Evaluating Heterogeneity

1. Advanced Statistical Techniques: New statistical methods have been developed to better detect and quantify heterogeneity. For instance, Bayesian meta-analysis approaches provide a framework for incorporating prior knowledge and uncertainty into the analysis, offering a more nuanced assessment of heterogeneity.



2. **Improved Measures of Heterogeneity:** Researchers are increasingly recognizing the limitations of traditional measures like  $I^2$  and Q tests. In response, enhanced measures that provide a more detailed understanding of heterogeneity are being developed. These include the incorporation of prediction intervals, which offer a range within which the true effect size of a new study is expected to lie, acknowledging the variability across studies.
3. **Meta-Analysis of Individual Participant Data (IPD):** IPD meta-analysis, where raw data from each study are analyzed, rather than summarized results, has gained traction. This approach allows for a more thorough investigation of heterogeneity, especially in terms of patient-level characteristics and responses.

#### *4.2 Technological Advancements and Software Tools*

1. **Automation in Literature Search and Data Extraction:** Advances in AI and machine learning have led to the development of tools that can automate the often laborious processes of literature search and data extraction, reducing the time and potential biases inherent in manual methods.
2. **Sophisticated Meta-Analysis Software:** New software and updates to existing platforms have made complex statistical analyses more accessible to researchers. Tools like RevMan, Stata, and R packages (e.g., 'metafor') offer advanced functionalities for heterogeneity assessment, including graphical representations, sensitivity analyses, and subgroup analyses.
3. **Interactive and Dynamic Reporting:** There's a growing trend towards interactive meta-analysis reports, where readers can manipulate parameters to see how conclusions might change under different assumptions. This dynamic approach offers a deeper understanding of the impact of heterogeneity on meta-analysis results.

#### *4.3 Future Directions in Heterogeneity Analysis*

1. **Integration of Diverse Data Types:** As research becomes more interdisciplinary, meta-analyses will increasingly need to integrate heterogeneous data types, including qualitative data, big data, and real-world evidence. Developing methods to handle this diversity while accurately assessing heterogeneity is a key future challenge.
2. **Personalized Medicine and Heterogeneity:** In the era of personalized medicine, understanding heterogeneity is crucial for tailoring treatments to individual patient characteristics. Future research might focus on how meta-analyses can contribute to personalized healthcare by dissecting heterogeneity at a granular level.
3. **Enhancing Transparency and Reproducibility:** There is a growing emphasis on transparency and reproducibility in research. Future advancements in heterogeneity evaluation will likely include standardized reporting practices and open-source tools, enhancing the reliability and credibility of meta-analytic findings.
4. **Cross-Disciplinary Methodologies:** As different fields grapple with heterogeneity in their meta-analyses, cross-disciplinary methodological exchanges are expected to grow. Innovations in one field could inform and enhance heterogeneity assessment in others.
5. **Ethical and Regulatory Considerations:** With increasing complexity in meta-analyses, ethical and regulatory considerations, particularly in the context of patient privacy in IPD meta-analyses and the use of AI in data handling, will become more prominent.

In conclusion, the field of heterogeneity evaluation in meta-analyses is rapidly evolving, driven by statistical, technological, and methodological innovations. These advancements promise to enhance the depth, accuracy, and applicability of meta-analytic research, ultimately contributing to more informed decision-making in various scientific and clinical domains.

### **5. Case Studies: Methods Used in Meta-Analyses and Their Alignment with Advanced Methodologies**

This paper discusses various methodologies for assessing and addressing heterogeneity in meta-analyses. To contextualize these methods, we can examine how they were applied in four different meta-analytic studies.

1. Study: "Barriers and facilitators of childhood obesity prevention policies: A systematic review and meta-synthesis" (Taghizadeh et al., 2022)

- Methods Used: The study employed a systematic review approach to synthesize barriers and facilitators of childhood obesity prevention policies, incorporating both qualitative and quantitative analyses.
- Alignment with Advanced Methodologies:
  - Heterogeneity Evaluation: Given the diverse nature of the policies and settings, the study likely faced clinical and methodological heterogeneity, aligning with the importance of recognizing different heterogeneity types as discussed in the review paper.
  - Subgroup Analysis and Meta-Regression: The focus on individual, sociocultural, and structural levels suggests a form of subgroup analysis, exploring how different factors influence policy implementation.

2. Study: "Diagnostic Accuracy of Ottawa Knee Rule for Diagnosis of Fracture in Patients with Knee Trauma; a Systematic Review and Meta-analysis" (Kazemi et al., 2023)

- Methods Used: This study, following PRISMA-DTA guidelines, conducted a systematic search across multiple databases and used QUADAS-2 for quality assessment. The heterogeneity was evaluated using the  $I^2$  statistic, and DerSimonian-Laird pooling method was employed for statistical analysis.
- Alignment with Advanced Methodologies:
  - Heterogeneity Evaluation: The use of  $I^2$  and DerSimonian-Laird method aligns with the methodologies discussed in the review paper for assessing and addressing statistical heterogeneity.

3. Study: "The Association Between Screen Use and Central Obesity Among Children and Adolescents: A Systematic Review and Meta-Analysis" (Ghasemirad et al., 2023)

- Methods Used: Adhering to PRISMA guidelines, the study involved a comprehensive database search and quality assessment using the AHRQ checklist. Statistical analysis included heterogeneity assessment with Cochran's Q and I-squared tests, subgrouping, meta-regression analysis, and publication bias evaluation.
- Alignment with Advanced Methodologies:
  - Heterogeneity and Meta-Regression: The use of Cochran's Q,  $I^2$ , and meta-regression for exploring heterogeneity sources is in line with the advanced methodologies discussed in the review paper.

4. Study: "Diagnostic Accuracy of Ultrasonography for Detection of Intussusception in Children; a Systematic Review and Meta-Analysis" (Rahmani, Amani-Beni, et al., 2023)

- Methods Used: Following PRISMA-DTA guidelines, this study utilized a systematic database search and QUADAS-2 for quality assessment. Statistical analysis included  $I^2$  and Cochran-Q tests for heterogeneity, and both DerSimonian-Laird and Mantel-Haenszel models were used depending on the heterogeneity levels. Publication bias was assessed using funnel plot, Egger's test, and Begg's test.
- Alignment with Advanced Methodologies:
  - Heterogeneity Assessment and Model Choice: The approach to heterogeneity assessment and the flexible use of statistical models depending on heterogeneity levels align well with the methodologies discussed in the review paper.

5. Study: "Effects of Biofeedback on Biomechanical Factors Associated with Chronic Ankle Instability" (Mousavi et al., 2023)

- Methods Used: This systematic review and meta-analysis, aiming to assess the impact of biofeedback on biomechanical parameters in individuals with chronic ankle instability (CAI), searched four databases including PubMed, Web of Science, Scopus, and Embase. The Downs and Black appraisal scale was used for quality assessment. The study focused on outcomes such as kinetics and kinematics, with data extraction carried out by two independent authors. The analysis included a range of biomechanical outcomes from various studies.

- **Alignment with Advanced Methodologies:**
  - **Comprehensive Search and Quality Assessment:** The thorough database search and use of a recognized quality assessment tool aligns with best practices in conducting systematic reviews and meta-analysis as discussed in the review paper.
  - **Subgroup Analysis and Data Synthesis:** The focus on specific biomechanical outcomes, such as center of pressure (COP) and lateral plantar pressure, and the distinction between auditory and visual biofeedback effects, reflects a detailed approach to subgroup analysis. This is important for understanding the nuances of heterogeneity in meta-analysis, as highlighted in the review paper.
  - **Clinical and Methodological Heterogeneity:** Given the variability in intervention types (auditory vs. visual biofeedback), participant characteristics, and biomechanical outcomes measured, the study likely encountered both clinical and methodological heterogeneity. This necessitates careful interpretation of the meta-analysis results, a key point emphasized in the review paper on heterogeneity evaluation.
  - **Implications for Future Research:** The study's conclusion, emphasizing the need for further research and development of user-friendly biofeedback devices, resonates with the review paper's emphasis on continuous methodological advancements and the application of meta-analysis findings in practical settings.

6. Study: "Effects of Prone Positioning on ARDS Outcomes of Trauma and Surgical Patients" (Phoophiboon et al., 2023)

- **Methods Used:** This systematic review and meta-analysis, conducted to assess the effects of prone positioning on acute respiratory distress syndrome (ARDS) outcomes in trauma and surgical patients, followed the PRISMA 2020 guidelines. The researchers conducted database searches in MEDLINE and EMBASE, supplemented by additional searches of primary literature and review articles. A random-effects model was used for estimating various clinical outcomes, including PF ratio, mortality rate, mechanical ventilator days, and intensive care unit length of stay, using Review Manager 5.4.1 software.
- **Alignment with Advanced Methodologies:**
  - **Comprehensive Search and PRISMA Compliance:** The study's adherence to PRISMA 2020 guidelines and thorough database search aligns with the best practices in conducting systematic reviews and meta-analysis as discussed in the review paper on heterogeneity evaluation.
  - **Random-Effects Model Usage:** The use of a random-effects model for data synthesis is particularly apt for studies like this, where clinical heterogeneity is expected due to varying patient characteristics and treatment protocols. This approach aligns with the recommendation in the review paper to consider heterogeneity when choosing the statistical model.
  - **Heterogeneity Assessment:** Although not explicitly detailed in the abstract, the use of a random-effects model suggests an acknowledgment of the potential for heterogeneity, which is a critical aspect of meta-analysis discussed in the review paper.
  - **Clinical Relevance and Future Research:** The study's focus on clinically relevant outcomes (like mortality rate and ventilator days) and the call for prospective multicenter studies reflect an understanding of the practical applications and limitations of meta-analysis findings, a point emphasized in the review paper.

These case studies, when compared with the methodologies discussed in this paper, offer practical insights into the application of heterogeneity evaluation techniques in diverse research contexts. They highlight the relevance and complexity of dealing with heterogeneity in meta-analyses and underscore the need for continuous methodological advancements to handle this multifaceted aspect effectively.

## 6. Conclusion

Meta-analysis, an integral component of evidence-based research, has evolved considerably, particularly in its approach to handling heterogeneity. This review has comprehensively explored the multifaceted nature of

heterogeneity in meta-analysis, addressing its types, methods for evaluation, and strategies for management, as well as the advancements and challenges in this field.

Understanding and appropriately managing heterogeneity are paramount for the reliability and validity of meta-analytic results. Heterogeneity can stem from a variety of sources, and its presence significantly impacts meta-analysis outcomes. High levels of heterogeneity necessitate cautious interpretation of results and may indicate that pooling data from the studies is inappropriate. However, heterogeneity also offers valuable insights into the variability of effects in different contexts, reflecting the diversity of research settings and populations.

Advanced statistical techniques have been developed for a more nuanced assessment of heterogeneity, including Bayesian meta-analysis approaches and improved measures of heterogeneity. The meta-analysis of individual participant data has emerged as a powerful tool, allowing for a more thorough investigation of heterogeneity, especially in terms of patient-level characteristics.

Technological advancements and software tools have revolutionized the meta-analytic process. Automation in literature search and data extraction, sophisticated software for heterogeneity assessment, and interactive and dynamic reporting of meta-analysis results have made complex analyses more accessible and transparent.

Looking ahead, the field faces several challenges and opportunities. As research becomes more interdisciplinary, meta-analyses must adapt to integrate diverse data types, including qualitative data and big data. The era of personalized medicine underscores the importance of understanding heterogeneity for tailoring treatments to individual patient characteristics. Future research in this field should focus on developing methods to handle the diversity of data while accurately assessing heterogeneity.

The case studies presented in this review demonstrate the practical application of heterogeneity evaluation techniques in various research contexts. They underscore the importance of rigorous methodology, careful consideration of heterogeneity, and the practical implications of meta-analysis findings.

In conclusion, the field of heterogeneity evaluation in meta-analyses is rapidly evolving, driven by statistical, technological, and methodological innovations. These advancements promise to enhance the depth, accuracy, and applicability of meta-analytic research, ultimately contributing to more informed decision-making in various scientific and clinical domains. As researchers and practitioners continue to grapple with the complexities of combining disparate studies, the insights provided in this review will be invaluable for navigating the challenges and harnessing the full potential of meta-analytic research.

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