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Phone: (6) 088-320 000 Fax: (6)088-321 377
Email: bej@ums.edu.my

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EDITORIAL Open Access

At the Edge of Elimination: Malaysia's Malaria Journey in a Zoonotic Era

Jenarun Jelip[1*]

[1]*Department of Public Health Medicine, Faculty Medicine and Health Sciences, Universiti Malaysia Sabah, Jalan UMS, 88400 Kota Kinabalu, Sabah, Malaysia*

*Correspondence Email: drjenarun@ums.edu.my

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Malaysia stands on the brink of a landmark public health success: the elimination of human malaria. From a peak of over 50,000 indigenous cases in the 1990s, the country has reported zero human malaria cases since 2018 - a trend sustained through 2022. This achievement reflects decades of strategic planning, innovation, and political commitment (World Health Organization [WHO], 2022). As Malaysia nears WHO certification for the elimination of the four main human species - *Plasmodium falciparum*, *P. vivax*, *P. malariae* and *P. ovale* - a new challenge emerges: the zoonotic transmission of *P. knowlesi*, now the predominant cause of malaria in the country (Cooper et al., 2020).

This editorial examines Malaysia's journey to malaria elimination, highlighting its integrated strategies, emerging challenges, and the imperative to rethink certification in the era of zoonotic malaria.

A Program Anchored in Integration and Innovation

Malaysia's malaria control program - spearheaded by the Vector-Borne Disease Control Division (VBDCD) under the Ministry of Health (MOH) - has evolved through phases of control, pre-elimination, and now elimination (MOH Malaysia, 2023). The national strategic plan emphasizes integrated vector management, case-based surveillance, and targeted interventions.

Innovations such as the real-time e-notification system and the Malaria Information System within the VEKPRO platform have strengthened surveillance, enabling rapid detection and response, even in remote and indigenous communities.

A key strength of Malaysia's approach lies in intersectoral collaboration. Partnerships between the Sabah State Health Department, the commercial agriculture sector, and the Sabah State Government's Forest Management Division have been crucial in mitigating cross-sectoral transmission risks.

Community engagement has also been instrumental. Grassroots initiatives such as Primary Health Care Volunteers in Sabah, Village Health Representatives in Sarawak, and Malaria Ambassadors in Peninsular Malaysia have supported surveillance, case detection, and vector control. The deployment of mobile teams targeting high-risk groups such as the Orang Asli and migrant workers, demonstrates a people-centered, equity-driven approach.

Zoonotic Malaria: The Next Frontier

While indigenous human malaria has been largely eliminated, *Plasmodium knowlesi*, a simian parasite transmitted from macaques via *Anopheles leucosphyrus* mosquitoes has emerged as a major public health concern, especially in Malaysian Borneo (Grigg et al., 2018). Unlike human-only malaria parasites, *P. knowlesi* cannot be eliminated through conventional human-targeted interventions.

Malaysia has responded by embracing One Health approaches that integrate human, animal, and environmental health. Current efforts include ecological risk mapping, community engagement in forest fringe areas, and operational research into personal protection and vector behavior (Wong et al., 2022). However, policy frameworks and funding structures remain centered on human malaria, highlighting the need for strategic realignment.

Certification in the Era of Zoonoses: A Call for Nuance

Despite meeting all prior criteria for elimination, Malaysia's certification has been delayed due to WHO's updated requirement: a "negligible risk" of zoonotic transmission (WHO, 2023). This poses a unique challenge for countries like Malaysia, where *P. knowlesi* though lacking sustained human-to-human transmission, remains entrenched in natural transmission cycles involving wildlife and sylvatic vectors (Singh & Daneshvar, 2013).

Expecting countries to demonstrate control over zoonotic reservoirs and forest-dwelling vectors shifts the burden from malaria elimination to broader ecological control, blurring the line between disease-specific certification and environmental health.

While *P. knowlesi* must be addressed through integrated strategies, penalizing countries for zoonotic malaria may set an unrealistic precedent. A revised certification framework is needed, one that recognizes the elimination of human malaria while supporting ongoing zoonotic control through a One Health lens.

Conclusions

Malaysia's malaria program exemplifies health system resilience, intersectoral coordination, and innovation. The elimination of human malaria is a milestone worth celebrating. Yet, the persistence of *P. knowlesi* demands sustained vigilance and a broader, integrated approach. As Malaysia navigates this evolving epidemiological landscape, it offers a model for the region and a compelling case for updating global malaria elimination frameworks.

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REVIEW ARTICLE Open Access

Factors Influencing Cholera Vaccination Effectiveness in Africa and Bangladesh: A Scoping Review

Airy Andrew Atoi[1], Safirah Jaan Jaafar[1]*, Azman Atil[1,2], Syed Sharizman Syed Abdul Rahim[1,2]

Abstract

Cholera remains a significant global public health challenge, particularly in areas with inadequate sanitation and water resources. Vaccination plays a critical role in addressing cholera outbreaks, but various factors can influence its effectiveness. This scoping review, with its potential to identify and analyse the key determinants affecting the effectiveness of cholera vaccination campaigns in Africa and Bangladesh, could significantly impact public health policies. The study aims to provide actionable insights into optimising cholera vaccine effectiveness, a goal of utmost importance and relevance to public health. We extensively searched electronic databases to locate relevant studies published from January 2020 to June 2024, ensuring that we included the most recent and up-to-date research. Our search covered databases such as PubMed, SCOPUS, and ScienceDirect. Our specific focus was on primary studies that examined the factors affecting the efficacy of cholera vaccination, particularly in areas where cholera is prevalent. The review encompassed eight articles examining costs, vaccine dosages, booster shots, age at vaccination, timeliness of vaccination, and vaccination coverage. The findings emphasise the importance of these factors in determining vaccine effectiveness and the need for targeted interventions to enhance sustained protection against cholera. Optimizing the cholera vaccine effectiveness requires a comprehensive approach that addresses cost considerations, adherence to vaccine schedules, precise timing of vaccination, and achieving high vaccination coverage. The insights from this scoping review will inform future efforts in controlling cholera, especially regarding cholera vaccination campaigns.

Keywords: Cholera vaccination effectiveness, Cholera vaccine, African continent, Bangladesh

*Correspondence Email: safirah.jaan@ums.edu.my

[1]*Department of Public Health Medicine, Faculty Medicine and Health Sciences, Universiti Malaysia Sabah, Jalan UMS, 88400 Kota Kinabalu, Sabah, Malaysia*

[2]*Borneo Medical and Health Research Centre (BMHRC), Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah, Jalan UMS, 88400 Kota Kinabalu, Sabah, Malaysia*

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INTRODUCTION

Cholera is a severe diarrheal condition caused by the bacterium Vibrio cholerae. If not treated, it can result in extreme dehydration and even death (Alemayehu et al., 2020). This disease remains a significant global public health issue, indicating inequity and lack of social development (WHO, 2023). While there are vaccines against cholera, their effectiveness can be affected by various factors. It is estimated that annually, there are between 1.3 and 4.0 million cases of cholera, resulting in 21,000 to 143,000 deaths worldwide (WHO, 2023). Since the beginning of 2023, as of March 31, 2024, a cumulative total of 824,479 cholera cases and 5,900 deaths have been reported from 31 countries across five WHO regions. The Eastern Mediterranean region recorded the highest numbers, followed by the African Region, the Americas, Southeast Asia, and the Western Pacific regions (WHO, 2024).

Cholera remains a critical public health challenge in Africa and Bangladesh, both regions experiencing significant burdens of the disease. From 2008 to 2012, it was estimated that there were approximately 2.9 million cases per year globally, with Sub-Saharan Africa accounting for a substantial portion of these infections, highlighting the continent's vulnerability to cholera introductions and outbreaks (Ali et al., 2015). The dynamics of cholera transmission in Africa are complex, with human factors playing a significant role in the persistence of cholera cases (Moore et al., 2018). Between 2010 and 2019, over 1 million cholera cases were reported in Sub-Saharan Africa alone (Zheng et al., 2021), indicating an ongoing epidemic situation that necessitates urgent intervention.

In Bangladesh, cholera is endemic, with significant annual infection rates. Data from a serosurvey indicated that around 16% of individuals in cholera surveillance zones had been infected in the year preceding the survey, suggesting that the total estimated infections could be much higher, given that many cases go undetected or unreported (Hegde et al., 2021). The burden of cholera in Bangladesh is exacerbated due to numerous socio-economic and environmental factors. Water sanitation issues compound the cholera risk, demonstrating how unsafe drinking water can be a pathway for the transmission of Vibrio cholerae (Rafique et al., 2016).

The introduction and successful administration of oral cholera vaccines (OCVs) have shown promising results in both regions. In Africa, studies have shown that OCVs provide short-term protection of up to 90% against cholera caused by V. cholerae O1 (Msyamboza et al., 2014). Campaigns in high-risk districts in Malawi have aimed to scale up this vaccination strategy, leading to enhanced immunity and reduced incidence rates in targeted areas (Msyamboza et al., 2014). In urban Bangladesh, vaccination campaigns have demonstrated that including children in vaccination protocols is particularly cost-effective (Khan et al., 2018).

Globally, the approach to cholera vaccination is gaining momentum. Investment in cholera vaccination programs has proven effective in mitigating outbreaks; however, it is estimated that only 5-10% of cholera cases globally are officially reported (Eruaga & Davis, 2024). This suggests that the actual effectiveness of vaccination programs might be greater than statistics indicate and emphasizes the need for improved surveillance systems to capture cholera epidemiology accurately. Furthermore, regions like Africa and Bangladesh reveal higher

efficacy outcomes in localized vaccination campaigns compared to global averages (Lessler et al., 2018).

Three WHO pre-qualified oral cholera vaccines exist: Dukoral®, Shanchol™, and Euvichol-Plus®. All require two doses for complete protection. Dukoral® is administered with a buffer solution and can be given to individuals over 2 years old, with a 7-day to 6-week interval between doses; it provides 2 years of protection and is mainly used by travellers. Shanchol™ and Euvichol-Plus® are administered without a buffer solution to individuals over one-year-old, with a 2-week interval between doses, providing at least three years of protection. Shanchol™ can be stored in a controlled temperature chain, allowing for more flexible vaccine management (WHO, 2023). This scoping review aims to pinpoint and analyse the key determinants affecting the efficacy of cholera vaccination campaigns, focusing on the African continent and Bangladesh, where cholera vaccination is actively and successfully conducted (Sack et al., 2021).

METHODS

Study Design

This scoping review presents a narrative synthesis by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) protocol (Page et al., 2021).

Data Sources and Search Strategies

An extensive investigation was conducted on various online databases, including PubMed, SCOPUS, and ScienceDirect, to identify relevant studies released between January 2020 and June 2024. MeSH terms and specific keywords, factors AND "cholera vaccination" OR "cholera vaccine" AND effectiveness, were utilised, employing Boolean operators. Furthermore, a careful review of the references cited within the scrutinised articles was undertaken to ascertain the presence of any supplementary pertinent studies (see Figure 1).

Inclusion Criteria

The review encompasses primary studies investigating the factors that impact the effectiveness of cholera vaccination. Inclusion criteria entail that study participants must be situated in African continent and Bangladesh where cholera vaccination is actively and successfully conducted (Sack et al., 2021). Additionally, the studies must have been published between January 2020 and June 2024, and be research articles from open access, subscribed journals, with free full text.

Search Outcomes

The initial search yielded 384 articles filtered within a 5-year from January 2020 to June 2024. After removing four duplicate records, 337 records were marked as ineligible by automation tools, and 21 records were removed for other reasons. Out of the remaining 22 articles, all were screened and retrieved, with none being removed. These 22 articles were then screened for eligibility, resulting in the removal of 1 old publication (2019) and 13 studies unrelated to factors influencing the effectiveness of the cholera vaccine. Finally, a total of 8 articles were deemed relevant to the review. The data abstraction process is depicted in Figure 1.

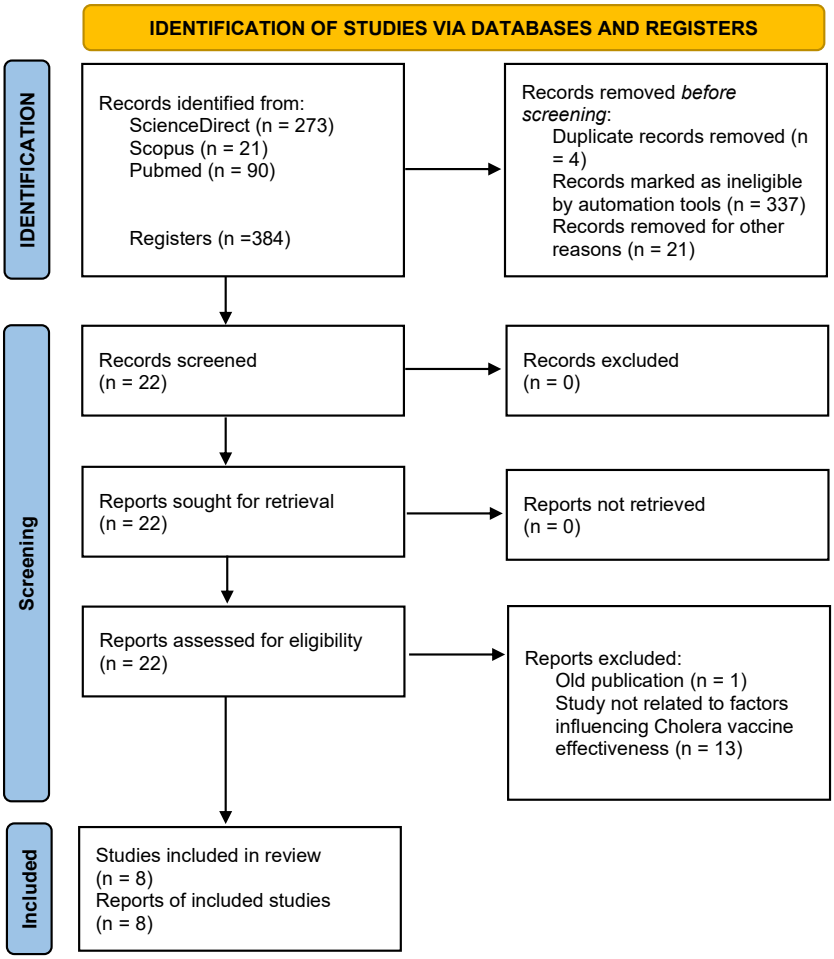

Figure 1: The Prisma flowchart for literature search and selection

Appraisal of Methodological Quality

The assessment of article quality utilised the Joanna Briggs Institute (JBI) Critical Appraisal checklist. (Barker et al., 2023), which is tailored to match particular study designs. Articles that scored over 50% on the relevant JBI checklist were eligible for inclusion in the study.

Data Extraction and Synthesis

The data was collected and analysed using a data matrix template. This template captured the following information from each study: authors, country, research design, sample sizes, factors influencing cholera vaccine effectiveness, key findings, and scoring (see Table 1). Due to variations in the scales and reported outcomes among the included studies, it was not possible to statistically combine the results. Therefore, a narrative synthesis was used to describe the outcomes.

RESULTS

Study Characteristics

Eight articles were included in the review. The research covered studies conducted in various locations, including Bangladesh (3), Africa (1), the Democratic Republic of the Congo (1), Haiti (1), Sudan (1), and Zambia (1). The sample sizes varied from 30 to 268896 participants. The study used a mixed-methods systematic review methodology to understand the research question fully. The study designs included in the review were 2 Analytical Cross-Sectional Studies, 2 Case-Control Studies, 1 Cohort Study, 1 economic evaluation, 1 Cluster Randomised Trial, and 1 Randomised Control Trial.

Methodological Quality Score

As per the Joanna Briggs Institute critical appraisal checklist, the articles included received moderate to high-quality scores, ranging from 62% to 90% of the total score. The articles include common issues related to the management and control of confounders.

Major Findings

The effectiveness of the cholera vaccine may be influenced by various factors as evidenced in the eight selected articles (Table 1). These factors include the cost of the cholera vaccination (Sarker et al., 2022), the total number of doses received (Malembaka et al., 2024a), the need for booster shots (Chowdhury et al., 2020), age at vaccination (Ali et al., 2021), timeliness of vaccination (El Bushra et al., 2024; Ng′ombe et al., 2022) and the extent of vaccination coverage (Bwire et al., 2020; Gelormini et al., 2023).

Table 1: Full Text Paper included

Authors	Country	Research Design	Samples	Factors	Key Findings	Quality Score
Sarker et al., 2022	Bangladesh	Economic evaluations	75170	Cost	• The total cost of the vaccination campaign was US$ 405,445. • Vaccine Procurement – The largest cost factor, accounting for 66.47% (US$ 269,519) of total expenditure. • Staff Salaries and Communication – The second-largest cost component at 18.09% (US$ 73,329). • Vaccine Delivery Cost – Estimated at US$ 1.95 per fully vaccinated individual. • Total Cost Per Fully Vaccinated Individual – US$ 6.11, while the cost for a single dose was US$ 2.86. • Provider vs. Recipient Cost – The total provider cost was US$ 6.01, whereas recipient-incurred costs were US$ 0.10. • The findings indicate that vaccine price and staff salaries were the key cost drivers.	- 8/11
Malembaka et al., 2024	Congo	Case-control sudy	658	Vaccine dosage	• A single-dose vaccine (Euvichol-Plus) for cholera shows a decreasing vaccine effectiveness (VE) over time. • The single-dose cholera vaccine shows an overall VE of 52.7% at 12-17 months, decreasing to 44.7% at 24-36	- 9/10

					months. In contrast, the dual-dose regimen is more effective, with VE 54% in the first year and 67% in the second year, providing more sustained protection.		
Chowdhury et al., 2020	Bangladesh	Randomized controlled trial	240	Booster shots	• Elevated plasma IgA responses to LPS after the first dose (Shanchol) were observed among the BI group (group with booster) compared to the PI group (Group without booster) among the young children therefore, VE is higher in the BI group compared to the PI group. • The geometric mean titres (GMT) of the BI group is higher at 40.98 compared to the PI group at 40.49	-	8/13
Ali et al., 2021	Bangladesh	Cluster randomized trial	268896	Age	• In younger children aged 1-4 years, the single-dose cholera vaccine (Shancol) had a vaccine effectiveness (VE) of 24% (95% CI: -30 to 56), whereas in older children aged 5 years and above, the VE was 49% (95% CI: 35 to 60). This indicates a notably higher and more consistent VE in older children than younger ones.		9/10

Ng′ombe et al., 2022	Zambia	Cohort study	223	Timeliness of vaccination	• Vibriocidal antibody titres rose significantly after vaccination but began to decline by 6 months post-vaccination, reaching nearly baseline levels at 12 months. • There was a resurgence in antibody levels at months 36 and 48, suggesting natural exposure rather than sustained vaccine-induced immunity. • Given the decline in immunity, the study suggests that booster doses should be administered before month 36 to maintain protection in cholera-endemic areas. • Vibriocidal antibodies may not be perfect correlates of long-term protection, as clinical immunity could persist despite declining titres.	-	7/11
Gelormini et al., 2023	Africa	Analytical cross-sectional study	7189	Coverage	• The two-dose vaccination (EuvicholTM) coverage was 56% (95% confidence interval (CI): 51.0–61.5), 44% (95%CI: 35.2–53.0) in rural and 57% (95%CI: 51.6–62.8) in urban areas. Vaccination coverage with at least one dose was 82% (95%CI: 77.3–85.5), 61% (95%CI: 52.0–70.2) in rural and 83% (95%CI: 78.5–87.1) • 90% of vaccinated respondents (95% CI: 88.5–92.0) had a positive opinion of the vaccine • 77% (95% CI: 73.1–81.4) reported that they were motivated to get vaccinated	-	6/8

					because they had prior knowledge of cholera and its risks		
Bwire et al., 2020	Uganda	Analytical cross-sectional study	1274	Coverage	• 94% (95% CI: 92%-95%) of the population received at least one dose and 78% (95% CI: 76%-81%) received both doses. • Individuals with at least primary school education were almost twice as likely to know the required doses compared to those with no education (OR = 1.90, 95% CI: 1.06-3.44, p = 0.03). This suggests that community education and awareness play a crucial role in achieving high vaccine uptake.	-	9/10
El Bushra et al., 2024	Sudan	Case-control study	199	Timeliness of vaccination	• The delay in vaccine deployment (100 days after the first case) may have contributed to a prolonged outbreak. • OCV is highly effective (80-81%), but it should be administered early, alongside improved hygiene and sanitation efforts. Effectiveness of OCV (Vaccine Effectiveness - VE): Unadjusted VE: 80% (95% CI: 69%-87%), Adjusted VE: 81.0% (95% CI: 56.0%-92.0%) • Protective Factors: I. a) Taking Oral Cholera Vaccine (OCV) reduced the odds of cholera infection (OR = 0.19, 95% CI: 0.08–0.44).	-	8/10

II. Handwashing with soap and water after defecation showed strong protection (OR = 0.01, 95% CI: 0.00–0.03).
III. Handwashing before eating also significantly reduced risk (OR = 0.15, 95% CI: 0.05–0.51).

- Risk Factors for Cholera:

I. Buying food or drinks from street vendors increased the odds of cholera (OR = 71.36, 95% CI: 16.58–307.14).
II. Living in an urban setting (Gadarif City) had a higher risk (OR = 5.38, 95% CI: 2.10–13.81).
III. Noticing open defecation in the neighborhood increased risk (OR = 4.25, 95% CI: 1.11–16.23).

DISCUSSION

Cost

The cost analysis of vaccination campaigns is a critical aspect of public health planning, as illustrated by the study conducted by Sarker et al. This research highlighted that the total vaccination campaign cost was US$ 405,445, predominantly driven by vaccine procurement costs, which represented 66.47% of total expenses (Sarker et al., 2022). This aligns with numerous studies that have indicated vaccine acquisition is typically the largest component of immunization costs, accounting for a significant portion, often upwards of 70-90% in various contexts (Orangi et al., 2022). For instance, the findings from Orangi et al. underscore that procurement plays a pivotal role in overall vaccination expenses, revealing that vaccine costs can dominate expenses in comparative studies across multiple diseases (Orangi et al., 2022).

Moreover, the study by Sarker et al. reported that delivery costs amounted to US$ 1.95 per fully vaccinated individual, culminating in a total expenditure of US$ 6.11 per person for vaccination, which also included considerable spending on staff salaries and communication (Sarker et al., 2022). This is consistent with research from Mvundura et al., which noted that service delivery costs—including logistical elements and human resources—generally account for a notable share of vaccination expenses, emphasizing the need for effective planning to manage these costs (Mvundura et al., 2015). Furthermore, the varying costs reported, depending on specific strategies and settings, reaffirm the necessity for tailored financial planning and resource allocation in vaccination campaigns (Brenzel, 2015; Ngabo et al., 2015).

Evidently, such insights underscore that understanding the cost structure, particularly the balance between procurement and delivery expenses, is essential for evaluating the effectiveness and sustainability of vaccination initiatives globally. Effective management of these costs can strengthen immunization programs, especially as evidenced during the COVID-19 vaccination efforts and their resultant economic implications (Gaythorpe et al., 2021).

Vaccine Dosage

A study by Malembaka et al. found that the single-dose cholera vaccine (Euvichol-Plus) has declining effectiveness, with VE dropping from 52.7% at 12–17 months to 44.7% at 24–36 months. In contrast, the dual-dose regimen offers greater and more sustained protection, with VE of 54% in the first year and 67% in the second year (Malembaka et al., 2024b).

Support for these findings is bolstered by Sialubanje et al., who demonstrated the significant effectiveness of a two-dose regimen during a cholera outbreak in Zambia, aligning with established evidence that emphasizes the superior protection conferred by multiple doses (Sialubanje et al., 2022). The advantages of a dual-dose strategy also resonate with recommendations from the WHO, which advocates for enhanced cholera vaccination strategies that consider the coverage and sustainability of protection across various populations (Poncin et al., 2017).

Moreover, the immunogenicity associated with two doses may be attributed to the generation of robust immune responses, aided by the booster effect, leading to more substantial

and prolonged protection against Vibrio cholerae, as supported by evidence from the studies analysed (Franke et al., 2018; Qadri et al., 2016). The dichotomy presented between single and dual-dose regimens underscores the importance of reevaluating vaccine strategies to ensure optimal disease prevention in cholera-endemic regions.

Booster shots

The study by Chowdhury et al. indicates that the administration of a booster dose of the Shanchol vaccine significantly enhances the immunogenic response in young children, as evidenced by the elevated plasma immunoglobulin A (IgA) levels in the booster (BI) group compared to the non-booster (PI) group. Specifically, the BI group exhibited a higher geometric mean titre (GMT) of 40.98 relative to 40.49 in the PI group (Chowdhury et al., 2020), suggesting that booster vaccinations may facilitate stronger protective mechanisms against pathogens by promoting mucosal immunity, an essential component in safeguarding young children from infectious diseases, including cholera (Nziza et al., 2023; Zambrano et al., 2023).

Mucosal antibodies, such as IgA, play a critical role in establishing protective immunity in the gastrointestinal tract, which is crucial given the oral nature of the Shanchol vaccine. Higher IgA responses correlate with improved vaccine effectiveness, emphasizing the importance of booster immunizations in pediatric vaccination schedules. Recent findings support this notion, revealing that robust antibody production following booster doses significantly correlates with reduced morbidity and mortality in various short- and long-term disease outcomes in children (Doyle et al., 2022; Syggelou et al., 2020). Thus, Chowdhury et al.'s results align with the broader immunological perspective regarding the importance of tailored vaccination strategies for optimizing protective immunity in young populations.

Age

Findings by Ali et al. indicate that the effectiveness of the single-dose cholera vaccine, Shanchol, varies significantly by age group. The study reported an effectiveness of 24% (95% CI: -30 to 56) in children aged 1–4 years, contrasting with a higher effectiveness of 49% (95% CI: 35 to 60) in older children aged 5 and above (Ali et al., 2021). This observation aligns with the broader literature, which suggests that oral cholera vaccines (OCVs) generally exhibit lower efficacy in younger populations. For instance, Jeon et al. indicated a two-dose efficacy for OCVs at approximately 30% for children under five, compared to 64% for older individuals (Jeon et al., 2021). Moreover, a study by Malembaka et al. emphasized the necessity for tailored vaccination strategies in endemic areas, particularly as one-dose efficacy is still being characterized for young children (Malembaka et al., 2023).

The impact of age on vaccine effectiveness may be attributed to physiological factors and the maturation of the immune system, which can vary significantly in the early years of childhood (Ali et al., 2021). Additional research underlines the importance of age-specific strategies in vaccination campaigns to enhance protection for younger children, thereby potentially reducing cholera incidence in this vulnerable demographic (Malembaka et al., 2023).

Timeliness of vaccination

Ng'ombe et al. demonstrated that vibriocidal antibody titres significantly increased after vaccination but returned near baseline levels within 12 months (Ng'ombe et al., 2022). In the other study by El Bushra et al, 100-day delay in vaccine deployment may have prolonged the outbreak. While OCV is highly effective (80-81%), timely administration alongside hygiene and sanitation measures is crucial (El Bushra et al., 2024). These observations suggest that while vaccination provides an initial immune response, the waning immunity necessitates the administration of booster doses, particularly in cholera-endemic areas. Their findings echo the conclusions drawn by Peak et al. who discuss the complexities of herd immunity and waning effects of vaccines, emphasizing that individual immunity may diminish over time due to external factors like human mobility and exposure to cholera pathogens (Peak et al., 2018). Furthermore, Falkard et al. highlight the longer-lasting memory B cell responses induced by the bivalent oral cholera vaccine, indicating that the immune system can still mount a response upon natural exposure, reinforcing the necessity for booster vaccinations (Falkard et al., 2019).

In addition, Iyer and Harris provide insights into correlates of protection, emphasizing that while vibriocidal antibodies are significant indicators of vaccine efficacy, they should not be viewed as sufficient for long-term immunity (Iyer & Harris, 2021). This is critical in interpreting Ng'ombe's findings, as they point out that the initial antibody surge may not ensure lasting protection against cholera. Therefore, continuous evaluation of vaccination strategies, including the timing of boosters and keeping populations informed about hygiene practices, is paramount for effective cholera management (Ng'ombe et al., 2022).

Vaccination Coverage

Gelormini et al. and Bwire et al. highlight the critical relationship between vaccine coverage and the effectiveness of cholera vaccines, emphasizing that higher coverage rates are necessary to maximize public health benefits (Bwire et al., 2020; Gelormini et al., 2023). Specifically, achieving high vaccine coverage, such as reaching at least 50% of a population, has been shown to significantly decrease cholera incidence. For example, mathematical models indicate that if a sufficient proportion of individuals is vaccinated, the overall disease burden can be reduced dramatically through herd immunity effects (Baltazar et al., 2018; Chitio et al., 2022).

Bwire et al. report that vaccination coverage exceeding the threshold necessary for herd immunity—around 67%—can effectively mitigate cholera outbreaks, as observed in their studies from Uganda (Bwire et al., 2022, 2023). Similarly, Gelormini et al. stress the importance of achieving broad vaccination coverage during cholera vaccination campaigns, as inadequate coverage has led to continued transmission and outbreaks in previous instances (Mukandavire et al., 2020). Overall, both studies converge on the point that optimal vaccine efficacy hinges on executing high-coverage campaigns to ensure community-wide protection against cholera.

CONCLUSIONS

Key factors such as cost, incomplete dosages, timing of vaccination, booster shots, age-specific strategies, and high vaccination coverage play pivotal roles in improving vaccine efficacy. Addressing these elements is essential for strengthening immunisation programs, preventing outbreaks, and informing evidence-based public health interventions. Policymakers and public health officials must leverage these insights to refine vaccination policies and ensure equitable access to effective cholera prevention measures.

Recommendations

Strategic planning is needed to ensure everyone receives the complete dosage during vaccination campaigns. Prioritizing high-risk areas can maximize impact. Where resources allow, maintaining a dual-dose regimen offers better and longer-lasting protection. Incorporating booster doses is also essential to sustain immunity, particularly for high-risk populations.

Early vaccination can boost immunity and reduce cholera cases, especially if timed with periods of highest risk. Rapid vaccination is crucial during outbreaks to control the spread and protect at-risk populations. A well-scheduled vaccination program, including timely booster doses, ensures long-term protection.

Improving vaccine coverage is vital for herd immunity and reducing disease transmission. Community engagement and involving leaders and healthcare professionals can build trust and acceptance. Addressing vaccine hesitancy, misinformation, and logistical barriers like access and flexible vaccination times can increase coverage.

Conflicts of Interest

The authors would like to declare there is no conflict of interest.

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REVIEW ARTICLE Open Access

The Impact of Maternal Nutritional Status on Child Malnutrition: A Systematic Review

Holly Girlchy Jastin [1], Safirah Jaan Jaafar [1*]

Abstract

Stunting, underweight, and wasting significantly affect children under five, especially in low- and middle-income countries (LMICs). Maternal BMI is a key determinant of child nutritional status, as it directly influences fetal growth, breastfeeding quality, and overall maternal health. This systematic review examines the impact of maternal BMI on child stunting and identifies key contributing factors. A comprehensive search was conducted across PubMed, Scopus, Web Science Direct, and Google Scholar for studies published between 2000 and 2024. The inclusion criteria were studies on maternal BMI and child stunting in children under five. Data extraction and risk of bias assessment followed the JBI Critical Appraisal Checklist. Ten studies were reviewed. Findings consistently showed significant associations between maternal BMI and child stunting. Low maternal BMI was linked to nutrient deficiencies and higher risks of stunting. High maternal BMI was associated with metabolic dysregulation and inflammation, also contributing to stunting. Socioeconomic factors like household wealth and maternal education were important determinants. Maternal BMI significantly influences child stunting in LMICs. Integrated nutritional interventions addressing maternal nutrition, socioeconomic factors, and regional disparities are essential to reduce child malnutrition. These findings underscore the need for policy-driven interventions that prioritize maternal nutritional health as a key strategy to improve child growth outcomes and break the cycle of malnutrition. Future research should further explore biological mechanisms linking maternal BMI to child health and develop effective, context-specific interventions.

Keywords: Maternal BMI, Child Stunting, Malnutrition, Low- and Middle-Income Countries, Nutritional Interventions, Socioeconomic Factors.

*Correspondence Email: safirah.jaan@ums.edu.my

[1]*Department of Public Health Medicine, Faculty Medicine and Health Sciences, Universiti Malaysia Sabah, Jalan UMS, 88400 Kota Kinabalu, Sabah, Malaysia*

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INTRODUCTION

Maternal nutritional status affects both her well-being and her child's growth and development. Good nutrition before and during pregnancy is crucial, as it helps prevent complications like low birth weight, preterm birth, and child malnutrition. Poor maternal nutrition, whether undernutrition (low BMI, micronutrient deficiencies) or overnutrition (obesity, excessive weight gain) can lead to serious health risks for both mother and baby. It is measured through anthropometric indicators like Body Mass Index (BMI) and mid-upper arm circumference (MUAC**)**, dietary assessments of food intake, and biochemical tests such as haemoglobin levels to check for anaemia. Monitoring maternal nutrition is essential to ensure healthy pregnancies, reduce risks of complications, and support the long-term well-being of both mother and child. Child malnutrition remains a significant global health concern, particularly in low- and middle-income countries (LMICs). In 2022, 149 million children under five were stunted, 45 million experienced wasting, and 37 million were overweight or obese (WHO, 2024). Malnutrition manifests in multiple forms, including undernutrition (wasting, stunting, underweight), micronutrient-related malnutrition, and overnutrition (overweight/obesity), all of which have profound long-term consequences on health, cognition, and socioeconomic outcomes. While food insecurity, inadequate healthcare, and socioeconomic inequalities are widely recognized as key drivers of child malnutrition, maternal nutritional status, particularly maternal BMI, plays a crucial yet often overlooked role. Maternal BMI influences fetal growth, birth weight, breastfeeding quality, and long-term child nutrition outcomes. Low maternal BMI is associated with undernourished offspring who are at higher risk for stunting, wasting, and weakening immunity. Conversely, high maternal BMI has been linked to metabolic complications, gestational diabetes, and childhood obesity (Bourassa et al., 2019).

Despite these associations, there is limited understanding of how maternal BMI contributes to child stunting across different regions, particularly in LMICs, where healthcare disparities persist. Research examining the maternal nutritional status and child malnutrition relationship is crucial for developing targeted interventions that address both maternal and child nutrition simultaneously. Many public health programs focus on child nutrition without adequately addressing maternal health, missing a critical opportunity to break the intergenerational cycle of malnutrition. Figure 1 illustrates this cycle, showing how maternal malnutrition perpetuates poor birth outcomes, leading to childhood stunting and long-term developmental consequences. To effectively combat childhood malnutrition, comprehensive strategies must integrate maternal health interventions, exclusive breastfeeding promotion, and improved access to healthcare and nutrition education. Addressing underlying socioeconomic factors, such as poverty, maternal education, and food security, is equally essential. This systematic review aims to fill the research gap by synthesizing existing evidence on the association between maternal BMI and child stunting, identifying key contributing factors, and proposing targeted intervention strategies. By focusing on maternal BMI as a key determinant of child nutritional outcomes, this review provides insights that can guide public health policies, ensuring maternal nutritional health becomes a central strategy in combating child malnutrition in LMICs. Figure 1 shows the intergenerational cycle of malnutrition. Malnourished women face inadequate food, health, and care, leading to low birth weight (LBW) babies at higher risk for mortality and chronic diseases. These children often experience stunted growth due to inadequate weaning and frequent infections.

Stunted children suffer from reduced mental capacity and continued nutritional deficiencies into adolescence and adulthood. As adults, they are less able to care for the next generation, perpetuating the cycle of malnutrition. This cycle underscores the need to address

malnutrition at all life stages to improve future generations' health outcomes. Addressing nutritional deficiencies in one generation can significantly impact subsequent generations' health and well-being. (see Figure 1: Intergenerational Cycle of malnutrition) (Ahmed et al., 2012). Comprehending the intricate interplay between maternal and child health elements and malnutrition in children under five is imperative for guiding focused interventions and policies directed at alleviating the burden of malnutrition in this vulnerable demographic. This systematic review aims to amalgamate the existing evidence concerning the correlation between maternal health practices and status and the prevalence of malnutrition among children under five.

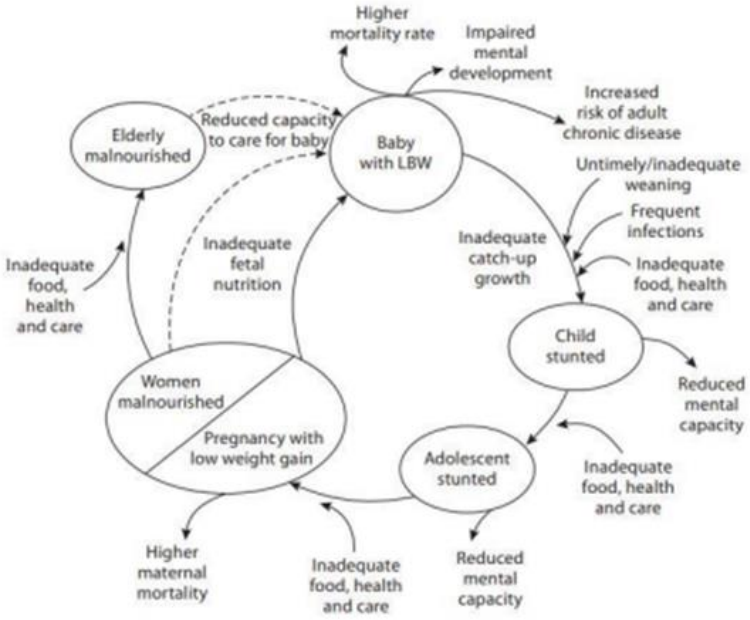

Figure 1: Intergenerational cycle of malnutrition (Ahmed et al., 2012)

METHODS

Study Population

The study population includes children under five years of age (0–59 months) and their mothers, focusing on the relationship between maternal nutritional status and child undernutrition.

Study Design

This systematic review investigates the association between maternal nutritional status and child undernutrition. Studies were selected based on their relevance to maternal anthropometric indicators and child growth outcomes.

Eligibility Criteria for Selecting Studies for Review

Inclusion Criteria:

- Studies assessing maternal nutritional status using anthropometric indicators (Body Mass Index - BMI) categorized as normal, underweight, and obese, with corresponding child growth outcomes (stunting in children aged 0–59 months).
- Studies published in English between 2020 and 2024 to ensure the inclusion of recent findings.
- Studies employing cross-sectional study designs, as they provide observational data on maternal BMI and child malnutrition prevalence.
- Studies conducted in low- and middle-income countries (LMICs) where stunting remains a major public health issue.

Exclusion Criteria:

- Studies that do not assess maternal BMI as a primary exposure variable. non-human studies, reviews, case reports, and editorials.
- Studies focused solely on high-income countries, as the public health context differs from that of LMICs.
- Articles published in languages other than English**,** due to translation limitations.

Study Period

The screening and data extraction process completed by May 2024. However, to ensure data completeness and minimize selection bias, an updated search conducted at the end of 2024 to capture newly published studies.

Search Strategy

A comprehensive literature search was conducted using four electronic databases Scopus, ScienceDirect, PubMed and Google Scholar. To maximize study identification**,** Boolean operators and PICO search strategies were used. The primary search keywords included "Maternal Undernutrition and child malnutrition", "Maternal BMI and child undernutrition", "Maternal nutrition and child health".

Data Extraction

All identified records were imported into a reference management software and converted into a CSV file for organization. The screening process followed three sequential steps.

1. Duplicate removal to avoid redundant studies.
2. Title and abstract screening to exclude irrelevant studies.
3. Full-text review against predefined inclusion and exclusion criteria**.**

Quality Assessment

A comprehensive quality assessment was conducted using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist, specifically designed for cross-sectional studies**.** This tool focusing on study design, sample representativeness, exposure measurement, and statistical analysis quality. The JBI tool evaluates inclusion criteria clarity, study population and setting, measurement validity of maternal BMI and child stunting, and assessment of confounding factors and appropriate statistical analyses. A high-quality rating was required for inclusion, ensuring robust and reliable study selection**.**

Prisma Diagram

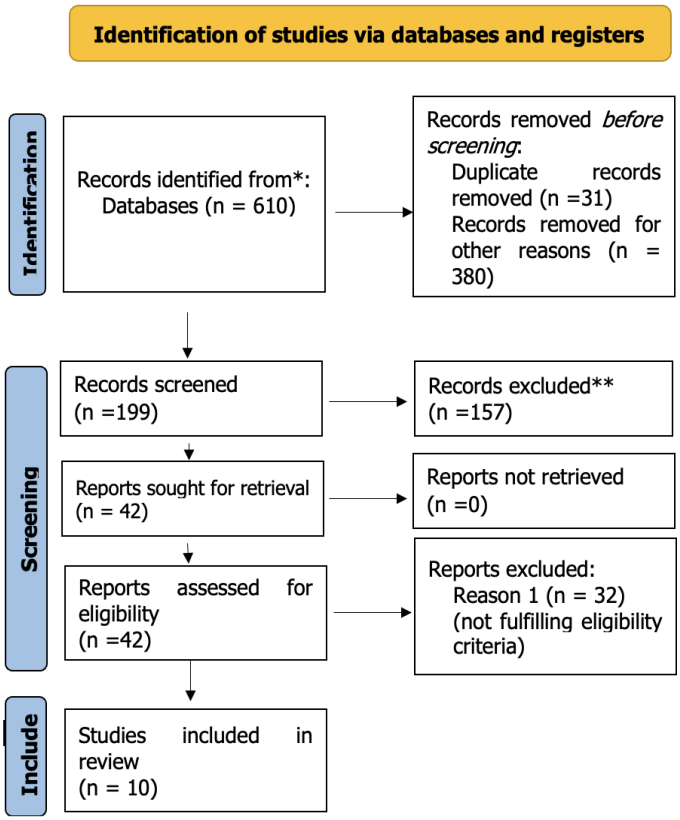

Figure 1: The Prisma flowchart of identified of studies via databases and registers.

RESULTS

Study Selection and Characteristics

A total of 10 studies were included in this review, covering African, Asian, South American, north American, Oceanian continents. The studies analysed the relationship between maternal nutritional status and child malnutrition, particularly focusing on stunting among children under five years old.

Demographic and Regional Distribution

The selected studies covered multiple geographic regions, including Southeast Asia, Africa, and Latin America**,** with varying levels of economic development, healthcare access, and maternal education. The total sample size ranged from 577 to 564,518 participants, with an overall representation of low- and middle-income populations**.** Prevalence rates of stunting, varied across regions but consistently highlighted the impact of maternal nutritional status.

Maternal Nutritional Status and Child Malnutrition

Maternal BMI and height were significant predictors of child stunting, Studies reported that children of underweight mothers (BMI <18.5) had increased odds of being stunted compared to those of normal-weight mothers (Wali et al., 2020). Meanwhile, maternal overweight (BMI ≥25) was linked to a paradoxical double burden of malnutrition higher rates of child stunting 25.2% (Blankenship et al., 2020). Short maternal height (<150 cm) was associated with higher odds of child stunting, with pooled ORs ranging from 1.9 to 4.7 (Li et al., 2020).

Socioeconomic and Household Factors

Studies consistently showed that lower maternal education was strongly associated with higher child malnutrition rates**.** Illiterate mothers had 1.58 times higher odds of having a stunted child compared to those with higher education (Kumar & Mohanty, 2022). Household wealth index was a significant determinant; children from the poorest quintile had 2.01 times higher odds of child stunting compared to the richest quintile (Kumar & Mohanty, 2022). Moreover, children from households without piped water have 1.59 times higher odds of being stunted compared to those with piped water (Gebreegziabher & Sidibe, 2024).

Table 2: Summarize of the findings

Reference	Study Area (Country, continent	Sample size	Findings
Li et al., 2020	35 LMICs (Global, multiple continents)	299,353	• Children of underweight mothers (BMI <18.5) had significantly higher odds of being stunted. Prevalence of stunting in children of underweight mothers: 49.7%, (aOR) = 1.6, $p < 0.001$. • Short maternal height (<145 cm) was the strongest predictor of child stunting. Prevalence of stunting in children of short mothers: 62.2%, aOR = 4.7, $p < 0.001$. • Children of mothers with no education had significantly higher odds of stunting. Prevalence of stunting in children of mothers with no education: 47.9%, aOR = 1.9, $p < 0.001$. • Children from the poorest households had the highest stunting prevalence. Prevalence of stunting in the poorest quintile: 51.2%, aOR = 1.7, $p < 0.001$.
Blankenship et al.,2020	Marshall Islands (Oceania)	581	• Maternal underweight (BMI <18.5) significantly increases the risk of child stunting (aOR = 1.00, prevalence = 43.4%). • Overweight and obese mothers had the lowest odds of stunting (aOR = 0.50 for BMI ≥30, prevalence = 19%). • Short maternal height (<150 cm) is the strongest predictor of child stunting (aOR = 6.62, prevalence = 62.2%). • Higher maternal education significantly reduces child stunting risk (aOR = 0.49 for higher education).

			• Children of working mothers were more likely to be stunted than those of non-working mothers.
Eshete et al., 2020	Ethiopia (Africa)	577	• Prevalence of stunted child-overweight/obese mother (SCOWT): 22.8%. • Overweight/obese mothers had a 23% likelihood of having a stunted child. • Maternal education significantly reduces child stunting risk (aOR = 0.18 for secondary education and above). • Children in rural areas were twice as likely to experience SCOWT compared to urban children (aOR = 2.06). • Older children (≥2 years) were nearly five times more likely to experience SCOWT than younger children (aOR = 4.94).
Kurniawan et al., 2022	Timor-Leste (Southeast Asia)	3,723	• Maternal underweight (BMI <18.5) increases the risk of child stunting. Children of underweight mothers (BMI <18.5) had a higher likelihood of being stunted. Prevalence of stunting in children of underweight mothers: 20.6%. Adjusted Odds Ratio (aOR) = 1.07 (95% CI: 0.87–1.31), p = 0.839. • Children of mothers with short stature (<145 cm) were more likely to experience stunting. Prevalence of stunting: 12.0%, aOR = 0.72 (95% CI: 0.56–0.93), p < 0.001. • Children of mothers with no formal education had a significantly higher risk of stunting. Prevalence of stunting: 42.8%, aOR = 0.8 (95% CI: 0.67–0.96), p < 0.001. • Children from rural households had a higher prevalence of stunting than urban households. Prevalence of stunting in rural areas: 71.5%, aOR = 1.036 (95% CI: 0.85–1.26), p = 0.003.

Anastasia et al., 2023	Indonesia (sulawesi)	4,423	• Maternal underweight (BMI <18.5) increases the risk of child stunting (APR = 1.02, p = 0.004). • Short maternal stature (<151 cm) significantly increases the likelihood of child stunting (APR = 1.3, p < 0.001). • Higher maternal education significantly reduces child stunting risk (APR = 1.9 for no education, p = 0.001). • Children from lower-income households have a higher risk of stunting compared to wealthier households (APR = 1.9, p = 0.021). • Increased maternal weight is protective against child stunting (APR = 0.9, p = 0.005).
Kumar & Mohanty, 2022	India (South Asia)	28,817	• Maternal short stature (<145 cm) is the strongest predictor of child stunting (aOR = 2.94, p < 0.001). • Higher maternal education significantly reduces the risk of child stunting (aOR = 1.58 for no education, p < 0.001). • Children from the poorest households had the highest likelihood of being stunted (aOR = 2.01, p < 0.001). • Younger maternal age (15–25 years) increases the risk of child stunting. • Maternal work status was not significantly associated with child stunting.
Gebreegziabher and Sidibe, 2024	Mali (West Africa)	8,908	• Maternal underweight (BMI <18.5) significantly increases the risk of child stunting. • Overweight and obese mothers had the lowest odds of stunting (aOR = 0.50 for BMI ≥30).

			• Higher maternal education significantly reduces child stunting risk. • Anaemic mothers had children with a higher likelihood of stunting. aOR = 1.47 (95% CI: 1.04–2.08), $p < 0.05$. • Children of pregnant mothers had significantly higher odds of stunting. aOR = 2.04 (95% CI: 1.28–3.26), $p < 0.01$.
Vijay & Patel, 2024	Nepal (South Asia)	2,381	• Maternal underweight (BMI <18.5) is a major risk factor for child stunting. Prevalence of stunting in children of underweight mothers: 43.4%. • Higher maternal education and longer birth intervals (>3 years) significantly reduce the risk of stunting. Birth interval >3 years significantly reduced stunting risk. Prevalence of stunting: 33.6%. aOR: 0.62, $p < 0.001$. • Children of working mothers were more likely to be stunted than those of non-working mothers. Prevalence of stunting: 40.2%. aOR**:** 1.26 (95% CI: 0.994–1.594).
Elmighrabi et al.,2024	North Africa (Algeria, Egypt, Sudan, Tunisia)	39,983	• Short maternal stature (<150 cm) is the strongest predictor of child stunting (aOR = 2.94, $p < 0.001$). • Maternal underweight (BMI <18.5) was unexpectedly associated with lower odds of child stunting (aOR = 0.30, $p < 0.001$). • Higher maternal education significantly reduces child stunting risk (aOR = 1.30 for no education, $p < 0.001$). • Children from the poorest households were twice as likely to be stunted compared to the richest households (aOR = 2.01, $p < 0.001$).

			• Younger maternal age (<20 years) increases the risk of child stunting (aOR = 1.30, p < 0.001).
Wali et al., 2020	South Asia (Bangladesh, India, Nepal, Maldives, Pakistan)	564,518	• Maternal underweight (BMI <18.5) significantly increases the risk of child stunting (aOR = 1.36, p = 0.001). • Short maternal stature (<150 cm) is the strongest predictor of child stunting (aOR = 3.80, p < 0.001). • Higher maternal education significantly reduces child stunting risk (aOR = 1.59 for no education, p < 0.001). • Children from the poorest households have a higher risk of stunting compared to wealthier households (aOR = 1.39, p = 0.002). • Younger maternal age (<20 years) increases the risk of child stunting (aOR = 1.30, p < 0.001).

Maternal Height

The review found a strong correlation between low maternal height and increased risk of child stunting, particularly in low- to middle-income nations. Low maternal height, a common risk factor for stunting, varies greatly across countries and is also linked to underweight children. The relationship between short maternal height and stunting has a biological basis, as chronic undernutrition and poor health during the mother's childhood lead to suboptimal fetal growth and development (Özaltin et al., 2010; Ahmed et al., 2012).

Maternal Education

Maternal education was significantly associated with stunting. This might be due to mothers with higher education having good nutritional knowledge and the ability to make better decisions and healthier choices when caring for their children (Tamir et al., 2022). Supported by other study that show result women with less than ten years of schooling are more likely to have malnourished children than their counterparts with more years. Higher rates of stunting correlated with lower maternal education levels, larger family sizes, and poorer sanitation conditions (Ndagijimana et al., 2024). Results also showed that improving housing quality reduces the likelihood of a child being malnourished by about nine percentage points. There was evidence of the mediating role of housing quality on the relationship between child maternal education and malnutrition (Tangwa et al., 2024).

Maternal education is significantly associated with child stunting. Higher education levels in mothers lead to better nutritional knowledge and healthier choices for their children (Tamir et al., 2022). Studies show women with less than ten years of schooling are more likely to have malnourished children. Higher stunting rates correlate with lower maternal education, larger family sizes, and poor sanitation (Ndagijimana et al., 2024). Improved housing quality can reduce child malnutrition by about nine percentage points, indicating its mediating role in the relationship between maternal education and child malnutrition (Tangwa et al., 2024).

The results revealed that women’s decision-making significantly positively affects children’s weight-for-age and weight-for-height (Adediran, 2024). Education empowers women to make rational choices regarding education, career, health, and relationships, leading to better health outcomes for themselves and their children (Dhiman, 2023; Kabeer, 2005). Addressing time constraints on caregivers is crucial for improving child feeding practices, emphasizing the need to reduce women's workloads and promote task-sharing within households (McClintic et al., 2022). Children under two in urban areas with working mothers are more likely to experience stunting than those in rural areas, partly due to increased consumption of processed and high-fat foods (Supadmi et al., 2024).

Geographical Variance

To address wealth disparities and geographical variations in malnutrition, all children must have equal access to essential nutrition and healthcare services, regardless of socio-economic status or location. Efforts to reduce wealth disparities and address geographical variations in malnutrition should include the following, firstly, governments and policymakers must prioritize and implement policies that target vulnerable populations in remote rural communities and urban slums.

Additionally, healthcare systems need to be strengthened to provide equal access to nutrition and healthcare services for all children. This includes improving healthcare infrastructure, increasing the availability of healthcare facilities, ensuring healthcare professionals are adequately trained, and utilizing mobile clinics and outreach programs to reach underserved areas.

Education and awareness campaigns are essential to raise awareness about the importance of nutrition and healthcare among parents, caregivers, and communities, enabling them to make informed decisions. Furthermore, efforts should be made to improve the availability and affordability of nutritious food. This can be achieved by promoting sustainable agriculture, supporting local food production, and implementing food assistance programs.

Overall, addressing wealth disparities and geographical variations in malnutrition requires a comprehensive approach involving policy changes, healthcare system improvements, education, and better access to nutritious food. By ensuring equal access to essential nutrition and healthcare services, we can strive to eliminate malnutrition disparities among children (Liou et al., 2020).

Socioeconomic

Poor living conditions, inadequate sanitation, and unsafe drinking water increase the risk of infections and diseases, impairing nutrient absorption and contributing to child malnutrition. Strengthening water and sanitation systems is crucial for improving early childhood nutrition and development outcomes (Leah Richardson et al., 2024). Access to clean water, adequate sanitation, and proper hygiene practices (WASH) prevents infections that impair nutrient absorption. Integrating WASH with nutrition programs creates safer environments, reducing malnutrition risks and supporting healthy growth.

Transformative WASH approaches ensure comprehensive and safe service delivery by promoting safe disposal of feces, handwashing with soap, clean play spaces, and safe food preparation. Case studies show that integrated WASH and nutrition interventions significantly improve child health outcomes. Investing in WASH systems is essential for sustainable improvements in child nutrition and overall public health.

Higher household wealth is linked to better access to nutritious food, healthcare, and education, improving child nutritional status. Lower household wealth limits these opportunities, increasing malnutrition risks. Household assets can impact child health outcomes, making them key targets for policy interventions in regions like India. Standardizing processes and interventions to meet regional standards is crucial as globalization and urbanization change the nutrition landscape (Nguyen et al., 2023). A One Health approach, recognizing the interconnectedness of human, animal, and environmental health, is proposed to tackle child stunting. Coordinating efforts across these sectors can more effectively reduce stunting in LMICs (Tyagi & Joshi, 2022).

Chinese government nutrition policies during the Millennium Development Goals period significantly improved maternal and child nutrition, particularly reducing undernutrition among children. These policies fostered a supportive environment for nutrition improvement, focusing primarily on reducing undernutrition through enhanced breastfeeding, with less emphasis on addressing overweight and obesity (Huang et al., 2020). Overall, China has made substantial progress in reducing undernutrition, contributing to a rapid decline in malnutrition

rates. With ongoing efforts, China is well on its way to achieving the Sustainable Development Goals (SDGs) related to child wasting, stunting, low birth weight, and anemia in women of reproductive age. Nevertheless, there is a need for targeted policies and interventions to further improve breastfeeding rates and to prevent and control childhood obesity in the future.

Nutrition-specific interventions include micronutrient supplementation, fortification, optimal breastfeeding, complementary feeding practices, and disease prevention to improve maternal, infant, and child health outcomes (Christian et al., 2015; Kinshella et al., 2021). The First 1,000 Days approach aims to reduce child stunting, with mothers playing a crucial role by improving their nutritional status during pregnancy and lactation (Kinshella et al., 2021).

Strengths and Limitations

This review's strength is its comprehensive search strategy, capturing a broad range of studies with large sample sizes, which helps reduce bias. However, limitations include study heterogeneity, variations in BMI and stunting measurements, potential publication bias, and reliance on self-reported data, introducing recall bias. The cross-sectional nature of many studies limits causal inference.

CONCLUSION

A systematic review found that children of mothers with low or high BMI had an increased risk of stunting. Household wealth and maternal education significantly contributed to regional disparities in child nutritional status. The complexity of malnutrition is highlighted by inconsistencies across studies, and limitations include potential publication bias and the inability to infer causality due to observational designs. These findings underscore the need for integrated approaches to maternal and child nutrition within a larger socioeconomic context. Strategies should be comprehensive, targeting both maternal and child nutrition to reduce stunting and improve long-term health outcomes.

Recommendation

To mitigate child undernutrition through enhanced maternal nutritional status, several interventions and policies are recommended. Firstly, nutritional programs targeted at pregnant and nursing mothers with low BMI should be implemented. These programs should provide individualized nutritional counseling and essential supplements like iron, folic acid, and multivitamins to improve maternal and child health outcomes. Education is crucial, so access to educational resources on balanced diets, breastfeeding, and nutrition before and after pregnancy should be enhanced. Utilizing multimedia technologies and local languages can ensure broad reach and comprehension. Socioeconomic support is also vital. Developing policies to reduce poverty and improve socioeconomic conditions for families will help. Providing low-income families with healthcare access, food vouchers, and financial assistance can alleviate the effects of poverty on child nutrition.

Addressing geographic differences in undernutrition involves developing nutritional interventions tailored to local food patterns and economic conditions. Establishing regional nutritional surveillance systems will help monitor and address areas with high rates of undernutrition. Researching environmental and cultural factors affecting nutrition is essential for tailoring interventions to local contexts, ensuring they are effective and culturally appropriate. Integrating maternal and child health services into existing healthcare systems is

necessary. Routine nutritional assessments and interventions should be ensured during prenatal and postnatal care visits. Advocating for policies that support maternal health, such as maternity leave and workplace accommodations for breastfeeding, is also important.

Promoting community-based seminars and support networks involving mothers, fathers, and caregivers can enhance maternal and child nutrition. Utilizing community health professionals and local leaders can increase participation and provide practical nutritional guidance and cooking demonstrations. These comprehensive strategies aim to improve maternal nutritional status and reduce child undernutrition by addressing both immediate needs and broader socioeconomic

Further Research

It is crucial to carry out additional research that investigates the causal processes connecting mother nutritional status to child undernutrition in order to fully address the issue of undernutrition in children. Gaining a greater understanding of these systems will help us better understand how maternal health influences children's nutritional outcomes, both directly and indirectly. To follow the nutritional state of a mother during her pregnancies, pregnancy, and breastfeeding, as well as the nutritional results of her offspring, longitudinal studies should be conducted. This entails investigating the effects on prenatal development and early childhood growth of the mother's BMI, micronutrient levels, and total dietary intake.

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REVIEW ARTICLE Open Access

Factors Related to Air Pollution and Impacts on Respiratory Health in Malaysia: A Scoping Review

Zainib Amirah binti Anwar[1,2], Safirah Jaan Binti Jaafar[1]*, Abdul Rahman Ramdzan[1]

Abstract

Air pollution, driven by urbanization, industrial activities, and transboundary haze, poses a significant threat to public health in Malaysia. It contributes to respiratory diseases such as asthma, chronic obstructive pulmonary disease (COPD), and bronchitis. Although advancements in monitoring have improved data accuracy, challenges remain in addressing regional disparities and climate-related factors. This review aims to explore air quality monitoring, factors influencing pollution, and its impacts on respiratory health in Malaysia. The aim of this study is to identify the scope of air quality monitoring, factors contributing to air pollution, and the associated impacts on respiratory health in Malaysia. A scoping review methodology was employed, using databases such as ScienceDirect, Scopus, and Google Scholar. Studies were included if they were conducted in Malaysia, published in English within the last five years, and investigated the relationship between air pollution and respiratory diseases. Data extraction focused on pollutants, study settings, and key findings. The review included 19 studies. Key findings indicate that urbanization, vehicular emissions, and transboundary haze are primary contributors to air pollution. Pollutants such as PM10, PM2.5, and NO2 are significantly associated with respiratory diseases, particularly asthma and COPD. Monitoring data shows that urban areas face greater challenges, while transboundary pollution affects rural and suburban regions. Air pollution remains a pressing issue in Malaysia, exacerbated by urbanization and transboundary haze. Strengthening air quality policies, enhancing monitoring systems, and promoting public awareness are crucial to reducing health risks. Future research should prioritize underrepresented regions, long-term health impacts, and the effectiveness of regulatory measures. Collaborative and region-specific interventions are essential to combat this multifaceted challenge.

Keywords: Air quality, air pollution, respiratory diseases, asthma, COPD

*Correspondence Email: safirah.jaan@ums.edu.my

[1] *Department of Public Health Medicine, Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah, Jalan UMS, 88400 Kota Kinabalu, Sabah, Malaysia*

[2] *Sabah State Health Department, Ministry of Health, Malaysia*

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INTRODUCTION

Air quality, a key environmental health indicator, varies globally due to industrial activities, traffic emissions, agriculture, and natural events. Urban areas, especially in developing countries, often face higher pollution levels from rapid industrialization and population growth, while rural areas may be affected by agriculture and natural dust and smoke (WHO, 2021). Air pollution significantly impacts global health, causing about 7 million premature deaths annually. Pollutants such as PM2.5, PM10, NO2, SO2, O3, and CO are linked to respiratory infections, heart disease, stroke, lung cancer, and COPD, with vulnerable groups like children, the elderly, and those with preexisting conditions being particularly at risk (WHO, 2021).

Extensive Air Pollution Index (API) monitoring can ideally be achieved by integrating new technologies such as ground-based smart sensors, satellite remote sensing systems, geospatial technologies, and computational advancements like machine learning, artificial intelligence, and the Internet of Things (IoT) (Singh et al., 2021). The Global Environment Monitoring System for Air (GEMS Air) under the United Nations promotes a coordinated framework to track air quality and forecast pollution events globally, emphasizing standardization and accessibility of data (UNEP).

The Department of Environment (DOE) Malaysia monitors air quality using a variety of advanced instruments installed in Continuous Air Quality Monitoring (CAQM) stations. These stations are equipped with analyzers for measuring particulate matter (PM10 and PM2.5), nitrogen dioxide (NO2), sulfur dioxide (SO2), carbon monoxide (CO), and ozone (O3) (DOE Malaysia). The analyzers operate continuously, providing real-time data essential for assessing air quality and identifying pollution trends (DOE Malaysia). As of 2011, the DOE monitored the country's ambient air quality through a network of 52 continuous monitoring stations; by 2023, this network had significantly improved, expanding to include 65 automatic monitoring stations, 14 manual monitoring stations, and 3 mobile monitoring stations, reflecting a strengthened commitment to comprehensive air quality monitoring. (DOE Malaysia, 2011; 2023).

In 2017, chronic respiratory diseases (CRDs) impacted 544.9 million individuals globally, with chronic obstructive pulmonary disease (COPD) as the leading cause of mortality, resulting in 3.91 million deaths. Consequently, CRDs ranked as the third leading cause of death worldwide, with smoking and air pollution recognized as significant risk factors (Soriano et al., 2020). In Southeast Asia, recurrent haze episodes have adversely affected respiratory health, resulting in heightened hospitalizations for conditions such as bronchial asthma and COPD exacerbations. Healthcare utilization is notably elevated during haze periods compared to non-haze periods (Jaafar et al., 2021). In Malaysia, particulate matter (PM2.5) pollution was

responsible for 9781 excess deaths in 2013, significantly affecting respiratory health, especially in relation to conditions such as COPD and asthma (Mazeli et al., 2023). The seasonal haze in Malaysia exacerbates respiratory issues, leading to increased outpatient visits and hospitalizations, which highlights the significant health challenges associated with air pollution (Jaafar et al., 2021).

Therefore, this scoping review aims to identify the provision of air quality monitoring, factors related to air pollution, and highlight the impacts of air pollution on respiratory health in Malaysia.

METHODS

Search Strategy

A detailed search approach was devised to identify appropriate studies for this scoping review. The search will include multiple electronic databases, such as ScienceDirect, Scopus, and Google Scholar. Articles from Google Scholar were cross-checked with respective authors' institutional affiliations or professional profiles. The search criteria will consist of a combination of keywords and terminologies pertaining to air quality, air pollution, and respiratory disorders in Malaysia. The following terms will be included in the search: "air pollution," "air quality, "Malaysia," "asthma", "COPD," "bronchitis," "lung cancer," and "respiratory diseases." The search terms were suitably combined using Boolean operators, namely "AND" and "OR". In addition, the reference lists of the included research will be examined to find any more relevant articles.

Inclusion and Exclusion Criteria

Inclusion criteria ensured the review included relevant papers: research conducted in Malaysia, published in English within the last five years, investigating the link between air pollution and respiratory disorders. Both observational studies and systematic reviews with empirical evidence were eligible. Exclusion criteria eliminated studies outside Malaysia, non-English publications, non-peer-reviewed works, and those lacking significant data on air pollution or respiratory disorders.

Data Extraction and Synthesis

Data extraction was performed using a standardized form to collect essential information such as study title, authors, publication year, study design, sample size, population characteristics, air quality parameters, reported respiratory outcomes, primary findings, and statistical significance. The data synthesis involved an analysis by the author of this article of the included studies, summarizing key findings on the associations between air pollution and respiratory diseases in Malaysia.

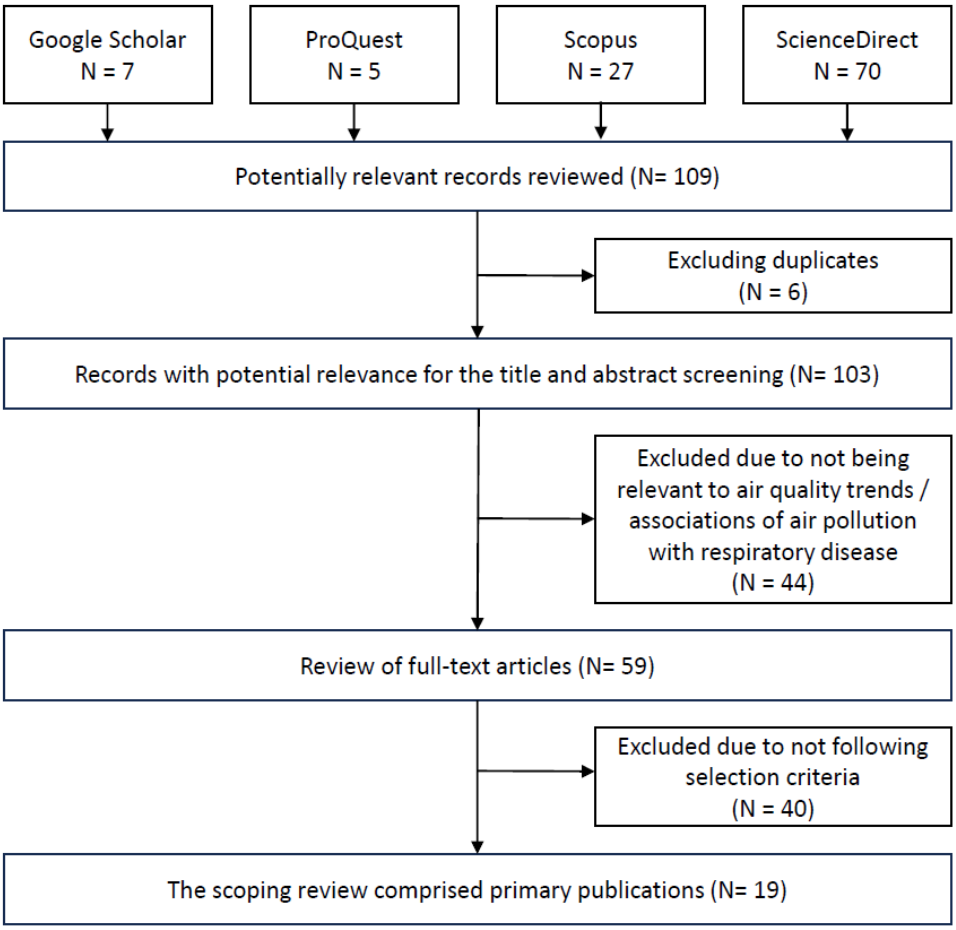

Figure 1: Systematic Selection of Records - Flow Diagram

RESULTS

The author initially conducted a search for pertinent publications that primarily focused on three key areas: abstract, findings, and discussion. The data collected from the selected studies were consolidated and analyzed using a charting technique that relies on a descriptive approach. The authors' names, publication year, research setting, study design, methodology, and any available study findings were recorded by adhering to this approach. The data from the articles was compiled and summarized using Microsoft Excel and Microsoft Word. The results sections of each article were examined to identify statements pertaining to the factors that exhibited associations with air quality and the incidence of respiratory disorders in Malaysia.

Table 1: Summary of Selected Articles on Air Quality Across Different Regions in Malaysia (n = 9)

Author(s)	Title	Period of Study	Region	Objective of Study	Data Source	Pollutants and Other Parameters Measured	Key Findings
Abdul Halim et al., 2020	Spatial assessment of land use impact on air quality in mega urban regions, Malaysia	2000 - 2015	Kuala Lumpur Extended Mega Urban Region (covers the area from Bernam River Basin, south Perak to Linggi River Basin in Negeri Sembilan, extending to Melaka River Basin, Melaka. Area is about 11 982 km^2	Assess the impact of land use changes on air quality in a mega urban region in Malaysia	Continuous air quality monitoring stations managed by DOE in Tg Malim , Petaling Jaya, Klang, Shah Alam, Nilai, Seremban, Bandaraya Melaka, and Bukit Rambai	PM10, NO, NO2, NOx, CO, SO2	Land use changes (increase in built-up land, decrease in vegetation and water bodies) contributed to spatial expansion of air pollutants like NO, NO2, CO, and SO2.
Abdullah et al., 2020	Air quality status during 2020 Malaysia Movement Control Order (MCO) due to	March 2020 – April 2020	Malaysia	Examine changes in air pollutant levels during the Movement	68 air quality monitoring stations managed by Department of	PM2.5	PM2.5 levels showed significant reductions (up to 58.4%) during the MCO, particularly in red zone areas with high COVID-19 cases.

	2019 novel coronavirus pandemic			Control Order (MCO) in 2020	Environment Malaysia		
Drahman et al., 2024	Twenty years of air pollutant index trend analysis in Kuching, Sarawak, Malaysia (2000–2019)	2000 - 2019	Kuching, Sarawak, Malaysia	Analyze API trends over 20 years in Kuching to assess long-term air quality fluctuations	Air pollutant index (API) for the monitoring station located at Medical Store Kuching, Sarawak	SO2, PM10, PM2.5, O3, NO2, CO	Elevated API readings were primarily due to transboundary haze from Indonesia; Fourier model predicted data well.
Mohd Halim et al., 2022	Air quality status during the pandemic Covid-19 in urban and sub-urban areas in Malaysia	January 2020 – Decembe r 2020	Kangar (suburban), Cheras (urban)	Assess the impact of the COVID-19 pandemic on air quality in urban and suburban areas	Malaysian Air Pollutant Index website	Air Pollutant Index (API)	API showed reductions in urban areas during lockdown phases, while suburban areas showed minimal changes.
Lee et al., 2020	Evaluation of air quality in Sunway City, Selangor, Malaysia from a mobile monitoring campaign using air	Septemb er 2018 – March 2019	Sunway City, Selangor, Malaysia	Evaluate air quality using a mobile monitoring campaign in a high-density urban area	Measurements collected via mobile monitoring campaign (using Aeroqual Series 500 portable	CO2, NO2	CO2 and NO2 concentrations varied significantly with traffic and meteorological conditions; urbanization contributed to pollutant levels.

	pollution micro-sensors				monitoring sensors)		
Naidin et al., 2023	Decade-long analysis: Unravelling the spatio-temporal dynamics of PM10 concentrations in Malaysian Borneo	2006 - 2016	Malaysian Borneo (Sabah and Sarawak)	Study long-term PM10 trends and transboundary air pollution effects in Malaysian Borneo	Air quality monitoring station data from 13 monitoring sites in Borneo, provided by the DOE	PM10	Southern Malaysian Borneo recorded the highest PM10 levels; biomass burning and El Niño were significant contributors to high pollution.
Rahim et al., 2023	Variability of PM10 levels with gaseous pollutants and meteorological parameters during episodic haze events in Malaysia	1997, 2005, 2013, 2015	Klang, Melaka, Pasir Gudang, Petaling Jaya	Analyze variability of PM10 with gaseous pollutants and meteorological parameters during haze episodes	Hourly dataset from Department of Environment Malaysia (PM10, gaseous pollutants, weather parameters)	NOx, SO2, NO2, O3, CO, PM10. Meteorological parameters such as wind speed, relative temperature, humidity	PM10 showed strong correlations with CO and moderate correlations with SO2; haze episodes were strongly influenced by transboundary pollution from Sumatra.
Sentian et al., 2019	Long-term air pollution trend analysis in Malaysia	1997 - 2015	Malaysia (20 monitoring stations)	Conduct long-term analysis of pollutant trends and	Data from 20 air quality monitoring stations in Malaysia	CO, NOx, PM10	Transboundary pollution from Indonesia during the southwest monsoon was a key contributor to PM10 levels; urban areas had

				identify pollution sources			additional local emission sources.
Zheng et al., 2023	Assessing the impacts of climate variables on long-term air quality trends in Peninsular Malaysia	2000 - 2019	Peninsular Malaysia	Investigate the impacts of climate variables on long-term air quality trends	Ground-based observations from climate and air quality monitoring stations (2000–2019)	PM10, O3, CO, NO2, SO2. Meteorological data such as temperature, precipitation, relative humidity, wind speed, wind direction.	Air quality worsened with rising temperatures, with increases in PM10 and O3 concentrations linked to global warming.

Table 2 : Summary of Selected Articles on Associations between Air Pollution with Respiratory Disease (n = 10)

Author(s)	Title	Study Location	Study Design	Study Objective	Data Source/ Sample Size	Independent Variables	Dependent Variable (s)	Key Findings
Anuar et al., 2023	Impact of haze event on daily admission of respiratory system patients in Peninsular Malaysia	Peninsular Malaysia	Cross-sectional (Generalized linear lag model)	Evaluate the impact of haze on respiratory admissions	Dataset June – September in year 2019 from DOE and 92 hospitals under MOH	Air pollutant levels (SO2, NO2, CO, O3, PM10,P,2.5), meteorological data (wind direction, wind speed, relative humidity, ultraviolet radiation, temperature)	Daily hospital admissions for respiratory diseases	Significant correlation between PM10 concentration and average daily number of respiratory disease hospitalization. Variability on the daily admission rate of patients with respiratory diseases to hospitals during haze period.
Awang et al., 2020	Assessment of micronucleus frequency and respiratory health	Klang Valley	Cross-sectional	Assess micronucleus frequency and respiratory	160 traffic policemen; 149 office workers	BTEX, PM2.5 exposure levels	Micronucleus frequency; respiratory symptoms	Higher exposure to BTEX and PM2.5 is linked to elevated micronucleus

	symptoms among traffic policemen exposed to BTEX and PM2.5 in Klang Valley, Malaysia			symptoms among traffic policemen				frequency and increased respiratory symptoms.
Ibrahim et al., 2022	Children's exposure to air pollution in a natural gas industrial area and their risk of hospital admission for respiratory diseases	Bintulu	Time-series analysis (Distributed Lag Non-linear Model)	Assess children's hospital admission risk in a natural gas industrial area	Children's admission data (2010 - 2019)	Air pollutant levels (PM10, PM2.5, SO2, NO2, O3, CO)	Children's hospital admission rates	Short-term exposure to PM2.5 and SO2 associated with hospital admissions for respiratory diseases in children.
Jaafar et al., 2021	The impact of haze on healthcare utilizations for acute respiratory diseases: Evidence from Malaysia	Selangor (Petaling, Klang, Kuala Selangor, Kuala Langat)	Cross-sectional	Investigate haze's impact on acute respiratory healthcare utilization	Haze/non-haze data (from CAQM DOE) and healthcare utilization records (public hospital and	Haze episodes	Healthcare utilization for respiratory diseases	Haze episodes significantly increase healthcare utilization for acute respiratory diseases.

					health clinics) in year 2012 – 2015.			
Khamal et al., 2019	Indoor particulate matters, microbial count assessments, and wheezing symptoms among toddlers in urban daycare centers in the district of Seremban, Malaysia	Seremban	Cross-sectional	Analyze indoor air quality and wheezing symptoms among toddlers in daycare	10 daycare centers; toddlers aged 1-4 years	Indoor air quality (PM2.5, PM10, CO2, total bacterial count, total fungal count)	Wheezing symptoms in toddlers	Indoor air quality exceeding standards and increased levels indoor air pollutants is associated to a higher prevalence of wheezing symptoms in toddlers.
Morrissey et al., 2021	The effects of air quality on hospital admissions for chronic respiratory diseases in Petaling Jaya, Malaysia, 2013 - 2015	Petaling Jaya	Time-series analysis (Distributed Lag Model)	Examine air quality effects on chronic respiratory admissions	Hospital admissions data (2013 - 2015)	Air Quality Index (API) changes	Hospital admissions for chronic respiratory diseases	A 10 µg/m^3 increase in API significantly raises hospital admissions for chronic respiratory conditions.

Norback et al., 2021	Asthma symptoms and respiratory infections in Malaysian students: Associations with ethnicity and chemical exposure at home and school	Johor Bahru	Cross-sectional	Identify chemical exposure links to asthma and respiratory issues	462 junior high students	Chemical exposure at home and school	Asthma symptoms and respiratory infections	Para-dichlorobenzene exposure at schools is associated with increased asthma and respiratory infections.
Shafie et al., 2022	Influence of urban air pollution on the population in the Klang Valley, Malaysia: A spatial approach	Klang Valley	Spatial Analysis	Examine urban air pollution's spatial risks on public health	Population density (Census of Population and Housing Malaysia), PM10 data (DOE) and health data from Klang Valley	Urban air pollution levels (PM10)	Chronic bronchitis risk (AirQ+ model)	High PM10 levels in Klang Valley correlate with increased chronic bronchitis risk among adults.
Sofwan et al., 2021	Risks of exposure to ambient air pollutants on the admission	Kuala Lumpur	Time-series analysis	Assess air pollutants' risks on respiratory and	Hospitalization data from Hospital Canselor Tunku	Ambient air pollutants (PM10, CO, NO2, SO2), meteorological variables (ambient	Respiratory and cardiovascular admissions	Significant associations found between air pollutants and hospital

	of respiratory and cardiovascular diseases in Kuala Lumpur		(Distributed Lag Non-linear Model)	cardiovascular health	Muhriz UKM, Hospital Kuala Lumpur, and MOH; pollutant concentrations from CAQMs in Batu Muda, Petaling Jaya, and Cheras	temperature, relative humidity)		admissions for respiratory and cardiovascular diseases.
Tajudin et al., 2019	Risk of concentrations of major air pollutants on the prevalence of cardiovascular and respiratory diseases in urbanized area of Kuala Lumpur, Malaysia	Kuala Lumpur	Time-series Analysis (Generalized Additive Model)	Evaluate air pollutants' impact on cardiovascular and respiratory disease prevalence	Hospitalization data from HCTM; and data from DOE's CAQM at Bandar Tun Razak (2010 - 2014)	Concentrations of air pollutants (SO2, NO2, PM10, CO, O3), meteorological variables (temperature, relative humidity)	Prevalence of cardiovascular and respiratory diseases	Delayed effects of NO2 and SO2 on hospitalizations for respiratory and cardiovascular conditions were observed.

Table 3 : Descriptive Results Summary (n = 19)

Type of Study	n
Cross-sectional	10
Longitudinal cohort	1
Longitudinal ecological	3
Time series analysis	4
Spatial analysis	1
Location/Setting	
Nationwide	4
Selangor	4
Kuala Lumpur	3
Negeri Sembilan	1
Sabah / Sarawak	3
Various locations (Peninsular Malaysia)	4
Year of Publication	
2019	3
2020	4
2021	4
2022	3
2023	4
2024	1

DISCUSSION

Measurement of air quality across Malaysia

Air quality in urban regions like the Kuala Lumpur Extended Mega Urban Region (KLEMUR) has been well-captured, showing significant correlations between land use changes and pollutants such as PM10, NO, NO2, and CO, which are heavily influenced by vehicular and industrial emissions (Abdul Halim et al., 2020). The COVID-19 Movement Control Order (MCO) provided a unique opportunity to observe reductions in PM2.5 levels across Malaysia, with decreases of up to 58.4%, demonstrating the responsiveness of monitoring systems during specific events (Abdullah et al., 2020). In Kuching, Sarawak, long-term Air Pollutant Index (API) trend analyses over 20 years have

been conducted, employing sophisticated models to compensate for missing data, suggesting a robust capability to track air quality fluctuations and seasonal transboundary pollution (Drahman et al., 2024). Similarly, monitoring in suburban and urban areas like Kangar and Cheras revealed notable differences in API changes during the MCO, emphasizing variability in monitoring precision between urban and suburban zones (Mohd Halim et al., 2022).

Advanced monitoring techniques, such as mobile sensors with GPS, have been employed in Sunway City to provide comprehensive spatial data on pollutants like CO2 and NO2, addressing limitations of fixed monitoring stations and enhancing localized data collection (Lee et al., 2020). Long-term analyses at multiple monitoring stations across Malaysia have revealed decreasing trends in pollutants like PM10, while transboundary haze remains a persistent issue, indicating that monitoring captures both local and regional pollution sources (Sentian et al., 2019). Climate-driven changes have also influenced air quality trends, with significant increases in pollutants like PM10 and O3 linked to warming temperatures, demonstrating the evolving challenge of air pollution measurement under climate change scenarios (Zheng et al., 2023).

The fixed monitoring stations, while useful, often lack sufficient spatial coverage, especially in high-density urban areas and suburban or rural regions, leading to gaps in capturing localized variations (Lee et al., 2020; Mohd Halim et al., 2022). The monitoring system struggles to address the impact of transboundary pollution, particularly from biomass burning in neighboring Indonesia, which remains a persistent challenge during seasonal haze episodes (Naidin et al., 2023; Rahim et al., 2023). Data gaps in long-term pollutant trends, such as PM10, often require advanced models for accurate prediction, highlighting limitations in consistent data collection (Drahman et al., 2024). Additionally, the system has yet to fully integrate climate variables, such as rising temperatures and changing precipitation patterns, which significantly influence pollutant trends under evolving environmental conditions (Zheng et al., 2023).

Urbanization-related changes, including increased built-up areas and reduced vegetation, are also not adequately reflected in current assessments, despite their clear role in exacerbating pollution levels (Abdul Halim et al., 2020). While the COVID-19 Movement Control Order demonstrated the adaptability of the monitoring network in capturing pollutant reductions, the system needs to further enhance its responsiveness and real-time capabilities (Abdullah et al., 2020).

Air quality trend in Malaysia

Air quality trends in Malaysia vary significantly between urban and suburban or rural areas due to differences in pollutant sources, urbanization, and the influence of transboundary pollution. In urban areas, the Kuala Lumpur Extended Mega Urban Region (KLEMUR) from 2000 to 2015 saw increasing concentrations of pollutants such as PM10, NO, NO2, and CO, driven by rapid urbanization and changes in land use. These trends reflect the growing contribution of vehicular and industrial emissions in densely populated regions (Abdul Halim et al., 2020). Similarly, a six-month study in Sunway City, Selangor, from

September 2018 to March 2019, revealed that traffic-related pollutants like NO2 and CO2 were dominant, highlighting the localized effects of urban activities on air quality (Lee et al., 2020).

Nationwide, urban areas experienced significant improvements in air quality during the COVID-19 Movement Control Order (MCO) in 2020, with PM2.5 levels reducing by up to 58.4%. This reduction demonstrated the immediate impact of decreased vehicular and industrial activities during lockdowns (Abdullah et al., 2020). However, haze events in urban areas during specific years—1997, 2005, 2013, and 2015—showcased the persistent challenge of transboundary pollution, as PM10 levels consistently exceeded recommended guidelines. Strong correlations were observed between PM10 and CO levels during these episodes, with urban centers bearing significant impacts (Rahim et al., 2023). Additionally, from 2000 to 2019, urban areas in Peninsular Malaysia recorded increasing levels of PM10 (+16.4%) and O3 (+39.5%), trends closely linked to warming temperatures and urbanization, underscoring the influence of climate change on air quality (Zheng et al., 2023).

In contrast, suburban and rural areas display different air quality dynamics. During the COVID-19 MCO, suburban Kangar showed smaller reductions in API compared to urban Cheras, reflecting lower baseline emissions in less industrialized and densely populated regions (Mohd Halim et al., 2022). In Malaysian Borneo (Sabah and Sarawak), from 2006 to 2016, PM10 levels varied across regions: urbanized areas like Miri and Limbang experienced increases, while rural areas such as Kuching and Bintulu saw significant decreases. This variability highlights the complex interaction of local emissions and transboundary pollution from biomass burning in neighboring countries (Naidin et al., 2023).

Kuching, Sarawak, provides a particularly illustrative case of long-term trends in a suburban setting. Between 2000 and 2019, the Air Pollutant Index (API) showed periodic increases during transboundary haze episodes, driven by regional biomass burning. These events significantly affected rural and suburban regions, demonstrating their vulnerability to external pollution sources (Drahman et al., 2024). Nationwide monitoring from 1997 to 2015 revealed that while PM10 levels generally decreased across most of the 20 monitoring stations, suburban and rural areas were disproportionately affected by seasonal transboundary haze, whereas urban regions faced additional pressures from local emissions (Sentian et al., 2019).

Factors Related to Air Pollution in Malaysia

In Malaysia, air pollution is affected by a variety of human activities, natural events, and climatic conditions. Urbanization and changes in land use, including the expansion of built-up areas and the decrease in vegetation, are important factors in regions such as KLEMUR. These changes have led to an increase in pollutants like PM10 and NO2, primarily due to emissions from industrial activities and vehicles (Abdul Halim et al., 2020). In high-density urban areas such as Sunway City, vehicular emissions, especially CO2 and NO2, are predominant. This issue is further intensified by the increasing

population and dependence on private transportation (Lee et al., 2020). Industrial activities significantly impact air quality, especially in urban and industrialized areas, where emissions of PM10 and SO2 are major contributors to its deterioration (Zheng et al., 2023). Seasonal haze episodes, frequently caused by transboundary biomass burning from neighboring Indonesia, increase pollution levels, leading to periodic spikes in PM10 concentrations in areas such as Malaysian Borneo and urban centers throughout Peninsular Malaysia (Naidin et al., 2023; Rahim et al., 2023; Sentian et al., 2019).

Climatic factors exacerbate air pollution, as phenomena such as El Niño and the southwest monsoon influence the dispersion and concentration of pollutants, especially during haze events (Naidin et al., 2023; Sentian et al., 2019). Increased temperatures and altered precipitation patterns have been associated with higher levels of pollutants such as PM10 and O3, illustrating the relationship between climate change and air quality (Zheng et al., 2023). The insufficient enforcement of environmental regulations during periods of peak pollution, along with inadequate proactive policies, worsens the situation, especially during transboundary haze events (Rahim et al., 2023).

Table 4: Factors Related to Air Pollution in Malaysia

	Factors	Studies
1.	Urbanization, Land Use Changes	Abdul Halim et al., 2020
2.	Vehicular Emissions	Lee et al., 2020
3.	Industrial Activities	Zheng et al., 2023
4.	Biomass Burning, Transboundary Pollution	Naidin et al., 2023; Rahim et al., 2023; Sentian et al., 2019;
5.	Seasonal and Climatic Influences	Naidin et al., 2023; Sentian et al., 2019; Zheng et al., 2023
6.	Reduced Environmental Regulations During Peak Pollution Events	Rahim et al., 2023
7.	Population Growth	Lee et al., 2020; Abdul Halim et al., 2020

Impacts of air pollution to respiratory health

Indoor air quality refers to the quality of air within buildings, influenced by factors like temperature, humidity, ventilation, and pollutants such as VOCs and particulate matter (Bhattacharya, Sridevi, & Pitchiah, 2012), while outdoor air quality pertains to air quality

in external environments, affected by sources like transportation and industry, with significant health impacts including respiratory and cardiovascular risks (Turner et al., 2020).

Poor indoor air quality, particularly in urban environments, contributes to respiratory issues, especially among vulnerable populations. For example, Khamal et al. (2019) found that high levels of PM2.5, PM10, and microbial counts in daycare centers were associated with increased wheezing symptoms among toddlers. Similarly, Norbäck et al. (2021) highlighted that indoor chemical emissions, such as para-dichlorobenzene in classrooms and homes, increased asthma and respiratory infections among Malaysian students. While indoor air pollution is often linked to chemical emissions from cleaning products, furniture, and paints, these sources can be mitigated with interventions like improved ventilation and reduced use of harmful products (Khamal et al., 2019; Norbäck et al., 2021).

In contrast, outdoor air quality is predominantly affected by broader environmental factors such as traffic emissions, industrial activities, and haze events, posing systemic challenges to respiratory health. Shafie et al. (2022) observed that outdoor PM10 levels in the Klang Valley significantly exceeded WHO guidelines, leading to an increased risk of chronic bronchitis. Similarly, Ibrahim et al. (2022) linked short-term exposure to outdoor pollutants, such as PM2.5 and SO2 in a natural gas industrial area, to higher hospital admissions for respiratory diseases in children. Additionally, Tajudin et al. (2019) highlighted that pollutants like NO2 and SO2 contributed to both immediate and delayed effects on respiratory and cardiovascular health in urbanized Kuala Lumpur. These findings underscore the need for systemic interventions, such as stricter emission controls and urban planning strategies, to mitigate outdoor air pollution and its health impacts (Shafie et al., 2022; Ibrahim et al., 2022; Tajudin et al., 2019).

CONCLUSIONS

The results of this scoping review highlight the various issues that air pollution presents and how seriously it affects respiratory health in Malaysia. Despite significant advancements in air quality monitoring and the identification of major sources of pollution, more effective and region-specific actions are still urgently required. In order to lessen the effects of urbanization, transboundary haze, and climate change, comprehensive, multi-sectoral policies are required. To protect health outcomes, air quality regulations must be strengthened, climate adaption strategies must be incorporated, and public awareness must be raised. To provide a comprehensive strategy to reducing air pollution, future research should concentrate on underrepresented areas, long-term health implications, and the efficacy of current regulations. Malaysia can effectively tackle air pollution and its detrimental health effects by exploiting technological developments in monitoring and promoting regional cooperation.

Recommendations

Enhancing air quality and mitigating respiratory health risks in Malaysia necessitate a thorough strategy involving various sectors. Policy and governance should prioritize enhancing regional collaboration to address transboundary haze and implement stricter regulations on vehicular and industrial emissions (Drahman et al., 2024; Lee et al., 2020). Incorporating climate change mitigation into air quality policies and maintaining low-emission practices established during the COVID-19 movement control order can lead to a further decrease in pollutants (Zheng et al., 2023; Abdullah et al., 2020). Urban and regional planning should focus on sustainable land use, the development of green spaces, and the enhancement of public transportation infrastructure to mitigate the effects of urbanization and decrease traffic-related emissions (Abdul Halim et al., 2020). Stricter emission regulations aimed at industrial and vehicular pollutants are essential for improving outdoor air quality, especially in urban areas like Kuala Lumpur and the Klang Valley (Tajudin et al., 2019; Shafie et al., 2022). Advancing low-carbon energy sources and cleaner transportation alternatives is crucial for achieving sustained reductions in outdoor pollution (Shafie et al., 2022). Strategies for urban planning, such as the establishment of pollution-free zones and the reduction of residential exposure to industrial emissions, are essential (Ibrahim et al., 2022; Shafie et al., 2022).

Minimizing the use of volatile organic compounds (VOCs) in household and school products is essential to reduce risks associated with chemical exposure (Norbäck et al., 2021). Stricter indoor air quality standards can enhance protection for vulnerable populations, especially children, against harmful exposure (Khamal et al., 2019). Enhancing ventilation systems in daycare centers, schools, and homes can substantially decrease the buildup of pollutants, including PM2.5, PM10, and microbial counts (Khamal et al., 2019). Safe indoor practices, including the use of non-toxic cleaning products and the maintenance of adequate airflow, can strengthen individual initiatives aimed at improving indoor air quality (Norbäck et al., 2021). Public awareness campaigns can inform communities about the health risks associated with outdoor pollution and the preventative measures that can be taken, such as minimizing exposure during haze events (Jaafar et al., 2021; Ibrahim et al., 2022).

Policymakers ought to utilize localized research findings to develop region-specific solutions that tackle challenges such as haze episodes and industrial emissions (Anuar et al., 2023; Ibrahim et al., 2022; Jaafar et al., 2021). Enhancements in monitoring and data collection are essential, particularly through the expansion of localized air quality stations and mobile monitoring campaigns to improve spatial data coverage (Lee et al., 2020; Mohd Halim et al., 2022). Monitoring and enforcing compliance with indoor air quality guidelines offer a systematic approach to protecting respiratory health (Khamal et al., 2019; Norbäck et al., 2021). Health surveillance systems must be established to monitor trends in air quality and to inform timely interventions (Khamal et al., 2019; Shafie et al., 2022).

Predictive modeling and climate forecasting tools can assist in anticipating and managing future challenges related to air quality (Zheng et al., 2023). Public health interventions, including early warning systems for haze and awareness campaigns, are crucial for mitigating health risks (Rahim et al., 2023). It is essential to address industrial emissions and establish inter-country agreements on transboundary pollution, in addition to implementing strategies for adapting to climate-related risks (Naidin et al., 2023; Rahim et al., 2023).

Collectively, these measures can establish a comprehensive framework for effectively addressing Malaysia's air quality and respiratory health challenges.

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REVIEW ARTICLE Open Access

Exploring The Global Public Health Impacts of Armed Conflict: A Systematic Review

Veshny Ganesan[1], Safirah Jaan Jaafar[1*]

Abstract

Armed conflicts are catastrophic disasters that significantly impact human health and well-being. Current research on the long-term and indirect health effects of armed conflicts is insufficient, and it often overlooks the unique health requirements of vulnerable populations, such as women, children, the elderly, and those with disabilities. This systematic review aims to investigate these impacts and identify the distinct health requirements of at-risk groups. Following the PRISMA guidelines, a systematic review was conducted on studies published in English from 2019 to 2024. We searched databases like Scopus, Science Direct, PubMed, and Google Scholar using PICO framework. The quality of the included studies was assessed using the JBI appraisal tool. A total of 22 studies met the inclusion criteria, highlighting the notable public health consequences of armed conflicts. Among the included publications, 19 were quantitative studies and three were qualitative studies. Six themes categorized these impacts: health effects, disruptions and shortages in healthcare infrastructure and services, disruptions in food security and malnutrition, environmental health effects, humanitarian crises and displacement, and long-term health outcomes and resilience. The synthesis of existing literature highlights the importance of robust mental health support frameworks, enhanced healthcare access, and integrated recovery strategies that consider social, cultural, political, and environmental factors. Future research should focus on including non-English studies and improving longitudinal data collection to better understand and address the public health impacts of armed conflicts, informing effective policy and practice.

Keywords: Armed Conflict; Public Health Consequences, Systematic Review

*Correspondence Email: safirah.jaan@ums.edu.my

[1] *Department of Public Health Medicine, Faculty Medicine and Health Sciences, Universiti Malaysia Sabah, Jalan UMS, 88400 Kota Kinabalu, Sabah, Malaysia*

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INTRODUCTION

Armed conflicts remain one of the most catastrophic disasters to human beings, with devastating effects on people's health and well-being. War is a tragic occurrence that violates the rights of humans. According to the Uppsala Conflict Data Program (UCDP), an armed conflict occurs when two parties, one of which is the government of a state, use military force against each other, resulting in at least 25 battle-related deaths per year (Żakowska, 2020). Geneva Conventions 1949 and Additional Protocols classified armed conflict into two types, which are international armed conflict (IAC) between two or more states, including belligerent occupation, and non-international armed conflict (NIAC) between a State and non-State armed groups. These are commonly referred to as civil wars (Milanovic & Hadzi-vidanovic, 2012). International humanitarian law specifically exists to govern and regulate conduct in armed conflict. International Humanitarian Law (IHL) and International Human Rights Law (IHRL) are vital in defending human lives, health, and dignity from various perspectives. IHL and IHRL are intertwined in the evolution of international law, to safeguard human rights and dignity (Ashri, 2019).

Armed conflicts have affected many countries worldwide, including Afghanistan, Ethiopia, the Democratic Republic of the Congo, Syria, Ukraine, and most recently reported in Gaza. The worldwide landscape of armed conflict has changed progressively over the last few decades. Modern conflicts are predominated by complex sociopolitical processes and extended periods of instability (Badanta et al., 2024). The health implications of these conflicts are serious and diverse.

While there is extensive research on the immediate and long-term health implications of armed conflicts, the existing knowledge is insufficient regarding the long-term and indirect health effects of armed conflicts, especially for the post-conflict disease burden, which includes mental health disorders, chronic diseases, malnutrition, and reproductive health challenges. Furthermore, current research frequently fails to provide a targeted examination of vulnerable populations, including women, children, the elderly, and those with disabilities, resulting in broad conclusions that overlook their unique health requirements. This systematic review seeks to thoroughly investigate the long-term and indirect health impacts resulting from armed conflicts. Furthermore, it aims to pinpoint the distinct health requirements of at-risk groups, including women, children, the elderly, and those with disabilities— tackling the existing research gap. This review synthesizes existing literature to emphasize essential areas for public health intervention and to guide evidence-based policies aimed at alleviating the long-term health consequences of armed conflicts.

METHODS

Search Strategy

The research questions and objectives for this systematic review were formulated using the PICO (Population, Interest, Context, Outcome) framework. PICO Framework is a common tool for developing clear and well-defined research questions (Tawfik et al., 2019). The search strategy for this study followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) standards (Tawfik et al., 2019). The electronic search utilised the following search terms: Boolean operators (AND, OR), which were used to combine search terms effectively. Search strategy based on a combination of the following terms was used ("armed conflict" OR "warfare" OR "civil war") AND (“public health implications” OR “health

effect" OR "public health consequences"). A systematic search was conducted in electronic databases such as Scopus, Science Direct, PubMed, and Google Scholar. Keywords related to armed conflict, warfare, public health consequences, public health impact were used to identify relevant studies. The reference lists of included studies and relevant systematic reviews were manually searched for additional articles. Grey literature, including government reports, technical reports, conference proceedings, and policy briefs, was also considered to enhance the dataset.

Inclusion and Exclusion Criteria

The inclusion criteria for this systematic review encompass studies published in English from 2019 to 2024, focusing on the overall public health consequences of armed conflicts on civilian populations, the environment, food security, and healthcare access and delivery. Additionally, grey literature, facility-based data, and reports from international organizations were included to ensure comprehensive coverage of the topic. The exclusion criteria for this review included reviewed articles in the form of systematic, scoping, or narrative reviews, as well as books or conference abstracts. Studies without full text, those covering multiple disasters including natural and other man-made disasters, were also excluded to maintain a focused analysis on armed conflicts specifically. Furthermore, articles with a critical appraisal standard of quality below 70% were excluded to ensure the inclusion of high-quality studies.

Quality Assessment

These studies evaluated the risks of bias, sample representativeness, the validity of outcome measures, and the generalizability of the results. Quality appraisal for the finalized article done by 2 appraisers using the Joanna Briggs Institute (JBI) Critical Appraisal tool for quantitative and qualitative studies (Lockwood et al., 2015). Each article was assessed using a pre-defined items checklist, with each item assigned a score of "yes," "no," "unclear," or "not applicable". A score of 1 point was assigned for each criterion marked as "yes," while other scores were assigned a value of zero. The scores for each article were then calculated and summed. They are then categorised into "low", "moderate" and "high" quality. Only studies with a score more than 70 % are termed as high quality and included in this study.

Data Extraction and Data Synthesis

The titles and abstracts of the retrieved publications were evaluated for eligibility using the inclusion criteria. Full-text papers that met the eligibility requirements were assessed, and data was extracted using a standard format. The data synthesis summarized key results comprising the author, year of publication, conflict zone, the population affected, size of sample, and findings of the articles (see Table 2). To identify the recurring consequences of armed wars on public health, a thematic approach was adopted.

RESULTS

Among the included publications, 19 were quantitative studies and three were qualitative studies. Included in the quantitative studies were four cohort studies and 15 cross-sectional studies. The data from these studies is heterogeneous and collectively, they provide a body map of the public health consequences by armed conflict. Articles searched were high indexed article from PubMed, Scopus and Science Direct and Google Scholar. Fig. 1 illustrates the study selection process. The PRISMA flow diagram guided the conduct of this study, which involved

four stages: identification, screening, eligibility, and inclusion. The initial database search identified 777 articles; after removing duplicate records and abstracts from conferences and books, 658 articles remained. The articles were screened based on their titles and abstracts. The full-text review included 117 articles in total.

Among these studies, nine articles were excluded due to their reviewed paper status, 20 articles were excluded due to their lack of standard sampling, 22 articles were excluded for not analyzing the effects of war on public health, 10 articles were excluded for lacking data on the number of affected individuals, 24 articles were excluded for failing to meet the study's objectives, and 10 articles had a low critical appraisal score. The study ultimately included 22 articles.

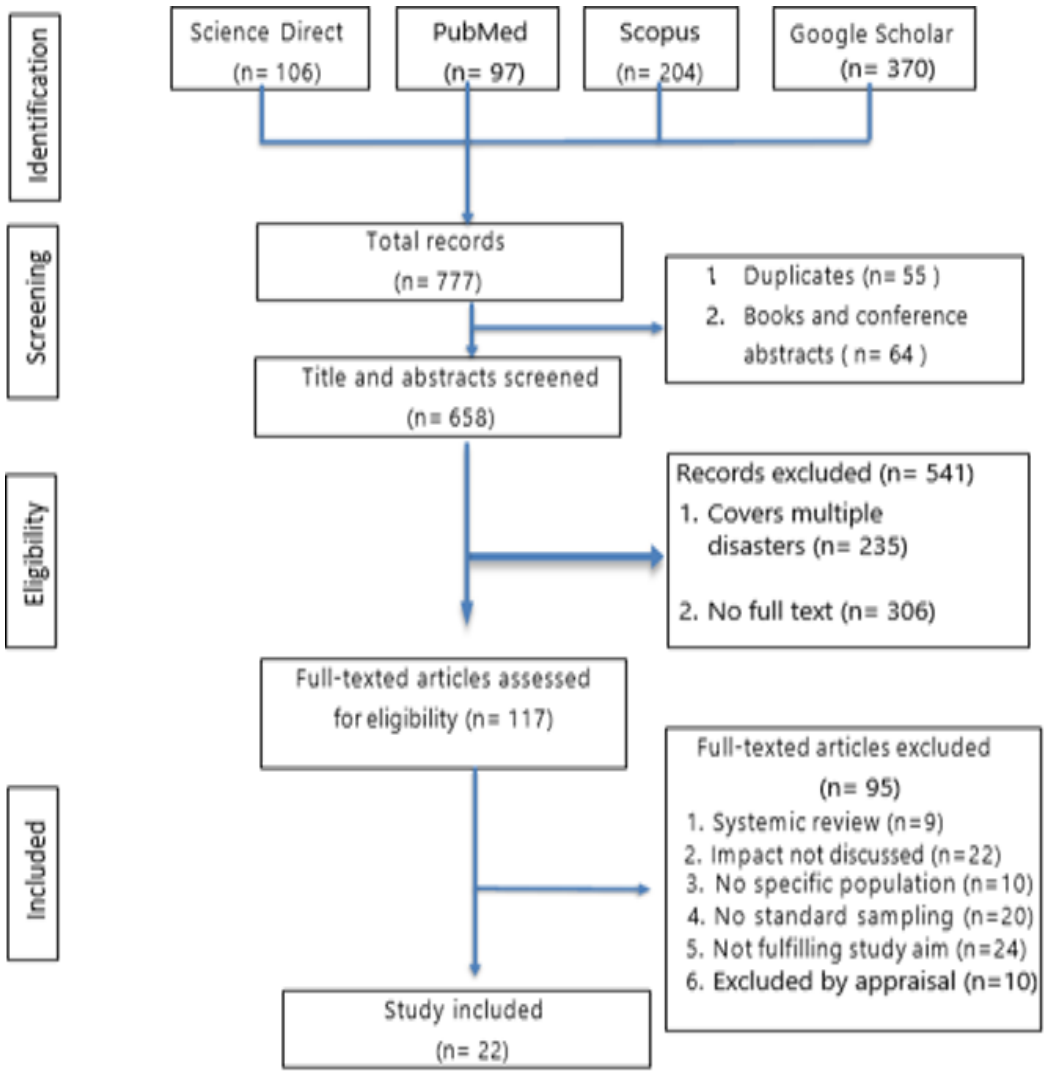

Figure 1: Flow Chart of Included Studies

Table 1 provided information on the author(s), year of publication, study source, study design, and JBI critical appraisal. This table helped summarizes the characteristics of the included studies. Findings from included articles are summarized in Table 2.

Table 1: Study characteristics of the reviewed literature

No	Author (year)	Database Source	Study Design	JBI Critical Appraisal
1	(Tarabay & Golm, 2024)	Science Direct	Cross-Sectional	No strategy for confounding factors, but met all other review criteria
2	(Smeeth et al., 2023)	PubMed	Cross-Sectional	Unclear on participants status at the beginning if the study and no strategies described to address incomplete follow up. Met all other criteria.
3	(Haas & Ramirez, 2022)	Google Scholar	Cohort	Unclear on participants status at the beginning if the study and no strategies described to address incomplete follow up. Met all other criteria.
4	(Haque et al., 2022)	Scopus	Cross-Sectional	No strategy for confounding factors but met all other review criteria.
5	(Belew et al., 2023)	Scopus	Cross-Sectional	Comply all Criteria
6	(Zhang et al., 2023)	Scopus	Cohort	Unclear on participants status at the beginning if the study and no strategies described to address incomplete follow up. Met all other criteria.
7	(Rawers et al., 2024)	Science Direct	Cross-Sectional	Comply all Criteria
8	(Goliaei et al., 2023)	Scopus	Qualitative	No statement locating the researcher culturally or theoretically and the influence of the researcher on the research not addressed
9	(Dwanyen et al., 2024)	Science Direct	Qualitative	Comply all Criteria
10	(Rahman et al., 2024)	Science Direct	Cross-Sectional	Unclear measurement of the exposure
11	(Kakaje et al., 2022)	Scopus	Cross-Sectional	Unclear strategy for confounding factors but met all other review criteria.

12	(Piotrowicz et al., 2022)	Scopus	Cross-Sectional	Comply all criteria
13	(Malytska et al., 2024)	Science Direct	Cross-Sectional	Comply all criteria
14	(Rudolfsen et al., 2024)	Google Scholar	Cross-Sectional	Comply all criteria
15	(Boos et al., 2022)	PubMed	Cohort	Unclear on follow up completion. Met all other criteria
16	(Fisseha et al., 2023)	Scopus	Cross-Sectional	Comply all criteria
17	(Rzońca et al., 2024)	Science Direct	Cross-Sectional	Comply all criteria
18	(Kassaye et al., 2023)	Scopus	Cross-Sectional	Comply all criteria
19	(Arage et al., 2023)	Google Scholar	Qualitative	No statement locating the researcher culturally or theoretically and the influence of the researcher on the research not addressed
20	(Lushchak et al., 2024)	Scopus	Cross-Sectional	No strategy for confounding factors but met all other review criteria.
21	(Béné et al., 2024)	Science Direct	Cross-Sectional	No strategy for confounding factors but met all other review criteria.
22	(Ruhnke et al., 2024)	Science Direct	Cross-Sectional	Comply all criteria

Table 2: Summary of Included Articles

No	Author	Conflict Zone	Population	Sample Size, N	Findings
1	(Tarabay & Golm, 2024)	Lebanon	Lebanese parent and adult offspring who had experienced the Lebanese civil war	220	Results showed an interaction effect between parents' war exposure intensity and their perceived social support. War exposure predicted psychopathology for parents with moderate (B= 2.00, SE=.54, t = 3.74, p < .001, 95% CI [.94, 3.07]) and high levels of social support (B = 3.02, SE =.78, t = 3.86, p < .001, 95% CI [1.47, 4.57])
2	(Smeeth et al., 2023)	Syria	Syrian refugee children and adolescents aged 6 to 18 years	1,591	Hair cortisol concentrations were linked to war-related events in children and adolescents, especially those aged 12 and above. This represents a 0.32% increase in HCC for each point on the PTSD symptom scale, equivalent to a 17.7% increase in HCC In comparison, the same model estimates females to have 72.5% higher HCC than males.
3	(Haas & Ramirez, 2022)	Europe	Older European cohorts aged fifty and above who had experienced war during their childhood years.	19,181	The findings conclude that there is a significant association between war exposure and a profound lifetime risk of cardiovascular disease, diabetes, high cholesterol, and hypertension.
4	(Haque et al., 2022)	Ukraine	People of Ukraine	24,000	The Russia-Ukraine war caused 5552 civilian deaths and 8513 injuries in Ukraine. The war has destroyed homes, schools, roads, bridges, and healthcare facilities in 21 cities resulting in interruptions to healthcare services. The increase in infectious diseases such as HIV/AIDS, tuberculosis, and COVID-19 cases further creates health challenges with medication shortages. The war poses risks of exposure to toxic chemicals, radiation, and air pollution.
5	(Belew et al., 2023)	North Gondar, Northwest Ethiopia	Pregnant and lactating mothers	1,560	The study showed that over 34.3% of pregnant and lactating women in war-affected areas are severely malnourished.

6	(Zhang et al., 2023)	Chad, the Central African Republic (CAR), the Democratic Republic of Congo (DRC), and the Republic of Iraq.	Women aged 15-49 years	55,683	Women in conflict-affected regions faces challenges in accessing comprehensive maternal and child health services, including limitations in sustaining ANC8+ throughout pregnancy due to security issues, collapse of the medical system, and unsustainability of health assistance.
7	(Rawers et al., 2024)	Syria	Displaced Syrian refugee in Turkey	593	The study identified three latent trauma classes among Syrian refugees in Turkey: multiple traumas, war and human suffering, and low exposure, combat-exposed.
8	(Goliaei et al., 2023)	Afghanistan	Afghan refugee families in the San Joaquin Valley, California	24	Afghan refugees face challenges: religious practices, financial difficulties, language barriers, limited transportation access, and lack of culturally specific food items can further exacerbate food insecurity.
9	(Dwanyen et al., 2024)	Liberia	Liberian refugees in the U.S	20	War-affected Liberian refugees are experiencing unresolved traumatic stress, engaging in substance use as a coping mechanism, and mental health stigma, which could act as a barrier to seeking and accessing mental health services. The long-term effects of war trauma and resettlement have disrupted community dynamics, leading to challenges in functioning and cohesion.
10	(Rahman et al., 2024)	Myanmar	Forcibly Displaced Myanmar Nationals (Rohingya)	679	The study found that 66.42% of the refugee camp's population was infected with scabies, indicating a significant burden of scabies infection among the FDMNs in Cox's Bazar with individuals aged 19–36 and those over 55 exhibiting the highest prevalence rates.
11	(Kakaje et al., 2022)	Syria	Secondary school students in Syria	1,369	Study found that 53% of the students suffered from PTSD, 62% of the students experienced problematic anger, 46% reported fair or worse general health and 61% of the students had moderate or severe mental health issues. War-related stressors were associated with negative habits like cigarette and shisha smoking. War exposure was found to have significant impact on PTSD, anger, and health-related quality of life (HRQL).

12	(Piotrowicz et al., 2022)	Ukraine	Older Ukrainian refugees, defined as aged 55 years or older	109, 985	The study highlighted the expected increase in burden of diseases such as hypertension, myocardial infarctions, strokes, and tuberculosis among older Ukrainian refugees, necessitating assessment, medications, and active screening for these conditions.
13	(Malytska et al., 2024)	Ukraine	Analyzing the effects of hostilities on tropospheric NO2 levels in Ukraine	-	The crisis in Ukraine has had a mixed effect on NO2 emissions, with localized rises in NO2 levels in conflict-affected areas as a result of fires linked to the conflicts and a decrease in industrial emissions as a result of economic interruptions.
14	(Rudolfsen et al., 2024)	Ukraine	Ukrainian citizens aged 18-55 residing in settlements	1,081	The study shows that Ukrainians experienced food insecurity that is one in every three people, indicating a significant proportion of the population is affected by armed conflict and experiencing food insecurity. Geographical proximity to violence also played a crucial role in determining food insecurity.
15	(Boos et al., 2022)	Afghanistan	Male adult UK combat veterans (UK-Afghanistan War 2003–2014)	1,144	The study highlighted that CRTI was associated with an increased prevalence of MetS and arterial stiffness. Factors such as age, injury severity (New Injury Severity Score), physical activity, and socioeconomic status also influenced cardiovascular risk in individuals with CRTI.
16	(Fisseha et al., 2023)	Tigray, Northern Ethiopia	Women of reproductive age (15–49 years)	5,171	Studies found that 43.3% of women experienced gender-based violence. Among them 9.7% of the women faced sexual violence, 28.6% experienced physical violence, and 40.4% underwent psychological violence. 82.2% of sexual violence cases were rape, with 68.4% gang-raped. Young women aged 15-24 years were predominantly affected by sexual violence. Common issues: physical trauma, STIs, HIV, unwanted pregnancy, depression.
17	(Rzońca et al., 2024)	Ukraine	Ukrainian civilian physicians and paramedics	435	The study showed that more physicians than paramedics met the criteria for PTSD according to the ICD-11 diagnostic rule (5.1% of physicians vs. 1.2% of paramedics). More physicians than paramedics met the criteria for anxiety disorders (16.5% of physicians vs. 10.0% of paramedics). The criteria for depression were met by 14.5% of participants.
18	(Kassaye et al., 2023)	North East Ethiopia	Adult residents of Woldia town in North East Ethiopia	597	Prevalence of PTSD was 56.28% among war-affected residents in Ethiopia. Factors like property destruction (AOR =1.6,95%CI,1.11–2.47) and family member murder increased PTSD risk (AOR = 2.1,95% CI,1.37–3.22). Direct witness to family member murder raised

					PTSD likelihood by 1.6 (AOR = 1.6,95% CI,1.01–2.71). According to research, those who have been unlawfully imprisoned are 1.7 times more likely (AOR = 1.7, 95%CI, 1.06–2.74) to acquire PTSD than those who have not experienced such imprisonment.
19	(Arage et al., 2023)	North Wollo, Ethiopia	Patients, pregnant women, elders, community and religious leaders, and health professionals	100	The conflict has significantly affected the population's health, leading to violence, insecurity, forced crisis and displacement. It disrupted the healthcare system, causing medication shortages, famine, and food insecurity. Long-term effects include medical facility devastation, immunization suspension, posttraumatic stress disorders, and permanent disabilities.
20	(Lushchak et al., 2024)	Ukraine	Adult residents of Ukraine at the time of the invasion	3,173	The research highlighted disparities in stress, anxiety, and PTSD prevalence among NDPs, IDPs, and refugees. Refugees appeared to be the most vulnerable group, while IDPs reported higher levels of distress compared to NDPs.
21	(Béné et al., 2024)	Burkino Faso, Western Africa	Food traders operating in conflict zone	-	The study emphasized the disruptions caused by armed conflicts on the local food system and the need for adaptation by food traders to navigate the challenges posed by insecurity and conflict
22	(Ruhnke et al., 2024)	Syria	Syrian refugees residing in Lebanon and Turkey	2,491	The study found that Syrian refugees in Lebanon experienced higher levels of mental distress compared to those in Turkey. Factors such as poverty, unemployment, discrimination based on nationality and religion, and challenges in accessing healthcare services were identified.

The themes emerged from a systematic thematic analysis focused on the recurring public health consequences. Essential processes included methodical data extraction, coding of the impacts, and the grouping of the identified impacts into larger themes, resulting in the establishment of six main themes illustrated in Fig 2. The themes underwent a thorough refinement process, validated against the included articles to ensure they accurately reflect the most significant and frequently reported health consequences of armed conflicts. The summary of principal findings is summarized in Table 3.

Figure 2: Public Health Consequences of Armed Conflict

Table 3: Summary of Principal Findings

Findings	Articles
Health Effects	(Smeeth et al., 2023), (Haas & Ramirez, 2022), (Haque et al., 2022), (Zhang et al., 2023), (Rawers et al., 2024), (Dwanyen et al., 2024), (Rahman et al., 2024), (Kakaje et al., 2022), (Piotrowicz et al., 2022), (Fisseha et al., 2023), (Arage et al., 2023)
Healthcare Infrastructure and Services	(Haque et al., 2022), (Zhang et al., 2023), (Piotrowicz et al., 2022), (Rahman et al., 2024), (Fisseha et al., 2023), (Kassaye et al., 2023), (Arage et al., 2023)
Food Security and Malnutrition	(Belew et al., 2023), (Goliaei et al., 2023), (Rudolfsen et al., 2024), (Fisseha et al., 2023), (Arage et al., 2023), (Béné et al., 2024)
Environmental Health Effects	(Haque et al., 2022), (Zhang et al., 2023), (Malytska et al., 2024), (Arage et al., 2023), (Béné et al., 2024)
Humanitarian Crisis and Displacement	(Haque et al., 2022), (Rawers et al., 2024), (Zhang et al., 2023), (Goliaei et al., 2023), (Rahman et al., 2024), (Arage et al., 2023)
Recovery and Resilience	(Tarabay & Golm, 2024), (Haas & Ramirez, 2022), (Rawers et al., 2024), (Dwanyen et al., 2024), (Kakaje et al., 2022), (Piotrowicz et al., 2022), (Boos et al., 2022), (Rzońca et al., 2024), (Arage et al., 2023), (Lushchak et al., 2024), (Ruhnke et al., 2024)

DISCUSSION

According to UCDP, numerous violent conflicts persist worldwide as of 2024, with catastrophic consequences (Conflict et al., 2023). The confrontation between Israel and Hamas in Gaza has escalated substantially since October 2023, leading to grave humanitarian catastrophes (Elfversson, 2021). The enduring confrontation between Russia and Ukraine continues to be one of the most prominent and lethal, resulting in extensive devastation and the loss of human lives. Afghanistan is currently facing ongoing hostilities with the Taliban, ISIS, and other rebel organizations, which are causing significant security and humanitarian issues (Davies, 2023).

The physical health consequences are extensive and grave, since multiple studies indicate a high prevalence of trauma-induced injuries such as gunshot wounds, shrapnel injuries, burns, and explosion injuries. These injuries frequently lead to enduring disability, persistent suffering and catastrophic mortality (Sidel & Levy, 2008). Limb amputations and traumatic brain injuries are most commonly reported injuries and physical disability (Bendavid et al., 2021). According to Al Jazeera news reports, at least 37,266 people have been killed and 85,102 wounded in Israel's war on Gaza in 6 months (Abudayya et al., 2023). In Gaza, a total of 148 UN personnel and non-governmental organization staff have been killed, and 134 United Nations Relief and Works Agency for Palestine Refugees in the Near East (UNRWA) facilities have been damaged (UNHCR, 2023). This data only takes into consideration reported deaths, bodies, and injuries, however, the data could be lacking the actual figure due to underreporting or unrecovered bodies buried amid a catastrophic event.

The sustained injuries and disabilities are further complicated by disruption of healthcare services due to damaged infrastructure and injured healthcare personnel. Conflict inflicts damage on healthcare facilities, interrupts medical supply chains, and results in the destruction of medical equipment and all related infrastructure. According to the BBC's report, the ongoing crisis in Gaza has resulted in the unfortunate loss of 37,000 lives in the Palestinian War. Over 83,000 individuals have sustained injuries. To worsen the condition, the destruction of all 25 hospitals left the injured untreated, leading to their eventual death. In Tigray, Ethiopia reported that the region has been under a de facto blockade and siege, preventing the entry of medications, medical equipment, and humanitarian aid (Gesesew et al., 2021). This situation becomes a bottleneck in delivering the necessary health services and hampers the healthcare workers from providing medical services to sufferers.

The interruption in healthcare service worsens public health crises, particularly infectious disease transmission. The deterioration of sanitation and healthcare systems resulted in higher rates of cholera and AIDS in conflict-affected communities. Various infectious diseases occur, including AIDS, Hepatitis B, Tuberculosis, Cholera, in regions affected by conflicts in Europe, the Middle East, Asia, and Africa (Marou et al., 2024). Factors that contribute to disease emergence and transmission in conflict situations include population displacement, destruction of vital infrastructure, reduced healthcare systems and personnel, disruption of disease control programs (e.g., reduced surveillance, diagnostic delays, and interrupted vaccinations), limited access to healthcare providers, and increased population vulnerability (Malek & Okhuysen, 2022). Conflict-affected countries require disease-specific interventions to educate populations, improve healthcare infrastructure, and provide necessary medical services. Such interventions include healthcare system investments, mobile clinics, telemedicine, and primary and emergency care gaps. To avoid vaccine-preventable disease outbreaks, especially in displaced and vulnerable communities, intensify immunization campaigns. Mobilizing resources, implementing sustainable public health policies, and building resilience in war-torn areas require political commitment and interagency engagement.

Managing the long-term health effects of violent wars requires a multi-sectoral approach combining governments, humanitarian agencies, and local organizations (Babakura et al., 2021).

Armed conflicts force millions of people to flee their homes, seeking safety and refuge in neighboring countries or within their borders. Israel's military operations in Gaza have forcibly displaced 1.9 million civilians, or an astounding 85% of Gaza's total population (UNHCR, 2023). Displaced populations face numerous health challenges, including overcrowded living conditions, inadequate sanitation, and limited access to healthcare, increasing their vulnerability to infectious diseases and malnutrition (Forces et al., 2024). Within displaced populations, specific demographic groups like women, children, the elderly, and those with disabilities encounter increased vulnerabilities and distinct health obstacles (United Nations High Commissioner for Refugees, 2023). UNICEF is collaborating with partners to build sanitary facilities to address the declining sanitation services for internally displaced individuals residing in overcrowded shelters (Response & Status, 2024). It is crucial for humanitarian efforts to prioritize their efforts, in particular women, children, the elderly, and individuals with disabilities (United Nations High Commissioner for Refugees, 2023).

The psychological and emotional consequences of armed conflict are significant, with a high incidence of mental health illnesses such as PTSD, depression, anxiety, and acute stress reactions among combat populations. Civilians, soldiers, healthcare workers, as well as humanitarian workers are subject to high levels of violence and trauma, which greatly increase the likelihood of developing mental health problems. Research repeatedly indicates that individuals residing in areas of conflict frequently suffer from high prevalence rates of post-traumatic stress disorder, primarily due to their exposure to traumatic incidents such as bombings, shootings, and the bereavement of close relatives (Carpiniello, 2023). The disturbance of everyday existence, the deprivation of means of subsistence, and the collapse of social frameworks contribute to a widespread feeling of hopelessness and desolation. Internally displaced individuals (IDPs) and refugees are particularly vulnerable to harm, as the emotional distress resulting from forced displacement exacerbates the challenges, they already encounter due to violence (Alemi et al., 2023).

Social support networks and coping techniques are essential in mitigating the mental health impact of armed conflict, given the significant psychological suffering experienced. Communities and individuals employ diverse coping mechanisms, such as seeking assistance from relatives and acquaintances, practicing religious or spiritual rituals, and participating in communal events (Schwarzer, 2024). Mobile psychiatric units and community-based support groups have demonstrated the potential to deliver essential mental health care in areas affected by war. These initiatives can assist in addressing the disparity in mental health treatment by providing accessible and culturally sensitive care. The involvement of international organizations and non-governmental organizations (NGOs) is critical in the execution and support of these mental health efforts. However, it is vital to have consistent funding and lasting dedication to achieve their desired outcomes.

Warfare poses significant environmental health risks, resulting in water contamination, the destruction of agricultural land, soil degradation, and air pollution from explosives. Aerial bombing exacerbates these effects by damaging trees, disrupting soil, and decimating wildlife populations, leading to further air and water contamination. These environmental hazards create long-term health risks for inhabitants, such as poisoning and respiratory diseases, while post-war restoration efforts are often limited and insufficient. According to Solokha et al. (2023), the occurrence of metals in soil profiles is heightened by armed conflict. Certini et al. (2013) found that hazardous elements such as Cd, Cu, Ni, Pb, and Fe in war metal and non-metal debris led

to soil degradation. Furthermore, military activities had an impact on dams, water wells, and water reservoirs (Schillinger et al., 2020). An important aspect of the environment that is affected during war is air pollution. The use of various military weapons and explosive material increases greenhouse gases. Significant air pollution was seen during the Russia-Ukraine War (Tollefson, 2022), leading to an increase in greenhouse gas emissions in the atmosphere. (Kicaj et al., 2023). In situations where conflicts arise, establishing no-fight zones can effectively protect the delicate environment.

There is a widespread issue of insufficient access to food and inadequate nutrition because of interrupted agricultural output and supply networks. Conflicts disrupt food production and supply lines, destroy means of livelihood, and inflict food deficit, price hikes, and acute malnutrition. Consequently, in numerous cases, conflict-affected populations of vulnerable groups are at higher risk of malnutrition (United Nations High Commissioner for Refugees, 2023). Conflict disrupts economies, affecting numerous people with poverty, unemployment, and loss of livelihoods. The 2022 global report on food crises revealed that 140 million individuals in Africa were experiencing severe food insecurity, while in the 2023 report, it was highlighted that over 22.6 million Ethiopians require food assistance due to drought, conflict, and rising food prices (Figures, 2024). Rapid distribution of emergency food assistance through strategic provisions and quick response teams to ensure immediate access. Supplementary feeding programs that specifically focus on vulnerable populations, such as children, pregnant women, and the elderly, play a crucial role in preventing acute malnutrition. The World Food Programme (WFP), which is affiliated with the United Nations, reported that 1.1 million individuals are experiencing cataclysmic levels of starvation. The organization requires US$341 million to fund its operations until the end of 2024 (Food and Agriculture Organization, 2024). UNICEF is collaborating with UNRWA in Gaza to provide safe drinking water to displaced families, treatment for critically malnourished children, medical supplies and vaccines for children in hospitals and shelters, and other life-saving items. Ready-to-use therapeutic food (RUTF) can assist malnourished children in regaining strength and recovering from malnutrition (Response & Status, 2024).

Chronic health conditions and social disruptions, along with disabilities, continue to affect populations for years or even generations after conflicts end. Therefore, efforts to rebuild health systems and address ongoing health needs must be long-term (Haas & Ramirez, 2022). Armed conflicts result in significant and long-lasting health effects that extend beyond the immediate generation directly affected by violence. The transmission of trauma between generations is an intriguing problem, as the offspring of individuals who have experienced violence often acquire psychological and emotional wounds (Tarabay & Golm, 2024). Furthermore, the persistent consequences of violence frequently hinder their parents' capacity to provide stable and prosperous conditions, exposing these children to socio-economic inequalities.

Therefore, recovery and resilience following armed conflicts necessitate a multi-sectoral approach to reconstruct healthcare systems, reinstate essential services, and guarantee long-term stability. Efforts should prioritize rebuilding healthcare infrastructure, strengthening public health systems, and integrating mental health and psychosocial support to effectively address trauma in affected populations. Programs for economic empowerment, educational initiatives, and social protection policies are crucial for enhancing community resilience. Additionally, effective governance and international collaboration support sustainable recovery. Investment in disease surveillance, access to clean water, and advancements in digital health are essential for preventing secondary crises and fortifying health systems against future

challenges. These interventions restore stability, improve health outcomes, and enhance the resilience of conflict-affected communities, thereby reducing their vulnerability to future crises.

Strength

The comprehensive scope of this study encompasses a broad range of research methodologies and geographic settings, allowing for a deeper understanding of the diverse health effects of armed conflicts. Incorporating contemporary research on environmental health hazards and food scarcity provides up-to-date insights and aids in propagating actions and interventions. Furthermore, the study places strong emphasis on continuous engagement and assistance, underscoring the critical importance of ongoing international involvement and support.

Limitation

Conflict settings pose significant challenges to data quality, with chaotic environments, security risks, and population displacement posing potential inaccuracies and incomplete datasets. Besides, the systematic review primarily synthesized English-language articles, which could potentially exclude valuable research from non-English-speaking regions, thereby reducing the reliability and validity of the studies. Longitudinal research is also lacking, which is crucial for understanding the long-term impacts of armed conflicts. Current research mostly provides snapshots of health impacts at specific points in time, lacking the continuity to observe how health outcomes evolve. Longitudinal studies help capture chronic health conditions and the cumulative effects of repeated trauma, enabling the development of comprehensive public health strategies.

CONCLUSION

This systematic review highlights the extensive and multifaceted public health impacts of armed conflicts, encompassing direct health effects, crises and displacement, healthcare access and delivery, food security and malnutrition, environmental health risks, and long-term health consequences and resilience. It emphasizes the importance of robust mental health support frameworks, enhanced healthcare access, and integrated recovery strategies that consider social, cultural, political, and environmental factors. Moving forward, future research should focus on expanding geographic representation of armed conflicts including non-English studies. Studies using mixed method approach and longitudinal data collection will provide a more comprehensive understanding of the public health impacts of armed conflicts and inform effective policy and practice.

Recommendation

The systematic review recommends establishing a comprehensive framework for mental health care to effectively address the needs of populations affected by traumatic events or recurring disasters. This framework should include a methodical process for identifying previous traumatic experiences and PTSD, actively providing mental health services with a focus on vulnerable populations such as children and families and creating trauma-sensitive counselling protocols. It is crucial to establish psychosocial support programs to promote resilience and provide training for local professionals to assess the health impacts of past disasters. Enhancing communication and collaboration among governments, NGOs, and communities, as well as creating channels for sharing information and community involvement, is critical. Holistic healing programs must consider historical trauma and incorporate social, cultural, political, and environmental factors. Ultimately, supportive public policies and consistent funding are vital for the sustained operation and effectiveness of mental health services. Addressing food security

in conflict zones involves a multifaceted approach, including rapid emergency food aid distribution, support for local food production, and the implementation of supplementary feeding and nutrition education programs. Establishing a pooled funding system would streamline resource collection and allocation, enhance resource management, and ensure equitable and strategic distribution of aid. This would address the challenges associated with currently collecting funds independently.

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REVIEW ARTICLE Open Access

Importance of Hazard Analysis Critical Control Points (HACCP): A Review

Mohd Fazeli Sazali[1,2*]

Abstract

Hazard Analysis and Critical Control Points (HACCP) is one of the essential public health interventions to ensure food safety and quality. HACCP has significantly improved public health by reducing the incidence of foodborne illnesses through systematic identification and control of food safety hazards. Economically, it enhances trade opportunities by aligning with international food safety standards, ensuring that food products meet stringent market requirements, and fostering global consumer trust. Industries' role in adhering to the requirements assures the consumers, which subsequently helps to protect public health and the economy. Increasing awareness of the importance of the HACCP is vital to ensure adherence to the HACCP standards. Therefore, this article aims to describe the importance of HACCP. Infectious agent ability; host vulnerability; public awareness; behaviour; methodological advancement; environmental contamination; urbanization and industrialization; and the impact of globalization are among the importance of the HACCP. Adherence to HACCP is indispensable and should be adopted by every level of the food industry to enhance food safety and quality for the public.

Keywords: Hazard Analysis Critical Control Points; HACCP; food safety; food quality.

*Correspondence Email: drmohdfazeli@moh.gov.my

[1] *Communicable Disease Control Unit, Public Health Section, Pahang State Health Department, Jalan IM 4, Bandar Indera Mahkota, 25582 Kuantan, Pahang, Malaysia*

[2] *Department of Public Health Medicine, Faculty Medicine and Health Sciences, Universiti Malaysia Sabah, Jalan UMS, 88400 Kota Kinabalu, Sabah, Malaysia*

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INTRODUCTION

HACCP (Hazard Analysis Critical Control Points) is a standard and globally recognized food safety assurance method to identify and manage food safety-related risks. In other words, HACCP is a management system where food safety is addressed by identifying food safety hazards. Subsequently, it will be analyzed and controlled from raw material production, procurement, and handling, to manufacturing, distribution, and delivery of the finished food product to the consumer. HACCP ensures the accountability of industries to adhere to requirements to ensure public health and protect economic consequences from food contamination from biological, chemical, and physical contaminants. In various countries, including Malaysia, food manufacturers must be certified for food safety assurance programs; one of the programs includes HACCP (Bahagian Keselamatan dan Kualiti Makanan, n.d.).

HACCP has become the cornerstone of modern food safety management systems worldwide. Its adoption is mandatory in many countries for food production and processing, ensuring compliance with international trade regulations and protecting public health (Domenech et al., 2013; Osimani et al., 2013). For instance, HACCP is integral to food safety regulations in the European Union, the United States, and other high-income nations (Williams et al., 2020; Hunter, 2016). Developing countries also implement HACCP to enhance their export capabilities, ensuring their products meet stringent global standards. Moreover, HACCP aligns with international food safety guidelines, such as the Codex Alimentarius, reinforcing its universal applicability and effectiveness in mitigating risks associated with biological, chemical, and physical food contaminants. Its preventive framework not only safeguards public health but also fosters consumer confidence and economic growth through safer and higher-quality food products.

Since the dawn of history, food safety has been considered one of the significant public health issues. There was much past evidence that there are rules and recommendations related to protecting health impact arising from foodborne disease or food adulteration. Understanding the importance of food safety assurance programs, especially HACCP, is vital so that the food industries, public health officials, and community can take appropriate action to ensure food safety to prevent harmful health, social, and economic consequences. Despite the proven effectiveness of HACCP in ensuring food safety, there is limited understanding from various stakeholders which leads to barriers to HACCP protocols, particularly in low- and middle-income countries (Woh et al., 2016). Therefore, in addressing the issue, this article aims to describe the importance of HACCP. By shedding light on the importance of HACCP, this article can serve as an essential resource for multiple stakeholders, including food manufacturers, public health officials, policymakers, and consumers.

Infectious Agent Ability

Exposure to various biological agents in food can be potentially infectious, toxic, and even cancerous to humans. The common biological agents that cause food borne diseases include bacteria (*Bacillus cereus*, *Campylobacter jejuni*, *Clostridium botulinum*, Clostridium perfringens, *Cronobacter sakazakii*, *Escherichia coli*, *Listeria monocytogenes*, Salmonella spp., *Shigella spp*., *Staphylococcus aureus*, *Vibrio spp*. and *Yersinia enterocolitica*), viruses (Hepatitis A and Noroviruses) and parasites (*Cyclospora cayetanensis*, *Toxoplasma gondii*, and *Trichinella spiralis*) (Bintsis, 2017). *Bacillus cereus* group, for example, can survive various stressful environmental conditions such as heat, ultraviolet, acid, and desiccation. Meanwhile,

salmonella can survive in hardy conditions, including dry environments and water, for several months (World Health Organization, n.d.; Knodler & Elfenbein, 2019).

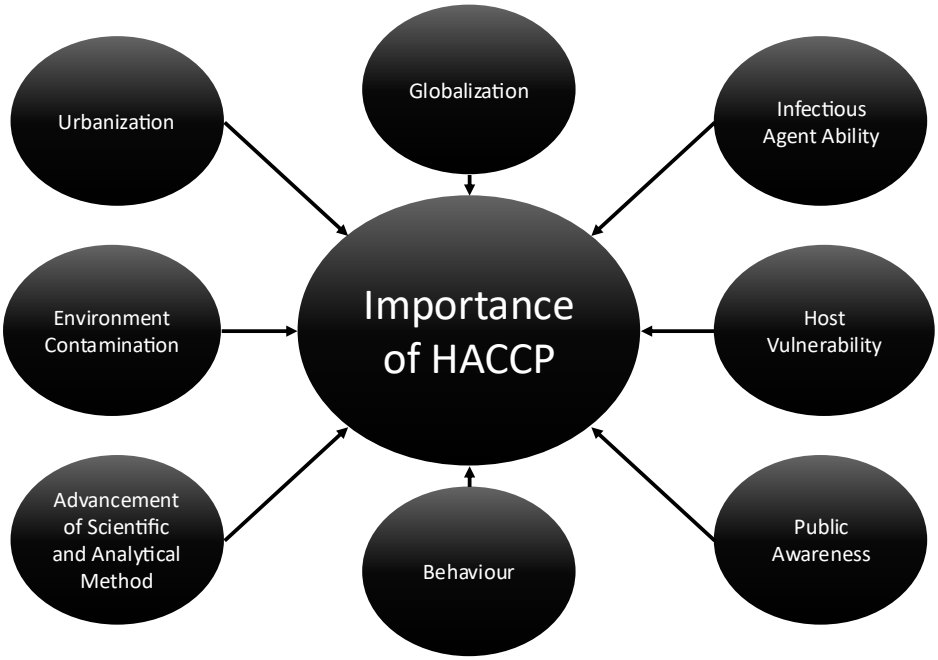

Figure 1: Importance of HACCP

The unique feature of these organisms makes the human susceptible to infection. It causes severe, life-threatening illnesses if the host has low immunity, such as in children and the elderly. World Health Organization (WHO) estimated that almost one out of ten people were ill after eating contaminated food, with more than 400,000 deaths annually (World Health Organization, n.d.). Most pathogens can cause gastrointestinal, neurological, gynaecological, and immunological problems. For example, acute gastroenteritis disproportionately affects children and is among the most common cause of death in children aged five years and below (World Health Organization, n.d.). In addition, people with low social status are more vulnerable to foodborne disease and its impact (Godinez-Oviedo et al., 2020). The emergence and spread of antimicrobial resistance in salmonella and campylobacter serotypes have also become a global public health concern (Marchello et al., 2019; Thomas et al., 2020). These pathogens were ubiquitous in food, animals, and meat (World Health Organization, n.d.), which potentially could be consumed by humans and cause infection.

HACCP serves as a crucial framework for preventing infectious disease risks posed by biological agents in food by systematically identifying, evaluating, and controlling potential hazards throughout the food production process. This proactive system operates by targeting critical control points (CCPs) where contamination risks are most likely to occur, such as during food processing, storage, or transportation. By implementing monitoring and corrective actions at these points, HACCP ensures that foodborne pathogens like Salmonella spp., Escherichia coli, Listeria monocytogenes, and others are effectively controlled before reaching consumers.

For example, temperature controls in CCPs can inhibit the growth of bacteria like Clostridium botulinum, which thrives in anaerobic conditions, while robust cleaning and sanitization practices can reduce the presence of pathogens such as Staphylococcus aureus and Campylobacter jejuni. HACCP also emphasizes the early detection of contamination risks

through regular inspections, microbial testing, and employee training. These measures are particularly important for addressing the unique survivability and resilience of pathogens such as Bacillus cereus and Salmonella, which can persist under extreme conditions.

Host Vulnerability

Most foodborne disease cases cause mild illnesses in humans. However, it can cause severe illness, significant morbidity, and mortality if individuals with the immunocompromised condition are affected. The population such as children, the elderly, immunocompromised states such as diabetes mellitus, people living with HIV, and long-course steroid medication use are vulnerable to severe infection from foodborne illness. According to WHO, the prevalence of HIV-infected people is increasing in trend. There were 37.7 million people estimated to be living with HIV by the end of 2020, with around 680,000 people dying from HIV-related causes (Frydrych et al., 2018). Meanwhile, individuals with uncontrolled diabetes mellitus are physiologically frail and at increased risk of infection and mortality due to sepsis. This condition is believed to be caused by immune system dysfunction triggered by chronic low-grade inflammation (Farouhi & Wareham, 2019). Globally, the prevalence of diabetes is increasing in trend. The number of people with diabetes was estimated to rise from 425 million in 2017 to 629 million by 2045 (Bahia & Suardi, 2019). The rising prevalence of diabetes was fueled by the increasing prevalence of obesity and changing lifestyles such as unhealthy diets and physical inactivity. The impact of globalization also fueled the excessive intake of fat, sugar, and salt, leading to the rising prevalence of diabetes and other associated health conditions.

HACCP is therefore vital in safeguarding vulnerable populations, such as children, the elderly, and individuals with immunocompromising conditions like diabetes and HIV. These groups are at heightened risk of severe outcomes from foodborne illnesses, including life-threatening complications such as sepsis, prolonged hospitalizations, and increased mortality. HACCP's preventive measures address these risks by implementing a structured and proactive system to control foodborne hazards at critical points throughout the food production and distribution process. For example, HACCP protocols ensure strict temperature controls to inhibit bacterial growth, proper handling and processing to avoid cross-contamination, and regular microbial testing to detect potential hazards early. For vulnerable populations, these measures provide a critical layer of protection, as their immune systems are less capable of fighting infections that might be mild in healthy individuals.

Following HACCP standards also ensures consistent monitoring and corrective actions to maintain food safety at every stage, from raw material procurement to consumer delivery. This systematic approach minimizes the risk of foodborne disease outbreaks, which disproportionately affect high-risk groups. Moreover, HACCP fosters accountability within the food industry, ensuring compliance with food safety regulations that protect vulnerable populations.

As the global prevalence of diabetes, HIV, and various comorbidity continues to rise, the implementation and adherence to HACCP become increasingly critical in reducing the burden of foodborne illnesses among these high-risk populations. By prioritizing food safety, HACCP not only protects public health but also reduces healthcare costs and improves the quality of life for the most vulnerable in society.

Public Awareness

Increased access to health information contributes to increased consumer awareness of food safety. Recently, public health officials often used social media and mainstream electronic media to reach various consumer backgrounds to enable every layer of society to access the needed health information. According to Global System for Mobile Communication Association (GSMA), almost half of the world's population are connected to the internet, which mainly contributes to the increased affordability of owning a mobile phone and increased internet access (Gedikoğlu & Gedikoğlu, 2021). High accessibility to mobile phones and internet access provides an opportunity for public health officials to utilize the medium to increase the reachability of food safety information to the public.

Increasing awareness about food safety is vital to enable the community to take action to prevent food-related illnesses. Community is encouraged to protect themselves from foodborne disease by practising self-hygiene, appropriately handling raw and ready-to-eat food, looking for food labelling before buying, and avoiding unhygienic food stalls. Consumer awareness regarding food safety allows the bottom-up approach to advocating the policy maker to improve their confidence about food safety through accreditation activities such as HACCP. A study conducted in the United States (US) found that 50% of its respondents (N=1,016) were willing to pay a premium price for HACCP-certified products (Hossain et al., 2023). Another study in Bangladesh indicates that the consumers are willing to pay a premium of 24.62% more for HACCP-certified frozen major carps (Rane, 2011). The findings show that HACCP certification significantly impacts consumer preferences and behavior by enhancing their confidence in food safety, encouraging informed purchasing decisions, and demonstrating a willingness to pay premium prices for HACCP-certified products, reflecting the growing value placed on food safety assurance.

The public's awareness and desire could drive the policy maker and food manufacturer to adhere to international standards for food safety. World Food Safety Day that is celebrated annually on 7th June can used as a medium for every stakeholder raising awareness regarding food safety that eventually can lead to better cooperation by the industries to adhere to the HACCP standards.

People’s Behavior

In today’s fast-paced world, many consumers rely heavily on external food sources, such as restaurants, food delivery services, and ready-to-eat meals, due to their busy schedules. This reliance heightens the risk of exposure to foodborne illnesses, as these food sources often involve complex supply chains and multiple handling stages where contamination can occur. A previous study found that food stalls are the source of food safety issues involve microorganisms belonging to genus Bacillus, Staphylococcus, Clostridium, Vibrio, Campylobacter, Listeria, and Salmonella (Law et al., 2014). The implementation of HACCP in such contexts is crucial to ensure that these external food sources adhere to rigorous food safety standards, minimizing the risk of biological, chemical, or physical contamination. By establishing critical control points across food preparation and distribution processes, HACCP ensures that food consumed by busy individuals remains safe, enabling them to trust the food industry with their health while maintaining their fast-paced lifestyles. In countries that have a robust HACCP certification program, its implementation has shown evidence of improvement in public health outcomes. In the United States, the implementation of HACCP in the meat, poultry, and seafood industries under the oversight of the USDA and FDA has contributed to a

reduction in foodborne illnesses caused by pathogens like Salmonella and Listeria (Williams et al., 2020).

Advancement of Scientific and Analytical Method

The availability of rapid detection tools to detect various food contaminants through the advancement of scientific and analytical methods emphasized the importance of HACCP in ensuring food safety. Rapid detection tools applied several methods in detection of food contaminants, including nucleic-acid based (i.e., simple polymerase chain reaction [PCR], multiplex PCR, real-time PCR, nucleic acid sequence-based amplification [NASBA], loop-mediated isothermal amplification (LAMP) and oligonucleotide DNA microarray), biosensor method (i.e., optical, electrochemical, and mass-based biosensors), and immunological-based method (i.e., enzyme-linked immunosorbent assay [ELISA] and lateral flow immunoassay) (Rather et al., 2017). The rapid detection tool helps prevent foodborne illness as it generally has high sensitivity and specificity, is cost efficient, saves time, reduces labour needs, and is more reliable than the conventional method. These rapid detection tools allow for the early identification of contaminants in food, thus providing information for policymakers and the public regarding food safety. Information regarding food contaminants emphasized the importance of food safety accreditation programs such as HACCP so that manufacturers are made accountable for the food manufacturing process to protect public health.

The integration of rapid detection tools strengthens HACCP by enabling the early identification of potential hazards at critical control points in the food production process. These methods provide high accuracy and quick results, allowing food manufacturers to act promptly to prevent contaminated products from reaching consumers. Additionally, these tools help food manufacturers maintain accountability, as the data generated can be used to demonstrate compliance with HACCP standards. For policymakers, the availability of precise information about food contaminants supports better decision-making and enforcement of food safety regulations. For the public, it increases trust in food safety systems, ensuring that HACCP-certified products meet stringent safety standards and protect public health effectively.

Environmental Contamination

Food contamination from the environment could occur due to natural phenomena or be introduced artificially by human activities. Many points in food manufacturing, from the processing of harvesting raw materials, processing, packaging, transportation, and storage, could be potentially at risk of contamination by biological, physical, and chemical contaminants (Wigley et al., 2005). Naturally occurring contamination in food can occur in several mechanisms, such as:

(i) some bacteria, viruses, and parasites have naturally inhabited the surface of foods;
(ii) raw food materials also can be contaminated by surrounding conditions such as sewage, soil, water, and animals that might be carrying the pathogenic organism;
(iii) the food materials originated from diseased animals; or
(iv) food materials also can be contaminated by chemicals that were accidentally consumed by the animal or plants.

Meanwhile, food contamination also can occur during food production, processing, packaging, delivery, and storage phases. In the production phase, the activity includes growing the plants to be harvested or raising the animal for future consumption. In the production phase, one example of food contamination is that Salmonella enterica serovar Pullorum can infect an

egg's yolk from an infected hen's reproductive organ (OECD, n.d.). During food processing, for example, animal slaughtering or cutting into pieces before the packaging, contaminants can enter the food materials. Subsequently, during the packaging, contaminants can enter the food product by a foreign object (i.e., glass, wood, stones, metal, etc.), chemical contamination from the packaging itself, or biological contamination due to improper packaging practices.

Furthermore, the food product can be contaminated during transportation because of prolonged exposure to suboptimal temperatures for food storage in the loading docks. Therefore, HACCP is required to identify critical points for controlling any identified hazard systematically. In addition, the rapid development of economic activities may also involve the innovation of new food products, which further emphasizes the importance of food safety accreditation activity.

Urbanization and Industrialization

Urbanization has become a global phenomenon in the 21st century. Urbanization has predominantly risen because of economic interest, leading to increased migration, the growth of new urban areas and the extension of urban administrative boundaries. Some people tend to move from one location to another due to pull and push factors. Urbanization occurs when there is an increasing proportion of population in certain areas, leading to a large number of people becoming concentrated in a relatively small area, forming a city (Abdullah et al., 2012). Urbanization can be an issue contributing to food safety. Urbanization can result in soil, air, and water pollution from waste and emissions from residential areas, industries, and vehicles.

A study in Klang Valley, Malaysia, one of the urban areas in Malaysia, found that the metropolitan area has severe acidified rain with the highest number of unhealthy days of air quality level (Hossain et al., 2015). The increased concentration of ground ozone level, particulate matter and various air pollutants could contaminate the soil and water and subsequently contaminate the feeding area for livestock and plants for human consumption. Another study in Gebeng Industrial City, Pahang, Malaysia, shows high mean concentrations of arsenic, barium, cadmium, copper, mercury, nickel, lead, and zinc in industrialized soils (Onakpa et al., 2018). The soil and water pollution, as well as the usage of pesticides in the urban and industrialized area, are most likely to cause heavy metal contamination to food crops and is associated with an adverse health outcome, such as cancer (FAO, 2024). Furthermore, urbanization can result in higher food demand to meet increasing population density. Protection of food safety through HACCP can potentially help prevent contamination of heavy metals and other contaminants into food products for urban inhabitants' consumption. Additionally, with urbanization comes the rise of food delivery services, which introduce risks related to improper handling, temperature abuse, and microbial growth during transportation. HACCP implementation in urban food service providers helps monitor and maintain the cold chain, ensures proper packaging, and reduces risks of contamination, ensuring the safety of ready-to-eat meals delivered to urban dwellers.

Integration of food safety measures into the design and management of urban environments could ensure sustainable and safe living conditions for growing urban populations. For example, urban farming initiatives are becoming a popular solution for increasing local food production in cities. HACCP can be applied to identify and control risks such as soil contamination, water quality issues, and improper use of fertilizers and pesticides (Hannan et al., 2022). This ensures that food produced in urban areas is safe for consumption and aligns with public health goals.

Globalization

Globalization is a process of interaction and integration related to social, cultural, and economic aspects. Globalization has accelerated economic growth, partly due to advancements in transportation and communication technology. The development of a new city stimulates the migration of people, contributing to the increasing population. High population density subsequently contributes to the growing food demand. To meet the rising food demand requires large-scale food production and process and will be distributed over greater distances. Expansion of food trading has increased the chance of unsafe food produced in one country and affects consumers in other countries.

Furthermore, the high volume of imported foods, as well as the diversified origin and growing complexities of technology used, the traditional method of monitoring food safety might no longer be adequate. Without a standardised form of overseeing trading partners' production process, it is pretty impossible for authorities in charge of food safety to adequately address the issue and protect the consumer in the country. Implementing a food assurance program such as HACCP that is universally recognized and accepted food assurance could potentially ensure that imported food is safe for consumption in the receiving countries.

The United States mandates HACCP compliance for seafood imports under FDA regulations. Countries like Vietnam and Thailand, major seafood exporters, implemented HACCP systems in their processing plants to meet U.S. safety standards, resulting in increased market access and reduced rejection rates of their exports. A study showed that Thailand's adoption of HACCP for shrimp processing improved product quality and helped maintain its position as a leading exporter to the U.S. and European Union (Hannan et al., 2022). In addition, the European Union (EU) requires all imported dairy products to comply with HACCP standards. Countries such as New Zealand, known for its robust HACCP implementation in dairy production, successfully export high volumes of dairy products to the EU without significant regulatory barriers (Fonterra, n.d).

CONCLUSION

The HACCP is an effective method for food safety assurance. Its implementation effectively prevents harmful social, health, and economic consequences. Implementation of HACCP through targeted control of significant food risks, the industry can assure its customers that its food products are safe based on the scientific method. Furthermore, reduction of food risk also can enhance public health protection. The increasing trend of food and waterborne disease, drug-resistant infection, ageing population and non-communicable disease, changing consumption patterns, advancements in scientific and analytical methods, environmental contamination, urbanization, and globalization emphasized that HACCP is indispensable and should be adopted by every food industry.

Conflicts of Interest

The author would like to declare that there is no conflict of interest.

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REVIEW ARTICLE Open Access

Telehealth Utilization Among The Older Adults During Covid-19 Pandemic: A Scoping Review

Nur Adilah Zainal[1], Noor Fadzilah Zulkifli[1*]

Abstract

The COVID-19 pandemic has global impact, especially to vulnerable populations such as older adults. This population may be affected with health issues in which telehealth appears to be a potential platform to improve their quality of life. The study aimed to review current literature on the benefits of telehealth among older adults during COVID-19 pandemic. The review emulates the five-phase framework of scoping reviews by Arksey and O'Malley, using three databases: MEDLINE, Scopus, and EBSCOhost. The MeSH term used were (("older adults" OR "elderly" OR "geriatric" OR "aged people") AND ("COVID-19" OR "COVID-19 pandemic)) AND ("telehealth " OR "telemedicine" OR "virtual consultation" OR " teleconsultation" OR "telecare"). A total of 390 articles were screened, of which 21 full-text articles were included. The papers were of systematic or scoping reviews (n=4), cross-sectional studies (n=6), longitudinal cohort studies (n=3), case reports (n=1), randomized control trials (n=1), qualitative studies (n=5) and 1 mixed method study. This review enlightened the role and benefits of telehealth services among the older adults in personal, psychosocial and environmental aspects. The barriers include their physical, cognitive and technical issues which limit telehealth utilization. Thus, recommendations were structured to enhance the efficiency in terms of technologically enabled aspects, patient-related factors, and provider-related factors. A rapid scale-up of telehealth services is significant for the provision of healthcare services among older adults. The accessibility of telehealth must be prioritized for older patients, their caregivers and health care provider to improve the quality of healthcare during the COVID-19 pandemic and beyond.

Keywords: Telehealth, Older adults, COVID-19

*Correspondence Email: nfadzilahz@usim.edu.my

[1]*Faculty of Medicine and Health Sciences, Universiti Sains Islam Malaysia, Bandar Baru Nilai, 71800, Nilai, Negeri Sembilan, Malaysia.*

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INTRODUCTION

The COVID-19 pandemic declared by WHO in March 2020 has shifted into an endemic phase (Biancolella et al., 2022; Cucinotta & Vanelli, 2020). This transition is contributed by vaccinations which provide protection and herd immunity to the community. The older adults was among the vulnerable populations who are likely to experience the biggest consequences (Martins Van Jaarsveld, 2020). WHO defines the older adults population as people aged 60 years and above (WHO, 2022). This population is more prone to get infections as their immune response is weakened. They usually have more comorbidities and hospitalizations which increases their chances of contracting the COVID-19 (Banerjee, 2020b). This COVID-19 not only altered the routines of older people but, exacerbates their physical, psychological, and cognitive health (Colucci et al., 2022). The government policies such as lockdowns and social gathering restrictions which are important to reduce the transmission of COVID-19 to the ageing population, has negatively impacted their psychological status causing distress such as anxiety, depression, and loneliness (Sepúlveda-Loyola et al., 2020). It also increases their lack of access to information and health care services (Lebrasseur et al., n.d.). In particular, older adults people shield away from seeking medical attention out of fear of infection. Thus, remote medical services like telehealth were thereafter acknowledged as a crucial adjustment system to preserve the continuity of healthcare provision.

Telehealth has developed as a significant tool to manage the communicable and non-communicable diseases among older adults prior to the pandemic. The concept is to minimize person-to-person contact and provide a remote assessment and healthcare provision (Smith et al., 2020). Telehealth technologies include video conferencing, store-and-forward imaging, streaming media, and wireless connectivity (Buis, 2020; Infinit-O, 2018). While telemedicine and telecare are subsets of telehealth which involves the use of electronic telecommunications technology or sensors and wearable devices. These interventions are also a form of healthcare services provided to people who are physically less capable for an in-person visit (Infinit-O, 2018). During the pandemic, telehealth has enabled physicians to deliver consulting services that address the home health care needs of older adults patients, as well as effective pre-hospital screening for early COVID-19 symptoms and signs (Buis, 2020; Smith et al., 2020). The proportion of older persons who participated in telehealth visit increased dramatically from 4% in May 2019 to 30% in June 2020 (Buis, 2020). However, adopting telehealth services among the older adults is accompanied by great challenges. The most prominent concerns expressed by the older adults about telehealth services are the lack of quality of services provided compared to in-person care, lack of personal connection to the health care provider and privacy issues (Buis, 2020; Martins Van Jaarsveld, 2020). Most countries are also lacking in regulating, integrating, and compensating for the telehealth regulatory framework during outbreaks (Smith et al., 2020). In the absence of a structured telehealth strategy, it is critical to have telehealth guidelines available to aid the telehealth service coordination and delivery during an emergency occurrence.

Several systematic or scoping review reports only highlighted the telehealth impacts among the general population (Doraiswamy et al., 2020; Garfan et al., 2021; Monaghesh & Hajizadeh, 2020). There is only one scoping review conducted among geriatricians regarding the telehealth services during COVID-19 (Doraiswamy et al., 2021). However, it does not

explain the impact and benefits of telehealth services, the barriers and challenges among the older adults during COVID-19. Besides, little is known regarding the potential interventions and recommendations to improve the telehealth services among older adults during the pandemic. Thus, this study aimed to collect and synthesize the relevant evidence which provide structured key points to comprehend the importance and challenges of telehealth, and to maximize the utilization of this digital platform among this older population effectively. This information will provide appropriate insight for stakeholders, including patients, clinicians, healthcare providers, and funders for the improvement of telehealth services during emergency events such as this pandemic and in the future.

METHODS

The scoping review was conducted in accordance with the study protocol and framework outlined by Arksey and O'Malley (Hilary Arksey & Lisa O'Malley (2005). The reporting items using Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) were also referred to summarize the existing literature on telehealth among older adults during COVID-19.

The keywords utilized include (("older adults" OR "older adult" OR "geriatric" OR "aged people") AND ("COVID-19" OR "COVID-19 pandemic" OR "SARS-COV-2" OR "2019-nCov" OR "Coronavirus Disease 2019" OR "Severe Acute Respiratory Syndrome Coronavirus 2")) AND ("teleconsultation" OR "telemedicine" OR "virtual consultation" OR "telehealth" OR "telecare"). These terms were inserted in the three databases: MEDLINE, Scopus, and EBSCOhost which includes studies from January 1st, 2020 to May 31st, 2022. This scoping review aims to capture evidence about telehealth among the older adults during the COVID-19 pandemic. The inclusion criteria were reports published in English, addressing the outcomes such as the roles/benefits, barriers and recommendations for telehealth/ teleconsultation/telemedicine (any equivalent term) used among the older adults during the COVID-19 pandemic and papers that focused on general population older adults aged >60 years old during the COVID-19 pandemic. Papers were excluded if telehealth provided focused on specialized services (e.g., psychiatry), among the older adults of a specific group or clinicians addressing older adults. Only original studies published in full manuscripts were included. Full-text articles were obtained for those that fulfilled the inclusion criteria. Duplicates were excluded. All the articles were read carefully, and relevant information was extracted for analysis. Systematic or scoping reviews, cross-sectional studies, longitudinal cohort studies, case reports, randomized control trials and qualitative research were among the papers included. The selected studies were then analyzed using an adaptive thematic analysis, and relevant ideas were classified into descriptive themes. For each theme, a narrative description of the evidence was written; benefits, barriers and recommendations for telehealth among the older adults during the COVID-19 pandemic.

RESULTS

Based on the keywords in the databases, 390 papers were identified. A total of 84 papers were duplicates; thus, they were removed. Out of 306 selected papers, only 21 papers (6.9%) were included in the final analysis after three separate phases of screening for eligibility: title, abstract, and full text. Figure 1 depicts the flow diagram for the scoping review search strategy for telehealth among the older adults during the COVID-19 pandemic. The literature was grouped thematically after reading the full text and synthesizing significant evidence.

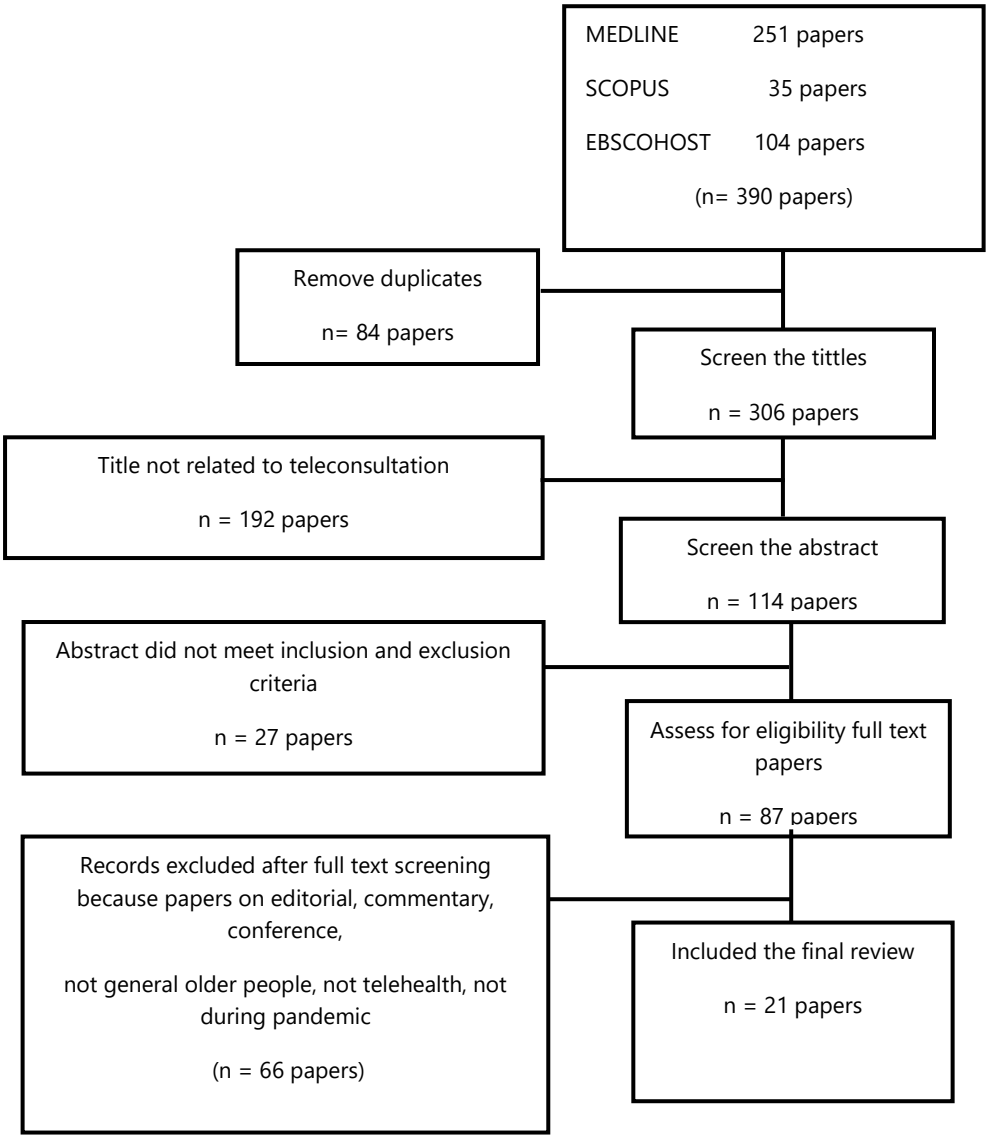

Figure 1: Flow diagram of search strategy for literature selection

Data Extraction and Synthesis

A total of 21 reports were included in this review (Table 1). The reports originate from 8 countries which are the United States (n=9), Canada (n=4), Korea (n=2), Ireland (n=2), the United Kingdom (n=1), Qatar (n=1), Singapore (n=1), and Israel (n=1). The papers include systematic or scoping reviews (n=4), cross-sectional studies (n=6), longitudinal cohort studies (n=3), case reports (n=1), randomized control trials (n=1), qualitative studies (n=5) and 1 mixed method study. Following the data analysis, three themes were identified: benefits, barriers and recommendations for the telehealth among older adults during the COVID-19 pandemic.

Table 3: Full Text Paper included

No	Author, year	Country	Research design	Study population, n	Objective	Result
1.	(Bartlett & Keir, 2019)	UK	Prospective cohort study	Geriatric patients at clinic	To study the effect of virtual consultation and PPE on the carbon footprint of a Geriatric Medicine clinic, in order to inform design of a service that addresses both the health of our patients and our environment.	**Environmental effect:** - Pre pandemic: The carbon footprint of a face-to-face clinic consultation is 4.82 kgCO2e, most of which is patient travel, followed by staff travel and use of PPE. - During pandemic: The footprint of a virtual consultation is 0.99kg CO2e, most of which is staff travel, followed by data use. - Using our hybrid model for a single session clinic reduced our annual carbon footprint by an estimated 200kg CO2e
2.	(Briones-Claudett et al., 2021)	Ecuador, South America	Case Report	72 y/o male, 82 y/o female and 58 y/o male patient who had confirmed COVID-19	To report the original results of the first three patients who were treated by the team using a telehealth home-based care approach during the COVID-19 pandemic in Guayas	**Social:** - Telehealth and home-based treatment serve great outcomes of the care of these severely ill patients living in a low-resource setting - collapsed health care system by preventing and identifying progressive deterioration in a timely manner in deprived settings.
3.	(Choi et al., 2022)	Texas, United States	Retrospective Longitudinal study	3961 participants aged 70+	To examine the association of telehealth participation during the COVID-19 outbreak with sociodemographic and health related characteristics, ICT device ownership, prior online experience, and technology instruction among older adults aged 70+	During COVID-19 outbreak, in person visits decreased by 31% ($p<.001$) and the telehealth used during outbreak increased to 21.1% ($p<.001$) The telehealth users are higher in patient with chronic medical conditions ($p<.001$), Instrumental activities of Daily Living (IADL) received help ($p<.002$), and mental health problem ($p<.009$) **Recommendation:** - Provide the technology-enabling factors (ICT devices ownership, online use experience, and learned to use the new technology program (Zoom or Facetime) to go online), moved in with someone or had others move in with them (AOR= 1.36, 95% CI= 1.04-1.76) can increase the efficiency of telehealth use among older adults during COVID-19
5.	(Senderovich & Wignarajah, 2022)	Ireland	Qualitative study	Geriatric patients	To explore the benefits and challenges to implement virtual care in day-to-day care for the geriatric patient during COVID-19 pandemic.	**Benefits:** - Reducing transmission - Better access to care for people lives in remote or suburban areas (specialist who may not be available in person) – prevent unnecessary transfer - Therapeutic alliance – communication (no need face mask), decrease level of stress

						Barriers: - Consent – risk unauthorized disclosure - Learning curves - - Cognitive Impairment - Technical challenges – inadequate internet connection, volunteers - Access to examination and diagnostic testing
6.	(Ng et al., 2022)	USA	Cross-sectional	Community-dwelling Medicare beneficiaries aged ≥ 65 years old and above	To examined factors associated with accessibility and utilization of tele-health among older adults during the COVID- 19 pandemic.	- Having more comorbidities was associated with a higher likelihood of using telehealth when offered [e.g., those with 2– 3 chronic conditions were 7.3% (CI = 2.5% to 12.1%) more likely to use telehealth than those with 0– 1 chronic condition] **Barriers:** - Those who reported having no access to the internet and no prior participation in video/voice calls/conferencing were 8.2% (CI = −12.8% to −3.7%) and 6.6% (CI = −9.2% to −4.1%) less likely to be offered telehealth services during COVID- 19
7.	(Murphy et al., 2020)	Ireland	Rapid systematic review	Nine studies with 975 patients met the inclusion criteria.	To describe the satisfaction, clinic productivity, clinical benefit, and costs associated with the virtual geriatric clinic model of care	**Seven of the nine studies reported on clinical benefit outcomes:** - cost effectiveness, - transport saving, - shortened waiting time - reduce acute hospitalization event, increased awareness and education about medication side effects, successfully used to implement a falls prevention programme) **Barriers:** - Technical difficulties - issues with confidentiality (perceiving that patients or caregiver were unable to speak openly), - communication issues (mainly hearing impairment)
8.	(Ho & Merchant, 2022)	Singapore	Cross sectional	42 Patients aged ≥60 years	To investigate perception and acceptability of digital technology among Asian older adults	- Most of the participants (n=38, 91%) agreed that technology is good - 79% (n=33) agreed that technology would allow them to be independent for longer. - Through digital HAPPY (Healthy Ageing Promotion Program for You), 45% (n=19) of participants reported feeling stronger, 48% (n=20) had improved spirits, and 40% (n=17) and 38% (n=16) had improved mood and memory, respectively
9.	(Haimi & Gesser-	Israel	Systematic Review	older adults population	To explore the availability, application, and	11 studies were finally included after reviewing the full text - for control and triage during the outbreak of the COVID-19 pandemic,

	Edelsburg, 2022)			(age 65 years and more)	implementation of telehealth services during the Covid-19 era, designed for the aged population (age 65 and more).	- for distance monitoring and treatment, - for follow-up online visits for patients residing in health centers - for the treatment and surveillance of chronic conditions
10.	(Doraiswamy et al., 2021)	Qatar	Scoping Review	older people over 65 years of age	to summarize learning from evidence synthesis for telehealth use in geriatric care	**Benefits:** - preventative, curative, and rehabilitative services but with a greater focus on curative services **Barriers:** - physical and cognitive limitations - inequity and the lack of standardization in the provision of age-friendly telehealth services. **Recommendations:** - Older People and Caregivers (training) - Physicians and Other Health Care Provider (get trained, provide resources) - Technology (accommodate IT) - Governance/Health Systems (educational outreach)
11.	(Schifeling et al., 2020)	United States	Cross sectional	190 Geriatric patients aged 75 years or older	To describe the rapid transition to telehealth (i.e., telephone and video visits) to meet the needs of geriatric primary care patients during the COVID-19 pandemic.	**Barriers:** - lack of equipment (54/100, 54%) - patient preference (32%, 32/100) - cognitive problems (23%, 23/100).
12.	(Mao et al., 2022)	United states	Cross Sectional	249 participants aged 60 years old and above	To better understand the barriers to telehealth in community-dwelling older adults to improve the access to and experience of virtual visits	**Barriers:** - hearing difficulties (n=89, 35.7%), - not being familiar with how to use technology or the internet (n=75,30.1%) - not knowing how to get connected to the telehealth platform (n=74, 29.7%) - language barriers (n=66, 26.5%) - not interested seeing provider outside of the clinic (n=24) - not having stable internet connection (n=16) - impairment attention and memory (n=13) - no smart device (n=13) - difficulty seeing (n=8)
13.	(Liu et al., 2021)	Canada	Cross-sectional	330 patients in geriatric clinic aged more	to identify patient-specific factors associated with accessing videoconference assessments, as opposed to	**Barriers:** Reduced utilization of videoconference compared with telephone assessment in;

				than 70 years old	telephone-based assessments, in a diverse population of older adults.	- Patients with frailty (adjusted OR 0.62, 0.45 to 0.85; adjusted RD -0.08, −0.09 to−0.06) - Patients who did not have a caregiver present at their virtual assessment (adjusted OR 0.12, 0.06 to 0.24; adjusted RD -0.35, −0.43 to−0.26)
14.	(Hawley et al., 2020)	USA	exploratory sequential mixed-methods	veterans who attended a geriatrics-renal clinic	To identify and address patient-perceived barriers to integrating home telehealth visits	**Barriers:** - Access to care - Access to technology (6 (12%) did not have access to either internet and compatible device) - Confidence (less than half (21 (42%)) of individuals were confident that they could participate in a home telehealth visit.) **Implementation Strategies to Address Patient-Perceived Barriers:** - Assessing for readiness and identifying barriers and facilitators (four phenotypes based on their interest and capability to complete a home telehealth visit: interested and capable, interested and incapable, uninterested and capable, and uninterested and incapable)
15.	(Beauchet et al., 2020)	Canada	Qualitative study	Montreal's housebound community-dwelling older adults	To evaluate the housebound older adults' health and social condition by ESOGER as a clinical tool and to improve the care provided to these older adults through additional research that incorporates data collected during the COVID-19 pandemic	- Short assessment known as "Evaluation SOcio-GERiatrique" (ESOGER) was designed, in late March 2020, for simple risk classification and intervention for older community dwellers. Recommendations involving two categories of interventions: - Free phone call interventions are offered to older adults at high risk levels in the psychological stress, social isolation and caregiver burden subdomains, by the health or social care providers - Contacting the family physician and/or a professional at the support program for senior autonomy (SAPA), which provides health and social home services
16.	(Chu et al., 2022)	California, United State	Prospective Longitudinal study	1427 patients aged >65 years old	To describe the Video Visits for Older adults Projects (VVEP), to help the older adults access video visits at an academic primary practice	- 312 (30.4%) were already video enabled, 192 (18.7%) accepted assistance to video-enable their electronic devices. - Notably, most of those successfully video-enabled with the help of VVEP staff as well as those already video-enabled did complete their visits via video (76%)
17.	(Dikaios et al., 2020)	Montreal, Canada	Cross-sectional	200 Older adults aged >60 years old	To assess the efficacy of Telehealth Intervention Program for Older Adult (TIP-OA during COVID-19 pandemic.	- Telephone based care by trained volunteer is likely able to serve the largest population of older adults - weekly friendly calls to older adults which to assess: - Perceived Stress Scale (PSS) - COVID Fear Scale - Patient Health Questionnaire-9 (PHQ-9) - Generalized anxiety disorder (GAD-&) - Technology in Geriatric scale

18.	(Weiss et al., 2021)	New York, United State	Qualitative study	85 older adults patients	To demonstrate a unique approach to reach vulnerable population using telehealth program, Coordinated Care at Risk/Remote Older adults Program (CCARRE)	**The CCARRE telehealth visits include:** - Start on the phone and move to video (increase compliance of patients and caregiver) - Use video visits to conduct a 'real time' safety evaluation (allow evaluation of navigational obstacle, medication review and possible elder neglect, home assessment and urgent follow up if needed) - Address advance care planning and goals of care during COVID-19 - Address patient/caregiver stress & their needs including providing (patients centered leisure activities, psychological support therapy and behavioral management techniques) - Link with local community-based organization to provide caregiver support service virtually
19.	(Hoffman et al., 2020)	USA	Qualitative study	Geriatric patient	We present a conceptual discussion of disability, environmental, and social risk factors that are exacerbated during a pandemic, then introduce a framework for addressing these risks	**Expanding virtual support by framework:** - Bridging the digital divide - Bridging age divide – intergenerational support - Building aging friendly physical and social infrastructure (trusted organization)
20.	(Khanassov et al., 2022)	Canada	Systematic review	Older adults patient aged 65 years old and above	To identify the themes on the attitude towards TM use, facilitators, and barriers to optimal use of TM by the older adults and clinicians during COVID-19.	**Consolidated Framework for Implementation Research (CFIR):** - Patient related (Older adult with a simple medical condition) - Primary care facility related (Availability of a coordinator – to navigate the patient) - Technology related (Adaptability User- friendly platform with simple access to TM visit)
21.	(Ha et al., 2021)	Korea	Qualitative study	Older adults	To investigate smartphone applications that may be helpful in managing the health of the older adults during COVID-19.	**Twelve applications were finalized based on 6 domains:** - Social and emotional health promotion and maintenance (Wysa & MindDoc) - Symptom and condition management (Ada & Diseases Dictionary) - Communication with the health care system (Telehealth &Blood Pressure Diary) - Medication management (Medisafe & MyTherapy) - Physical activity (FitOn &Samsung Health) - Nutritional management (Lifesum & Health and Nutrition Guide)

Synthesis of Results

Benefits/Role of Telehealth Among Older adults During COVID-19 Pandemic

Among the reports reviewed, a total of 9 papers discussed the role of telehealth among the older adults, which can be categorized into personal, psychosocial, and environmental aspects. Two papers described the utilization of telehealth services among the older adults during the COVID-19 pandemic which was influenced by pre-existing co-morbidities either medical conditions or mental health problems (Choi et al., 2022; Ng et al., 2022). For personal aspects, telehealth services improved the access to healthcare among older adults people living in remote or suburban areas (Haimi & Gesser-Edelsburg, 2022; Murphy et al., 2020; Senderovich & Wignarajah, 2022). Senderovich et. al. reported that virtual care for geriatric patients improved therapeutic alliance and treatment adherence as well as decreased the no-show rates among the older adults during this pandemic (Senderovich & Wignarajah, 2022). This result was supported by a systematic review which showed telehealth is cost-effective, transport saving and can shorten the waiting time compared to in-person face-to-face related care (Murphy et al., 2020).

In the psychosocial aspect, Ho et. al. revealed that digital technology improved the psychological well-being of the older adults population which showed 45% (n=19) of participants reported feeling stronger, 48% had improved spirits, and 40% and 38% had improved mood and memory, respectively through digital HAPPY (Healthy Ageing Promotion Program for You) program (Ho & Merchant, 2022). In addition, a case report from Briones et. al. revealed that telehealth can improve the healthcare outcomes of severely ill older adults patients living in a low-resources healthcare system (Briones-Claudett et al., 2021). The result was consistent with other studies which demonstrated that telehealth reduced the progressive deterioration of older adults patients conditions (Doraiswamy et al., 2021; Haimi & Gesser-Edelsburg, 2022). Besides, this tool may also act as a preventive measure for the rapid COVID-19 transmission among the older adults (Senderovich & Wignarajah, 2022).

Apart from that, Bartlett et. al. reported that the carbon footprints following the hybrid model of geriatric clinic sessions were reduced significantly from 4.82 kgCO2e pre-pandemic to 0.99 kgCO2e during the period of the COVID-19 pandemic. This reduction in carbon footprint is mostly contributed by the lesser staff travel and lesser usage of PPE which positively impact the environment (Bartlett & Keir, 2022).

Barriers to Telehealth Among Older adults During COVID-19 Pandemic

Most of the studies discussed the challenges of telehealth services faced by the older adults during the COVID-19 pandemic. The common barriers noted are subcategorized into 3 components which are physical, cognitive and technical issues.

Eight papers discussed the technical issues which hinder the effective utilization of telehealth services among the older adults during the pandemic. Schifeling et. al. reported that the main barriers to telehealth usage among the older adults in the United States are due to the lack of equipment (54%) (Schifeling et al., 2020). This result is consistent with other studies that revealed lack of access to compatible devices, internet connection and lack of standardization in the aged-friendly telehealth services. Various designs and interfaces increase challenges for the older adults to utilize telehealth effectively (Doraiswamy et al., 2021; Hawley et al., 2020; Mao et al., 2022; Ng et al., 2022; Senderovich & Wignarajah, 2022). Besides,

Murphy et. al. in the systematic review described the issues of confidentiality and privacy concerns among older adults patients and healthcare providers. This issues result in reduced trust of the older adults to speak and communicate openly (Murphy et al., 2020).

Recommendation to Improve the Telehealth Among Older adults During COVID-19 Pandemic and Beyond

The majority of the papers (n=11) described the potential interventions to improve telehealth services among the older adults during the COVID-19 pandemic. The recommendations can be structured into 3 parts which are technology-enabled factors, patient-related factors and provider-related factors.

- **Technology enabling factors**: Choi et. al. suggested the participation of telehealth among the older adults can be enhanced by technology enabling factors such as providing ICT devices ownership and skills to use the new technology program (Choi et al., 2022). A few studies also suggested similar recommendations in which video-enabled by adaptability friendly user platform (Khanassov et al., 2022) as well as providing assistance of healthcare staff (Beauchet et al., 2020; Chu et al., 2022; Dikaios et al., 2020; Doraiswamy et al., 2021) increased the success rate to complete their virtual visits. In addition, recent work from Korea reported that smartphone applications may help manage and monitor the older adults's health during COVID-19 (Ha et al., 2021).
- **Provider-related factors:** Many studies revealed that provider-related factors are significantly associated with the improvement of telehealth utilization among the older adults. A study from Canada suggested a framework to improve the optimal use of telehealth which includes increasing the availability of the coordinator to navigate older adults patients (Khanassov et al., 2022). Similar findings were recorded in other studies. Engagement with trusted organization in providing training to the healthcare staff and the patient's caregiver will help the older adults during virtual visits session (Beauchet et al., 2020; Doraiswamy et al., 2021; Hoffman et al., 2020; Weiss et al., 2021). The results were emphasized by Choi et. al. which reported that telehealth efficiency is enhanced when the older adults had an assistance/caregiver (AOR=1.36, 95% CI=1.04-1.76).
- **Patient-related factors:** Apart from that, few studies reported that patient-related factors can influence telehealth utilization. Hawley et. al. revealed the implementation strategies to address patients-perceived barriers including assessment for readiness, barriers and facilitators among the older adults before offering telehealth services to them (Hawley et al., 2020).

Another systematic review revealed a framework to implement effective telehealth among the older adults by tailoring the service based on patients' underlying medical conditions (Khanassov et al., 2022).

DISCUSSION

Benefits/Role of Telehealth Among Older adults During COVID-19 Pandemic

According to the literature, the telehealth service during COVID-19 impacts the personal, psychosocial and environmental aspects of the older adults. The telehealth improves feasibility and convenience for the older adults to seek treatment during the pandemic crisis. By using live video conferencing or a phone call, telehealth enables medical professionals to gather necessary data, prioritize and determine whether a patient is allowed to self-monitor symptoms at home or needs hospitalization (Zhai et al., 2020). This could decrease the face-to-face contact of medical services to minimize the risk of COVID-19 transmission. Hence, telehealth was shown to be a practical, feasible, and effective medium to improve healthcare outcomes (Hong et al., 2020).

Furthermore, telehealth also acts as a tool to reduce psychological distress amongst the older adults. A study showed that senior citizens expressed mild-to-moderate and severe peritraumatic discomfort concerning the COVID-19 pandemic (Fadila et al., 2021). The vulnerability of older people is exacerbated by the pandemic's uncertainty as well as the experience of fear of dying or losing their loved ones (Banerjee, 2020a). Hence, telehealth may provide a remote service which can respond to mental health needs while upholding the standard of care particularly at times of public health crises, national and international emergencies (Whaibeh et al., 2020).

Apart from that, telehealth promotes a healthy environment and reduces the greenhouse effects. A study revealed that telehealth services result in higher emissions savings in rural communities (Ravindrane & Patel, 2022). This net environmental advantage is dependent on both reduced travel distance and energy consumption by transportation (Ravindrane & Patel, 2022).

Barriers to Telehealth Among Older adults During COVID-19 Pandemic

The barriers to optimal telehealth utilization among the older adults during the COVID-19 pandemic are mostly associated with technical, cognitive and physical issues. This review demonstrated that higher levels of digital literacy increased the likelihood of remote medical care participation (Bhaskar et al., 2020). This is consistent with findings that revealed inadequate access to Internet or Wi-Fi facilities is the primary impediment to telehealth implementation (Smolić et al., 2022). A study by Hirko showed that older people living in rural areas has lacking access to the internet which hindered them to utilize telehealth services (Hirko et al., 2020). Hence, age-related digital devices issues and poor socioeconomic status may continue to place a strain on healthcare outcomes, impeding telehealth capabilities.

In addition, cognitive impairment, such as Alzheimer's disease, hinders the older adults from using telehealth services. A study by Lam et. al. demonstrated telehealth unreadiness is higher in dementia patients (Lam et al., 2020). This can be explained by difficulties to care accompanied by a lack of resources, and medical complications which reduced the effectiveness of telehealth (Weiss et al., 2021). As a result, engagement in remote care by the older adults with declined cognitive was significantly reduced (Kim et al., 2017).

Other than that, telehealth utilization was hindered in older adults with physical impairment such as hearing or visual difficulties. According to a report by Nieman et. al, hearing

loss is practically common in older adults, with about two-thirds of persons aged 70 years or older having clinically substantial hearing loss (Nieman & Oh, 2020). Furthermore, as telehealth takes place virtually, the possibility of noise, distractions, and missing visual cues increases, thereby limiting both patient and provider comprehensibility (Overcoming Telehealth Barriers and Engaging Older Adults in Virtual Care | MedPro Group, n.d.). This hearing and vision impairment are natural ageing processes, but they can make interaction via digital tools challenging.

Recommendations for Improvement of Telehealth Among Older Adults During COVID-19 Pandemic and Beyond

Among the recommendations discussed in this review are the need to improve on the technology, providers and patients related factors. As technical challenges were the most frequent issues encountered, offering technological components such as age-friendly interface devices, Wi-Fi, and cellular connection are crucial to the successful implementation of telehealth (Zhang et al., 2021).

Telecommunications equipment ought to be covered as a medical necessity, especially to reduce the gap between poverty and telehealth readiness. (Lam et al., 2020). Besides, several smartphone applications should be available to assist older adults in navigating isolation during the COVID-19 epidemic. For instant, applications of Doctor on Demand, Teladoc, and K Health give users access to licensed doctors for non-emergency medical issues and comply with the Health Insurance Portability and Accountability Act of 1996 (HIPAA) (Arizona Telemedicine program, 2015; Banskota et al., 2020). During emergency closures and periods of high demand for medical services, these platforms can connect patients with remote physicians (Banskota et al., 2020).

Factors such as caregivers or volunteer assistance are significant to gain optimal utilization of telehealth among the older adults. A study revealed the importance of caregivers' participation in addressing questions and concerns, as well as facilitating their older adults to access telehealth care (Raj et al., 2022). This telehealth makes it easier for family caregivers to care for their loved ones by providing them with direct access to healthcare specialists.

CONCLUSION

In conclusion, this scoping review added to the knowledge that telehealth services significantly benefit the vulnerable older adults population during the COVID-19 pandemic. Telehealth improves the feasibility, therapeutic alliance and psychological well-being of the older adults, besides preventing the transmission of illness to others. The utilization of telehealth among the older adults is hindered by various factors/barriers which are related to technical, physical and cognitive issues. Thus, a variety of recommendations were put into practice to address the shortcomings of telehealth, including broadening access to technology and enhancing provider and patient-related factors. With the rapid evolution of COVID-19, this review suggests that stakeholders such as healthcare workers, caregivers and patients collaborate for the optimal telehealth utilization experience. Telehealth will continue to play a vital role in enhancing healthcare accessibility and quality of life beyond the COVID-19 pandemic. As a key tool for delivering care in future emergencies, it will ensure the safety of both patients and healthcare professionals while driving innovation in remote healthcare solutions.

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Conflicts of Interest

The authors of this study declare that there is no conflict of interest.

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REVIEW ARTICLE Open Access

Rabies Pre-Exposure Prophylaxis: A Systematic Review on Safety, Immunogenicity and Booster Recommendations

Mohd Fazeli Sazali[1*], Nafsah Dulajis[2], Puteri Nureylia Amir[3]

Abstract

Rabies infection is a serious and fatal disease that disproportionately affects children and low socioeconomic groups. Pre-exposure prophylaxis (PrEP) is a preventive strategy to protect high-risk groups. Timely updating recommendations for rabies PrEP are needed, especially to meet the needs of the underserved population. This review aimed to find recent evidence available to evaluate the safety and immunogenicity of rabies PrEP of reduced dose and duration; intramuscular (IM) and intradermal (IM) administration; and to assess booster recommendations following rabies PrEP. The literature review was conducted according to PRISMA guidelines for systematic reviews and meta-analyses. A literature search of PubMed, Google Scholar and Scopus was performed from the database for studies in the past five years (1st Jan 2017-30th May 2021). Of 45 studies identified, 15 publications met the inclusion criteria for safety, dosage, immunogenicity and booster recommendations. Most studies identified that the recommended dose and duration is safe and immunogenic for children and adults. Rabies vaccine booster is indicated for occupational exposure. The current recommendation on rabies PrEP is safe for adults and children, and the immunogenicity is not inferior to the 1-dose 3-visit regime, with equivalent effectiveness via both routes (ID and IM).

Keywords: Rabies, Pre-exposure prophylaxis, Safety, Immunogenicity.

*Correspondence Email: drmohdfazeli@moh.gov.my

[1]*Ministry of Health Malaysia, Communicable Disease Control Unit, Public Health Section, Pahang State Health Department, Jalan IM 4, Bandar Indera Mahkota, 255282, Kuantan, Pahang, Malaysia*

[2]*Ministry of Health Malaysia, Sandakan Are Health Office, Tingkat 6, Bangunan Persekutuan, 90009, Sandakan, Sabah, Malaysia*

[3]*Ministry of Health Malaysia, Pejabat Kesihatan Daerah Kinta, Jalan Aman, 31000, Batu Gajah, Perak, Malaysia*

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INTRODUCTION

Rabies is an infectious disease caused by rabies virus which is responsible for approximately 59,000 deaths in over 150 countries, mainly in Asia and Africa (Taylor & Nel, 2015). The disease disproportionately affects children below 15 years old, especially among poor communities in rural areas. However, most of these cases are underestimated, as the affected regions often underreported deaths (*Rabies*, n.d.). The disease is highly fatal once the infected person develops neurological symptoms due to rabies encephalitis (Jackson, 2016). The death from rabies infection could be preventable through various strategies, such as prevention at the reservoir through canine vaccination or by administration of rabies vaccines as well as rabies immunoglobulin following rabies virus exposure, either through bites, scratches, or licking from suspected rabid animals (World Health Organization (WHO), 2014).

Pre-exposure prophylaxis (PrEP) is another preventive strategy involving giving a course of rabies vaccine either through the intramuscular or intradermal route. Administration of PrEP could protect from rabies infection as the vaccine enables fast recall of memory immune responses once the person re-exposes to the virus. PrEP-protected individuals may only require fewer doses of post-exposure prophylaxis and may not require rabies immunoglobulin, which is expensive and largely inaccessible in many parts of the world. Prevention through PrEP could provide benefit for those at high risk of rabies virus exposure, particularly among occupational exposure to rabies virus (e.g., veterinary staff and laboratory worker that is regularly handling specimens with Lyssavirus), among the population that is living in an endemic area with high dog bite incidence (more than 5% per year), or among traveller that planned to visit remote areas that is endemic with the disease where the post-exposure prophylaxis medication is inaccessible (World Health Organization, 2018a).

In 2018, the World Health Organization (WHO) updated their recommendations regarding PrEP, especially the dosage, regimens, and the number of visits to get PrEP vaccination (World Health Organization, 2018a). In 2018 WHO recommendations, the dosage of intramuscular vaccine is a one-site injection, either 0.5mL or 1.0mL, depending on the volume of each vial. The regimen has been reduced from three visits on day 0, day 7, and day 21 or day 28 (in 2014 recommendations) to only two visits on day 0 and day 7. Reduction of visits can help to enhance compliance and, at the same time, achieve adequate protection as effective as three doses of vaccine. Meanwhile, the same position paper has maintained its recommendations on six monthly rabies antibody serological monitoring for high occupational risk. WHO also recommended administering booster doses if the titer falls below 0.5 IU/mL with a one-site intradermal or one-site intramuscular booster vaccine. Hence, to meet the need of a high-risk population, more evidence is needed to achieve better outcomes but shorter, less costly, and more feasible PrEP protocols without compromising their safety & effectiveness (Safety, 2012). This review aims to evaluate evidence on the safety and immunogenicity of rabies PrEP schedule for intramuscular and intradermal administration, the reduced dose and duration, and the rabies vaccine booster recommendations.

METHODS

The literature review was intended to update the evidence on pre-exposure prophylaxis following the 2018 WHO rabies vaccine position paper. The literature review was conducted according to PRISMA guidelines for systematic reviews and meta-analyses (Page et al., 2021). Two web-based search engines and one database were used in the literature search. PubMed, Google Scholar and Scopus databases were searched to identify relevant studies, and only studies in the past five years were included (1st Jan 2017-30th May 2021). The only original

article included for review while unpublished manuscripts, letters to the editor, systematic reviews, articles not measuring the outcome of interest, articles involving animal studies, non-English articles and conference abstracts were excluded. The literature review was done by including both open access and non-open access articles. The last search was conducted on 30th May 2021.

The search strategy was already used in another study before (Kessels et al., 2017). The search string used was: "rabies" AND "pre-exposure" AND ("prophylaxis" OR "vaccin*"). Filters applied, including 'search in the title or abstract only' and 'last 5 years.' The selection and data collection process were done in two phases in which the first phase was screening by reading the title and abstract. The second phase was done by reading the full text. All of the processes were done by the reviewer independently. Since there were three reviewers, an agreement was achieved by choosing the option with two votes.

Data synthesis was done with selected articles' characteristics were first compiled in a spreadsheet and characterized by general information such as citation reference, publication year, study location, type of study, study design and type of vaccine used. Spreadsheets were uploaded in Google drive, which makes them transparent for all reviewers. Data were then extracted from respective articles according to the three objectives of this systematic review in different spreadsheets. All extracted data in different spreadsheets was analyzed and discussed before a final consensus was gained among reviewers.

RESULTS

The literature search yielded 45 published articles, of which 28 publications remained after the removal of duplicates. These publications were screened for eligibility, and 13 were excluded. Fifteen publications met the inclusion criteria for safety, dosage, immunogenicity and booster recommendations (Table 1). The PRISMA flowchart shows identified articles' selection and screening (Figure 1).

Table 4: Summary of the included publications

Reference	Publication type/ year	Study design	Study location	Prophylaxis	Vaccines
Janewongwirot, P. (Janewongwirot et al., 2019)	Journal article/ 2019	Randomized control trial	Thailand	PVRV	Children
Recuenco, S. (Recuenco et al., 2017)	Journal article/ 2017	Randomized control trial	Atlanta	PCECV	Adults
Soentjens, P. (Soentjens, De Koninck, et al., 2019)	Journal article/ 2019	Randomized control trial	Belgium	PCEV	Adults
Damanet, B. (Damanet, Costescu Strachinaru, et al., 2020;	Journal article/ 2020	Retrospective study	Belgium	PCECV, vaccination against yellow fever, tetanus,	Adults

Damanet, Strachinaru, et al., 2020)				diphtheria, pertussis and meningococcal group A, C, W and Y	
Angsuwatcharakon, P. (Angsuwatcharakon et al., 2020)	Journal article/ 2020	Randomized control trial	Thailand	PVRV, JE-CV	Children
Furuya-Kanamori, L. (Furuya-Kanamori et al., 2021)	Journal article/ 2021	Retrospective study	Australia	HDCV (MIRV), PCECV, PVRV	Adults
De Pijper, C. A. (Cornelis A De Pijper et al., 2021)	Journal article/ 2021	Prospective study	Amsterdam	PCECV	Adults
Soentjens, P. (Soentjens, Andries, et al., 2019)	Journal article/ 2019	Randomized control trial	Belgium	HDCV (MIRV)	Adults
De Pijper, C. A. (Cornelis Adrianus De Pijper et al., 2018)	Journal article/ 2018	Prospective study	Netherlands	PVRV	Adults
Huttner, A. (Huttner et al., 2021)	Journal article/ 2021	Retrospective study	Switzerland	PCECV/HDCV (MIRV) if short supply of PCECV	Adults
Hardanahalli S., R. (Hardanahalli S et al., 2017)	Journal article/ 2017	Prospective study	India	PCECV	Children, adults
Parize, P. (Parize et al., 2021)	Journal article/ 2021	Retrospective study	France	PVRV, PCECV	Adults
Van Nieuwenhove, M. D. M. (Van Nieuwenhove et al., 2019)	Journal article/ 2019	Retrospective study	Belgium	PCECV	Adults
T. P. Endy et al. (Endy et al., 2020)	Journal article/ 2020	Randomized control trial	USA	PCECV	Adults

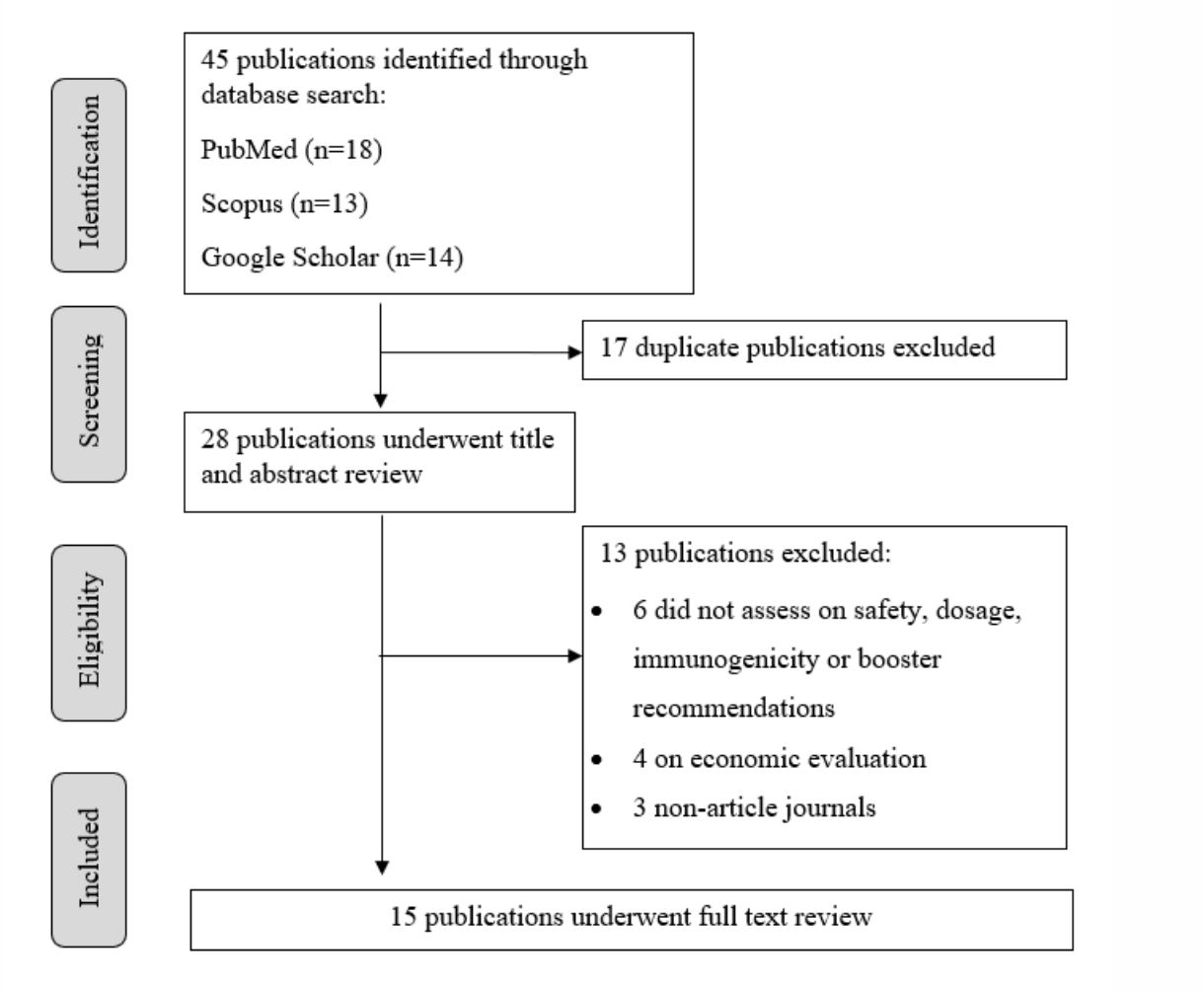

Figure 1: The PRISMA flowchart of identified articles' selection and screening

Safety

The study search identified seven studies evaluating the safety of rabies vaccination prophylaxis with or without immunogenicity (Angsuwatcharakon et al., 2020; Endy et al., 2020; Hardanahalli S et al., 2017; Huttner et al., 2021; Recuenco et al., 2017; Soentjens, Andries, et al., 2019; Soentjens, De Koninck, et al., 2019). Among them, three studies included the safety evaluation using the latest regimes recommended by the World Health Organization (WHO) (Angsuwatcharakon et al., 2020; Endy et al., 2020; O'Brien & Nolan, 2019; Soentjens, Andries, et al., 2019). In total, five studies were conducted after WHO had updated its recommendations in 2018 (Angsuwatcharakon et al., 2020; Endy et al., 2020; Huttner et al., 2021; Soentjens, Andries, et al., 2019; Soentjens, De Koninck, et al., 2019). However, another two studies were conducted before 2018 (Hardanahalli S et al., 2017; Recuenco et al., 2017). The latter were included because their results were still relevant to our study (Hardanahalli S et al., 2017; Recuenco et al., 2017). Most studies found that the dose and duration were safe and immunogenic to adults (Angsuwatcharakon et al., 2020; Endy et al., 2020; Soentjens, Andries, et al., 2019; Soentjens, De Koninck, et al., 2019) and children (Angsuwatcharakon et al., 2020; Hardanahalli S et al., 2017).

The current vaccination prophylaxis regime was safe for adults (Angsuwatcharakon et al., 2020; Endy et al., 2020; Soentjens, Andries, et al., 2019). Mild and transient local irritation at the injection site were the common effects that occurred after primary injection (43.4%) as compared to 0.1ml one intradermal dose in a 3-visit regime (p-value 0.07) (Soentjens, Andries, et al., 2019). Nevertheless, three participants in the study experienced severe adverse effects, one from a 3-visit regime following primary injection and another two from the current schedule following booster dose. These two participants had esophagitis, dyspnea, angioedema and urticaria (Soentjens, Andries, et al., 2019). Table 2 summarises the adverse events experienced by the study participants.

Two studies among children identified that the vaccine was safe for children (Angsuwatcharakon et al., 2020; Hardanahalli S et al., 2017). A group of 150 children from a poor urban locality aged 5 to 10 years were selected in a study (Hardanahalli S et al., 2017), and 49 children aged 12 to 16 months were enrolled in another study (Angsuwatcharakon et al., 2020). Some children only developed local adverse reactions such as pain, redness, pruritus and itching, and some had fever and headache. No severe adverse reactions were recorded (Angsuwatcharakon et al., 2020; Hardanahalli S et al., 2017).

A study in Switzerland was done on Multiple Sclerosis (MS). Only 10.9% of their patients had relapsed after a year post rabies vaccination. Some patients even received up to seven repeated doses of the rabies vaccine, and the authors did not find any relation to MS relapse (Huttner et al., 2021). Furthermore, a study in Thailand administered the rabies vaccine simultaneously with the Japanese encephalitis (JE) vaccine on day 0 to their healthy children. No immediate or severe adverse vaccine reactions were identified (Angsuwatcharakon et al., 2020).

Table 5: Adverse events recorded

Reference	Route/ Regime/ Vaccine type	Adverse events	No. (%) of cases	Remarks
Recuenco, S. (Recuenco et al., 2017)	1ID/ 1IM/ day 0, 7, 21/ PCECV	No severe adverse events (Erythema, induration, tenderness, headache, fatigue, fever, insomnia)	-	-
Soentjens, P. (Soentjens, De Koninck, et al., 2019)	2ID/ day 0/ PCEV	No severe adverse events. Mostly has local irritation (redness, swelling, rash, itching)	14.9%	-
Angsuwatcharakon, P. (Angsuwatcharakon et al., 2020)	2ID/ day 0, 28/ PVRV	No severe adverse events	-	-
	1ID/ day 0, 7, 28/ PVRV		-	-
Soentjens, P. (Soentjens, Andries, et al., 2019)	3ID/ day 0, 7 28/ HDCV	Reversible diplopia and hemianopsia	1	14 days after final rabies vaccination and some days after receiving MMR vaccines in other centers (violating protocol)
	2ID/ day 0, 7/ HDCV	Esophagitis	1	After booster dose

		Dyspnea, angioedema, urticaria	1	
Huttner, A. (Huttner et al., 2021)	Not stated	Not associated with Multiple Sclerosis (MS) relapses	-	A study among MS patients
Hardanahalli S., R. (Hardanahalli S et al., 2017)	3ID/ day 0, 7, 21/ PCECV	Mild reactions and subsided without any complication (Local reactions: pain, redness, itching. Systemic reactions: fever, myalgia, fatigue, headache)	5.1% (children)	-
			5.0% (rag pickers)	-
			10.4% (veterinary students)	-
T. P. Endy et al. (Endy et al., 2020)	3IM/3ID/ day 0, 7, 21 or 28/ PCECV	More adverse events in ID groups compared to IM groups (pain, itching, swelling, fatigue, low-grade fever, muscle aches)	66.7% (IM group) 91.7% (ID group)	-
	2IM/2ID/ day 0, 7/ PCECV		66.7% (IM group) 90.9% (ID group)	-

Immunogenicity

New Regime

With the new dose and route recommended by WHO (O'Brien & Nolan, 2019), the adequate antibody level was reached in more than 86% of the participants (Angsuwatcharakon et al., 2020; Endy et al., 2020; Furuya-Kanamori et al., 2021; Soentjens, Andries, et al., 2019). Rabies serum antibody concentration of 0.5 IU/ml or more indicated an adequate serum conversion. It can be achieved after 14 days post-primary vaccine and day 7 post-booster (Angsuwatcharakon et al., 2020; Endy et al., 2020; Soentjens, Andries, et al., 2019; World Health Organization, 2018b).

Australia

From 2000 until 2016, travellers who attended a specialized travel medicine clinic in Adelaide were given the ID rabies vaccine according to three different schedules (Table 3). The choice was based on the clinician, cost, time and ability of the patient to return to the clinic for the subsequent doses. As overall, 92.5% of all travellers achieved adequate rabies antibody levels. Among them, 93.4% of the patients who received a single dose for three visits had adequate rabies antibody levels, compared to two-dose for two visits (86.2%) and four-dose for a single visit (76.2%) schedule. Younger travellers aged less than 30 also had more adequate antibody levels than those aged 30 and above. However, the antibody level depends on the timing of the test, in which the reading was the lowest if it was done less than 14 days post-primary vaccine, and the reading peaked if it was done between 14 to 34 days post-primary vaccine (Furuya-Kanamori et al., 2021).

Different routes of administration

Two studies were identified comparing immunogenicity differences among the intramuscular and intradermal routes. In these studies, all participants had adequate rabies antibody levels post-primary vaccine, regardless of the route (Angsuwatcharakon et al., 2020; Recuenco et al., 2017). The geometric mean titer (GMT) for both routes among adults peaked at 14 days post-primary vaccine and maintained its titer of more than 0.5 IU/ml up until 160 days (Recuenco et al., 2017). The titer among children remained above the threshold level for up to a year (Angsuwatcharakon et al., 2020). There was no difference in the GMT values between both routes in both studies (Angsuwatcharakon et al., 2020; Recuenco et al., 2017).

Different Dose and Duration

Three studies were identified evaluating the vaccine schedules with different doses and durations (Damanet, Strachinaru, et al., 2020; Janewongwirot et al., 2019; Van Nieuwenhove et al., 2019). In a study among healthy children of 2 to 12 years old in Thailand comparing two-visit and three-visit regimes, all had rabies virus antibody titer of 0.5 IU/ml or more at day 14 post-primary vaccination. Notably, 100% of those in the three-visit regime were able to maintain the titer at one year compared to only 80% of those in the two-visit regime. The remaining 20% of the children were from the two-visit regime with titers of less than 0.5 IU/ml at one-year post-primary vaccine, predominantly males and children aged more than six years (Janewongwirot et al., 2019). Another two studies were conducted among the armies. Both provided a single-dose 3-visit intradermal rabies vaccine to the participants. However, the variability occurred when some participants received the dose earlier than scheduled, at the

correct timing, late and very late than scheduled. Regardless of the variability, 99.9% to 100% of the participants' rabies virus antibodies developed an antibody level of 0.5 IU/ml (Damanet, Strachinaru, et al., 2020; Van Nieuwenhove et al., 2019). The antibody level was significantly influenced by the timing of the test, in which the level was higher in 7 to 28 days post-primary vaccination as compared to those later than 28 days ($p = 0.047$) (Van Nieuwenhove et al., 2019). Being female, age younger than 30 years, and the normal timing of the serology (7 to 28 days post-primary vaccination) significantly influenced the antibody titer level to be 3 IU/ml or more (Damanet, Strachinaru, et al., 2020).

Booster

There were six studies evaluating the effect of boosters on immunogenicity. All of them demonstrated that adequate rabies antibody titer could be achieved from 98.7% up to 100% of participants (Cornelis A De Pijper et al., 2021; Furuya-Kanamori et al., 2021; Janewongwirot et al., 2019; Parize et al., 2021; Soentjens, Andries, et al., 2019; Soentjens, De Koninck, et al., 2019) regardless of the timing of booster, a booster dose (Soentjens, De Koninck, et al., 2019) or vaccine schedules (Cornelis A De Pijper et al., 2021; Parize et al., 2021; Soentjens, Andries, et al., 2019). P. Janewongwirot et al.'s study revealed that the rabies antibody titers were above the threshold level in all of the children. The titers increased from 0.8 IU/ml pre-booster to 20.9 IU/ml 7-day post-booster in the 2-visit regime and from 1.7 IU/ml pre-booster to 22.2 IU/ml 7-day post-booster in 3-visit regime (Janewongwirot et al., 2019). Participants with a 4-dose ID booster have significantly higher rabies antibody titer than a 2-dose ID booster ($p = 0.0228$) (Soentjens, De Koninck, et al., 2019).

Meanwhile, participants who received the current recommended vaccine regime by WHO had significantly higher antibody titer after the booster dose as compared to the previous regime ($p < 0.001$) (Soentjens, Andries, et al., 2019). Nevertheless, both regimes had a titer of more than 0.5 IU/ml (Soentjens, Andries, et al., 2019; Soentjens, De Koninck, et al., 2019). Some participants maintained adequate titers more than five years after a single booster dose (Parize et al., 2021). Only two cases were observed to have severe adverse reactions after booster dose (Table 3) (Soentjens, Andries, et al., 2019). In contrast, others only had local irritation at the injection site, such as redness, swelling, rash and itching (Soentjens, Andries, et al., 2019; Soentjens, De Koninck, et al., 2019).

Table 6: Pre-exposure rabies prophylaxis

Reference	Year	Schedule	Route	Booster	Sample specification	Serology result	Safety
Janewongwirot, P. et al. (Janewongwirot et al., 2019)	2019	1. Single-dose 2-visit (day 0, 28) 2. Single-dose 3-visit (day 0, 7, 28)	0.5ml IM	0.5ml IM (day 365)	Healthy children aged 2-12 years with. No history of rabies vaccination. Randomized to receive vaccine 2-doses or 3-doses group	1. Day 14: 100% of participants from both groups had RVNA titers ≥ 0.5 IU/ ml after primary vaccination. 2. Day 365 (pre-booster): 2-doses group had 80% with RVNA titers ≥ 0.5 IU/ ml (GMT RVNA 0.8IU/ml). 3-doses group had 100% with RVNA titers ≥ 0.5 IU/ ml (GMT RVNA 1.7 IU/ml) (p=0.01) 3. Post-booster: Both groups had 100% RVNA titers ≥ 0.5IU/ml. The 2-doses group had GMT RVNA 20.9 IU/ml. The 3-doses group had	N/A

						GMT RVNA 22.2 IU/ml.	
Recuenco, S. (Recuenco et al., 2017)	2017	1. PrEP group: single dose day 0,7,21 (ID route) 2. PrEP group: single dose day 0,7,21 (IM route) 3. Booster group: a person with previous PrEP was given booster day 0 (ID route) 4. Booster group: a person with previous PrEP was given booster day 0 (IM route)	0.1ml ID or 1.0ml IM	N/A	CDC staff age 18 years and above.	1. RVNA titers day 14-21 increased at a similar rate for both ID and IM groups in the PrEP regime. 2. All group participants had RVNA titers > 0.5IU/ml after 14 days of complete vaccination.	No serious adverse reaction. Common reactions were erythema, induration and tenderness at the injection site.
Soentjens, P. (Soentjens, De Koninck, et al., 2019)	2019	0.1ml 2-dose single visit day 0	ID	After 1 year PrEP regime: 1. Booster single visit 4-	Belgian Armed Forces age 18-54 years	1. Day 7 post-booster: 99.3% participants in both booster groups had	No serious adverse event. Only 14.9% had mild to transient local irritation after PrEP.

				dose 0.1ml 2. Booster single visit 2-dose 0.1ml		antibody titers > 0.5IU/ml 2. Day 7 post-booster: Significant higher GMT after 4-dose booster (20IU/ml) compared to 2-dose booster (14IU/ml) (p=0.0228)	Post-booster local irritation was seen higher in the 4-dose booster regime compared to the 2-dose booster regime (53% vs 49.6%).
Damanet, B. (Damanet, Costescu Strachinaru, et al., 2020)	2020	0.1ml 2-dose 2-visit 1. Early (day 0, ≤6) 2. Correct (day 0,7) 3. Late (day 0, 8-56)	ID	N/A	Belgium Armed Forces who had never received any vaccination before study	1. 98.7% had RVNA ≥0.5IU/ml 2. 39.5% had a "very good protection against rabies" (RVNA > 10 IU/mL) 3. 4 subjects (1.3%) had RVNA < 0.5 IU/mL 4. There is a significantly higher RVNA in 'late" second dose administration than correct the	N/A

						second dose on day 7.	
Damanet, B. (Damanet, Strachinaru, et al., 2020)	2020	Single-dose 3-visit 0.1ml 1. Early (day 0, ≤6, ≤20) 2. Correct (day 0, 7,21-28) 3. Late-variable (day 0, 8-35, 29-56) 4. Late- vary variable (day 0, >35, >56)	ID	N/A	Belgium Armed Forces	1. All participants seroconverted with RVNA ≥0.5 IU/ml. 2. Better immune response in participants aged less than 30 years compared to other age groups. 3. Female is a predictor for RVNA ≥ 3IU/ml. 4. Very late vaccination schedule is a predictor to RVNA >10IU/ml compared to "correct" schedule	N/A
Angsuwatcharakon, P. (Angsuwatcharakon et al., 2020)	2020	PrEP: 1. Group A: 0.1ml ID 2-dose 2-visit (day 0, 28) + JE-CV (day 0, 365)	ID, IM	N/A	Healthy children age 12-16 months.	1. Day 42 post vaccination: All children had RVNA > 0.5IU/ml. 2. Day 365 post vaccination: 92.3% children in Group A and	No vaccine-related severe adverse effect observed. Common local reaction: Group A had erythema and

		2. Group B: 0.5ml IM 1-dose 3-visit (day 0, 7, 28) + JE-CV (day 0, 365)				92.3% children in Group B had RVNA >0.5IU/ml.	pruritus at the site of injection. Group B had pain at the injection site.
Furuya-Kanamori, L. (Furuya-Kanamori et al., 2021)	2021	PrEP: 1. 0.1ml 1-dose 3-visit (day 0, 7, 21-28) 2. 0.1ml 2-dose 2-visit (day 0, 7) 3. 0.1ml 4-dose 1-visit (day 0)	ID	Some had ID boosters after 12 months of primary vaccination	Travellers	Serology tested either (1) after primary ID PrEP or (2) after a booster. 1. 92.5% of travellers had antibody titer ≥0.5IU/ml. Group 1 PrEP had the highest proportion of antibody titer ≥0.5IU/ml compared to other groups. Aged 50 years and above had 89.4% antibody titer ≥0.5IU/ml. 2. 98.7% of travellers had antibody titer ≥0.5IU/ml. Aged 50 years and above had 97.9%	N/A

						antibody titer ≥0.5IU/ml. That booster, for more than 3 years, had all antibody titer ≥0.5IU/ml.	
De Pijper, C. A. (Cornelis A De Pijper et al., 2021)	2021	PrEP at least 10 years before study 1. 3-dose IM 2. 3-dose ID 3. Divergent (2 or 3 dose regime)	IM	1ml IM	Healthy volunteers aged 18 years and older	1. All participants had antibody titer ≥0.5IU/ml after a 1-week booster.	N/A
Soentjens, P. (Soentjens, Andries, et al., 2019)	2019	PrEP: 1. Control group: 0.1ml 1-dose 3-visit (day 0, 7, 28) 2. Intervention group: 0.1ml 2-dose 2-visit (day 0, 7)	ID	0.1ml ID booster 1-3 years after primary vaccination	Belgian Armed Forces	1. Day 7 post-booster: 100% participants had RFFIT >0.5IU/ml. 2. Day 7 post booster: 96% in the intervention group had antibody titer >10IU/ml compared to the control group (83%). 3. GMT was higher in the control group after	1. One case had a severe adverse event (reversible diplopia and hemianopsia) 14 days after the last dose of the primary vaccine (control group). 2. One case had esophagitis after booster (intervention group). 3. One case with dyspnea, angioedema, and

						primary vaccination. But GMT was higher in the intervention group after the booster.	urticaria after booster (intervention group). 4. Local irritation occurred more frequently in the control group after primary vaccination. 5. Local irritation occurred more frequently in the intervention group after the booster dose.
De Pijper, C. A. (Cornelis Adrianus De Pijper et al., 2018)	2018	0.1ml (day 0, 7, 21-28)	ID	N/A	Military personnel	1. 99.3% had antibody titer > 0.5IU/ml after 2 doses (GMT 7.59 IU/ml) 2. Another 3 participants seroconverted after third dose.	N/A
Huttner, A. (Huttner et al., 2021)	2021	At least one dose PrEP	N/A	N/A	Multiple Sclerosis patients. They were receiving disease-modifying therapy during the study period. 91% received at least	N/A	The annualized relapse rates in the pre-exposure risk, exposure-risk, and post-risk periods were 0.44, 0.22, and 0.10, respectively

					one other vaccine during the study period.		(the rate ratio for exposure-risk to pre-exposure periods was 0.509)
Hardanahalli S., R. (Hardanahalli S et al., 2017)	2017	PrEP: 0.1ml 1-dose 3-visit (day 0, 7, 21)	ID	N/A	Group 1: Children from an urban poor locality Group 2: Rag-pickers Group 3: Government Veterinary college students	N/A	Overall adverse drug reactions: 5.1% in children. 5.0% in rag-pickers. 10.4% in veterinary students. Common local reactions were pain, redness and itchy at the injection site. Systemic ADRs were fever, myalgia, headache and fatigue.
Parize, P. (Parize et al., 2021)	2021	Had received PrEP regime before study period (1-dose IM, 3-visit)	IM	Had received a booster dose before the study period	Laboratory workers of the Institut Pasteur of Paris	1. 17.2% of participants had inadequate antibody titer after primary vaccination (without booster) 2. 0.5% had an inadequate response after booster 3. Significant factors for	N/A

						inadequate antibody titer were male, more than 6 months intervals between primary vaccine and serology test, and simultaneous administration with non-rabies vaccine during PrEP	
Van Nieuwenhove, M. D. M. (Van Nieuwenhove et al., 2019)	2019	0.1ml 1-dose 3-visit schedules: 1. Early (day 0, ≤6, ≤ 20) 2. Correct (day 0, 7, 21-28) 3. Late-variable (day 0, 8-35, 29-56) 4. Late- very variable (day 0, >35, >56)	ID	N/A	Belgian Armed Forces	1. 99.9% developed RVNA ≥0.5IU/ml. 2. A higher proportion of RVNA >10IU/ml in a very late variable group compared to the correct group (p=0.047) 3. Normal timing for serology determination had a significantly higher frequency of RVNA > 10IU/ml than	N/A

						later-than-planned.	
T. P. Endy et al. (Endy et al., 2020)	2020	PrEP: Group 1: 1ml IM 3-visit (day 0, 7, 21 or 28) Group 2: 0.1ml ID 3-visit (day 0, 7, 21 or 28) Group 3: 1ml IM 2-visit (day 0, 7) Group 4:0.1ml ID 2-visit (day 0, 7)	IM, ID	1ml IM at 1 year after first dose	Adults aged 18-60 years at the State University of New York Upstate Medical University (SUNY-UMU) in Syracuse, New York	1. All participants in groups 1-4 achieved >0.5IU/ml rabies antibody titer by day 14 and 28 posts primary vaccine and on day 372 after the booster. 2. At day 365, only 64% in group 1, 45% in group 2, 58% in group 3 and 60% in group 4 had rabies antibody titer > 0.5IU/ml, with p-value of 0.39, 0.79 and 0.86 respectively as compared to group 1.	1. Common adverse events at the injection site: pain, itch, swelling. 2. Common systemic adverse events: fatigue, low-grade fever, muscle ache. 3. Those who received ID vaccines experienced more local (91.7%) and systemic (90.9%) adverse events compared to those who received IM vaccine (66.7% and 66.7% for local and systemic adverse events, respectively.

DISCUSSION

The conventional rabies vaccine previously recommended by WHO had been practised differently (O'Brien & Nolan, 2019). For example, in Belgium, their military personnel have received rabies PrEP before deployment since 2009. Due to their nature of work, instead of providing their armies with conventional rabies PrEP regime, the 2-dose 0.1ml ID 2-visit schedule has been practised (Damanet, Costescu Strachinaru, et al., 2020). There were also timescale variations in the rabies vaccination schedule because they could not comply with the vaccine's exact timing as they had deployed away from their centre (Damanet, Costescu Strachinaru, et al., 2020; Damanet, Strachinaru, et al., 2020), similarly to travellers from Australia. Due to tight departure timing, cost and ability of the travellers to return to the clinic, the treating clinician helped to provide a suitable rabies vaccine schedule, which can be different from the conventional regime (Furuya-Kanamori et al., 2021). Hence, WHO has updated the regime to improve access to the rabies vaccine, especially among the high-risk populations (O'Brien & Nolan, 2019; World Health Organization, 2017a).

Studies demonstrated that rabies vaccine is safe in adults and children (Angsuwatcharakon et al., 2020; Endy et al., 2020; Hardanahalli S et al., 2017; Huttner et al., 2021; Recuenco et al., 2017; Soentjens, Andries, et al., 2019; Soentjens, De Koninck, et al., 2019). The current recommended dose, route and duration of primary rabies vaccine is immunogenic and comparable with the conventional dose, route and duration (Angsuwatcharakon et al., 2020; Damanet, Strachinaru, et al., 2020; Cornelis Adrianus De Pijper et al., 2018; Endy et al., 2020; Furuya-Kanamori et al., 2021; Janewongwirot et al., 2019; Parize et al., 2021; Recuenco et al., 2017; Soentjens, Andries, et al., 2019; Van Nieuwenhove et al., 2019). Additionally, it can be safely administered simultaneously with the JE vaccine in children (Angsuwatcharakon et al., 2020). It is also safe to give MS patients as it does not associate with MS relapse (Huttner et al., 2021).

The circulating rabies virus antibody was detectable even after 9 years post-primary vaccination; up to 80% of participants received the vaccine through the IM route. No booster dose was given in that study (World Health Organization, 2017b, 2018b). Rabies vaccine booster dose after PrEP also confers higher and long-term immune response. Seropositivity can be detected as early as 7 days post-booster dose up to more than 5 years (Cornelis A De Pijper et al., 2021; Endy et al., 2020; Furuya-Kanamori et al., 2021; Parize et al., 2021; Soentjens, Andries, et al., 2019; Soentjens, De Koninck, et al., 2019). Current WHO recommendation indicated that no further PrEP booster doses are needed after primary vaccination for individuals living in and travellers going to high-risk areas (World Health Organization, 2018b). Individual assessment is needed in which booster dose can be considered in frequent travellers that have the potential of direct contact in an extended period in remote settings where rabies is enzootic. (World Health Organization, 2017a). In occupational exposure, professionals continuously exposed to the risk will be required to have regular serology monitoring. A booster dose will be provided if the antibody falls below 0.5 IU/ml (World Health Organization, 2017a, 2018b).

Hence, in general, PrEP with or without booster is recommended to individuals with occupational exposure, such as individuals involved with rabies research and exposed to rabies biological products, animal disease control, wildlife management, involved in dog vaccination campaigns, military and religious individuals that work or reside in remote areas (World Health Organization, 2017a). Frequent travellers to endemic rabies areas will be evaluated for eligibility for receiving PrEP (World Health Organization, 2017a, 2018b). Providing PrEP at the population level will not be cost-effective. Hence, in extreme circumstances where the

rabies exposure is more than six per cent, and rabies immunoglobulin will be difficult to access, PrEP is recommended after being assessed by individual country (World Health Organization, 2017a).

Even though some studies mentioned that the conventional regime using the 3-visit schedule has a higher proportion of participants with higher rabies antibody level and persist at least up to a year as compared to the new recommended regime using a 2-visit schedule (Angsuwatcharakon et al., 2020; Furuya-Kanamori et al., 2021; Janewongwirot et al., 2019; Soentjens, Andries, et al., 2019), even a single visit of PrEP can result with adequate seroconversion (World Health Organization, 2018b). This information is useful for adapting high-risk occupations to easily comply with the new rabies vaccine schedule, such as those in the military (Soentjens, Andries, et al., 2019). Furthermore, administering the rabies vaccine through ID does not mean it is inferior to the IM administration. Evidence has shown that its immunogenicity and effectiveness can be equivalent (Denis et al., 2019; O'Brien & Nolan, 2019).

This review provides the latest evidence on rabies pre-exposure prophylaxis' safety, immunogenicity and booster, which could help policy decision-makers to protect vulnerable populations from rabies mortality.

This review is not without limitations. Our study only included published articles in English, excluding local reports in other languages and the grey literature. The strength of this review is most of the articles have study designs that are RCTs and cohort studies which provide good quality evidence even though the risk of bias due to heterogeneity is undeniable. However, most of the included articles did not assess the safety and immunogenicity of novel PrEP schedules for special populations, such as infants, pregnant women or immunocompromised persons, such as people infected with HIV. The use of PrEP in these subpopulations is highly relevant and was included as a priority question by the SAGE working group on rabies. Furthermore, Meta-analysis is not included in this review due to the limited number of literatures that meet the inclusion criteria, which could raise the publication or reporting biases and are likely to produce an inappropriate summary.

CONCLUSION

The now recommended PrEP schedule by WHO provides a shorter vaccine regime that can help reduce the cost, the quantity of vaccine use and the number of visits. It is important that it still provides adequate immunogenicity and effectiveness while simultaneously maintaining user safety for children and adults at high risk.

Conflicts of Interest

No potential conflict of interest was reported by the authors(s).

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Distribution and Trend of COVID-19 Cases and Death among Population in Bachok, Kelantan

Che Muhammad Nur Hidayat Che Nawi[1], Kamarul Imran Musa[1*], Mohamad Hazni Abd Rahim[1], Norain Ahmad[2], Razan Ab. Samat[2]

Abstract

The COVID-19 infection has been widely spread since it was first declared as a pandemic in late 2019. The trend of COVID-19 cases and death varies across regions. The study sought to describe the distribution and trend of COVID-19 cases and death in the Northeast Malaysia region for 2021. This cross-sectional study analyzed data on COVID-19 infection cases and death in 2021 from the COVID-19 surveillance database (eCOVID system). All confirmed COVID-19 cases and death in Bachok, Kelantan from 1 January 2021 until 31 October 2021 were included in the study. Descriptive analysis of trend and distribution of COVID-19 cases and deaths were conducted using R software. A total of 8384 and 151 COVID-19 cases and death were respectively recorded between the study period. Age less than thirty (34%), females (57%), unemployment (44%), clinical category 2 (86%), and unvaccinated individuals (47%) contributed mostly to COVID-19 cases. Meanwhile, only the age category more than 50 (51-60: 22%, 61-70: 30%, > 70: 36%) contributed most to the COVID-19 deaths in Bachok, Kelantan. The COVID-19 cases and deaths peaked in August 2021. The distribution and trend of COVID-19 cases and death vary across different sociodemographic categories and echoed the national and global trends, respectively.

Keywords: COVID-19, Cases, Death, Northeast Malaysia.

*Correspondence Email: drkamarul@usm.my

[1]*Department of Community Medicine, School of Medical Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian Kelantan, Malaysia.*

[2]*Bachok District Health Office, 16300 Bachok, Kelantan.*

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INTRODUCTION

The COVID-19 pandemic has infected 245 million people globally, killing over 5 million, and the pandemic is far from over (WHO, 2021). Meanwhile, in Malaysia, the Covid-19 infections have increased to nearly 2.8 million cases and caused more than 30 thousand death by end of December 2021 (MOH, 2021a). As for Kelantan, the confirmed cases of COVID-19 were nearly 170 thousand and the death toll was nearly 13 hundred deaths for the year 2021 (MOH, 2021a).

Our local COVID-19 situation echoed the trend and distribution of COVID-19 cases and death at the national and global levels. Events such as low compliance to COVID-19 standard operation procedure, the emergence of new COVID-19 variance, and the high prevalence of chronic diseases contributed to the increase in COVID-19 infection cases and deaths in our region (Bernama, 2021; MOH, 2021b; National Institutes of Health (NIH), 2019).

Epidemiological surveillance is the foundation of all preventative and control efforts. Covid-19 surveillance is monitoring the disease's spread to ascertain its progression patterns, including mortality, and to implement preventative and control measures (Ibrahim, 2020). Identification of high-risk patients in hospital and community settings, as well as insights from population-based research, will be critical in assisting us in focusing our community- and hospital-based public health programs (Madahar, Wunsch, Jha, Slutsky, & Brodie, 2021).

Studies regarding the trend and distribution of COVID-19 cases and deaths based on local epidemiological surveillance have been limited. Furthermore, reports on COVID-19 instances and fatalities fluctuate by geographic region, resulting in disparities in outcomes and risk factors (Huang et al., 2020; Sim et al., 2020; Surendra, Elyazar, & 2021, 2021a). The effectiveness of government regulations, epidemic readiness and response, and bias in reporting the real number of COVID-19 cases and deaths have all been speculated as reasons for the gap (Rajgor, Lee, & 2020, 2020). Thus, the present study aimed to provide current distribution and trends on COVID-19 cases and death due to COVID-19 in the northeast Malaysia region for 2021.

METHODS

Study design and data collection

This was a cross-sectional study to observe the distribution and trend of COVID-19 cases and death in Bachok, Kelantan, Northeast Malaysia region. Data were collected from the Bachok eCOVID system (an online database for infectious diseases under the governance of the Ministry of Health Malaysia) and recorded in the patient's proforma. The eCOVID system capture date for the whole and each district in Kelantan state. We applied a universal sampling method to obtain the study sample. The study population included all Polymerase Chain Reaction (PCR), Nasopharyngeal Antigen Rapid Test Kit (NPS RTK-Ag), and Saliva Antigen Rapid Test Kit (Saliva RTK-Ag) verified by healthcare professional confirmed COVID-19 patients recorded by the Bachok District Health Office who either died or were alive between January 2021 until October 2021. We excluded patients with positive home-based self saliva COVID-19 test in our study.

Variables

The retrieved information for independent variables included socio-demographic and clinical characteristics such as age, age group, gender, occupation, ethnicity, citizenship, case category, clinical category, reinfection, and vaccination status. The occupation is divided into six

categories that are not under state control. The private sector category refers to a group of workers in registered private groups or companies. Meanwhile, the self-employed categories is a group of freelance workers or owner of unregistered business. Besides, vaccination status was categorized as complete vaccination if the COVID-19 patients received two doses injection of COVID-19 vaccine of more than fourteen days and non-vaccinated if vice versa. The uncomplete vaccination status is when the COVID-19 patients received only one dose of COVID-19 vaccine or two doses in less than 14 days after getting the COVID-19 infection. The dependent variable will be the COVID-19 status of either of the confirmed cases and death. We review for all individuals investigated for COVID-19 notified for the period indicated.

Statistical analysis

Secondary data with no identifiers were utilized for analysis using R version 4.1.2, a language and environment for statistical computing (R Core Team, 2020). Descriptive analysis of trend and distribution of COVID-19 cases and death were performed using *gtsummary* and *incidence* packages in R (Sjoberg, Whiting, Curry, Lavery, & Larmarange, 2021; Thibaut Jombart, 2020). Sociodemographic and COVID-19 infection characteristics were summarized in table. Meanwhile, frequency histograms were used to depict the COVID-19 trend over the time.

RESULTS

Sociodemographic characteristics and distribution of the COVID-19 cases and death in Bachok, Kelantan

Our analyses for 8535 COVID-19 cases and death in Bachok showed that the majority of the cases were recovered from COVID-19 infection with an overall fatality rate of 1.8%. The age category was predominated by an age group of less than thirty (34.0%), followed by an aged group of thirty-one to forty (22.1%), forty-one to fifty (15.9%), and other age groups. The distribution of COVID-19 infections in our sample was higher in the younger age group. Meanwhile, the dead were mostly occurred among those aged forty years and above (94.7%).

In terms of gender, the occurrence of COVID-19 infection was were higher among females (57.0%) and males (43.0%), respectively. The COVID-19 related deaths were higher among males (56.0%) than females (44.0%). The type of occupation showed that the unemployed category dominated the total COVID-19 infection cases (44.0%) as well as the death (71.8%). Ethnically, the majority of the COVID-19 cases and death were predominated by Malay, 98.4% and 98.6%, respectively. Nearly all of the COVID-19 cases and death were Malaysian.

The COVID-19 cases were categorized based on clinical category upon diagnosis which will help the decision for the admission. Clinically, COVID-19 cases were divided into five categories depending on the severity of the symptoms and signs. In Bachok, nearly 85.0% of the COVID-19 cases were in category 2 upon diagnosis. On the other hand, a total of 55.1% of COVID-19 death recorded among cases in clinical category 3 and above. The rate of reinfection in our sample was 0.2%.

Besides, the occurrence of COVID-19 infection and death varied upon vaccination status with 62.0% of the cases occurring among unvaccinated and incomplete vaccination categories. In addition, a similar trend also occurred for COVID-19 related death as 77.0% of death occurred in those categories. All related information is available in Table 1.

Table 1: Characteristics of the participants

Characteristic	N	Overall, N = 8,535[1]	Recovered, N = 8,384[1]	Dead, N = 151[1]
Age category	8,535			
< 30		2,865 (34.0%)	2,863 (34.2%)	2 (1.3%)
31-40		1,889 (22.1%)	1,883 (22.4%)	6 (4.0%)
41-50		1,353 (15.9%)	1,343 (16.2%)	10 (6.6%)
51-60		1,143 (12.9%)	1,110 (13.1%)	33 (22.1%)
61-70		799 (9.4%)	754 (9.0%)	45 (30.0%)
> 70		486 (5.7%)	431 (5.1%)	55 (36.0%)
Gender	8,535			
Female		4,832 (57.0%)	4,765 (57.0%)	67 (44.0%)
Male		3,703 (43.0%)	3,619 (43.0%)	84 (56.0%)
Occupation	8,535			
Government sector		1,065 (12.2%)	1,059 (13.0%)	6 (4.0%)
Pensioner		159 (1.9%)	149 (1.8%)	10 (6.6%)
Private sector		1,719 (20.2%)	1,712 (20.0%)	7 (4.6%)
Self-employed		1,330 (16.0%)	1,311 (16.0%)	19 (13.0%)
Student		488 (5.7%)	488 (5.8%)	0 (0%)
Unemployed		3,774 (44.0%)	3,665 (43.4%)	109 (71.8%)
Ethnicity	8,535			
Malay		8,405 (98.4%)	8,256 (98.4%)	149 (98.6%)
Chinese		31 (0.4%)	30 (0.4%)	1 (0.7%)
Indian		4 (0.1%)	4 (0.1%)	0 (0%)
Others		41 (0.5%)	41 (0.5%)	0 (0%)
Siamese		54 (0.6%)	53 (0.6%)	1 (0.7%)
Citizenship	8,535			
Malaysian		8,438 (98.9%)	8,288 (98.9%)	150 (99.3%)
Non-Malaysian		97 (1.1%)	96 (1.1%)	1 (0.7%)
Case category	8,535			
Local case		8,447 (99.0%)	8,296 (99.0%)	151 (100.0%)
Import case		88 (1.0%)	88 (1.0%)	0 (0%)
Clinical category (upon diagnosis)	8,535			
Category 1		1,071 (13.0%)	1,059 (13.0%)	12 (7.9%)
Category 2		7,252 (84.3%)	7,196 (85.2%)	56 (37.0%)
Category 3		49 (0.6%)	42 (0.5%)	7 (4.6%)
Category 4		112 (1.3%)	82 (1.0%)	30 (20.3%)
Category 5		51 (0.6%)	5 (0.1%)	46 (30.2%)
Reinfection, Yes	8,535	17 (0.2%)	17 (0.2%)	0 (0%)
Vaccination status	8,535			
Unvaccinated		4,018 (47.0%)	3,916 (47.0%)	102 (67.7%)
Complete		3,241 (38.0%)	3,206 (38.0%)	35 (23.0%)
Incomplete		1,276 (15.0%)	1,262 (15.0%)	14 (9.3%)

[1]n (%) for categorical, mean (SD) for numerical

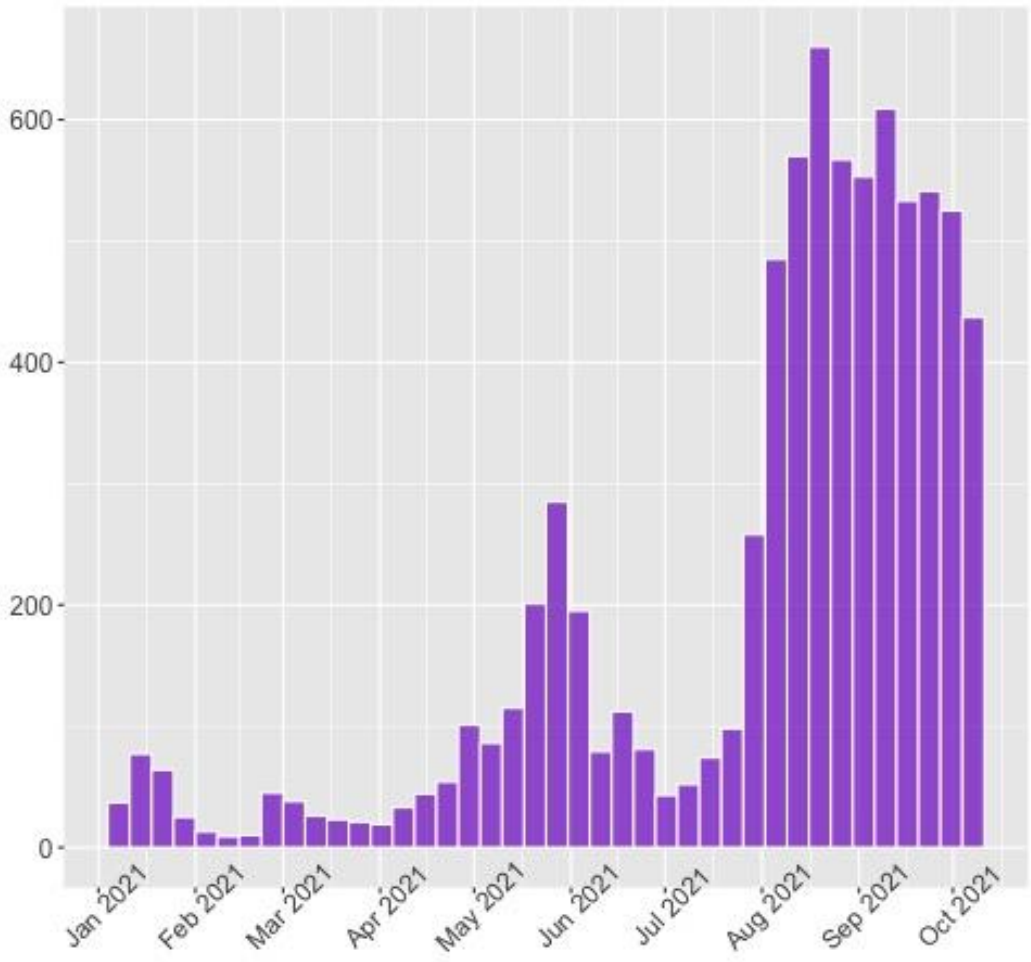

Figure 1: Weekly COVID-19 cases trend in Bachok

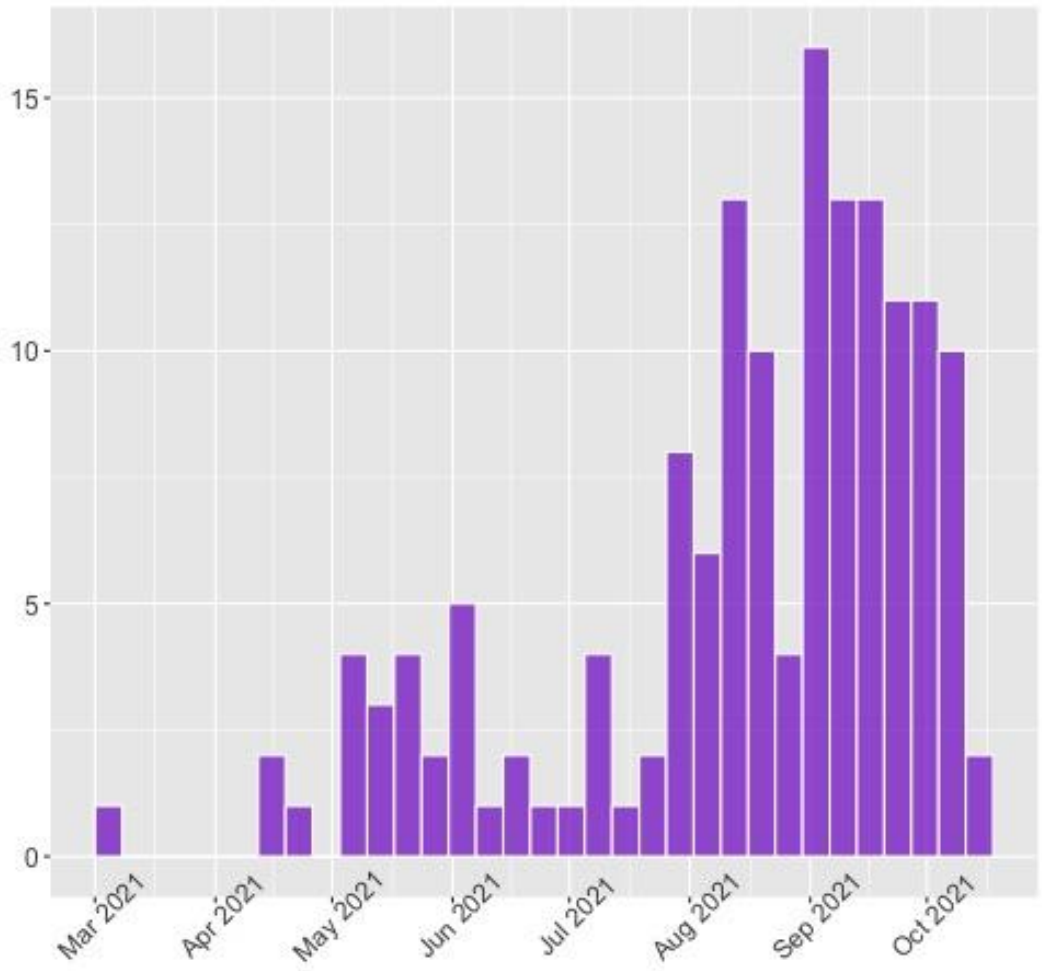

Figure 2: Weekly COVID-19 death trend in Bachok.

Figure 1 and Figure 2 depicted the trend for COVID-19 cases and death in Bachok for the year 2021. In early 2021, the recorded COVID-19 cases were less than a hundred cases while less than five deaths were recorded per week. The COVID-19 cases and death were increasing in a trend started in May and July 2021, reaching the peak in June and August 2021, respectively. The peak of the COVID-19 cases reached nearly six hundred cases per week and nearly 15 deaths were recorded at the end of August 2021. The decreasing trend of COVID-19 cases and death per epidemiological week can be observed after September 2021 onwards.

DISCUSSION

Our analysis showed that younger age group, female, unemployed, clinical category 2, incomplete vaccination, and unvaccinated individuals contributed to the majority of the COVID-19 cases in Bachok, Kelantan. Meanwhile, COVID-19 death mostly occurred among the older age group, males, unemployed, clinical category 3 and above, incomplete vaccination, and unvaccinated individuals. The trend for COVID-19 cases and death showed remarkable increment started in May 2021 and July 2021 and peaked in June 2021 and August 2021, respectively.

The distribution of COVID-19 cases and death in our population is contradicted according to age group. Our findings showed that the younger age group (aged less than forty)

contributed to most of the COVID-19 cases and parallel to findings in other studies (Boehmer, DeVies, & 2020, 2020; Ecdc, 2020; Stokes, Zambrano, & 2020, 2020). Meanwhile, the COVID-19 death in our population was predominated by the older aged group. Similar findings were also reported in Indonesia and the United Kingdom which showed that the older population had a high rate of death as compared to their counterparts (Bhaskaran, Bacon, Evans, & 2021, 2021; Surendra, Elyazar, & 2021, 2021b). The contradicted finding of the rate of COVID-19 infection and death between age groups occurred due to a higher prevalence of comorbidities were identified in the older age group (Guo et al., 2020; MV Blagosklonny - Aging (Albany NY) & 2020, 2020).

The gender distribution of COVID-19 cases in our population was higher in females than in males and the COVID-19 death was higher in males as compared to females. A study conducted across ten European countries also showed a similar trend when females outnumbered the COVID-19 infection cases than males (Sobotka, Brzozowska, Muttarak, Zeman, & di Lego, 2020). Whereas study conducted in China depicted the distribution of COVID-19 cases was equal between males and females (Jin et al., 2020). However, two other studies in China showed contradicted findings where 51% and 73% of the COVID-19 cases were males, respectively (Huang et al., 2019; Wu, Jama, & 2020, 2020). In terms of death distribution, multiple studies in various regions showed that males had a higher rate of death than females due to the presents of co-morbidities and severe COVID-19 infection (Ecdc, 2020; Guo et al., 2020; Jin et al., 2020; MedRxiv & 2020, 2020; MV Blagosklonny - Aging (Albany NY) & 2020, 2020; Williamson, Walker, Bhaskaran, Nature, & 2020, 2020).

Our data showed that unemployment contributed the largest proportion of COVID-19 cases and death for the year 2021. These findings were consistent with sociodemographic and epidemiological trends of the population in Ecuador (Ortiz-Prado et al., 2021). The authors stated that the case fatality rate for unemployed was nearly 17% in Ecuador and at higher risk of death. Unemployment is associated with low education and low net income which predisposed them to COVID-19 infection and death due to lack of health-seeking behavior (Amal, Paramesarvathy, & 2011, 2006; Drefahl, Wallace, Mussino, & 2020, 2020).

The Ministry of Health, Malaysia categorized the confirmed COVID-19 infection cases into five clinical categories as stated in the guidelines (MOH, 2020). Our findings showed that the proportion of COVID-19 cases in category 3 and below was higher as compared to the national data (Sim et al., 2020). Meanwhile, the proportion of COVID-19 cases in categories 4 and 5 is lower as compared to the national data (Sim et al., 2020). The COVID-19 death in Bachok mostly occurred among patients in category 3 and above upon diagnosis. This finding was consistent with two studies conducted among the Indonesian and Indian population which showed that severe clinical category of COVID-19 infection was associated with a higher rate of mortality (Mahendra, Nuchin, Kumar, Shreedhar, & Mahesh, 2021; Surendra et al., 2021a).

COVID-19 vaccination help to protect individuals against severe COVID-19 infection their related death (Bermingham et al., 2021; Nunes et al., 2021; Sadarangani et al., 2021). Our data showed that the mortality rate of COVID-19 infection was decreasing among fully vaccinated individuals which is consistent with the study conducted in the United States (Scobie et al., 2021). The study depicted that the incidence of COVID-19 death was significantly reduced from an incidence rate ratio of 16.6 (95% CI=13.5-20.4) to 11.3 (95% CI=9.1-13.9) when the population achieved the targetted vaccination coverage.

The trend of COVID-19 cases and death in Bachok echoed the national trend reported by the Ministry of Health, Malaysia on the COVIDNOW webpage available at covidnow.moh.gov.my (MOH, 2021a). The national data showed increasing in COVID-19 cases and death in early May and July 2021 which is similar to our COVID-19 cases' trend.

The increase of COVID-19 cases and death during the period was due to the emergence of new COVID-19 variants namely variant of concern and variants of interest which increased the transmission of the disease and causing high fatality rate (CDC, 2021; Loo & Letchumanan, 2021). Besides, a similar trend was also observed in multiple regions of the world as depicted in the World health Organization COVID-19 dashboard which is available at covid19.who.int (WHO, 2021).

This study has a limitation that must be acknowledged as we did not include variables related to pre-existing co-morbidities such as cardiovascular and cerebrovascular diseases. As a result, the COVID-19 cases and deaths cannot be comapred to the distribution and trend of patients' comorbidities.

CONCLUSION AND RECOMMENDATION

The distribution of COVID-19 cases in Bachok predominantly occurred in the younger age group, females, unemployed, and incomplete and unvaccinated individuals. Meanwhile, The COVID-19 deaths in Bachok mainly occurred among the elderly, males, severe clinical category, and incomplete and unvaccinated individuals. The trend of COVID-19 cases and deaths in Bachok followed the national and global trend of COVID-19. We recommend future study to search for signifiacant sociodemographic risk factor associated with COVID-19 death among population in Bachok, Kelantan.

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This study was performed following the principles of the Helsinki Declaration. Ethical approval was obtained from the Medical Research and Ethics Committee of the National Institute of Health, Ministry of Health Malaysia NMRR ID-22-00191-8PM (IIR).

Patient consent was waived as this dataset is secondary data, and we did not take new data from the participants. To obtain permission to reanalyze the data, we have obtained ethical approval from the Medical Research and Ethics Committee, Ministry of Health Malaysia.

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ACKNOWLEDGEMENTS

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