BORNEO EPIDEMIOLOGY JOURNAL | BEJ

REVIEW ARTICLE Open Access

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

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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

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Received: 22/07/2024
Accepted: 11/12/2024

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.

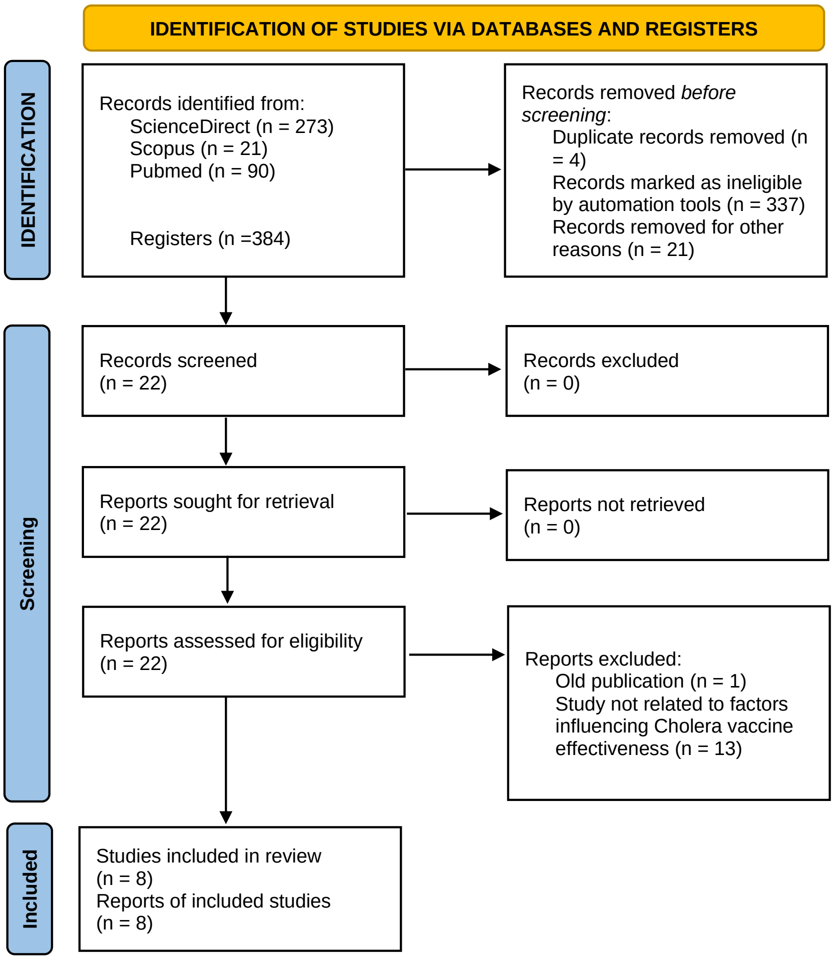

Figure 1: The Prisma flowchart for literature search and selection

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.

Acknowledgements

The authors sincerely thank all the lecturers within the Public Health Medicine Department at Universiti Malaysia Sabah and the peers from the MPH program session 2023/2024 for their consistent support and invaluable assistance in completing this review.

Funding

This review was self-funded.

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