Trials

COMMENTARY Open Access

Collecting and reporting adverse events in low-income settings—perspectives from vaccine trials in the Gambia

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Abstract

Background Despite Africa's significant infectious disease burden, it is underrepresented in global vaccine clinical trials. While this trend is slowly reversing, it is important to recognize and mitigate the challenges that arise when conducting vaccine clinical trials in this environment. These challenges stem from a variety of factors peculiar to the population and may negatively impact adverse event collection and reporting if not properly addressed.

Methods As a team of clinical researchers working within the MRCG (Medical Research Council Unit The Gambia), we have conducted 12 phase 1 to 3 vaccine trials over the past 10 years. In this article, we discuss the challenges we face and the strategies we have developed to improve the collection and reporting of adverse events in low-income settings.

Outcome.

Healthcare-seeking behaviors in the Gambia are influenced by spiritual and cultural beliefs as well as barriers to accessing orthodox healthcare; participants in trials may resort to non-orthodox care, reducing the accuracy of reported adverse events. To address this, trial eligibility criteria prohibit self-treatment and herbal product use during trials. Instead, round-the-clock care is provided to trial participants, facilitating safety follow-up.

Constraints in the healthcare system in the Gambia such as limitations in diagnostic tools limit the specificity of diagnosis when reporting adverse events. To overcome these challenges, the Medical Research Council Unit maintains a Clinical Services Department, offering medical care and diagnostic services to study participants.

Sociocultural factors, including low literacy rates and social influences, impact adverse event collection. Solicited adverse events are collected during home visits on paper-based or electronic report forms.

Community engagement meetings are held before each study starts to inform community stakeholders about the study and answer any questions they may have. These meetings ensure that influential members of the community understand the purpose of the study and the risks and benefits of participating in the trial. This understanding makes them more likely to support participation within their communities.

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Conclusion Conducting ethical vaccine clinical trials in resource-limited settings requires strategies to accurately collect and report adverse events. Our experiences from the Gambia offer insights into adverse event collection in these settings.

Keywords Adverse events, Clinical trials, Low-income countries, Sub-Saharan Africa

Introduction

Clinical trials play a crucial role in assessing the efficacy and safety of medicines, vaccines, and other treatment methods before licensure and in subsequently optimizing their use in new populations and according to new dosing schedules [1]. However, while Africa comprises 17% of the world's population and carries around 25% of the global disease burden [2, 3], this is not reflected in the number of clinical trials undertaken on the continent [4, 5]. Conducting clinical trials in Africa is vital for developing vaccines and treatments for diseases that primarily burden the region [6]. First, significant progress has been made in the development of vaccines for malaria and Ebola virus disease only through clinical trials conducted here [7, 8]. The high incidence of malaria, with over 90% of cases occurring in the region [9], makes it possible to assess efficacy while keeping in line with the ethical principles of equity and justice. Second, extrapolating data from other settings and populations to guide policy in Africa may be unsafe due to distinct socioeconomic, genetic, and environmental differences between regions [6, 10, 11]. For example, while the efficacy of the oral rotavirus vaccines in trials conducted in high-income countries was over 90% over the first 2 years of life, in low-income settings in Africa and elsewhere, the efficacy was considerably lower at below 35% over the first 2 years of life [12]. Finally, as demonstrated during COVID-19, the continent cannot rely on the equitable distribution of vaccines, even in the context of a global pandemic [13]. The Partnership for African Vaccine Manufacturing (PAVM), led by the African Union and Africa Centres for Disease Control and Prevention, is addressing this and aims for 60% of vaccines to be manufactured locally on the continent by 2040 [14]. Conducting clinical trials in Africa will contribute to this vision by building local expertise and capacity as well as establishing regulatory frameworks and quality standards essential for vaccine manufacturing.

International ethical standards, including the Declaration of Helsinki and the International Council on Harmonization Guidelines for Good Clinical Practice (ICH-GCP), have been established to harmonize the conduct of clinical trials across settings and ensure the safety of participants [15, 16]. According to the ICH-GCP (ICH GCP, E6(R2) 1.2), an adverse event (AE) is defined as "any untoward medical occurrence in a participant administered a study product, which does not necessarily have a causal relationship with the study product itself." An adverse event is defined as serious (i.e., an SAE) if it results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, and results in persistent or significant disability/incapacity or a congenital anomaly/birth defect [17]. Good clinical practice guidelines require that all serious adverse events be reported to the relevant sponsor and institutional review board; hence, the identification and reporting of adverse events are important components of ensuring safety in vaccine clinical trials [18]. Furthermore, vaccines are generally held to a higher safety standard than other medications as they are generally administered to healthy individuals for disease prevention rather than treatment [19]. Consequently, accurately collecting and reporting adverse events comprehensively in vaccine clinical trials is vital to ensuring public trust in the vaccine development process [20, 21].

Context

The Gambia has a population of 2.4 million people, with a gross domestic product per capita of $808 [22]. Although progress has been made in recent years [23], the under-5 mortality rate, of 47.9 deaths per 1000 live births, is significantly above the average of 5 deaths per 1000 live births in high-income countries [24, 25]. Lower respiratory tract infections and diarrheal diseases are major contributors to child morbidity and mortality [26–28]. The physician and nurse density in the Gambia is 1.4 doctors and 19.4 nurses and midwives per 10,000 population respectively, compared to an average of 33.4 doctors and 114.9 nurses and midwives in high-income countries [29].

English is the official national language of the Gambia; however, adult literacy rates are relatively low, at 51.2% for women and 65.2% for men [30]. A wide range of languages are spoken, but they are not commonly used in written form. These include Mandinka (38%), Wolof (18%), and Fula (21%) [31, 32]. Thirty-three per cent of the population have access to the Internet [33]. Overall, 95% of the Gambian population is Muslim, with Christianity and West African traditional religions making up the remainder [31].

The Medical Research Council Unit The Gambia (MRCG) is a research institution that has been

conducting medical research in the Gambia and elsewhere in West Africa for over 75 years. The first trials as well as key efficacy trials of *Haemophilus influenzae* type b (Hib) and pneumococcal-conjugate vaccines and the first trials of the RTS/S malaria vaccine in Africa were conducted at the Unit [34–40]. As a team of researchers working within the MRCG, we have conducted 12 phase 1 to 3 vaccine trials over the past 10 years. These trials have ranged in size from less than 100 to more than 3000 participants, enrolling newborns, infants, children, and adults as well as a series of trials enrolling pregnant women, achieving retention rates ranging from 603/660 [91.4%] to 345/346 [99.7%]. Consequently, we have gained considerable experience collecting and reporting adverse events in this setting.

In this article, we explore the context-specific issues and the strategies we have developed to ensure we collect robust safety data in our context.

Health-seeking behavior

Healthcare-seeking behaviors are defined as actions an individual undertakes to find a remedy when they have a health problem [41]. These behaviors are influenced by religious and cultural beliefs as well as the availability, accessibility, and affordability of healthcare [42, 43]. Health-seeking behaviors are particularly important in vaccine trials because participants are typically healthy and may dismiss mild symptoms as unrelated to the study product. A study conducted in the Gambia revealed that only half of parents of children under 5 with a febrile illness sought initial care at a health facility, with 12% first visiting a pharmacy and 5% consulting a traditional healer. Forty-nine percent of individuals chose to seek care from alternative health providers due to their greater accessibility within the local community [42].

Self-medication

When participants or their parents (in pediatric populations) opt for self-treatment, we find that they may not disclose clinical events they experience to clinical trial staff. Furthermore, side effects of these unreported concomitant medications may be incorrectly reported as adverse events due to the investigational product. This is especially important as the country has historically lacked the necessary laboratory facilities for quality control checks on imported drugs, leading to instances of unsafe medications being available over the counter. For instance, between June to September 2022, 66 children died due to contaminated cough syrup containing diethylene glycol and ethylene glycol sold over the counter [44]. This was traced to an Indian pharmaceutical manufacturer and has resulted in a significant tightening in the application of import regulations.

Traditional/spiritual healers

It has been estimated that over 80% of the population of sub-Saharan Africa uses traditional medicines, either independently or as an adjunct to orthodox medicine [45]. Many Gambians believe illness has either a biomedical basis (referred to as *kuraŋ keso* in Mandinka) or is a result of supernatural causes (*ming kesa sande* in Mandinka), such as djinn spirits and witchcraft [46]. For example, seizures are often believed to be of spiritual origin. These strongly held beliefs about the spiritual origin of disease can be resistant to change. Participants seeking the services of a traditional healer may forget to report adverse events once symptoms resolve or may choose to conceal them, perceiving them to be outside the realm of biomedicine.

Additionally, some herbal medications have been reported to be toxic to the liver or kidneys [47, 48]. For example, a study conducted in Nigeria found that over one-third of cases of acute tubular necrosis were due to the use of traditional herbal medicines [49]. It is frequently challenging to clearly define the impact of the concurrent use of traditional medicines and their associated side effects in the reporting and assessment of adverse events in clinical trials. Moreover, in most cases, there is limited information about the nature of the medications taken, which are not labeled or regulated in the same way, making it difficult to establish definitively what was consumed.

Strategies

To limit the impact of self-medication, a requirement for participants to abstain from self-treatment and the use of herbal products during the trial is typically included within the eligibility criteria for the trial [50–52]. This is reaffirmed at each study visit. Furthermore, study sites maintain an on-call rota of clinicians, nurses, field workers, and drivers to respond to any concerns out-of-hours, thus minimizing the need to seek alternative forms of care. Participants are provided with mobile phones that enable free phone calls to the trial staff. This enables participants to contact the study team at any time and allows the study team to reach out for safety follow-up. When a participant calls the team to report a medical concern, different approaches are taken depending on the nature of the complaint; the participant may be reassured, visited at home, or transported to the MRCG clinic for an in-person consultation, where free treatment is provided according to accepted medical standards in the Gambia. In cases where participants are visited at home, all decisions about health concerns are made together with a study doctor. This ensures that all adverse events and concomitant medications are captured and recorded.

When encouraging participants to avoid traditional medicines, it is crucial to approach this non-judgmentally, to avoid under-reporting related to social desirability and the perceived biomedical focus of the study team. Participants are encouraged to disclose any herbal products used and reminded to contact study staff for all clinical concerns. One study indicated that over 50% of users of traditional medicine failed to disclose their use to their healthcare providers [53].

Health systems

The Gambia, like many sub-Saharan African countries, has a healthcare system with finite human resources, physical infrastructure, and diagnostic and clinical supply capacity. The collection and reporting of adverse events must be considered with such limitations in mind.

Healthcare provision

Providing free healthcare to participants in the context of a constrained healthcare system can paradoxically result in overreporting adverse events due to participants reporting illnesses to obtain free medication for other family members. In addition, the provision of free medical care may be perceived as an undue influence on a participant's decision to join a trial and risks some parents allowing their child to join a study solely for access to medication, rather than making an informed decision based on understanding the purpose, risks and benefits of the trial.

Diagnostic limitations

With limited support from routine laboratory and radiological services, clinicians depend more heavily on clinical skills alone to make diagnoses. This limitation typically reduces the specificity of diagnoses. Moreover, cultural beliefs and the short time to burial following death in the Islamic religion, as well as limited capacity for postmortem examination, reduce the ability to determine the cause of death, even in trial participants.

Lack of reliable background data

The absence of robust epidemiological and surveillance data may hinder the analysis of vaccine safety signals. During active follow-up on adverse events in trials, there may be an increase in reported safety events due to the nature of follow-up, compared to data based on passive reporting which may or may not be available. This risks generating apparent safety signals in trials and raising safety concerns that may not be warranted.

Strategies

Accurate collection of adverse events offers indirect benefits to the parents, providing an opportunity for health education on optimal feeding practices and other relevant healthcare-related topics. In addition, MRCG has an established Clinical Services Department (CSD) that provides outpatient and inpatient medical care to study participants as well as the local population. The department also runs ISO15189 and Good Clinical Laboratory Practice (GCLP) accredited laboratory services and radiology services. Furthermore, studies may establish trial-specific additional capacity to characterize adverse events of special interest more fully, such as using respiratory virus multiplex panels and bacterial culture and serotyping. In cases where participants die outside a healthcare facility, verbal autopsies are conducted. These involve standardized interviews with the deceased person's next of kin to determine the cause of death. One study found 67% to 80% concordance between the diagnosis from verbal autopsy and the diagnosis on the death certificate [54]. The use of the minimally invasive autopsy procedures currently under development in related context may further improve this in the future [55].

To limit the overreporting of illnesses during clinical trials, clinical guidelines are used to ensure only medications routinely used in the Gambian healthcare system are prescribed and that thorough clinical assessments are undertaken ensuring the provision of medications to trial participants alone based on clinical indication. The MRCG has also conducted a wide variety of epidemiological studies to enhance the understanding of background disease rates including within three established Health and Demographic Surveillance Systems.

Sociocultural considerations

Literacy rates

In many clinical trials conducted in high-income settings with high literacy rates and internet penetration, participants are provided with diary cards or smartphone apps to document solicited adverse events in the days following the administration of the study product [56, 57]. While this approach facilitates the systematic and real-time collection of adverse events, replicating it in settings in which literacy is limited and internet access inconsistent is challenging. Participants may struggle to reliably self-report adverse events on a diary card or smartphone app.

Highly mobile population

Due to historical factors and shared linguistic and cultural features, tribes and families span international borders, leading to significant internal and international migration between the Gambia, Senegal, Guinea-Bissau, and Guinea-Conakry [58]. Participants frequently travel across international borders, presenting challenges in collecting adverse events, particularly when they do so

without informing the study team in advance. Rarely, this leads to participants being lost to follow-up, resulting in incomplete data and unreported adverse events.

Social dynamics

Social influence significantly affects individuals' decisions to participate in trials and report adverse events to study staff [42, 59]. Healthy participants in vaccine trials may have lower incentives to participate in the trial and report adverse events accurately. Additionally, friends and family may influence study participants to seek care from alternative healthcare providers, leading to potential underreporting of adverse events. In the Gambia, a patriarchal society, women often require approval from husbands, fathers, or other significant male figures before seeking medical care for themselves or their children. This contributes to delayed reporting of adverse events when women are compelled to wait for approval from their fathers or husbands before contacting the study team.

The MRCG has developed significant visibility in the communities in which clinical studies are conducted. In our studies, we do not offer financial incentives to participants, yet we achieve high participation rates through robust community engagement and support. The Unit is well regarded due to the positive impact of research on the communities involved. However, rumors, particularly regarding MRCG "selling" blood samples, persist, which may make people reluctant to enroll in studies and participants less likely to accept blood sampling as part of safety follow-up.

Strategies

Field staff are crucial members of the team who help to mitigate the challenges mentioned above. To replace diary cards given to participants, field staff conduct home visits to collect adverse events. They are provided with paper or electronic case report forms on tablets with online and offline functionality which they use during daily visits to participants' homes following vaccination. We rely on participants providing detailed directions to their homes, due to the lack of street names and house numbers in many parts of the Gambia. In addition, to ensure data quality and consistency, a percentage of these home visits undergo spot checks by senior field staff with data subsequently being reviewed by a trial clinician.

To mitigate the challenge of participants moving out of the study area, we ensure that potential participants have no imminent travel plans for the duration of the study. Field staff are assigned to individual participants to maintain regular contact throughout the study period, increasing the likelihood that we are aware if participants plan to relocate. When a participant travels out of the study area, contact is maintained via telephone and a field worker is dispatched to their location to collect adverse events. Given the small size of the Gambia, we regularly follow participants across the country.

To ensure community engagement and support during clinical trials, community sensitization meetings are held at the beginning of every trial, with community advisory boards (CAB) increasingly playing a role in the design and set up of the studies being conducted. Community sensitization meetings inform the community about the upcoming trial, address questions and rumors, and obtain permission from the village chief (Alkalo) and other key stakeholders to conduct research in the community. At the end of a clinical trial, open days are held to feedback the results of the trial to the community. Community meetings, CABs, and open days are in line with Good Participatory Practice [60] and ensure that not only potential participants but also other influential members of the community understand why the trial is being conducted as well as its procedures, risks, and benefits. This understanding makes them likely to accommodate and support participation within communities. Most members of the field team are resident in the local communities and are therefore able to detect rumors early and arrange additional community sensitization meetings to address these rumors. Our community engagement activities have led to routinely high recruitment and retention rates. The key challenges we have encountered and strategies we have implemented to address them are summarized in Table 1.

Discussion

The challenges we face in collecting adverse events are not unique to the Gambia, as similar conditions are prevalent in other low-income countries. These countries often have similar health-seeking behaviors and social dynamics, weak health systems, and populations with low literacy rates. Therefore, we expect that the strategies we have developed will be generally applicable in other low-income contexts.

Implementing some strategies can be relatively straightforward, such as organizing community sensitization meetings and open days to improve community engagement. Requiring participants to abstain from self-medication and herbal products during the study also helps improve adverse event collection; however, studies that implement such requirements will benefit from committing to providing healthcare for participants throughout the study. This can be achieved by partnering with clinics and hospitals to ensure that participants receive standardized care throughout the study. Conducting home visits to collect adverse events can also be implemented in clinical trials. This active method of collecting adverse events improves the accuracy of reported adverse events.

Table 1 Summary of challenges encountered and strategies to overcome them

	Challenges	Strategies
Health-seeking behavior	Self-medication	• Require participants to abstain from self-treatment during the trial • Provide free, round-the-clock medical care to participants
	Traditional healers	• Require participants to avoid using herbal products during the trial • Provide free, round-the-clock medical care to participants • Maintain a non-judgmental approach
Health systems	Healthcare provision	• Work with MRCG CSD to provide inpatient care for participants
	Diagnostic limitations	• Offer laboratory and radiology services at MRCG CSD • Conduct verbal autopsies as required
	Lack of reliable background data	• Conduct epidemiological studies to understand background disease rates • Establish Health and Demographic Surveillance Systems
Sociocultural considerations	Literacy rates	• Conduct home visits to collect information on adverse events
	Highly mobile population	• Ensure potential participants have no imminent travel plans during the study • Maintain regular contact throughout the study period • Send field workers to collect adverse events from participants who travel
	Social dynamics	• Organize community sensitization meetings • Use community advisory boards • Hold open days for engagement

Other strategies, such as conducting epidemiological studies and establishing health demographic surveys, may be more difficult to implement. These are made possible by the resources available at established research institutions like the MRCG. We recommend increased collaboration between researchers and institutions to allow for the pooling of resources. This will also allow researchers to benefit from the resources available in large institutions across the continent.

This commentary represents the experiences of a diverse team of researchers who have worked together over time. However, we recognize that valuable additional strategies may have been excluded. While many of the points raised apply beyond the Gambia, we also recognize some strategies are context-specific, and local knowledge is essential in their application in other low-income countries.

Conclusion

Conducting clinical research according to international ethical standards in resource-limited settings is vital but poses challenges. We have developed strategies to ensure adverse event data are robust in vaccine trials conducted in the Gambia. While context specific, these insights may be of value to researchers undertaking vaccine and other clinical trials in related settings.

Abbreviations

AE	Adverse event
Africa CDC	Africa Centres for Disease Control and Prevention
CSD	Clinical Services Department
GCLP	Good Clinical Laboratory Practice
ICH-GCP	International Council on Harmonization Guidelines for Good Clinical Practice
MRCG	Medical Research Council Unit The Gambia
PAVM	Partnership for African Vaccine Manufacturing
SAE	Serious adverse event

Acknowledgements
Ikechuckwu Adigweme for substantial reviewing and proofreading

Authors' contributions
Concept and design—AAB, EC.
Drafting of the manuscript—AAB.
Critical revision of the manuscript for important intellectual content—AAB, AOU, AB, MO, MY, DOA, AF, AN, SA, MBJ, LK, LA, OAO, LBJ, MK, BD, AZ, EC.
Supervision—EC.
All authors provided critical feedback and provided final approval of the version to be published.

Funding
Not applicable.

Availability of data and materials
Not applicable.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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Received: 31 March 2024 Accepted: 21 August 2024
Published online: 02 September 2024

References

1. Hansson SO. Why and for what are clinical trials the gold standard? Scandinavian Journal of Public Health. 2014;42(13_suppl):41–8.

2. Niohuru I. Disease Burden and Mortality. In: Niohuru I, editor. Healthcare and disease burden in Africa: the impact of socioeconomic factors on public health. Cham: Springer International Publishing; 2023. p. 35–85.
3. Worldometer. Africa population [11 Jan 2024]. Available from: https://www.worldometers.info/world-population/africa-population/#:~:text=Africa%20Population%20(LIVE)&text=Africa%20population%20is%20equivalent%20to,%22)%2C%20ordered%20by%20population.
4. Viergever RF, Li K. Trends in global clinical trial registration: an analysis of numbers of registered clinical trials in different parts of the world from 2004 to 2013. BMJ Open. 2015;5(9): e008932.
5. Taylor-Robinson SD, Spearman CW, Suliman AAA. Why is there a paucity of clinical trials in Africa? QJM. 2021;114(6):357–8.
6. Marincola E, Kariuki T. Quality research in Africa and why it is important. ACS Omega. 2020;5(38):24155–7.
7. Agnandji ST, Lell B, Soulanoudjingar SS, Fernandes JF, Abossolo BP, Conzelmann C, et al. First results of phase 3 trial of RTS, S/AS01 malaria vaccine in African children. N Engl J Med. 2011;365(20):1863–75.
8. Sulis G, Peebles A, Basta NE. Lassa fever vaccine candidates: a scoping review of vaccine clinical trials. Trop Med Int Health. 2023;28(6):420–31.
9. Organization WH. World malaria report 2023: World Health Organization; 2023.
10. Fortes-Lima C, Schlebusch C. Closing the gaps in genomic research. Trends Genet. 2021;37(2):104–6.
11. Campbell MC, Tishkoff SA. African genetic diversity: implications for human demographic history, modern human origins, and complex disease mapping. Annu Rev Genomics Hum Genet. 2008;9:403–33.
12. Clarke E, Desselberger U. Correlates of protection against human rotavirus disease and the factors influencing protection in low-income settings. Mucosal Immunol. 2015;8(1):1–17.
13. Africa faces 470 million COVID-19 vaccine shortfall in 2021 WHO Africa [30 March 2024]. Available from: https://www.afro.who.int/news/africa-faces-470-million-covid-19-vaccine-shortfall-2021.
14. A Breakthrough for the African Vaccine Manufacturing Africa CDC [20 Mar 2024]. Available from: https://africacdc.org/news-item/a-breakthrough-for-the-african-vaccine-manufacturing/#:~:text=The%20goal%20of%20the%20PAVM,30%20per%20cent%20by%202030.
15. Declaration of Helsinki. http://www.med or jp/wma/helsinki02_j html. 1964;World Medical Association.
16. Integrated addendum to ICH E6(R1): Guideline for Good Clinical Practice E6(R2) International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) [27 Feb 2024]. Available from: https://database.ich.org/sites/default/files/E6_R2_Addendum.pdf.
17. Edwards IR, Biriell C. Harmonisation in pharmacovigilance. Drug Saf. 1994;10(2):93–102.
18. World Health Organization. Handbook for good clinical research practice (GCP): guidance for implementation. Geneva: World Health Organization; 2005.
19. Al Khames Aga QA, Alkhaffaf WH, Hatem TH, Nassir KF, Batineh Y, Dahham AT, et al. Safety of COVID-19 vaccines. J Med Virol. 2021;93(12):6588–94.
20. Yao B, Zhu L, Jiang Q, Xia HA. Safety monitoring in clinical trials. Pharmaceutics. 2013;5(1):94–106.
21. Ozawa S, Stack ML. Public trust and vaccine acceptance–international perspectives. Hum Vaccin Immunother. 2013;9(8):1774–8.
22. World Bank. GDP per capita (current US$) - Gambia, The [30 Mar 2024]. Available from: https://data.worldbank.org/indicator/NY.GDP.PCAP.CD?locations=GM.
23. Rerimoi AJ, Jasseh M, Agbla SC, Reniers G, Roca A, Timæus IM. Under-five mortality in The Gambia: comparison of the results of the first demographic and health survey with those from existing inquiries. PLoS ONE. 2019;14(7): e0219919.
24. UNICEF. Gambia (GMB) - Demographics, Health & Infant Mortality - UNICEF DATA [19 March 2024]. Available from: https://data.unicef.org/country/gmb/.
25. World Bank. Mortality rate, under-5 (per 1,000 live births) - high income [27 March 2024]. Available from: https://data.worldbank.org/indicator/SH.DYN.MORT?locations=XD.
26. Black RE, Cousens S, Johnson HL, Lawn JE, Rudan I, Bassani DG, et al. Global, regional, and national causes of child mortality in 2008: a systematic analysis. The Lancet. 2010;375(9730):1969–87.
27. Barrow AAA, Azubuike PC, Cham D. Prevalence and determinants of acute respiratory infections among children under five years in rural settings of the Gambia: evidence from a national survey. GJEID. 2022;2(1):23–32.
28. Saha D, Akinsola A, Sharples K, Adeyemi MO, Antonio M, Imran S, et al. Health Care Utilization and Attitudes Survey: understanding diarrheal disease in rural Gambia. Am J Trop Med Hyg. 2013;89(1 Suppl):13–20.
29. Measuring the availability of human resources for health and its relationship to universal health coverage for 204 countries and territories from 1990 to 2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet. 2022;399(10341):2129–54.
30. World Bank. Adult literacy in the Gambia is lower among women than among men (2021) 2021 [16 Jan 2024]. Available from: https://genderdata.worldbank.org/countries/gambia-the/.
31. National Review Report on Implementation of the Beijing Declaration and Platform for Action (BPFA) +25 UN Women [16 Jan 2024]. Available from: https://www.unwomen.org/sites/default/files/Headquarters/Attachments/Sections/CSW/64/National-reviews/Gambia.pdf.
32. Juffermans K, McGlynn C. A sociolinguistic profile of The Gambia. Socioling Stud. 2009;3(3):329–55.
33. World Bank. Individuals using the Internet (% of population) - Gambia, The The World Bank [24 Feb 2024]. Available from: https://data.worldbank.org/indicator/IT.NET.USER.ZS?locations=GM.
34. Campbell H, Byass P, Ahonkhai VI, Vella PP, Greenwood BM. Serologic responses to an Haemophilus influenzae type b polysaccharide-Neisseria meningitidis outer membrane protein conjugate vaccine in very young Gambian infants. Pediatrics. 1990;86(1):102–7.
35. Mulholland EK, Byass P, Campbell H, Fritzell B, Greenwood AM, Todd J, Greenwood BM. The immunogenicity and safety of Haemophilus influenzae type b-tetanus toxoid conjugate vaccine in Gambian infants. Ann Trop Paediatr. 1994;14(3):183–8.
36. Mulholland K, Hilton S, Adegbola R, Usen S, Oparaugo A, Omosigho C, et al. Randomised trial of Haemophilus influenzae type-b tetanus protein conjugate vaccine [corrected] for prevention of pneumonia and meningitis in Gambian infants. Lancet. 1997;349(9060):1191–7.
37. Leach A, Ceesay SJ, Banya WA, Greenwood BM. Pilot trial of a pentavalent pneumococcal polysaccharide/protein conjugate vaccine in Gambian infants. Pediatr Infect Dis J. 1996;15(4):333–9.
38. Cutts FT, Zaman SM, Enwere G, Jaffar S, Levine OS, Okoko JB, et al. Efficacy of nine-valent pneumococcal conjugate vaccine against pneumonia and invasive pneumococcal disease in the Gambia: randomised, double-blind, placebo-controlled trial. Lancet. 2005;365(9465):1139–46.
39. Bojang KA, Milligan PJ, Pinder M, Vigneron L, Alloueche A, Kester KE, et al. Efficacy of RTS, S/AS02 malaria vaccine against Plasmodium falciparum infection in semi-immune adult men in the Gambia: a randomised trial. Lancet. 2001;358(9297):1927–34.
40. Doherty JF, Pinder M, Tornieporth N, Carton C, Vigneron L, Milligan P, et al. A phase I safety and immunogenicity trial with the candidate malaria vaccine RTS, S/SBAS2 in semi-immune adults in the Gambia. Am J Trop Med Hyg. 1999;61(6):865–8.
41. Latunji OO, Akinyemi OO. Factors influencing health-seeking behaviour among civil servants in Ibadan. Nigeria Ann Ib Postgrad Med. 2018;16(1):52–60.
42. Hossain I, Hill P, Bottomley C, Jasseh M, Bojang K, Kaira M, et al. Healthcare seeking and access to care for pneumonia, sepsis, meningitis, and malaria in rural Gambia. Am J Trop Med Hyg. 2021;106(2):446–53.
43. Terefe B, Mulat B, Shitu K, Assimamaw NT. Individual and community level factors associated with medical treatment-seeking behavior for childhood diarrhea among the Gambian mothers: evidence from the Gambian demographic and health survey data, 2019/2020. BMC Public Health. 2023;23(1):579.
44. World Health Organization. Medical Product Alert N°6/2022: Substandard (contaminated) paediatric medicines: World Health Organization; [18 March 2024]. Available from: https://www.who.int/news/item/05-10-2022-medical-product-alert-n-6-2022-substandard-(contaminated)-paediatric-medicines.
45. World Health Organization. Guidelines for Registration of Traditional Medicines in the African Region WHO Africa [21 Feb 2024]. Available from: https://www.afro.who.int/publications/guidelines-registration-traditional-medicines-african-region.
46. O'Neill S, Gryseels C, Dierickx S, Mwesigwa J, Okebe J, d'Alessandro U, Peeters GK. Foul wind, spirits and witchcraft: illness conceptions and health-seeking behaviour for malaria in the Gambia. Malar J. 2015;14:167.

47. Okaiyeto K, Oguntibeju OO. African herbal medicines: adverse effects and cytotoxic potentials with different therapeutic applications. Int J Environ Res Public Health. 2021;18(11).
48. Chitturi S, Farrell GC. Herbal hepatotoxicity: an expanding but poorly defined problem. J Gastroenterol Hepatol. 2000;15(10):1093–9.
49. Kadiri S, Ogunlesi A, Osinfade K, Akinkugbe OO. The causes and course of acute tubular necrosis in Nigerians. Afr J Med Med Sci. 1992;21(1):91–6.
50. Haidara FC, Umesi A, Sow SO, Ochoge M, Diallo F, Imam A, et al. Meningococcal ACWYX conjugate vaccine in 2-to-29-year-olds in Mali and Gambia. N Engl J Med. 2023;388(21):1942–55.
51. Adigweme I, Akpalu E, Yisa M, Donkor S, Jarju LB, Danso B, et al. Study protocol for a phase 1/2, single-centre, double-blind, double-dummy, randomized, active-controlled, age de-escalation trial to assess the safety, tolerability and immunogenicity of a measles and rubella vaccine delivered by a microneedle patch in healthy adults (18 to 40 years), measles and rubella vaccine-primed toddlers (15 to 18 months) and measles and rubella vaccine-naïve infants (9 to 10 months) in the Gambia [Measles and Rubella Vaccine Microneedle Patch Phase 1/2 Age De-escalation Trial]. Trials. 2022;23(1):775.
52. Clarke E, Bashorun AO, Okoye M, Umesi A, Badjie Hydara M, Adigweme I, et al. Safety and immunogenicity of a novel 10-valent pneumococcal conjugate vaccine candidate in adults, toddlers, and infants in the Gambia-results of a phase 1/2 randomized, double-blinded, controlled trial. Vaccine. 2020;38(2):399–410.
53. James PB, Wardle J, Steel A, Adams J. Traditional, complementary and alternative medicine use in Sub-Saharan Africa: a systematic review. BMJ Glob Health. 2018;3(5): e000895.
54. Pacqué-Margolis S, Pacqué M, Dukuly Z, Boateng J, Taylor HR. Application of the verbal autopsy during a clinical trial. Soc Sci Med. 1990;31(5):585–91.
55. Breiman RF, Blau DM, Mutevedzi P, Akelo V, Mandomando I, Ogbuanu IU, et al. Postmortem investigations and identification of multiple causes of child deaths: an analysis of findings from the Child Health and Mortality Prevention Surveillance (CHAMPS) network. PLoS Med. 2021;18(9): e1003814.
56. Jiang F, Zhang R, Guan Q, Mu Q, He P, Ye X, et al. Immunogenicity and safety of a live attenuated varicella vaccine in children 1–12 years of age: a randomized, blinded, controlled, non-inferiority phase 3 clinical trial. Contemp Clin Trials. 2021;107: 106489.
57. Laursen SL, Helweg-Jørgensen S, Langergaard A, Søndergaard J, Sørensen SS, Mathiasen K, et al. Mobile diary app versus paper-based diary cards for patients with borderline personality disorder: economic evaluation. J Med Internet Res. 2021;23(11): e28874.
58. Mitsch JF. Bordering on national language varieties: political and linguistic borders in the Wolof of Senegal and the Gambia: The Ohio State University; 2016.
59. Fehr A, Nieto-Sanchez C, Muela J, Jaiteh F, Ceesay O, Maneh E, et al. From informed consent to adherence: factors influencing involvement in mass drug administration with ivermectin for malaria elimination in The Gambia. Malar J. 2021;20(1):198.
60. World Health Organization. Good Participatory Practice [30 March 2024]. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-trial-of-covid-19-vaccines/good-participatory-practices#:~:text=Good%20Participatory%20Practice%20for%20Emerging%20Pathogens%20(GPP%2DEP)%3A%20a,emerging%20and%20re%2Demerging%20pathogens.

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