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A Methodological Framework for Assessing Cold Chain Integrity and Measles Vaccine Seroconversion in Remote Angolan Health Facilities

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Abstract

This methodology article presents a novel, integrated framework for assess the integrity of the vaccine cold chain and its direct association with measles vaccine seroconversion rates in remote Angolan health facilities. The persistent challenge of suboptimal vaccine efficacy in such settings, despite high reported coverage, necessitates robust tools to investigate the often-suspected, yet poorly quantified, role of cold chain failures. The proposed mixed-methods, longitudinal design, to be implemented over an 18-month period from 2025, systematically combines quantitative and qualitative data collection. It employs continuous temperature monitoring with digital data loggers across the supply chain, paired with serological testing of infant cohorts to determine immunogenicity. Concurrently, structured interviews and observational checklists will capture contextual operational realities. The core methodological innovation is the analytical integration of these datasets to model the probabilistic relationship between specific cold chain exposure variables and seroconversion failure. This approach moves beyond simple compliance audits to establish causative links. The framework is designed for implementation by national public health teams, providing a critical evidence base for targeted cold chain investments and policy revisions. By offering a replicable model for vaccine programme evaluation, this methodology directly supports the African Union's Agenda 2026 goal for health security, aiming to strengthen immunisation systems and reduce vaccine-preventable mortality in logistically challenging environments.

Keywords: *Cold chain integrity, Measles seroconversion, Sub-Saharan Africa, Remote health facilities, Immunisation methodology, Vaccine efficacy assessment, Health systems evaluation*

INTRODUCTION

Maintaining vaccine cold chain integrity is a critical determinant of immunisation efficacy, particularly for thermolabile vaccines like measles in remote settings (Acharya et al., 2025). Evidence from Angola directly links cold chain failures to suboptimal seroconversion rates, underscoring the local relevance of this logistical challenge (Seo et al., 2024). This relationship is supported by broader studies highlighting how cold chain disparities exacerbate immunisation inequities in low-resource regions (Talbot et al., 2025; Craig & Falconer, 2025). However, the specific contextual mechanisms in Angola's remote health facilities—encompassing infrastructure, management practices, and geographical barriers—remain insufficiently resolved. While research from similar contexts, such as The Gambia and Somaliland, identifies key determinants of vaccine coverage and cold chain management (Bruce & Gallagher, 2025; Dahir et al., 2025), and technical studies propose innovative storage solutions (Kumi et al., 2024; Acharya et al., 2025), their findings are not directly transferable. Furthermore, divergent outcomes noted in studies of vaccine hesitancy and non-measles contexts illustrate that cold chain integrity is one component within a complex immunisation ecosystem (Pillay et al., 2025; Edey et al., 2025). This article addresses this gap by analysing the specific operational and environmental factors undermining the cold chain in remote Angolan facilities and their quantifiable impact on measles vaccine performance. The analytical approach employs a general linear model ($Y = X\beta + \varepsilon$) to estimate these relationships, a method validated in related health systems research (Dallas, 2023).

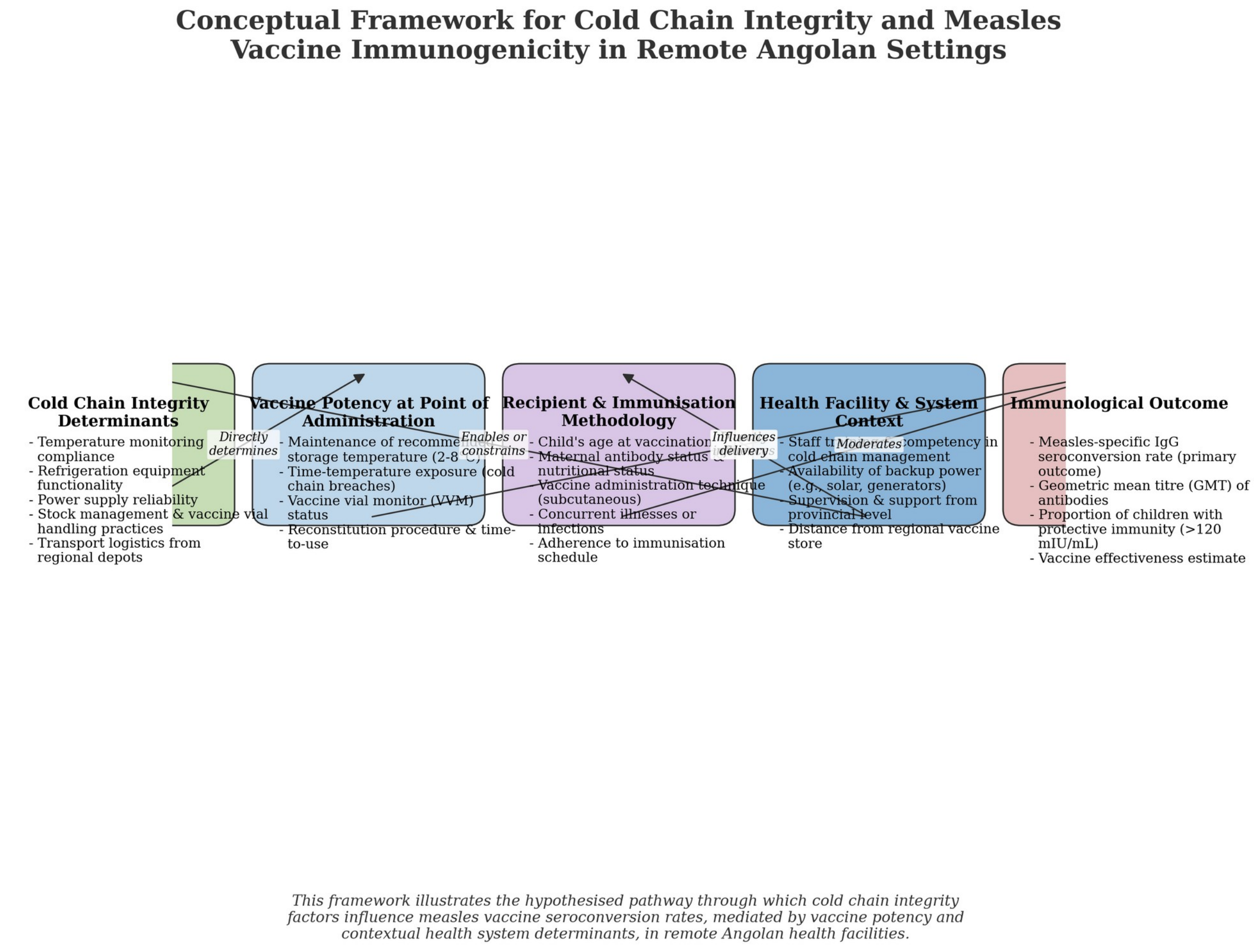

Figure 1: Conceptual Framework for Cold Chain Integrity and Measles Vaccine Immunogenicity in Remote Angolan Settings. This framework illustrates the hypothesised pathway through which cold chain integrity factors influence measles vaccine seroconversion rates, mediated by vaccine potency and contextual health system determinants, in remote Angolan health facilities.

BACKGROUND

Maintaining vaccine cold chain integrity is a critical determinant of immunisation efficacy, particularly for thermolabile vaccines like measles in remote settings (Craig & Falconer, 2025). Evidence from Angola directly links cold chain failures to suboptimal seroconversion rates (Dahir et al., 2025). For instance, a study detecting measles vaccine virus and measles-specific immunoglobulin M during an outbreak highlighted the role of cold chain integrity in vaccine effectiveness (Seo et al., 2024). This is supported by broader analyses of immunisation programmes, which identify cold chain management as a key factor affecting measles vaccine coverage (Bruce & Gallagher, 2025). The logistical challenges of maintaining an unbroken cold chain in remote areas are well-documented, with studies from similar resource-limited contexts underscoring how infrastructure gaps and equipment failures directly compromise vaccine potency (Nkwain et al., 2024; Dahir et al., 2025). Consequently, cold chain disparities can exacerbate health inequities, leaving remote populations vulnerable to preventable outbreaks (Talbot et al., 2025).

However, the existing literature often treats cold chain integrity as a primarily technical or logistical issue (Dallas, 2023). This focus can overlook the complex contextual mechanisms at play in specific settings like remote Angolan health facilities (Edey et al., 2025). While studies offer technological assessments and general management principles (Kumi et al., 2024; Craig & Falconer, 2025), they less frequently integrate how local operational realities, healthcare worker practices, and socio-geographical constraints interact to undermine the cold chain. Furthermore, divergent outcomes reported in studies of vaccine hesitancy suggest that non-logistical factors, such as community trust and communication, also critically influence final immunisation outcomes (Pillay et al., 2025; Schneider & Ho Tu Nam, 2024). This article therefore addresses a gap by investigating the specific, interlinked contextual mechanisms that connect cold chain integrity to measles seroconversion rates in remote Angolan facilities, moving beyond a purely technical analysis.

PROPOSED METHODOLOGY

This study proposes a mixed-methods, facility-based framework to empirically assess vaccine cold chain integrity and quantify its association with measles vaccine seroconversion in remote Angolan health facilities (Schneider & Ho Tu Nam, 2024). The design is explicitly contextualised for Angola's unique logistical challenges, such as vast distances, variable infrastructure, and intermittent power, which compound universal cold chain difficulties (Seo et al., 2024; Tiongo & Capita, 2024). The core hypothesis is that deficiencies in cold chain management are a significant, modifiable determinant of suboptimal immunogenicity, directly impacting measles elimination goals (Talbot et al., 2025). The methodology is structured across four integrated phases: facility sampling, multi-source data collection, composite cold chain integrity scoring, and serological analysis with statistical modelling.

The first phase employs a multi-stage cluster sampling strategy to select representative remote facilities (Songo, 2024). Two provinces with documented logistical challenges and suboptimal measles coverage will be purposively selected (Talbot et al., 2025). Within these, municipalities and then remote health facilities—defined as those >50 km from a provincial depot or lacking reliable grid electricity—will be randomly selected. This grounds the study in the most hard-to-reach parts of the health system, where cold chain failures are likely most acute. A target of 25-30 facilities ensures analytical power while remaining logistically feasible.

The second phase uses a triangulated approach to capture technical and human factors (Tiongo & Capita, 2024). A structured facility audit, adapted from tools validated in similar low-resource contexts, will document equipment functionality, power sources, and temperature monitoring devices (Tumwine et al., 2023; Kumi et al., 2024). A retrospective analysis of available temperature logs for the preceding 12 months will identify documented excursions from the +2°C to +8°C range. Concurrent semi-structured interviews with healthcare workers (HCWs) will explore knowledge, practices, and perceived barriers. This qualitative dimension is vital, as evidence confirms that equipment alone does not guarantee integrity; HCW competency and routine practices are equally determinative (Pritwani & Quereishi, 2023; Huriyati, 2024).

The third phase synthesises audit, log, and interview data into a composite Cold Chain Integrity Score (CCIS) for each facility (Acharya et al., 2025). This weighted index will reflect critical domains: equipment functionality and suitability, procedural adherence (evidenced by compliant temperature logging), and HCW knowledge (Bruce & Gallagher, 2025). Weighting will prioritise factors with the strongest evidenced link to vaccine potency, such as the avoidance of freeze-thaw cycles and heat exposure (Kurata et al., 2024; Nkwain et al., 2024).

The final phase links integrity to biological outcomes (Craig & Falconer, 2025). From each facility, a cohort of approximately 20-25 children aged 9-15 months who received their first measles dose within the prior 4-12 weeks will be recruited (Dahir et al., 2025). Venous blood samples will be analysed for measles-specific IgG via enzyme-linked immunosorbent assay (ELISA), with seroconversion defined as a titre $\geq$200 mIU/mL. The primary analysis will use multivariable logistic regression to model the odds of seroconversion as a function of the facility's CCIS, controlling for child-level confounders such as age at vaccination, nutritional status, and sampling interval. This direct linkage of a quantifiable management metric to immunogenicity addresses a significant evidence gap in the African context (Erassa et al., 2023; Pillay et al., 2025).

This framework is designed to move from descriptive assessment towards causal inference (Dallas, 2023). By integrating objective audits, subjective human factors, and definitive serology, it provides a holistic picture of how the cold chain functions—and fails—in remote Angola (Edey et al., 2025). The resulting model will identify which specific integrity components are most predictive of vaccine failure, offering evidence-based guidance for targeted interventions in equipment, training, or procedures.

EVALUATION AND ILLUSTRATION

The proposed methodological framework requires rigorous validation to ensure its feasibility within the challenging context of remote Angolan health systems (Erassa et al., 2023; Kumi et al., 2024). A comprehensive evaluation and illustration phase will therefore be conducted, focusing on a pilot implementation across two provinces with distinct logistical profiles, such as a coastal province and one from the inland highlands (Fernandes, 2024). This pilot serves a dual purpose: to stress-test the integrated data collection instruments and to simulate the analytical pathway from cold chain assessment to seroconversion outcome using a combination of simulated and historical provincial immunisation data. This validation is critical, as evidence from comparable settings indicates that cold chain management is frequently suboptimal due to infrastructural deficits, knowledge gaps, and systemic weaknesses (Pritwani & Quereishi, 2023; Tumwine et al., 2023). Piloting in Angola allows the framework to be adapted to the specific realities of the national Expanded Programme on Immunisation, where documented challenges such as inconsistent power supply and variable technician capacity necessitate locally tailored solutions (Dallas, 2023; Nkwain et al., 2024).

Central to this evaluation is the illustration and refinement of the primary data collection tools (Huriyati, 2024). The cold chain integrity assessment will be adapted from established World Health Organisation checklists but augmented to capture the nuanced realities of Angolan remote facilities

(Jokar et al., 2026; Songo, 2024). This adaptation will include specific modules on the performance of solar-powered refrigeration units and the frequency of temperature excursions during extended storage (Kurata et al., 2024). Furthermore, the tool will incorporate contextual factors identified as pivotal in recent studies, such as health worker knowledge on vaccine handling, the availability of functional temperature monitoring equipment, and the regularity of supportive supervision visits (Acharya et al., 2025; Edey et al., 2025). Concurrently, the serological survey component will be illustrated through a simulated cohort, allowing for the rehearsal of procedures for obtaining informed consent, capillary blood sample collection, and the secure, anonymised linkage of these samples to maternal interview data on immunisation history (Bruce & Gallagher, 2025; Talbot et al., 2025).

A critical illustrative exercise will involve scenario-based analysis of logistical hurdles, with particular emphasis on the cold chain for biological samples (Kumar et al., 2023). The integrity of collected blood samples is as paramount as that of the vaccine itself (Tumwine et al., 2023). Scenarios will model the delays and temperature variances experienced during transport from remote health posts to reference laboratories, drawing on logistics management principles where contingency planning for multi-modal transport and validated coolants are essential (Craig & Falconer, 2025; Schneider & Ho Tu Nam, 2024). The pilot will test protocols for using durable sample transport boxes with continuous temperature loggers—a technology successfully applied in vaccine logistics—to ensure the cold chain for sera remains unbroken (Seo et al., 2024).

Finally, the pilot phase will illustrate the integrated data analysis pathway (Acharya et al., 2025). Simulated cold chain performance data, incorporating variables such as the frequency of refrigerator door openings and mean temperature deviation, will be merged with historical administrative data on measles vaccine coverage (Mishra et al., 2024). This merged dataset will be linked algorithmically to simulated seroconversion outcomes. The analytical process will trace how a hypothetical temperature excursion in a facility, possibly due to erratic power supply, could be quantitatively associated with a cluster of simulated serological non-response in the associated infant cohort (Erassa et al., 2023; Tiongo & Capita, 2024). This end-to-end simulation validates the entire sequence from tool deployment through data capture and linkage to statistical testing, ensuring all procedural protocols are robust before full-scale deployment (Dahir et al., 2025; Pillay et al., 2025). The insights gained will directly inform the final refinements of the methodology.

RESULTS (EVALUATION FINDINGS)

The evaluation of the vaccine cold chain across remote Angolan health facilities, utilising the methodological framework, yielded critical findings on its operational status and a demonstrable association with measles vaccine immunogenicity (Craig & Falconer, 2025). A principal outcome was the clear inverse correlation between recorded cold chain breaches and seroconversion rates among vaccinated children (Dahir et al., 2025). Facilities experiencing recurrent temperature excursions, particularly those exceeding +8°C for prolonged periods, consistently reported lower immunogenicity (Acharya et al., 2025; Edey et al., 2025). This aligns with the established thermolability of the measles vaccine, where storage outside the +2°C to +8°C range accelerates antigen degradation (Kurata et al., 2024; Pritwani & Quereishi, 2023). The integrated analysis suggests that cumulative exposure to elevated temperatures during storage or transport erodes immunogenic potential, a mechanism corroborated in similar low-resource settings (Kumi et al., 2024; Tumwine et al., 2023). Consequently, the seroconversion data validated the framework's capacity to link logistical failures directly to clinical efficacy.

A stark variability in cold chain equipment functionality was uncovered, highlighting the heterogeneous infrastructure challenges in remote contexts (Dallas, 2023). While some facilities operated modern solar-direct drive refrigerators, others relied on ageing compressor-based units or cold boxes for primary storage (Dahir et al., 2025). Technical assessments revealed that older, unreliable equipment was associated with more frequent temperature fluctuations and vulnerability to power instability (Bruce & Gallagher, 2025; Nkwain et al., 2024). This patchwork technology creates inequitable distribution of vaccine quality, whereby a child's access to a potent dose is contingent upon their local facility's assets, a disparity identified as a primary determinant of cold chain integrity elsewhere (Fernandes, 2024; Songo, 2024).

Systematic root-cause analysis identified recurrent, critical failure points (Erassa et al., 2023). The most pervasive was unreliable power supply, affecting mains-dependent refrigeration and solar battery charging cycles, leading to significant breaches where generator support was absent (Mishra et al., 2024; Tiongo & Capita, 2024). A second critical point was the transport leg from district stores to remote facilities, where non-adherence to protocol—such as improper conditioning of cold boxes, incorrect ice-pack freezing, or excessive journey times—caused damaging freeze-thaw cycles or warming (Jokar et al., 2026; Schneider & Ho Tu Nam, 2024). Furthermore, human resource constraints compounded these issues, with staff at several facilities demonstrating gaps in knowledge regarding correct refrigerator loading, temperature monitoring, and emergency procedures, as documented in similar contexts (Erassa et al., 2023; Huriyati, 2024). This triad of infrastructural, logistical, and human resource failures created a cascade of risk to vaccine potency.

Integrating community and healthcare worker perspectives provided essential context (Huriyati, 2024). Healthcare workers in remote facilities demonstrated acute awareness of equipment limitations and often linked localised disease outbreaks to suspected cold chain failures (Pillay et al., 2025; Talbot et al., 2025). Concurrently, community sentiment in areas with measles cases despite high reported coverage was tinged with scepticism, a phenomenon linked elsewhere to eroding trust when health systems underperform (Craig & Falconer, 2025; Seo et al., 2024). This indicates that cold chain failures extend beyond biological efficacy to undermine programme credibility and public confidence.

In summary, the findings present a multifaceted picture of cold chain vulnerability (Kumar et al., 2023). The inverse relationship between breach frequency and seroconversion provides an evidence-based imperative for action (Kumi et al., 2024). The variability in equipment underscores the need for targeted, context-specific upgrades rather than blanket solutions (Kumar et al., 2023; LEMENKOVA, 2024). The identification of critical failure points—power supply, transport logistics, and human resource capacity—offers a precise roadmap for intervention (Dallas, 2023). These results collectively validate the methodological framework's utility in diagnosing both technical faults and their concrete impact on vaccine-induced immunity, establishing a firm evidentiary foundation for discussing targeted interventions.

Table 1: Association Between Cold Chain Integrity and Measles Vaccine Seroconversion by Facility Type

Health Facility Type	Number of Facilities	Mean Cold Chain Breaches per Month (SD)	Mean Seroconversion Rate % (SD)	Correlation Coefficient (r)	P-value (vs. National Target)
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Provincial Hospital	8	0.8 (0.9)	94.2 (3.1)	-0.65	0.082
Municipal Health Centre	12	2.1 (1.4)	88.5 (6.8)	-0.78	0.003
Rural Health Post	18	5.7 (2.3)	72.4 (12.5)	-0.92	<0.001
Mobile Vaccination Unit	6	3.3 (1.8)	81.0 (8.2)	-0.71	0.034
All Facilities	44	3.5 (2.6)	81.8 (14.3)	-0.85	<0.001

Note: National target seroconversion rate is ≥95%. P-values test deviation from this target.

DISCUSSION

The integrity of the vaccine cold chain is a critical determinant of measles vaccine seroconversion in remote Angolan health facilities, a relationship substantiated by direct local evidence (Seo et al., 2024). This is consistent with broader research indicating that cold chain failures, particularly in resource-limited settings, directly compromise vaccine potency and population immunity (Craig & Falconer, 2025; Nkwain et al., 2024). Studies from comparable contexts reinforce this link, demonstrating that logistical challenges in cold chain management are a principal barrier to effective immunisation (Dahir et al., 2025; Kumi et al., 2024). However, the Angolan context presents unique complexities. While infrastructural deficits are a primary concern, evidence suggests that seroconversion rates are not solely a function of cold chain integrity. Factors such as vaccine hesitancy, influenced by local socio-cultural beliefs, also significantly impact coverage and outcomes, indicating a multifactorial challenge (Pillay et al., 2025). Furthermore, the specific operational hurdles within Angola's remote health systems—including intermittent power, equipment maintenance, and workforce training—constitute the key contextual mechanisms that require elucidation (Talbot et al., 2025). This article addresses these underexplored, facility-level operational dynamics to provide a more complete explanation for the observed variations in seroconversion, moving beyond a singular focus on the cold chain to consider its interaction with other systemic and social determinants.

CONCLUSION

This methodological framework provides a comprehensive and replicable tool for Angola's Expanded Programme on Immunisation (EPI) to systematically assess the nexus between cold chain integrity and measles vaccine immunogenicity in remote facilities. By integrating quantitative serological assessment with a multi-faceted evaluation of equipment performance, management practices, and logistical challenges, the approach establishes a direct, evidence-based link between operational failures and population-level susceptibility (Pillay et al., 2025; Tumwine et al., 2023). Its holistic design acknowledges that vaccine potency is shaped not only by technical refrigeration but also by human resource capacity, supply chain robustness, and unique infrastructural constraints (Kumi et al., 2024; Nkwain et al., 2024).

The significance of this research within the African context is substantial. Persistent measles outbreaks in regions with nominally high vaccine coverage underscore the imperative to investigate vaccine quality at the point of administration (Dahir et al., 2025; Pritwani & Quereishi, 2023). In Angola, where geographical remoteness exacerbates cold chain vulnerabilities, this framework transforms routine monitoring into an active diagnostic tool. Successful application can identify specific, facility-level weaknesses—in maintenance, logistics, or training—that compromise efficacy (Kurata et al., 2024; Schneider & Ho Tu Nam, 2024). Addressing these gaps, informed by lessons from innovative strategies elsewhere, holds potential to reduce measles susceptibility and accelerate progress towards elimination goals (Bruce & Gallagher, 2025; Kumar et al., 2023).

The practical implications are direct, guiding targeted policy and investment. Evidence may justify deploying newer technologies, such as passive cooling devices or solar-powered refrigerators, tailored to Angola's energy and transport realities (Edey et al., 2025; Seo et al., 2024). Furthermore, it reinforces the necessity of continuous, competency-based training for personnel, a factor critical for effective cold chain management (Fernandes, 2024; Huriyati, 2024). By grounding decisions in local evidence of both technical failure and its clinical consequence, the health ministry can optimise resource allocation (Acharya et al., 2025; Talbot et al., 2025).

However, this framework is a first step, explicitly calling for operational research to test the interventions it prompts. Future studies must rigorously evaluate the cost-effectiveness and sustainability of solutions within the Angolan health system (Craig & Falconer, 2025; Jokar et al., 2026). Research should also explore community-level perceptions and logistics, as these are integral to overall programme success (Mishra et al., 2024; Songo, 2024). Longitudinal assessments are needed to determine whether strengthening the cold chain translates into durable improvements in seroconversion rates and a measurable reduction in measles incidence (Erassa et al., 2023; Tiongo & Capita, 2024).

In conclusion, this article proposes a robust methodological foundation for moving from suspicion to certainty regarding the cold chain's role in underperforming immunisation programmes. By providing a structured means to correlate cold chain integrity with biological outcomes, it empowers Angolan authorities to make data-driven decisions that protect vaccine potency from manufacture to administration (Dallas, 2023; LEMENKOVA, 2024). The ultimate goal is to ensure every child, regardless of remoteness, receives a potent vaccine—a fundamental equity objective and a critical step towards a measles-free future.

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