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Vaccine vial monitor availability and use in low- and middle-income countries: A systematic review ☆

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ABSTRACT

Introduction: The vaccine vial monitor (VVM) registers cumulative heat exposure on vaccines over time. As low- and lower-middle-income countries transition beyond support from the Global Alliance for Vaccines and Immunization (Gavi), they will assume full responsibility for vaccine financing and procurement. It is unclear to what extent countries transitioning out of Gavi support will continue to include VVMs on their vaccines. This paper aims to systematically review evidence on VVM availability and use in low- and middle-income countries to document factors behind global access to and country demand for VVMs. Such results could help identify actions needed to ensure continued use of VVMs in countries that transition out of Gavi support.

Methods: We performed a systematic review of electronic databases, reference lists, and grey literature in English and French languages with publication dates from 2005 onwards. The studies included were analyzed for the following outcomes: (1) availability and deployment of VVM-labeled vaccines; (2) VVM practices and perceptions in the immunization system; (3) vaccine introduction and decision-making processes; (4) Gavi graduation and vaccine program sustainability.

Results: The study found that VVM availability and use was affected by multiple sourcing of vaccines and the extent to which VVM was included in the vaccine specification in the tendering documents when procuring vaccines. Knowledge about VVM and its impact on the EPI program was found to be high among health workers as well as decision-makers. However, the study also found that weak capacity in key national institutions such as NRA and NPA might impact on demand for VVM. As countries take decisions regarding the adoption of new vaccines, factors such as disease burden and vaccine price may assume greater importance than vaccine characteristics and presentation. Finally, the study found that countries rely largely on the advice and recommendations from technical partners such as WHO and PAHO.

Conclusion: The study concludes that global access to and country demand for VVM are dependent on policy statements and recommendations about VVM by key policy institutions such as WHO and UNICEF. The study also concludes that despite Gavi-eligible countries having access to VVM-labeled vaccines, inclusion is often below 100%. Weak institutional capacity in key national agencies such as NRA and NPA seems to be a contributing factor, while other factors include the procurement of clear national policies on the inclusion of VVM on vaccines, along with the capacity to enforce the policy. Finally, the study concludes that knowledge about VVM and its impact on vaccine program efficiency, safety, and cost is critical for transitioning countries' continuous demand for VVM.

1. Introduction

The World Health Organization (WHO) has issued guidelines recommending that all vaccines used in routine immunization be kept between two and eight degrees Celsius during in-country distribution (the "cold chain") [1]. Excessive heat exposure can

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damage vaccines and result in reduced potency, which can impair development of individual and population immunity. This temperature management recommendation has been standardized for programmatic simplicity.

The vaccine vial monitor (VVM) is a technology that registers cumulative heat exposure on vaccines over time [1]. The technology was developed as a temperature-monitoring device to help health workers know whether a vaccine was still effective and could be used following exposure to potentially damaging heat during, for example, a cold-chain break, or whether it should be discarded. The VVM label provides an indication of the integrity of the cold chain, both in routine storage, and when vaccines are removed from storage for final distribution prior to vaccination sessions. Since their introduction in 1996, VVMs have been placed on most vaccines obtained through United Nations procurement agencies, including those vaccines procured with financial support from the Global Alliance for Vaccines and Immunization (Gavi).

This low-cost technology is a critical support for program staff to promote good temperature management, and provides reassurance of the potency. This is especially important in low-resource settings where vaccines must be removed from the cold chain at the last point of distribution to enable vaccination in locations without refrigeration. The presence of VVMs has also helped avoid the unnecessary discard of vaccines when infrastructure has failed. A 2002 WHO technical review noted that VVMs had "become an invaluable tool to increase coverage through increased access in hard-to-reach communities and in areas with very weak . . . infrastructure" [2]. In 2014, WHO incorporated VVMs into programmatic pre-qualification requirements as a "critical characteristic"[1] needed to ensure vaccine safety and quality [3]. VVMs are incorporated into several indicators of vaccine management quality in the WHO Essential Vaccine Management program [4] that, for example, monitors the proportion of health facilities where vaccines are used are in use before VVMs discard point.

Since the launch of Gavi, low- and middle-income countries have rapidly expanded their EPI programs [5], leading to significant increases in the availability of life-saving vaccines and reductions in under-five mortality [6]. This expansion has also increasingly strained national health systems, including the immunization system and its supply and cold chains in particular [7–9]. As additional antigens are added to the immunization programs in Gavi-eligible countries, some of which are more heat-sensitive vaccines, the risk of vaccine damage due to excessive heat exposure will increase. The inclusion of VVMs on vaccines is therefore increasingly viewed as a critical element to ensure vaccine quality [1,10,24], maximize the use of vaccine stocks, and reduce the risk of administering heat-damaged vaccine.

Transitioning out of Gavi support means that countries assume full responsibility for the financing and procurement of vaccines. The transition period is divided into phases, during which the co-financing obligations rise as the national income grows, until it reaches the threshold (US$ 1580 GNI per capita). The country then transitions out of Gavi support over a period of 5 years. A total of 24 countries are projected to transition out of Gavi support by 2020, and another seven before 2022 [11,12].

Only few studies to date have assessed capacity at country level to address graduation challenges and the extent to which fully transitioned countries are in a position to sustain and expand EPI programs [13–15,25–27] after transition. These studies found institutional weaknesses of varying degrees related to vaccine procurement, financing, and management of EPI programs, which need to be addressed as part of transitioning planning.

[1] "Critical characteristic" is the level below "mandatory characteristic" in the PQS division of vaccine characteristics. It means that a vaccine characteristic such as inclusion of VVM can be excluded if there are strong reasons.

This paper aims to systematically review evidence on VVM availability and use in low- and middle-income countries, and to document factors behind global access to and country demand for VVM technologies. The aim is to identify actions needed to ensure continued use of VVMs in countries that transition out of Gavi support, and highlight the additional information needed to support continued deployment of this technology.

2. Methods

2.1. Search strategy

An electronic literature search was conducted in February–March 2016 that applied the PICOS framework to inform the search strategy [16]. The search aimed to identify peer-reviewed articles, unpublished documents or conference proceedings that reported the following program experiences in low- or middle-income countries: VVM availability and deployment; VVM perceptions and practices; vaccine introduction and decision-making processes (including procurement); and Gavi graduation and vaccine program sustainability. These themes were selected to capture information about the context within which decisions on inclusion of VVM would be made. Since there are no studies specifically looking at critical factors for VVM inclusion on vaccines, data on factors influencing vaccine introduction decision-makers were used as a proxy for conceptualizing decision-making in relation to inclusion of VVM. The primary outcome was global access to and country demand for VVMs.

The search was restricted to English or French language documents published in 2005 or later, which is the period when VVM was included as a minimum requirement for vaccines procured by United Nations agencies. Case studies, evaluation reports, cross-sectional surveys, qualitative studies, review articles, conference abstracts or proceedings, and cost-effectiveness analyses were considered for inclusion in this review. Policy briefs, technical briefs and organizational strategies were considered if retrieved from websites of organizations actively working in this area.

The search strategy included three different methods. First, a systematic database search was conducted in PubMed and Google Scholar using the following terms:

"vaccine vial monitor"
"vaccine AND temperature monitor"
"immunization AND temperature monitor"
"vaccine AND temperature monitoring"
"immunization AND temperature monitoring"
"vaccine demand AND [any of Gavi-eligible countries] AND cold chain"
"vaccine demand AND [any of Gavi-eligible countries] AND price"
"vaccine demand AND [any of Gavi-eligible countries] AND quality"
"vaccine demand AND [any of Gavi-eligible countries] AND sustainability"
"vaccine introduction AND low-income countries AND sustainability"
vaccines AND decision-making"
"Gavi graduation"

Second, reference lists from included studies were manually reviewed to identify other relevant articles. Third, websites of organizations active in this area were searched for relevant papers including WHO, UNICEF, Program for Appropriate Technology in Health (PATH), The Bill & Melinda Gates Foundation, and major pharmaceutical companies.