Mechanisms to Enhance Availability of Vaccines Against Epidemics: a Case Study of Ebola
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PROBLEM ARTICULATION

The frequency of outbreaks due to filoviruses, known for causing hemorrhagic fever, is growing:
• Recent outbreaks: DRC (Ebola – Zaire species / EBOV, 2022), Uganda (Ebola – Sudan species / SUDV, 2022), and Equatorial Guinea & Tanzania (Marburg / MARV, 2023)
• Shift from rural, hard-to-reach areas and conflict zones to more urban areas
• Endemic to Sub-Saharan Africa, but can lead to significant global health security risks

Numerous challenges hinder timely availability of vaccines against epidemic-prone pathogens:
• Limited commercial viability given small and sporadic demand, leading to a higher barrier to entry and opportunity cost than typical vaccine development and commercialization efforts
• Uncertainty around viral strain, clinical effectiveness and cost-effective post-licensure use of vaccines
• Low thermostability puts pressure on already-strained downstream supply chains

As EBOV is the only filovirus with approved vaccines, an overview of historical outbreaks (Figure 1) and phases of development for vaccines (Figure 2) are shown below.

RESULTS: CAUSAL LOOP DIAGRAMS

Objective: Design candidate vaccine
General dynamics: Spillover events (animal-to-human transmission) increase the disease burden, leading to rapid growth in the at-risk population (loop b). Non-pharmaceutical control strategies (loop a) are initially the only option to protect population, while shifting priority towards vaccine needs is a trade-off.

EBOV case: During outbreaks, emphasis is on containment strategies (e.g., isolation) and prophylactic interventions (e.g., safe and effective treatments). Most outbreaks were mostly in rural areas and short-lived, thus limited investment in pre-clinical vaccine development other than for biosafety reasons.

Criteria for transition: A sufficiently long period of EBOV transmission to further prioritize vaccines and start clinical trials.

Figure 1: A) Confirmed EBOV cases reported by country and outbreak year from the first recorded outbreak in 1976 until 2014; B) Monthly reported cases during the 2014-2016 West Africa Ebola Epidemic, the worst Ebola outbreak in history.

METHODOLOGY

Develop a dynamic hypothesis on protecting populations at-risk of EBOV infections, focusing on availability and uptake of EBOV vaccines

OBJECTIVES

Identify post-licensure challenges that jeopardize the sustainability of the EBOV vaccine supply chain

METHODOLOGY

Literature review – 50 sources: epidemiology, RM&D, manufacturing, supply chain, regulatory, finance, strategy

Stakeholder interviews – 20 interviews: industry, multilateral agencies, government, foundations, NGOs

Data collection – Standardized documentation process based on DataMatics (Fer et al., 2022) and qualitative analysis based on the genetically transmitted qualitative method (Tomassen-Contalto et al., 2022)

CLDs - SDFs

Validation – 45-50 SDQs: sustainability, safety, efficacy, cost-effectiveness, mechanism, translation, ethics, governance, accountability

Figure 3: System dynamics approach for developing causal loop diagrams (CLDs) and stock-and-flow diagrams (SDFs) based on existing frameworks focused on iterative analysis (e.g., Sterman, 2000; Luna-Rayes & Andersen, 2003; Decouttere et al., 2016).

Figure 2: A) Phases in the development and commercialization of EBOV vaccines; (B) Select events related to the supply of EBOV vaccines, showing a long delay to licensure by stringent authorities (FDA – U.S. Food & Drug Administration, EMA – European Medicines Agency). Two vaccines have receivedWHO pre-qualification: Merck – Ervebo (for outbreak use), Janssen – Zadonov/Influenza (for preventive use).

Figure 4: Description of dynamics following phases (colors) described in Figure 2: A) pre-clinical phase, B) clinical phase, C) post-licensure phase, specifically, emergency vaccine stockpile for use during outbreaks (Merck, and) D) post-licensure phase, specifically, preventive vaccine use prior to outbreaks (Janssen)

CONCLUSIONS

• Challenges emerge from diverging priorities (e.g., commercial, humanitarian, public health) and their incentives
• Support from partners (e.g., product development, GAVI funding) has significant impact on aligning supply-demand
• For each CLD, unique sources of delay and loop dominance influence dynamics, pointing to levers for transitioning towards a more sustainable system and lower disease burden

FUTURE WORK

Translate insights into SDFs and policy design to enhance sustainability
• Data collection, parameter estimation, and sensitivity analysis
• Replicate reference models and validate complex supply-demand dynamics with a broad group of stakeholders
• Quantitative simulation and scenario comparison for key problems in the post-licensure phase (e.g., vaccination strategies)

REFERENCES