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Intrapartum antibiotic prophylaxis for prevention of neonatal group B streptococcal disease: a review of key limitations and their implications for vaccine development

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Research Question: What are the key limitations of intrapartum antibiotic prophylaxis as means of preventing group B streptococcal disease among neonates (and others)?

INTRODUCTION

Group B Streptococcal (GBS) infections are a leading cause of perinatal morbidity and mortality worldwide, causing an estimated 90,000 neonatal and infant deaths, 57,000 stillbirths, and up to 3.5 million preterm births annually, among other outcomes.[1]

Intrapartum antibiotic prophylaxis (IAP) is the only currently available intervention to prevent neonatal early-onset GBS (EOGBS) and is the standard of care in most high-income countries and a growing share of low- and middle-income countries (LMICs).[2] Unfortunately, IAP has not eliminated EOGBS incidence even in countries with high coverage and has had negligible impact on late-onset disease, maternal disease, and stillbirths and preterm births **(Figure 1)**, illustrating the need for new tools and strategies to address the remaining GBS burden.

We conducted a literature review to critically evaluate the state of current IAP implementation globally and identify risks and limitations of IAP in anticipation of a future maternal GBS vaccine.

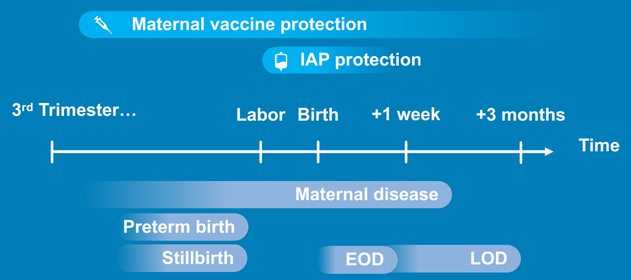


Figure 1: Timeline of GBS disease presentations and possible interventions. GBS disease may present before or after birth in mothers and infants; timing and mechanism of infection differ by presentation. IAP prevents GBS disease occurring among neonates in the first week of life (EOGBS) but is not efficacious against other presentations. By contrast, a maternal vaccine administered in the early third trimester may provide some protection against GBS in both mother and child for weeks before and after birth, including all the presentations indicated above.

Figure 2: Barriers to successful EOGBS prevention by IAP are encountered at each stage of care

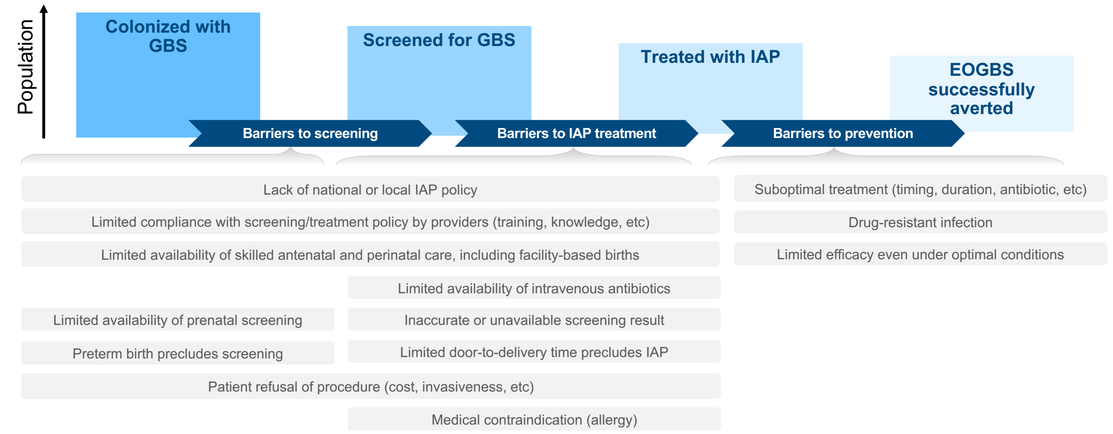
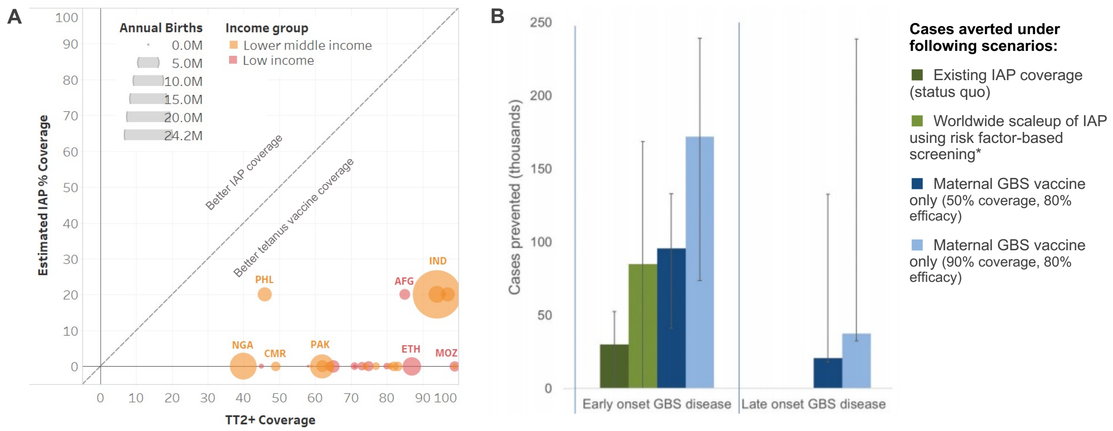


Figure 3: A GBS maternal vaccine may offer advantages for implementation and impact



In low- and lower-middle-income countries, IAP coverage lags behind maternal tetanus immunization. IAP coverage calculated as proportion of eligible women receiving IAP.[2] Maternal tetanus immunization (TT2+) calculated as proportion of pregnant women receiving 2nd or higher dose of a tetanus vaccine during pregnancy (Unicef data).

A future GBS vaccine could prevent large burden of disease not currently addressed by IAP. Reproduced from 2017 Seale et al.[1] Recent estimates indicate that a maternal GBS vaccine with 80% VE and 50% coverage may prevent more cases of GBS EOD than global scaleup of risk factor-based IAP. Such a vaccine may also be efficacious against disease presentations not preventable with IAP (LOD, fetal disease, and maternal disease).

METHODS

We searched PubMed, Google Scholar, and other databases for relevant articles using keywords and phrases related to IAP and GBS. We also manually searched reference lists of relevant articles and reviews for further studies of interest. We included peer-reviewed articles, government reports, internationally-funded health reports, and other clinical guidelines and professional society recommendations.

DISCUSSION

We found that IAP policies, practices, and coverage differ considerably among countries, with clear differences between high- and low-income contexts. Most LMICs do not have a national IAP guideline, and most low-income countries have negligible rates of IAP coverage (data not shown).[2] Factors preventing EOGBS elimination by IAP may include a lack of normative guidance, provider training and compliance, accuracy of screening methods, availability of high-quality antenatal and perinatal care, and efficacy of IAP itself **(Figure 2)**. There is mixed but concerning evidence regarding risks of IAP including antimicrobial resistance, infant gut dysbiosis, and other adverse health outcomes, warranting further investigation (data not shown). A maternal GBS vaccine meeting WHO's preferred product characteristics has the potential to address many of these risks and limitations as an adjunctive intervention to IAP.

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