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Progress towards a Group B streptococcal vaccine – where are we now?☆

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ABSTRACT

The global burden of Group B streptococcal (GBS) disease remains high and an effective vaccine in pregnancy is an unmet public health need. GBS vaccines have been in development for decades, with earlier work providing evidence of immunogenicity and safety but not resulting in a licensed product. More recently, two vaccine candidates have reached advanced stages of clinical development. This article reviews the progress towards a GBS vaccine, the challenges that lie ahead and how they might be overcome.

1. Background

Globally, Group B streptococcus (GBS) is an important cause of infant infection-related deaths [1], estimated to have caused 91,900 deaths in 2020 [2]. In high-income countries (HIC) GBS is responsible for more early-onset infections in the first week of life than any other bacterial pathogen [3–5]. It causes neonatal sepsis, meningitis and pneumonia as well as infections in pregnant people and is associated with stillbirths and preterm births [6].

Vaccination in pregnancy has the potential to prevent a wide spectrum of GBS-related disease, in contrast to currently available prevention strategies. A vaccine is both a longstanding, unmet public health need and an imminent possibility. Here, an overview of progress made towards this and the obstacles still to be overcome are reviewed.

1.1. GBS pathophysiology overview

Infant invasive GBS disease (iGBS) is typically divided into early-onset disease (EOD, occurring on days 0–6 of life) and late-onset disease (LOD, occurring between days 7–89 of life).

In EOD, transmission to the neonate is vertical: colonisation of the vagina/rectum during late pregnancy leads to ingestion or aspiration of bacteria either in-utero or during passage through the birth canal, allowing for bacterial adhesion and invasion via the respiratory or gastrointestinal tract and leading to sepsis or pneumonia [7], most often on the first day of life.

LOD pathogenesis is less well defined but involves adhesion of bacteria to mucosa and subsequent invasion [7,8] leading to sepsis and in around 40 % of cases, meningitis [9]. There is a higher risk of disease linked to certain GBS clonal complexes [10] and a number of GBS virulence factors are specifically linked to invasion of the blood-brain-barrier or brain microvascular endothelial cells [11]. Transmission route is not always clear but may occur after bacterial exposure from a variety of sources including acquisition at delivery, familial colonisation, nosocomial transmission, siblings in a multiple birth, breast milk and others [8]. Prevention of this category of disease is therefore more challenging and indeed current strategies do not address LOD burden [12].

1.2. Global epidemiology and burden of invasive infant disease

In a 2024 systematic review and meta-analysis of maternal and neonatal colonisation rates, a pooled prevalence in pregnant women was estimated to be 17.1 %, (95 % confidence interval (CI) 14.6–19.6) [13]. In another systematic review and meta-analysis of colonisation in pregnancy in 2017, 11–35 % of pregnant people were colonised globally, with significant regional variation: the highest rates reported in the Caribbean (38 %), a median of 19 % for developed regions and lowest in Eastern Asia (11 %) [14]. Based on studies in the pre-intrapartum antibiotic prophylaxis (IAP) era, 50 % of babies born to a colonised parent are also colonised, resulting in invasive disease in 1–2 % of these infants [15,16]. The 2024 meta-analysis estimated a pooled prevalence

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for vertical transmission of colonisation in infants of 1.4 % in countries with >50 % IAP coverage and 34 % in countries with ≤50 % IAP coverage [13].

The spectrum of clinical disease primarily includes neonatal sepsis, meningitis and pneumonia [17]. In 2020, there were an estimated posterior median of 231,800 cases EOD (95 % posterior interval 114,100–455,000) and 162,200 cases of LOD (95 % posterior interval 70,200–394,400) [2]. The same systematic review also estimated that in 2020 GBS was responsible for 91,900 neonatal deaths (44,800–187,800) and 37,100 children (14,600–96,200) with moderate to severe neurodevelopmental impairment. Given the burden of GBS meningitis, it's mortality and association with poor long-term neurodevelopmental outcomes, it's prevention is a key pillar in the World Health Organisation's (WHO) defeating meningitis by 2030 roadmap [18]. Africa, and in particular South Africa, tends to have the highest disease incidence across both EOD and LOD (1.12/1000 livebirths in Africa) with Asia, in particular South East Asia, experiencing the lowest disease incidence (0.30/1000 livebirths) [9]. However, regional variation in case ascertainment remains a challenge for accurate monitoring of global disease burden.

Beyond infant disease, GBS is also associated with an estimated 518,100 (95 % posterior interval 36,900–1,142,300) excess preterm births and 46,200 stillbirths (20,300−111,300) as well as a significant burden of disease in pregnant people [2]. Whilst disease incidence varies with geographical region [6], the greatest burden of morbidity and mortality is almost always experienced in low and middle income countries (LMICs), with sub-Saharan Africa, for example, representing an estimated 55 % of global GBS related infant deaths and south east and central Asia experiencing a high burden of GBS-related stillbirth [2].

2. Current prevention strategies

The predominant prevention strategy against infant invasive GBS is IAP which is implemented variably across regions. This involves administering intravenous antibiotics, most frequently a penicillin, at the time of delivery in the presence of either known GBS colonisation or known risk factors for EOD. The implementation of IAP has led to a significant reduction in EOD in high-income countries (HICs) [19] but has had no impact on LOD, disease in pregnant people, stillbirth and preterm birth [20].

Implementation of IAP is usually either via a universal GBS screening policy (via rectal and/or vaginal swabs obtained in late pregnancy) or a risk-based policy. The majority of HICs conduct universal screening; in the US for example, this has been in place since 2002 with widespread high uptake of testing [20]. The UK has adopted a risk-based policy, meaning IAP is indicated in the presence of risk-factors such as previous infant with invasive disease, GBS bacteriuria, intrapartum fever and preterm delivery [21]. Despite this, an increasing burden of EOD has been demonstrated in the UK through two enhanced surveillance studies conducted 15 years apart (2000–1 [22] and 2014–15 [23]): from 0.48/1000 livebirths (95 % CI 0.43–0.53) to 0.57/1000 livebirths (0.52–0.62).

There have been no randomised controlled trials comparing risk-based and universal screening approaches to EOD prevention. A large US retrospective cohort study [24] included over 600,000 births and estimated the relative risk of EOD for universal screening vs risk-factor screening-based IAP to be 0.46 (95 % CI 0.36–0.60). A recent meta-analysis [25] similarly found a reduced risk of EOD using a universal screening vs a risk-based policy (RR 0.43, 95 % CI 0.32–0.56).

Aiming to answer this question for a UK population, the GBS3 trial is a large, UK-wide cluster randomised trial of universal screening, either at delivery or antenatally, vs risk-based screening with a primary outcome of all-cause early-onset neonatal sepsis [26]. This study has completed recruitment and results are awaited.

IAP has thus far proven a relatively low-cost and successful intervention against EOD but has a number of limitations.

2.1. Limitations of current prevention strategies

A multistate surveillance study in the US [17] found that in 48 % of EOD cases between 2006 and 2015, IAP was not apparently indicated, i.e. almost half of EOD cases were not preventable by the available prevention strategy, predominantly due to a negative GBS screening result. This study [17] also found that even when IAP was indicated, 22 % of cases still did not receive it. This demonstrates the barriers to effective delivery of IAP, even in resource-rich settings. In resource-limited settings the delivery of IAP can be even more challenging, where access to screening as well as administration of the antibiotic may not be consistently available, if at all [27].

In a recent meta-analysis of risk-based vs universal screening IAP [25], 41 % of EO disease cases occurring in a risk-based IAP policy setting did not present any risk-factors that would trigger IAP. In universal screening settings, 24 % of EO cases were born after a negative screening result.

Overall, it has been shown that IAP is given in around 30 % of deliveries, in both risk-based and universal screening settings [25]. This extensive administration of antibiotics contributes to antimicrobial resistance (AMR) rates in invasive isolates, with reduced susceptibility demonstrated at low but increasing rates to beta-lactams [28] and at concerningly high rates to tetracycline and macrolide antibiotics [29,30]. It is important to distinguish between resistance to antibiotics which are commonly used to treat invasive disease (penicillin, gentamicin for example) and those antibiotics used for IAP (penicillin, macrolide and vancomycin resistance) as these differences guide antibiotic guidelines and policies. For example, for those with penicillin allergy, alternative antibiotic choice has often been macrolides such as erythromycin and clindamycin. Resistance to these antibiotics is found in between 30 and 35 % of isolates, worldwide [30]. IAP is also associated with negative effects on the neonatal microbiome [31].

Whilst effective against EO disease, IAP is not able to impact the burden of LO disease, GBS related preterm birth, stillbirth or maternal disease. A GBS vaccine given in pregnancy, by contrast, could address the full spectrum of disease, as well as the problem of AMR, and is widely accepted as the best option for prevention, officially recognised by the WHO as a priority in 2015 [32].

3. A GBS vaccine

3.1. Vaccine development: A long history

Vaccination as a strategy for prevention of iGBS has been supported by decades of previous work. In the 1930's Rebecca Lancefield demonstrated that protection against GBS infection in mice could be achieved using capsular polysaccharide (CPS)-specific rabbit sera [33]. Pivotal studies by Baker and colleagues showed that low levels of naturally occurring maternal antibody to CPS correlate with susceptibility of the neonate to iGBS disease for serotype III [34]. This work was subsequently replicated for serotypes Ia and Ib [35].

A number of mono, bi and multivalent polysaccharide-protein conjugate vaccines against serotypes Ia, Ib, II, III, and V have been studied in pre-clinical and clinical trials, in non-pregnant and pregnant people [36–40]. These candidate vaccines were demonstrated to be safe, immunogenic and to result in placental transfer of antibody with persistence of antibody in infants to at least two months of age [37]. GBS vaccines have traditionally targeted the CPS, but a more recent focus of vaccine development has included conserved surface proteins. None of these vaccines have yet progressed beyond phase II trials, although important lessons were learned along the way. For example, the trivalent CPS conjugate vaccine from GSK/Novartis employed reverse vaccinology for its development, thereby identifying several novel GBS antigens [41].

3.2. Vaccine targets and their global distribution

CPS is an important virulence factor of GBS and the most studied vaccine target [42]. There are 10 antigenically distinct capsular serotypes (Ia/Ib and II to IX). Of these, six serotypes cause over 95 % of infant invasive disease [6,9]. The most extensively examined surface-protein vaccine targets are the highly conserved Alpha-like protein (Alp) family [43]. These cell-wall anchored membrane proteins each have a functionally active N-terminal domain and almost all invasive isolates express at least one of the six Alp family antigens: Alpha C, Rib, Alp1, Alp2, Alp3 and Alp4 [29].

Estimates of the CPS serotype distribution, as well as expression of AlpN, in invasive isolates globally, are important in our understanding of the potential impact of these candidate vaccines. A meta-analysis of iGBS looked at global distribution of CPS-type across 6500 isolates [9]: overall, serotype III was responsible for 61.5 % of all infant disease, Ia 19.1 %, followed by V and Ib. This analysis demonstrated most serotype variability among EOD isolates with LOD being predominantly caused by serotype III (71.5 %). Whilst there is significant regional variation in serotype distribution, serotypes III and Ia still dominate in all regions.

In both a multicentre surveillance study in China [44] and a US multistate surveillance study [29], at least one of four AlpN proteins (Rib, Alpha C, Alp1, Alp 2/3) were expressed in over 98 % of infant invasive isolates. Expression of the Rib protein broadly corresponds with capsular serotype III: in the US surveillance study, 54.7 % of the 506 isolates from young infants were Rib positive with 89.2 % of these being serotype III[29] and in the surveillance data from China, Rib protein expression was found in 93.3 % of serotype III isolates [44]. Another study of South African iGBS isolates [45] found at least one Alp-family protein expressed in 92 % of 648 invasive isolates with Rib predominating in 58.2 % of these and Alp1 in 21.5 %.

3.3. Vaccine candidates

There are GBS maternal vaccine candidates in early stages of development [46], including IVT GBS-06, a hexavalent polysaccharide non-adjuvanted conjugate vaccine manufactured by Inventprise, Inc. and supported by PATH. IVT GBS-06 has entered phase I/II trials in healthy, non-pregnant women [47] (NCT06611371). The vaccine covers serotypes Ia, Ib, II, III, V, VII and a dose-finding study evaluating three dose levels started in November 2024 in the US and South Africa. GSK's Vaccine Institute for Global Health (GVGH) has recently published a proof of concept study for a new formulation of their polysaccharide conjugate vaccine, conjugated to nanoparticles and virus-like particles [48].

However, the two vaccine candidates that are most advanced in clinical development have both undergone phase II trials in pregnant individuals. GBS6 is a hexavalent conjugate vaccine developed by Pfizer, Inc. [49] and GBS-NN/NN2 is a 2-component fusion-protein vaccine developed by MinervaX [50].

GBS-NN/NN2 contains 2 fusion proteins; GBS-NN consisting of the N-terminal domains of Rib and AlpC and GBS-NN2 consisting of Alp1-N and Alp2/3-N. GBS6 contains equal amounts of CPS from serotypes Ia, Ib, II, III, IV, V, all individually conjugated to CRM_{197} protein.

Figs. 1 and 2 show a summary of key studies in the clinical development of the vaccine candidates, GBS6 and GBS-NN/NN2, to date.

For the GBS6 vaccine, dose-escalation trials in both non-pregnant and pregnant adults have demonstrated a good safety profile with a robust immune response, persisting to six months after a single dose of vaccine [49,51]. A 20 microgram per serotype dose has been found optimum for immunogenicity and has been selected for progression to further trials. This dose resulted in higher IgG concentrations in infants at birth when given between 27 and 36 weeks gestation [51]. An aluminium hydroxide adjuvant was shown not to enhance immunogenicity, and to result in increased frequency of pain at the injection site [49,51] and so has not been included in subsequent trials. Trials of a booster dose at 2 years and co-administration with the tetanus, diphtheria and acellular pertussis vaccine have also been carried out as well as a phase II in pregnant people living with HIV.

For the AlpN GBS vaccine, development of the single component formulation, GBS-NN demonstrated a good safety profile and was immunogenic in phase I trials in healthy non-pregnant females [43].

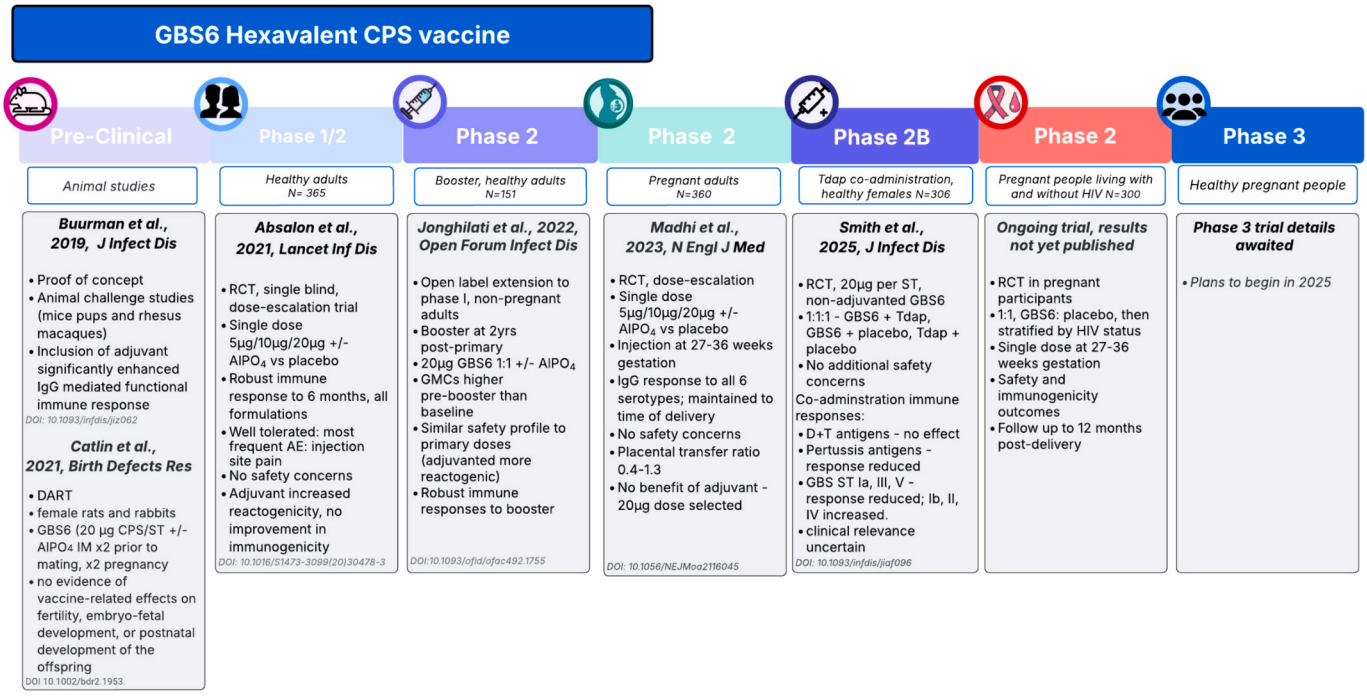

Fig. 1. Overview of key studies in the development of the hexavalent capsular polysaccharide conjugate vaccine candidate for GBS.
Abbreviations: IgG – Immunoglobulin G, AlPO4 – Aluminium Phosphate adjuvant, Tdap – Vaccine containing tetanus, diphtheria, acellular pertussis antigens, HIV – human immunodeficiency virus, ST – serotype, $AlPO_4$ – Aluminium phosphate adjuvant, GMC – Geometric mean concentration, RCT – Randomised controlled trial.

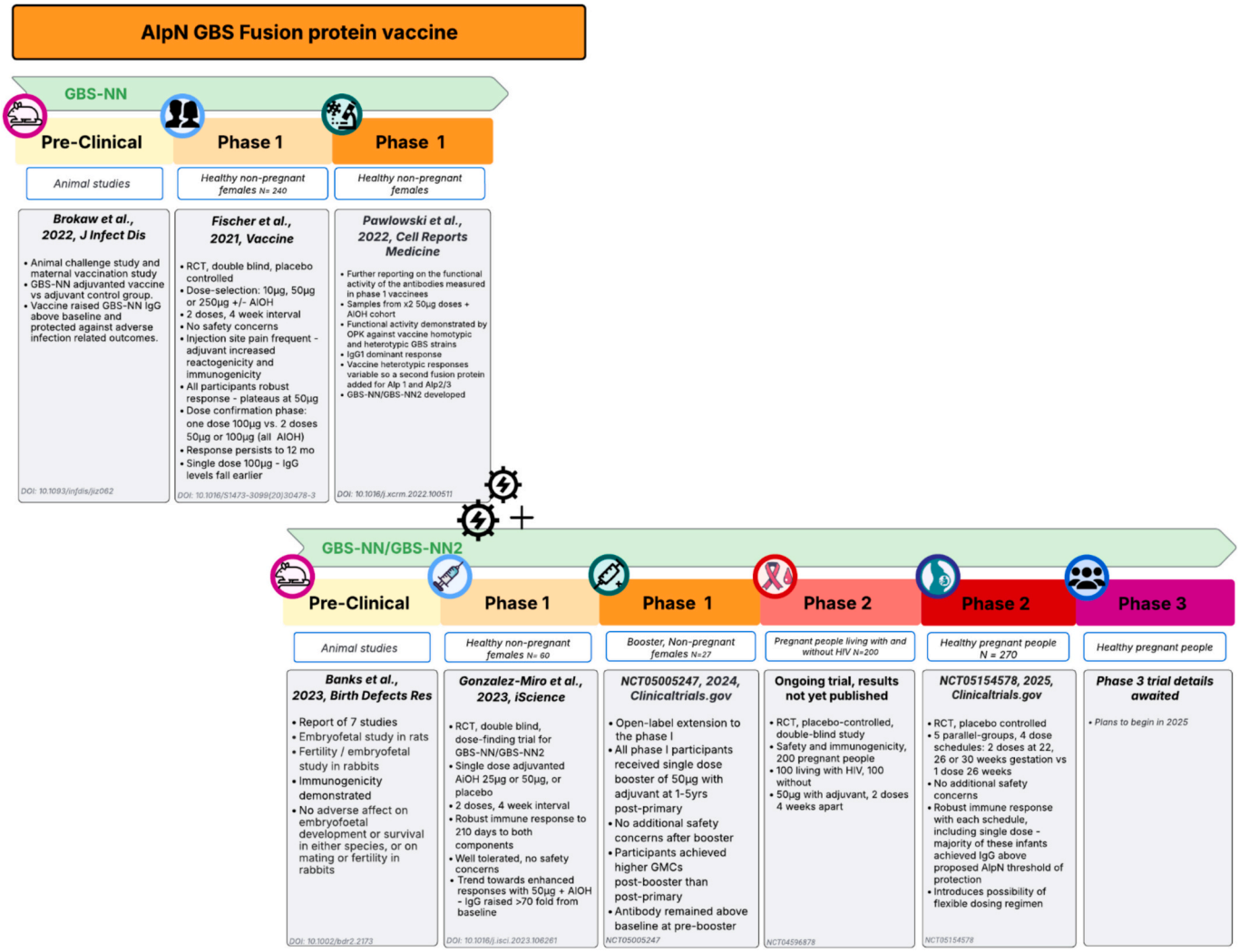

Fig. 2. Overview of key studies in the development of the two-component fusion-protein vaccine candidate for GBS.
Abbreviations: IgG (1) – Immunoglobulin G (class 1), AlOH – Aluminium hydroxide adjuvant, HIV – human immunodeficiency virus, ST – serotype, GMC – Geometric mean concentration, RCT – Randomised controlled trial.

However, although responses to vaccine homotypic Alp antigens were consistent, responses to vaccine heterotypic antigens were variable [52]. An N-terminal domain for Alp 1 and Alp 2/3 was therefore added in a second-generation formulation and GBS-NN/GBS-NN2 has continued in development. This formulation also demonstrated a good safety profile with injection site pain being the most frequently reported symptom [50]. An aluminium hydroxide (AlOH) adjuvant slightly increased reactogenicity but also significantly improved immunogenicity. Dose-finding and dose confirmation studies in non-pregnant adults selected a 50 µg dose with adjuvant [50]. A phase II trial in pregnant participants has shown that there is flexibility in scheduling with a 2 dose schedule at either 22 and 26 or 30 weeks gestation, or a single dose at 26 weeks, robustly immunogenic, allowing different schedules for implementation [53]. A booster dose trial and a phase II in pregnant people living with HIV have been carried out [54,55].

3.4. Barriers to progression

Progression to phase III, clinical efficacy trials has not been possible to date, predominantly due to the prohibitively large sample size of pregnant people and infants required for efficacy outcomes [56]. It is estimated that to demonstrate a vaccine efficacy of 80 % with a population disease incidence of 0.5–1.0/1000 livebirths, 62,000–122,000 pregnant people and their infants (120–250,000 participants) would need to be enrolled. In addition, as the disease endpoint is challenging to assess due to the rapid onset and progression of infant illness and the requirement for invasive samples for diagnosis it would require a sophisticated and comprehensive trial infrastructure. These factors render a clinical efficacy trial logistically challenging, time-consuming and commercially unviable.

Each vaccine candidate will also face its own challenges on the path to licensure. Much of the GBS vaccine-related research to date, including natural immunity studies, have focused on CPS antibody, so supportive evidence for CPS-based vaccines is more available than for surface-protein-based vaccines, although natural immunity and correlate of protection work has also been undertaken for the alpha-like proteins vaccine targets [45,57]. Standardisation of assays is also more advanced for anti-CPS IgG quantitative and functional assessments than for other antibodies such as AlpN IgG. An international consortium has published on standardising and validating these assays [58–60].

However, for CPS-based vaccines there is also the possibility of serotype escape or capsular switching [61], as has been seen with other encapsulated organisms such as pneumococcus [62], whereas protein-based vaccines might maintain longevity of isolate coverage. Serotype replacement may be less likely for GBS than pneumococcus however, due to a smaller number of serotypes and the variation in virulence

between GBS serotypes.

WHO published preferred characteristics for a GBS vaccine in 2017 [63] which gave vaccine manufacturers confidence to continue development, despite these challenges. WHO continues to support the development of GBS vaccines in pregnancy as a priority, publishing a full vaccine value assessment [32] and most recently, the clinical and regulatory development strategies for GBS vaccines in LMICs [64]. Additionally, both candidates have been given PRIME designation (Priority Medicine) by the European Medicines Agency (April 2022 for GBS6 [65] and September 2022 for AlpN GBS [66]) and granted Fast Track Designation by the U.S. Food and Drug Administration (FDA) (March 2017 for GBS6 and January 2023 for AlpN) and FDA Breakthrough Therapy Designation for GBS6 in September 2022. These regulatory designations recognise the potential for important public health impact of these vaccines and aim to facilitate licensure processes, where possible.

3.5. Alternative pathways to licensure

Given the challenges in completing clinical efficacy trials for a GBS vaccine, an alternative approach to licensure is via an immunological endpoint. This approach could enable an agreed serological marker against invasive infant disease to be embedded as an endpoint in an efficacy trial to reduce the sample size requirement and improve feasibility.

The terms *correlate* and *surrogate* of protection are used widely but inconsistently between authors, publications and regulatory agencies [67–69]. The term serological threshold of risk reduction (SToRR) is preferred and the recently published report from WHO-convened stakeholder consultations uses this term [64]. A SToRR can be defined as an immune marker, statistically correlated with reduced risk of invasive disease after vaccination and for GBS is likely to be defined initially by natural immunity studies [64]. A GBS SToRR could be either an immune marker which confers direct protection against disease (a mechanistic SToRR) or one which is correlated with protection but not necessarily related to the mechanism of protection (non-mechanistic) [70]. The validation of immune markers as a SToRR depends on meeting certain criteria, such as the Prentice criteria or the Qin framework [68]. WHO has previously published a review of the evidence needed for a GBS SToRR [56]. This pathway to licensure has been agreed, in principle, by regulatory authorities if there is adequate justification and evidence provided of such an immune marker.

A SToRR pathway to vaccine licensure also has precedent as other vaccines in recent history have been licensed successfully based on SToRR. For example the pneumococcal conjugate vaccine, licensed initially using an aggregate IgG concentration for a few key serotypes [71] with further evidence gathered on additional serotypes after licensure [72]. The *Haemophilus influenzae* type B (HiB) conjugate vaccine was licensed for infants based on a combination of antibody threshold and efficacy data from clinical trials [73]. A number of meningococcal vaccines, including most recently the four component protein meningococcal B vaccine, were also licensed using serum bactericidal assay titre SToRR [74].

However, for a GBS vaccine SToRR, there are a number of additional complexities [75]. In contrast to the above examples, there may be no efficacy data for any GBS vaccine formulation prior to licensure. For GBS a SToRR is likely to vary between EOD and LOD, and between different serotypes. An independent SToRR is also needed for antibodies against AlpN. An aggregate value is not likely to be sufficient given the differing immune responses to these variables and licensure is likely to be based initially on the most common infant disease-causing serotypes such as Ia and III, with less common serotypes being defined in post-licensure studies. Another question is whether binding antibody, functional antibody or both should form the basis of a SToRR for GBS. A functional antibody measurement, such as via opsonophagocytic killing activity assay (OPkA) can seem an attractive and logical choice to provide confidence that the antibody measured in vaccinees is active. However, the assays are difficult to interpret in the context of antibiotic presence in sera; a major problem considering the population studied in natural immunity studies include high, even close to universal, rates of antibiotic exposed sera. In addition, standardisation of these functional assays is more difficult than for binding antibody measurement and they are less scalable and not easily rendered high-throughput.

3.6. Seroepidemiological studies of natural immunity

Multiple case-control studies over the last 30 years have tried to define SToRR antibody levels. However, the results from these studies have not been fully comparable due to methodological differences. Studies have differed in their specimen sources (analysing either maternal or infant sera), antibody detection tests (ELISA or Luminex), standardisation approaches, and choice of statistical analysis – with some employing relative risk reduction calculations while others adopt absolute disease risk frameworks [42,75]. (Table 1).

3.7. Standardisation of approaches

Standardised immunoassays and validated statistical approaches are critical for deriving GBS SToRR. The GASTON (Group B Streptococcus Assay STandardisatiON) Consortium was formed to tackle longstanding challenges in measuring GBS antibody levels, where inconsistent laboratory methods had stalled progress in vaccine development [84]. The consortium developed harmonised protocols for both Luminex-based multiplex immunoassays (MIA) [58] and OPkA [59], establishing uniform procedures for antigen preparation, sample handling, and assay standardisation to minimise variability between laboratories [60]. In addition, GASTON is in the process of validating universal reference sera and quality-control panels for streamlining evaluations of GBS candidates [60].

The application of aligned statistical approaches – particularly the use of standardised case definitions, adjusted generalised linear models, and Bayesian frameworks for threshold estimation will allow for robust cross-study synthesis of protective antibody levels against different GBS serotypes [85].

Overall, this methodological harmonisation is critical for creating a unified evidence base to support a SToRR, particularly as three large-scale GBS seroepidemiological studies (South Africa, US, PREPARE consortium (Europe, Uganda, Malawi and UK)) are close to completion. The resulting pooled data will significantly enhance the power to establish a SToRR and inform a vaccine licensure pathway.

4. The global impact of a vaccine

It has been estimated that GBS vaccination could prevent between 127,000–231,000 (UR 63,000 to 507,000) cases in infants and pregnant people and 60,000–108,000 (UR 22,000–198,000) stillbirths/neonatal deaths annually, assuming 50–90 % coverage with 80 % efficacy [6]. Multiple country-specific or regional epidemiological studies across diverse settings – from sub-Saharan Africa to HICs like the UK, US, and Japan [86–92] have consistently demonstrated that GBS vaccination of pregnant people would likely be more cost-effective than current prevention strategies. A recent study used data from 183 countries to model how a GBS vaccine could reduce infections, deaths, and preterm births worldwide [93]. It calculated potential lives saved and healthcare costs, considering different vaccine prices and coverage levels, while also accounting for uncertainties in the data, such as protection against preterm birth. It was found that vaccination would be cost-effective across all income settings if competitively priced, with particularly transformative potential in high-burden LMICs where healthcare resources are most constrained [93]. These data provide policymakers with a robust evidence base, highlighting that GBS vaccination of pregnant people could not only save tens of thousands of lives annually but also reduce the

Table 1
A summary of the findings of natural immunity seroepidemiological studies of infant iGBS disease, to date.

Study (Year)	Design	Cases (Serotype)	Controls	Onset	Protective thresholds
Capsular polysaccharide					
Lin et al. (2001) [76]	Case-control	50 (Ia)	336	EOD	Ia: 5 μg/ml (maternal) 4 μg/ml (cord/infant)
Lin et al. (2004) [77]	Case-control	26 (III)	143	EOD	III: 10 μg/ml (maternal) 7 μg/ml (cord/infant)
Baker et al. (2014) [78]	Case-control	17 (Ia), 9 (III), 7 (V)	99	EOD	Ia: 0.5 μg/ml (maternal) III: 0.5 μg/ml (maternal)
Dangor et al. (2015) [79], (2021) [80]	Matched Case-control	27 (Ia), 29 (III)	74	EOD + LOD	Ia: 6 μg/ml (maternal) 2.52 μg/ml (infant) III: 3 μg/ml (maternal) 0.95 μg/ml (infant)
Fabbrini et al. (2016) [81]	Case-control	8 (Ia), 23 (III)	280	EOD	Ia: 1 μg/ml (maternal) III: 1 μg/ml (maternal)
Madhi et al. (2021) [82]	Case-control Cohort	14 (Ia), 23 (III)	128	EOD + LOD	Ia: 2.31 μg/ml (maternal) 1.04 μg/ml (cord/infant) III: 3.41 μg/ml (maternal) 1.53 μg/ml (cord/infant)
Madhi et al. (2023) [51]	Case-control Cohort	18 (Ia), 45 (III), 77 (all)	250	EOD + LOD	Ia: 0.755 μg/ml (cord/infant) III: 0.381 μg/ml (cord/infant) All: 0.494 μg/ml (cord/infant)
Saukkoriipi et al. (2024) [83]	Case-control	9 (Ia), 32 (III), 55 (all)	229	EOD + LOD	III: 0.266 μg/ml (cord) All: 0.404 μg/ml (cord)
Alpha-like protein					
Dangor et al. (2023) [57]	Case-control Cohort	46 (Rib), 24 (Alp1)	82	EOD + LOD	Rib: 0.428 μg/ml (cord/infant) Alp1: 0.112 μg/ml (cord/infant)

EOD: Early-onset disease; LOD: Late-onset disease.

substantial economic burden of preterm birth complications and long-term impairment.

5. Beyond licensure – challenges to implementation and monitoring

The licensure of a GBS vaccine represents only the first step in a complex journey. While immunogenicity-based approval may accelerate availability, significant challenges remain in ensuring equitable access, effective delivery, and robust monitoring in high-burden settings.

5.1. Integration into fragile health systems

A primary challenge lies in integrating GBS vaccination into existing maternal and child health platforms, particularly in LMICs [32]. Antenatal care (ANC) attendance varies widely, with sub-Saharan Africa and South Asia reporting the lowest coverage. Even where ANC services exist, competing priorities—such as HIV testing, iron supplementation, and ultrasound screenings—may overwhelm healthcare workers, leading to missed opportunities for vaccination. Strengthening ANC infrastructure and training providers to prioritise vaccine delivery will be critical. Additionally, the vaccine's recommended timing (second or third trimester) must align with local ANC visit schedules. With the WHO's update to antenatal care recommendations in 2016 [94], 8 antenatal visits are now recommended which could improve opportunities for vaccination.

5.2. Co-administration and safety monitoring

Pregnant people may now receive multiple vaccines, including tetanus-diphtheria (TT/Td) or tetanus-diphtheria-pertussis (Tdap), influenza, RSV and, in some HICs, COVID-19. The potential for immune interference or compounded reactogenicity with GBS vaccines remains uncertain, particularly in populations with high HIV prevalence or malnutrition where vaccine responses may be reduced or altered [95,96]. Post-licensure pharmacovigilance systems must be strengthened to detect rare adverse events, utilising networks like the Global Alignment of Immunisation Safety Assessment (GAIA). Standardised case definitions for maternal and neonatal outcomes will be vital to distinguish vaccine-related effects from background pregnancy complications.

5.3. Monitoring impact and serotype replacement

Post-introduction surveillance must address many key questions around the effectiveness of a vaccine against not only iGBS, but also stillbirths and preterm births [97]. In addition, real-world data will be needed to answer questions about the impact on antenatal GBS colonisation, dosing durability across pregnancies, and potential serotype replacement, each presenting unique methodological challenges. The vaccine's potential to reduce GBS-associated preterm births and stillbirths presents a huge opportunity. A vaccine probe study design could help establish causality by comparing rates of these outcomes between vaccinated and unvaccinated populations while controlling for confounding. Post-vaccine introduction, linking immunisation registries with birth outcome databases could provide large-scale observational data to address these questions. The durability of clinical protection across subsequent pregnancies will influence vaccination strategies. If antibody waning necessitates administration in every pregnancy, this could create implementation challenges in low-resource settings with inconsistent ANC attendance. Immunogenicity studies tracking antibody persistence and effectiveness evaluations in multiparous women will help determine optimal dosing intervals. Serotype dynamics require careful surveillance to detect potential shifts in circulating strains. While GBS shows less diversity than some pathogens, monitoring for emerging serotypes or antigenic variants will be crucial. Establishing sentinel surveillance sites with genomic sequencing capacity in high-burden regions should be prioritised to track these trends over time.

5.4. Behavioural and societal challenges

Vaccine hesitancy, fueled by misinformation or distrust in immunisation during pregnancy, could undermine uptake. Engaging local leaders, leveraging trusted community channels, and co-designing communication campaigns with pregnant individuals will be pivotal to building acceptance.

Overcoming these challenges demands a coordinated, multi-sectoral approach. Partnerships between governments, manufacturers, non-governmental organisations, and communities must align to strengthen health systems, ensure equitable access, and monitor the vaccine's real-world impact.

6. Summary and conclusions

In summary, the global burden of GBS-related disease remains high based on a number of recent estimates. The public health need for a GBS vaccine is therefore clear. Vaccine development efforts to date have demonstrated that a GBS vaccine in pregnancy could be safe and efficacious but have not yet resulted in a licensed product. The two most clinically advanced and promising candidates to date face significant challenges before licensure but a number of recent large, seroepidemiological studies, combined with efforts to align the approach to a SToRR definition, mean that licensure via an immunological endpoint is a real possibility. The vital and cross-cutting work needed to address issues of vaccine uptake, vaccine hesitancy, implementation and real-world effectiveness monitoring will require collaboration between many sectors to ensure that a GBS vaccine is able to deliver its full potential.

CRediT authorship contribution statement

N. Thorn: Writing – review & editing, Writing – original draft, Data curation. **K. Karampatsas:** Writing – review & editing, Writing – original draft, Data curation, Conceptualization. **K. Le Doare:** Writing – review & editing. **P.T. Heath:** Writing – review & editing, Supervision, Data curation, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: PTH and KLD act on behalf of their institution as investigators on studies funded/sponsored by multiple vaccine manufacturers including Pfizer and MinervaX. PTH and KLD are members of the UK Joint Committee on Vaccination and Immunisation (JCVI) and members of the WHO GBS Technical Advisory Group (TAG). KLD also carries out work in collaboration with PATH. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. All authors attest that they meet the ICMJE criteria for authorship.

Data availability

No data was used for the research described in the article.

References

[1] Oligbu G, Ahmed L, Ferraras-Antolin L, Ladhani S. Retrospective analysis of neonatal deaths secondary to infections in England and Wales, 2013–2015. Arch Dis Child Fetal Neonatal Ed 2021;106(4):363–9. https://doi.org/10.1136/archdischild-2020-319093.

[2] Gonçalves BP, Procter SR, Paul P, et al. Group B streptococcus infection during pregnancy and infancy: estimates of regional and global burden. Lancet Glob Health 2022;10(6):e807–19. https://doi.org/10.1016/S2214-109X(22)00093-6.

[3] Shane AL, Sánchez PJ, Stoll BJ. Neonatal sepsis. The Lancet 2017;390(10104):1770–80. https://doi.org/10.1016/S0140-6736(17)31002-4.

[4] Cailes B, Kortsalioudaki C, Buttery J, et al. Epidemiology of UK neonatal infections: the neonIN infection surveillance network. Arch Dis Childhood – Fetal Neonatal Ed 2018;103(6):F547–53. https://doi.org/10.1136/archdischild-2017-313203.

[5] Garvey M. Neonatal infectious disease: a major contributor to infant mortality requiring advances in point-of-care diagnosis. Antibiotics 2024;13(9):877. https://doi.org/10.3390/antibiotics13090877.

[6] Seale AC, Bianchi-Jassir F, Russell NJ, et al. Estimates of the burden of group B streptococcal disease worldwide for pregnant women, stillbirths, and children. Clin Infect Dis 2017;65(suppl_2):S200–19. https://doi.org/10.1093/cid/cix664.

[7] Nizet V, Ferrieri P, Rubens CE. Molecular pathogenesis of group B streptococcal disease in newborns. In: Streptococcal infections: clinical aspects, microbiology, and molecular pathogenesis. Oxford University Press; 2000. p. 180–210.

[8] Miselli F, Frabboni I, Di Martino M, et al. Transmission of group B Streptococcus in late-onset neonatal disease: a narrative review of current evidence. Ther Adv Infect Dis 2022;9. https://doi.org/10.1177/20499361221142732. 20499361221142732.

[9] Madrid L, Seale AC, Kohli-Lynch M, et al. Infant group B streptococcal disease incidence and serotypes worldwide: systematic review and meta-analyses. Clin Infect Dis 2017;65(suppl_2):S160–72. https://doi.org/10.1093/cid/cix656.

[10] Tazi A, Plainvert C, Anselem O, et al. Risk factors for infant colonization by hypervirulent CC17 group B Streptococcus: toward the understanding of late-onset disease. Clin Infect Dis 2019;69(10):1740–8. https://doi.org/10.1093/cid/ciz033.

[11] Tavares T, Pinho L, Bonifácio Andrade E. Group B streptococcal neonatal meningitis. Clin Microbiol Rev. 35(2):e00079-21. doi:https://doi.org/10.1128/cmr.00079-21.

[12] Jordan HT, Farley MM, Craig A, et al. Revisiting the need for vaccine prevention of late-onset neonatal group B streptococcal disease: a multistate, population-based analysis. Pediatr Infect Dis J 2008;27(12):1057. https://doi.org/10.1097/INF.0b013e318180b3b9.

[13] Lee KW, Yap SF, Murdan S, et al. Maternal and neonatal group B streptococcus colonisation: a systematic review and the meta-analysis of matched-pair studies. Acta Paediatr 2024;113(5):892–911. https://doi.org/10.1111/apa.17152.

[14] Russell NJ, Seale AC, O'Driscoll M, et al. Maternal colonization with group B Streptococcus and serotype distribution worldwide: systematic review and meta-analyses. Clin Infect Dis 2017;65(suppl_2):S100–11. https://doi.org/10.1093/cid/cix658.

[15] Baker CJ, Barrett FF. Transmission of group B streptococci among parturient women and their neonates. J Pediatr 1973;83(6):919–25. https://doi.org/10.1016/s0022-3476(73)80524-4.

[16] Ferrieri P, Cleary PP, Seeds AE. Epidemiology of group-B streptococcal carriage in pregnant women and newborn infants. J Med Microbiol 1977;10(1):103–14. https://doi.org/10.1099/00222615-10-1-103.

[17] Nanduri SA, Petit S, Smelser C, et al. Epidemiology of invasive early-onset and late-onset group B streptococcal disease in the United States, 2006 to 2015: multistate laboratory and population-based surveillance. JAMA Pediatr 2019;173(3):224. https://doi.org/10.1001/jamapediatrics.2018.4826.

[18] World Health Organisation. Defeating Meningitis by 2030: A Global Road Map. Accessed May 22, https://www.who.int/publications/i/item/9789240026407; 2025.

[19] Edmond KM, Kortsalioudaki C, Scott S, et al. Group B streptococcal disease in infants aged younger than 3 months: systematic review and meta-analysis. The Lancet 2012;379(9815):547–56. https://doi.org/10.1016/S0140-6736(11)61651-6.

[20] Schrag SJ, Verani JR. Intrapartum antibiotic prophylaxis for the prevention of perinatal group B streptococcal disease: experience in the United States and implications for a potential group B streptococcal vaccine. Vaccine 2013;31(Suppl. 4):D20–6. https://doi.org/10.1016/j.vaccine.2012.11.056.

[21] Prevention of early-onset neonatal group B streptococcal disease. BJOG 2017;124(12):e280–305. https://doi.org/10.1111/1471-0528.14821.

[22] Heath PT, Balfour G, Weisner AM, et al. Group B streptococcal disease in UK and Irish infants younger than 90 days. The Lancet 2004;363(9405):292–4. https://doi.org/10.1016/S0140-6736(03)15389-5.

[23] O'Sullivan CP, Lamagni T, Patel D, et al. Group B streptococcal disease in UK and Irish infants younger than 90 days, 2014–15: a prospective surveillance study. Lancet Infect Dis 2019;19(1):83–90. https://doi.org/10.1016/S1473-3099(18)30555-3.

[24] Schrag SJ, Zell ER, Lynfield R, et al. A population-based comparison of strategies to prevent early-onset group B streptococcal disease in neonates. N Engl J Med 2002;347(4):233–9. https://doi.org/10.1056/NEJMoa020205.

[25] Hasperhoven GF, Al-Nasiry S, Bekker V, Villamor E, Kramer BWW. Universal screening versus risk-based protocols for antibiotic prophylaxis during childbirth to prevent early-onset group B streptococcal disease: a systematic review and meta-analysis. BJOG 2020;127(6):680. https://doi.org/10.1111/1471-0528.16085.

[26] Routine testing for Group B Streptococcus in pregnancy (GBS3 trial). ISRCTN Registry. doi:https://doi.org/10.1186/ISRCTN49639731.

[27] Dangor Z, Seale AC, Baba V, Kwatra G. Early-onset group B streptococcal disease in African countries and maternal vaccination strategies. Front Public Health 2023:11. https://doi.org/10.3389/fpubh.2023.1214844.

[28] Kobayashi M, McGee L, Chochua S, et al. Low but increasing prevalence of reduced beta-lactam susceptibility among invasive group B streptococcal isolates, US population-based surveillance, 1998-2018. Open Forum Infect Dis 2020;8(2). https://doi.org/10.1093/ofid/ofaa634.

[29] McGee L, Chochua S, Li Z, et al. Multistate, population-based distributions of candidate vaccine targets, clonal complexes, and resistance features of invasive group B streptococci within the United States, 2015-2017. Clin Infect Dis 2021;72(6):1004–13. https://doi.org/10.1093/cid/ciaa151.

[30] Hsu CY, Moradkasani S, Suliman M, et al. Global patterns of antibiotic resistance in group B Streptococcus: a systematic review and meta-analysis. Front Microbiol 2025;16:1541524. https://doi.org/10.3389/fmicb.2025.1541524.
[31] Zimmermann P, Curtis N. Effect of intrapartum antibiotics on the intestinal microbiota of infants: a systematic review. Arch Dis Child Fetal Neonatal Ed 2020; 105(2):201–8. https://doi.org/10.1136/archdischild-2018-316659.
[32] World Health Organisation. Group B Streptococcus Vaccine: full value vaccine assessment. Accessed March 28, 2025, https://www.who.int/publications/i/item/9789240037526; 2021.
[33] Lancefield RC. Two serological types of group b hemolytic streptococci with related, but not identical, type-specific substances. J Exp Med 1938;67(1):25–40. https://doi.org/10.1084/jem.67.1.25.
[34] Baker CJ, Kasper DL. Correlation of maternal antibody deficiency with susceptibility to neonatal group B streptococcal infection. N Engl J Med 1976;294 (14):753–6. https://doi.org/10.1056/NEJM197604012941404.
[35] Boyer KM, Kendall LS, Papierniak CK, Klegerman ME, Gotoff SP. Protective levels of human immunoglobulin G antibody to group B streptococcus type Ib. Infect Immun 1984;45(3):618–24. https://doi.org/10.1128/iai.45.3.618-624.1984.
[36] Baker CJ, Paoletti LC, Wessels MR, et al. Safety and immunogenicity of capsular polysaccharide—tetanus toxoid conjugate vaccines for group B streptococcal Types Ia and Ib. J Infect Dis 1999;179(1):142–50. https://doi.org/10.1086/314574.
[37] Baker CJ, Rench MA, McInnes P. Immunization of pregnant women with group B streptococcal type III capsular polysaccharide-tetanus toxoid conjugate vaccine. Vaccine 2003;21(24):3468–72. https://doi.org/10.1016/s0264-410x(03)00353-0.
[38] Madhi SA, Cutland CL, Jose L, et al. Safety and immunogenicity of an investigational maternal trivalent group B streptococcus vaccine in healthy women and their infants: a randomised phase 1b/2 trial. Lancet Infect Dis 2016;16(8): 923–34. https://doi.org/10.1016/S1473-3099(16)00152-3.
[39] Donders GGG, Halperin SA, Devlieger R, et al. Maternal immunization with an investigational trivalent group B streptococcal vaccine: a randomized controlled trial. Obstet Gynecol 2016;127(2):213. https://doi.org/10.1097/AOG.0000000000001190.
[40] Madhi SA, Koen A, Cutland CL, et al. Antibody kinetics and response to routine vaccinations in infants born to women who received an investigational trivalent group B Streptococcus polysaccharide CRM197-conjugate vaccine during pregnancy. Clin Infect Dis 2017;65(11):1897–904. https://doi.org/10.1093/cid/cix666.
[41] Chen VL, Avci FY, Kasper DL. A maternal vaccine against group B Streptococcus: past, present, and future. Vaccine 2013;31(4):D13–9. https://doi.org/10.1016/j.vaccine.2012.12.080.
[42] Absalon J, Simon R, Radley D, et al. Advances towards licensure of a maternal vaccine for the prevention of invasive group B streptococcus disease in infants: a discussion of different approaches. Hum Vaccin Immunother 2022;18(1):2037350. https://doi.org/10.1080/21645515.2022.2037350.
[43] Fischer P, Pawlowski A, Cao D, et al. Safety and immunogenicity of a prototype recombinant alpha-like protein subunit vaccine (GBS-NN) against Group B Streptococcus in a randomised placebo-controlled double-blind phase 1 trial in healthy adult women. Vaccine 2021;39(32):4489–99. https://doi.org/10.1016/j.vaccine.2021.06.046.
[44] Ji W, Zhou H, Li J, et al. Distributions of candidate vaccine targets, virulence factors, and resistance features of invasive group B Streptococcus using whole-genome sequencing: a multicenter, population-based surveillance study. Vaccine 2024;42(16):3564–71. https://doi.org/10.1016/j.vaccine.2024.04.062.
[45] Gent V, Lu YJ, Lukhele S, et al. Surface protein distribution in Group B Streptococcus isolates from South Africa and identifying vaccine targets through in silico analysis. Sci Rep 2024;14:22665. https://doi.org/10.1038/s41598-024-73175-4.
[46] GBS vaccine clinical trial tracker. Accessed June 5, https://www.path.org/our-impact/resources/gbs-vaccine-clinical-trial-tracker/; 2025.
[47] Inc Inventprise. A Phase I/II, Observer-Blind, Randomized, Placebo-Controlled, Dose-Selection Study to Assess the Safety, Tolerability, and Immunogenicity of Hexavalent Group B Streptococcus Conjugate Vaccine Manufactured by Inventprise, Inc.. In: Healthy, Non-Pregnant, Adult Women of Childbearing Age (WOCBA) in the US and South Africa. clinicaltrials.gov; 2025. https://clinicaltrials.gov/study/NCT06611371. [Accessed 5 June 2025].
[48] Carboni F, Cozzi R, Romagnoli G, et al. Proof of concept for a single-dose Group B Streptococcus vaccine based on capsular polysaccharide conjugated to Qβ virus-like particles. NPJ Vaccines 2023;8(1):152. https://doi.org/10.1038/s41541-023-00744-5.
[49] Absalon J, Segall N, Block SL, et al. Safety and immunogenicity of a novel hexavalent group B streptococcus conjugate vaccine in healthy, non-pregnant adults: a phase 1/2, randomised, placebo-controlled, observer-blinded, dose-escalation trial. Lancet Infect Dis 2021;21(2):263–74. https://doi.org/10.1016/S1473-3099(20)30478-3.
[50] Gonzalez-Miro M, Pawlowski A, Lehtonen J, et al. Safety and immunogenicity of the group B streptococcus vaccine AlpN in a placebo-controlled double-blind phase 1 trial. iScience 2023;26(3). https://doi.org/10.1016/j.isci.2023.106261.
[51] Madhi SA, Anderson AS, Absalon J, et al. Potential for maternally administered vaccine for infant group B Streptococcus. N Engl J Med 2023;389(3):215–27. https://doi.org/10.1056/NEJMoa2116045.
[52] Pawlowski A, Lannergård J, Gonzalez-Miro M, et al. A group B Streptococcus alpha-like protein subunit vaccine induces functionally active antibodies in humans targeting homotypic and heterotypic strains. Cell Rep Med 2022;3(2): 100511. https://doi.org/10.1016/j.xcrm.2022.100511.
[53] Minervax ApS. A Multicentre, Multinational, Parallel Group, Observer-Blind, Randomised, Placebo-Controlled Study on the Group B Streptococcus Vaccine (GBS-NN/NN2), Investigating the Immunogenicity and Safety of Four Vaccination Regimens in Pregnant Woman, Assessing IgG Specific to AlpN Proteins in Cord Blood and Maternal Blood, and the Safety Profile in Mother and Infant up to 6 Months Post-Delivery. clinicaltrials.gov. Accessed April 2, 2025, https://clinicaltrials.gov/study/NCT05154578; 2025.
[54] Minervax ApS. A follow-on study to assess the safety and immunogenicity of a booster dose of GBS-NN/NN2 vaccine 1 to 5 years after GBS-NN/NN2 recipients in study MVX0002 have completed the primary vaccination course, in comparison with a single dose of GBS-NN/NN2 administered in placebo participants from study MVX0002 or vaccine naïve participants. clinicaltrials.gov. https://clinicaltrials.gov/study/NCT05005247. [Accessed 31 March 2025].
[55] Minervax ApS. A multi-centre study to evaluate the safety, tolerability and immunogenicity of two doses of a Group B Streptococcus vaccine (GBS-NN/NN2) in women who are pregnant and living with HIV and women who are pregnant and do not have HIV. clinicaltrials.gov. https://clinicaltrials.gov/study/NCT04596878. [Accessed 31 March 2025].
[56] Vekemans J, Crofts J, Baker CJ, et al. The role of immune correlates of protection on the pathway to licensure, policy decision and use of group B Streptococcus vaccines for maternal immunization: considerations from World Health Organization consultations. Vaccine 2019;37(24):3190–8. https://doi.org/10.1016/j.vaccine.2019.04.039.
[57] Dangor Z, Kwatra G, Pawlowski A, et al. Association of infant rib and Alp1 surface protein N-terminal domain immunoglobulin G and invasive Group B streptococcal disease in young infants. Vaccine 2023;41(10):1679–83. https://doi.org/10.1016/j.vaccine.2023.01.071.
[58] Gaylord MA, Larrier M, Giordano-Schmidt D, et al. Development and validation of a 6-plex Luminex-based assay for measuring human serum antibodies to group B streptococcus capsular polysaccharides. Hum Vaccin Immunother 2024;20(1): 2311480. https://doi.org/10.1080/21645515.2024.2311480.
[59] Leung S, Collett CF, Allen L, et al. Development of a standardized opsonophagocytosis killing assay for group B Streptococcus and assessment in an interlaboratory study. Vaccines (Basel) 2023;11(11):1703. https://doi.org/10.3390/vaccines11111703.
[60] Le Doare K, Gaylord MA, Anderson AS, et al. Interlaboratory comparison of a multiplex immunoassay that measures human serum IgG antibodies against six-group B streptococcus polysaccharides. Hum Vaccin Immunother 2024;20(1): 2330138. https://doi.org/10.1080/21645515.2024.2330138.
[61] Bellais S, Six A, Fouet A, et al. Capsular switching in group B Streptococcus CC17 hypervirulent clone: a future challenge for polysaccharide vaccine development. J Infect Dis 2012;206(11):1745–52. https://doi.org/10.1093/infdis/jis605.
[62] Weinberger DM, Malley R, Lipsitch M. Serotype replacement in disease after pneumococcal vaccination. Lancet 2011;378(9807):1962–73. https://doi.org/10.1016/S0140-6736(10)62225-8.
[63] World Health Organization WHO preferred product characteristics for group B Streptococcus vaccines. Geneva: World Health Organization; 2017. Licence: CC BY-NC-SA 3.0 IGO. Published online 2017. WHO/IVB/17.09.
[64] Le Doare K, Benassi V, Cavaleri M, et al. Clinical and regulatory development strategies for GBS vaccines intended for maternal immunisation in low- and middle-income countries. Vaccine 2025;58:127131. https://doi.org/10.1016/j.vaccine.2025.127131.
[65] FDA grants breakthrough therapy designation to Pfizer's Group B Streptococcus vaccine candidate to help prevent infection in infants via immunization of pregnant women. Pfizer; 2025. Accessed April 7, https://www.pfizer.com/news/press-release/press-release-detail/fda-grants-breakthrough-therapy-designation-pfizers-group-b.
[66] William. MinervaX announces that EMA has awarded PRIME Status for its Group B Streptococcal vaccine. MinervaX; 2022. Accessed April 7, 2025, https://minervax.com/minervax-announces-that-ema-has-awarded-prime-status-for-its-group-b-streptococcal-vaccine/.
[67] Plotkin SA. Vaccines: correlates of vaccine-induced immunity. Clin Infect Dis 2008; 47(3):401–9. https://doi.org/10.1086/589862.
[68] Qin L, Gilbert PB, Corey L, McElrath MJ, Self SG. A framework for assessing immunological correlates of protection in vaccine trials. J Infect Dis 2007;196(9): 1304–12. https://doi.org/10.1086/522428.
[69] World Health Organisation. Correlates of vaccine-induced protection: methods and implications. Immunization, Vaccines and Biologicals; 2013. Accessed May 16, 2025, https://www.who.int/publications/i/item/WHO-IVB-13.01.
[70] Pollard AJ, Bijker EM. A guide to vaccinology: from basic principles to new developments. Nat Rev Immunol 2021;21(2):83–100. https://doi.org/10.1038/s41577-020-00479-7.
[71] Siber GR, Chang I, Baker S, et al. Estimating the protective concentration of anti-pneumococcal capsular polysaccharide antibodies. Vaccine 2007;25(19):3816–26. https://doi.org/10.1016/j.vaccine.2007.01.119.
[72] Andrews NJ, Waight PA, Burbidge P, et al. Serotype-specific effectiveness and correlates of protection for the 13-valent pneumococcal conjugate vaccine: a postlicensure indirect cohort study. Lancet Infect Dis 2014;14(9):839–46. https://doi.org/10.1016/S1473-3099(14)70822-9.
[73] Käyhty H. Difficulties in establishing a serological correlate of protection after immunization with Haemophilus influenzae conjugate vaccines. Biologicals 1994; 22(4):397–402. https://doi.org/10.1006/biol.1994.1062.
[74] Toneatto D, Pizza M, Masignani V, Rappuoli R. Emerging experience with meningococcal serogroup B protein vaccines. Expert Rev Vaccines 2017;16(5): 433–51. https://doi.org/10.1080/14760584.2017.1308828.
[75] Le Doare K, Kampmann B, Vekemans J, et al. Serocorrelates of protection against infant group B streptococcus disease. Lancet Infect Dis 2019;19(5):e162–71. https://doi.org/10.1016/S1473-3099(18)30659-5.

[76] Lin FY, Philips JB, Azimi PH, et al. Level of maternal antibody required to protect neonates against early-onset disease caused by group B Streptococcus type Ia: a multicenter, seroepidemiology study. J Infect Dis 2001;184(8):1022–8. https://doi.org/10.1086/323350.
[77] Lin FYC, Weisman LE, Azimi PH, et al. Level of maternal IgG anti-group B Streptococcus type III antibody correlated with protection of neonates against early-onset disease caused by this pathogen. J Infect Dis 2004;190(5):928–34. https://doi.org/10.1086/422756.
[78] Baker CJ, Carey VJ, Rench MA, et al. Maternal antibody at delivery protects neonates from early onset group B streptococcal disease. J Infect Dis 2014;209(5):781–8. https://doi.org/10.1093/infdis/jit549.
[79] Dangor Z, Kwatra G, Izu A, et al. Correlates of protection of serotype-specific capsular antibody and invasive Group B Streptococcus disease in South African infants. Vaccine 2015;33(48):6793–9. https://doi.org/10.1016/j.vaccine.2015.10.019.
[80] Dangor Z, Kwatra G, Izu A, Khan M, Lala SG, Madhi SA. Infant serotype specific anti-capsular immunoglobulin G antibody and risk of invasive group B Streptococcal disease. Vaccine 2021;39(47):6813–6. https://doi.org/10.1016/j.vaccine.2021.10.022.
[81] Fabbrini M, Rigat F, Rinaudo CD, et al. The protective value of maternal group B Streptococcus antibodies: quantitative and functional analysis of naturally acquired responses to capsular polysaccharides and pilus proteins in European Maternal Sera. Clin Infect Dis 2016;63(6):746–53. https://doi.org/10.1093/cid/ciw377.
[82] Madhi SA, Izu A, Kwatra G, et al. Association of Group B Streptococcus (GBS) serum serotype-specific anticapsular immunoglobulin G concentration and risk reduction for invasive GBS disease in South African infants: an observational birth-cohort, matched case-control study. Clin Infect Dis 2021;73(5):e1170–80. https://doi.org/10.1093/cid/ciaa1873.
[83] Saukkoriipi A, Silmon de Monerri NC, Toropainen M, et al. Association between anti-capsular IgG levels at birth and risk of invasive group B streptococcus disease in Finnish newborns: a retrospective case–control study. The Lancet Microbe 2024;5(7):689–96. https://doi.org/10.1016/S2666-5247(24)00038-7.
[84] Davies HG, Carreras-Abad C, Le Doare K, Heath PT. Group B Streptococcus: trials and tribulations. Pediatr Infect Dis J 2019;38(6S):S72. https://doi.org/10.1097/INF.0000000000002328.
[85] Gilbert PB, Isbrucker R, Andrews N, et al. Methodology for a correlate of protection for group B Streptococcus: report from the Bill & Melinda Gates Foundation workshop held on 10 and 11 February 2021. Vaccine 2022;40(32):4283–91. https://doi.org/10.1016/j.vaccine.2022.05.016.
[86] Kim SY, Russell LB, Park J, et al. Cost-effectiveness of a potential group B streptococcal vaccine program for pregnant women in South Africa. Vaccine 2014;32(17):1954–63. https://doi.org/10.1016/j.vaccine.2014.01.062.
[87] Russell LB, Kim SY, Cosgriff B, et al. Cost-effectiveness of maternal GBS immunization in low-income sub-Saharan Africa. Vaccine 2017;35(49Part B):6905–14. https://doi.org/10.1016/j.vaccine.2017.07.108.
[88] Ahmed N, Giorgakoudi K, Usuf E, et al. Potential cost-effectiveness of a maternal Group B streptococcal vaccine in the Gambia. Vaccine 2020;38(15):3096–104. https://doi.org/10.1016/j.vaccine.2020.02.071.
[89] Giorgakoudi K, O'Sullivan C, Heath PT, et al. Cost-effectiveness analysis of maternal immunisation against group B Streptococcus (GBS) disease: a modelling study. Vaccine 2018;36(46):7033–42. https://doi.org/10.1016/j.vaccine.2018.09.058.
[90] Kim SY, Nguyen C, Russell LB, et al. Cost-effectiveness of a potential group B streptococcal vaccine for pregnant women in the United States. Vaccine 2017;35(45):6238–47. https://doi.org/10.1016/j.vaccine.2017.08.085.
[91] Hahn BA, de Gier B, van Kassel MN, et al. Cost-effectiveness of maternal immunization against neonatal invasive Group B Streptococcus in the Netherlands. Vaccine 2021;39(21):2876–85. https://doi.org/10.1016/j.vaccine.2021.04.001.
[92] Sorano S, Procter SR, Seale AC. Cost-effectiveness analysis of maternal vaccination against Group B streptococcus in Japan. Vaccine: X 2023;14:100332. https://doi.org/10.1016/j.jvacx.2023.100332.
[93] Procter SR, Gonçalves BP, Paul P, et al. Maternal immunisation against Group B Streptococcus: a global analysis of health impact and cost-effectiveness. PLoS Med 2023;20(3):e1004068. https://doi.org/10.1371/journal.pmed.1004068.
[94] World Health Organisation. WHO recommendations on antenatal care for a positive pregnancy experience. Accessed June 5, 2025, https://www.who.int/publications/i/item/9789241549912; 2016.
[95] Smith WB, Seger W, Chawana R, et al. A phase 2b trial evaluating the safety, tolerability, and immunogenicity of a 6-valent Group B Streptococcus vaccine administered concomitantly with tetanus, diphtheria, and acellular pertussis vaccine in healthy nonpregnant female individuals. J Infect Dis 2025:jiaf096. https://doi.org/10.1093/infdis/jiaf096.
[96] Duggal S, Chugh TD, Duggal AK. HIV and malnutrition: effects on immune system. Clin Dev Immunol 2012;2012:784740. https://doi.org/10.1155/2012/784740.
[97] Thorn N, Guy RL, Karampatsas K, et al. GBS vaccines in the UK: a round table discussion. F1000Res 2024;13:519. https://doi.org/10.12688/f1000research.147555.1.