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Maternal vaccination to prevent neonatal infections and combat antimicrobial resistance

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ABSTRACT

Maternal vaccination during pregnancy is emerging as a powerful strategy in protecting newborns from infectious diseases, improving neonatal outcomes, and potentially reducing antimicrobial use and resistance.

Maternal immunisation works by eliciting protective antibodies in the mother that are transferred to the fetus transplacentally and through breastmilk postnatally to provide the infant with passive immunity during the first vulnerable months of life. There is sufficient evidence to support the role of maternal vaccination in averting many neonatal infections that would otherwise require medical intervention.

By preventing infections in mothers and their newborn, maternal vaccination also holds significant potential for reducing antimicrobial use and antimicrobial resistance. Fewer neonatal infections translate to a reduced need for antimicrobial use in the neonatal period and in postpartum women, therefore lowering the selective pressure for drug-resistant bacteria.

Routine maternal vaccines (tetanus, diphtheria, acellular pertussis (Tdap), influenza, COVID-19, respiratory syncytial virus) already confer measurable antibiotic-sparing benefits by preventing infections that typically trigger antimicrobial therapy in mothers and neonates. Pipeline candidates (*Group B Streptococcus*, *Klebsiella pneumoniae*, *Escherichia coli*) could further lower neonatal sepsis burden, reducing broad-spectrum antimicrobial use in neonatal intensive care units to help slow antimicrobial resistance. Integrated with antibiotic stewardship and infection-prevention measures, maternal immunisation offers a practical, scalable practice to limit perinatal antibiotic exposure.

1. Introduction

Maternal immunisation is an important element of perinatal care to protect both pregnant individuals and their infants when they are most vulnerable to infection. Vaccine-induced maternal IgG is actively transported across the placenta, providing newborns with passive, antigen-specific protection in the first months of life before their own routine vaccines are given [1].

Real-world impact is evident from the reduction in neonatal morbidity and mortality associated with vaccine-preventable diseases. The introduction of maternal tetanus programmes has seen neonatal tetanus deaths fall dramatically since the late 1980s with the elimination of neonatal tetanus deaths in most priority countries [2]. Maternal Tdap (tetanus, diphtheria, acellular pertussis) vaccination given in late pregnancy provides high protection against disease in young infants demonstrated by studies from the UK and US which estimate 70–95 % effectiveness against infant pertussis and 90 % protection against cases before 2 months of age [3]. Maternal influenza vaccination also benefits both mother and child with randomised and observational studies showing a significant reduction in laboratory-confirmed influenza and infant influenza-associated hospitalisations [4]. Another major recent advance is prevention of respiratory syncytial virus (RSV). In 2023, a bivalent prefusion F vaccine (RSVpreF, Abrysvo®) was approved for administration in pregnancy after a phase 3 trial demonstrated efficacy against severe RSV-associated lower respiratory tract disease in infants in the first 3–6 months of life [5]. Importantly, a secondary analysis of a randomised maternal RSV vaccine trial suggested reduced antimicrobial prescribing in infants during the first 90 days of life, highlighting a

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potential added benefit [6].

By reducing vaccine-preventable disease, maternal gestational vaccination program potentially plays a crucial role in averting a high prevalence of antimicrobial resistance (AMR). In 2019, an estimated 4.95 million deaths were associated with bacterial AMR (1.27 million attributable), with the highest rates in parts of sub-Saharan Africa with children and infants disproportionally affected [7]. Neonatal sepsis is increasingly caused by pathogens, such as *Klebsiella pneumoniae,* with high resistance to first-line antibiotic regimens such as ampicillin and gentamicin [8]. Preventing infections to reduce the over usage of antibiotics may therefore be a central strategy alongside antibiotic stewardship.

In this review, evidence for maternal vaccines in current use (Tdap, influenza, RSV, COVID-19) and in development (*Group B Streptococcus*-GBS, *Klebsiella pneumoniae and E. coli)* as a strategy in reducing AMR will be considered focusing on efficacy/effectiveness for maternal and neonatal infection outcomes, impacts on neonatal morbidity (e.g. sepsis, pneumonia, meningitis), and its downstream effects on antibiotic use.

2. Antimicrobial resistance: A growing concern

Antimicrobial resistance (AMR) threatens neonatal health worldwide by eliminating the effectiveness of first-line management against invasive bacterial disease. AMR emerges through mutations and horizontal gene transfer of mobile genetic elements (plasmids, transposons), processes which are accelerated by antibiotic selection pressure in humans, animals, and the environment [9,10]. In the clinical setting, resistant organisms propagate via contaminated hands, equipment, and surfaces, resulting in the colonisation and infection of patients [10,11]. A vicious cycle ensues with increased antibiotic use encouraging selection for resistance.

AMR is now a significant contributor to the epidemiology of neonatal sepsis. *Klebsiella pneumoniae* has emerged as a leading global cause of neonatal sepsis and death and commonly exhibits resistance to first-line and second-line antibiotics [8,12,13]. Other priority pathogens include extended-spectrum β-lactamase (ESBL)–producing *Escherichia coli* and methicillin-resistant *Staphylococcus aureus* (MRSA), both implicated in neonatal intensive care unit (NICU) outbreaks and severe disease [1,14,15]. These patterns demonstrate how AMR amplifies the risk of treatment failure and mortality for neonates.

High antibiotic use in pregnancy and neonatal care further adds to resistance. Meta-analytic estimates indicate that approximately 24 % of pregnant women receive at least one antibiotic during pregnancy, with antibiotics accounting for a large portion of prescriptions in pregnancy [16–18]. Intrapartum antibiotic prophylaxis (IAP) to prevent early-onset Group B Streptococcus (GBS) disease is widely implemented and in settings with universal screening, a substantial proportion, often exceeding 15–30 %, of women receive IAP [19–21]. In neonates, empiric antibiotic thresholds are necessarily low because early bacterial sepsis is life-threatening. However, this practice can further drive resistance, especially when treatment is continued for longer periods in culture-negative cases. A large US study of more than 50,000 NICU admissions reported that 44.8 % of infants received antibiotics, predominantly ampicillin and gentamicin, despite relatively few culture-confirmed infections [22]. Similar or higher exposure has been reported for very-low-birth-weight infants and in resource-limited hospitals, where days of therapy per 1000 patient-days remain among the highest in paediatrics [23,24]. Antibiotic use also extends to viral illnesses where infants hospitalised with bronchiolitis frequently receive antibiotics despite guidelines, reflecting diagnostic uncertainty about bacterial co-infection [25,26].

Neonatal units can function as hot-spots for multidrug-resistant organism transmission. Several reports document ESBL-producing Klebsiella and MRSA outbreaks in NICUs, resulting in significant morbidity, mortality, and prolonged hospitalisation [11,14,27–29]. Whole-genome sequencing studies reveal complex transmission networks, environmental reservoirs, and evolution of resistance with the host, illustrating how quickly multi-drug resistant organisms can disseminate in NICUs [11,28]. In addition, resistant lineages that traverse facilities through patient transfers and travel, cause local outbreaks and have regional implications. This further reinforces the need to control unnecessary antibiotic use and ideally to prevent infections in the first place [10,11].

Preventing neonatal infections is therefore an important AMR strategy. Every averted case of suspected sepsis avoids an empirical broad-spectrum course of antibiotics and a reduced infection incidence allows antimicrobial stewardship programmes to narrow empiric protocols and shorten treatment duration. Maternal vaccination during pregnancy is a particularly promising means to achieve this. By allowing passive immunity to the newborn, maternal vaccines lower rates of neonatal infection therefore antibiotic consumption. This antibiotic-sparing effect of maternal vaccination during pregnancy has been demonstrated in a randomised trial where maternal RSV vaccination reduced infant antimicrobial prescribing by 12.9 % over the first 90 days of life, most likely through fewer bronchiolitis admissions and less empiric treatment for presumed bacterial pneumonia [8]. Additionally, vaccines that prevent viral illness (influenza, RSV, COVID-19) also reduce downstream antibiotic use from diagnostic uncertainty and prevention of secondary bacterial infections [6,25,26]. Further, modelling studies suggest that maternal vaccination against *Klebsiella pneumoniae* could prevent hundreds of thousands of sepsis episodes annually particularly in high burden regions [12]. At population level, the World Health Organization estimates that optimal deployment of existing and pipeline vaccines could reduce global antibiotic consumption by 22 % (2.5 billion daily doses per year) [30]. Along with antibiotic stewardship and infection-prevention measures, maternal vaccination during pregnancy supports the efforts to reduce AMR.

3. The role of maternal vaccination in neonatal health

Pregnancy offers a unique opportunity to protect newborns from infection by harnessing the mother's immune system. During pregnancy, maternal immunity is transferred to the fetus and newborn through active transplacental transfer of IgG antibodies before birth and through the provision of immune factors (lactoferrin and IgA) through breast milk during the postpartum period.

In late gestation, maternal IgG is actively transported across the placenta via the neonatal Fc receptor (FcRn) [31]. By the time of delivery, most infants carry a broad repertoire of their mother's pathogen-specific IgG. Vaccination during pregnancy boosts these titers, so babies start life with higher levels of targeted protective antibodies. Although the half-life of maternal IgG in infants is an estimated month, protective concentrations have been shown to persist for several months to span the vulnerable period before the infant's own routine vaccinations and immune maturity come into play [32]. After birth, breast milk adds another protective layer providing a source of secretory IgA, as well as IgG, immune cells, and cytokines that coat mucosal surfaces [33,34]. These antibodies act locally rather than entering the circulation, and the specific response can be improved through maternal vaccination during pregnancy. Influenza immunisation in pregnancy increases flu-specific IgA in milk, which has been linked to improved infant outcomes [35].

Determining optimal timing of maternal vaccination is essential to maximise maternal protection and neonatal benefit via transplacental IgG transfer. For COVID-19 and seasonal influenza, vaccination is recommended in any trimester, with administration at the earliest opportunity and preferably several weeks before delivery to allow antibody maturation and placental transfer. For Tdap, there is currently no consensus on the optimal timing of vaccination during pregnancy with different guidelines available, for example the US recommendation is for 27–36 weeks' gestation while the UK recommendation is for a broader interval of 16–32 weeks' vaccination. For RSV, a narrower window applies as illustrated in the United States' recommendation for a single

maternal dose at 32–36 weeks' gestation during the RSV season and the UK programme currently offers the vaccine from 28 weeks' gestation and onwards. In all settings, scheduling should allow sufficient time before delivery for efficient antibody transfer.

Examples of the impact of maternal vaccines in pregnancy include the introduction of maternal tetanus immunisation which reduced neonatal tetanus mortality with global programmes having achieved elimination in most countries [36]. For pertussis, a single Tdap dose in late pregnancy protects infants during their first months of life before they begin their own routine immunisation course. The rollout of vaccine programmes in the UK and US led to significant reductions in infant hospitalisations and deaths due to pertussis, with vaccine effectiveness estimated at 70–95 % against infant pertussis and higher against severe outcomes [37,38]. Influenza vaccination during pregnancy benefits both mother and baby. Pregnant individuals face risks of severe influenza and related complications such as pneumonia and preterm birth. Inactivated influenza vaccines, recommended in all trimesters, reduce influenza-related hospitalisations in pregnant women and confer partial protection to infants who cannot be vaccinated until six months of age. This is demonstrated in randomised and observational studies showing significant reductions in infant influenza and influenza-related hospitalisations [4,39].

The COVID-19 pandemic further highlighted the importance of maternal immunisation. Infection in pregnancy increases risks of admission to intensive care, mechanical ventilation, and adverse perinatal outcomes [40]. Vaccination has shown robust protection against severe maternal disease. In addition, through the transplacental transfer of vaccine-induced maternal antibodies across the placenta, infants born to vaccinated mothers have lower COVID-19 hospitalisation rates [41]. Large surveillance programmes have not identified increased adverse pregnancy outcomes, supporting vaccination during pregnancy [42]. A recent milestone is the introduction of maternal RSV vaccination. RSV is a leading cause of infant bronchiolitis and pneumonia, with peak severity in the first months of life. The first licensed maternal RSV vaccine (RSVpreF; Abrysvo®), substantially reduces severe RSV disease and medically attended lower respiratory tract infections in early infancy [8,11,12]. Together with long-acting monoclonal RSV antibody prophylaxis for infants (nirsevimab/clesrovimab), maternal RSV immunisation offers a powerful, complementary approach to reducing seasonal RSV burden [5].

Collectively, Tdap, influenza, COVID-19, and RSV vaccines have demonstrated safety and effectiveness in pregnancy, lowering maternal morbidity and improving newborn outcomes through passive protection. Their success validates maternal immunisation as a foundation for perinatal care and a promising platform for future vaccines targeting other neonatal diseases.

4. Contributions of routine maternal vaccines to reducing antibiotic reliance

4.1. Tetanus, diphtheria, and acellular pertussis (Tdap)

Administered in late pregnancy, Tdap induces high concentrations of anti-pertussis antibodies that are efficiently transferred across the placenta, protecting infants in the first months when disease is most severe. In the UK, vaccine effectiveness against infant pertussis less than 3 months of age was approximately 91 % (95 % CI 84–95) [3]. Similarly, a large US cohort analyses supported robust protection against pertussis through the first year of life [37]. By preventing infant disease, maternal Tdap reduces therapeutic macrolide use for index patients and post-exposure prophylaxis for close contacts. Tdap during pregnancy also boosts maternal tetanus and diphtheria immunity maternal antibodies may offer additional neonatal protection against diphtheria where transmission persists, and against tetanus, that would otherwise prompt adjunctive antimicrobial treatment, achieving elimination in most priority countries [3,37].

4.2. Inactivated influenza vaccine

Although influenza is viral, it frequently results in antibiotic prescribing in both adults and infants where clinicians consider secondary bacterial pneumonia and cannot immediately exclude bacterial infection. Randomised and observational studies show that maternal influenza vaccination protects mothers and infants. A randomised control trial in Bangladesh demonstrated a fall in infant laboratory-confirmed influenza up to 6 months of age by 63 %, along with reductions in febrile respiratory illness in mothers and infants following vaccination of pregnant women with an inactivated influenza vaccine [4]. Subsequent reviews and cohorts corroborate significant reductions in infant influenza and related hospitalisations, particularly when vaccination occurs later in pregnancy, aligning with maximal transplacental transfer [4]. Fewer influenza-associated febrile illnesses and hospitalisations translate to fewer antibiotic courses for presumed bacterial pneumonia or neonatal sepsis. At the population level, these vaccine-prevented viral illnesses reduce antibiotic use that would otherwise be driven by diagnostic uncertainty and concern for bacterial superinfection [4,30,43].

4.3. COVID-19 vaccines

Severe COVID-19 in pregnancy often triggers empiric broad-spectrum antibiotics, despite the relatively low prevalence of proven bacterial co-infection. Studies have demonstrated that approximately three-quarters of hospitalised COVID-19 patients had received antibiotics early in the pandemic [44,45]. Maternal vaccination reduces severe maternal disease and is associated with a significantly lower risk of COVID-19 hospitalisation among infants less than 6 months of age, consistent with placental antibody transfer with an estimated 61 % vaccine effectiveness against infant hospitalisation [41]. By avoiding severe maternal pneumonia, where antibiotics are commonly prescribed, and decreasing infant COVID-19 admissions, where febrile infants routinely receive empiric intravenous antibiotics pending cultures, maternal COVID-19 vaccination during pregnancy reduces antibiotic exposure for both mothers and neonates [41,44,45].

4.4. Respiratory syncytial virus (RSV) vaccine

The phase 3 MATISSE trial demonstrated that vaccination with bivalent prefusion F (RSVpreF) in late pregnancy reduces severe RSV-associated lower respiratory tract illness (LRTI) and medically attended RSV LRTI in infants through the first months of life [5]. This vaccine is now recommended in many countries. Importantly for antibiotic stewardship, analysis of a randomised maternal RSV vaccine trial found a 12.9 % reduction in antimicrobial prescribing among infants during the first 90 days of life, likely driven by fewer bronchiolitis admissions and fewer empiric antibiotics for presumed bacterial pneumonia [6]. This nicely quantifies an antibiotic-sparing effect of maternal RSV vaccination during pregnancy which shows the direct reduction of infant antibiotic exposure by preventing viral lower respiratory tract infections that often triggers antibiotic treatment in practice [5].

5. Vaccines in development for maternal immunisation

5.1. Group B Streptococcus (GBS)

GBS remains a leading cause of neonatal sepsis and meningitis. Intrapartum antibiotic prophylaxis (IAP) reduces early-onset disease but does not prevent late-onset disease, and necessitates broad spectrum antibiotic exposure contributing to antibiotic selection pressure. A maternal GBS vaccine could prevent both early and late-onset disease reducing the need for neonatal antibiotic treatment whilst also reducing reliance on IAP. A 2023 global modelling study (across 183 countries) estimated that a single-dose maternal GBS vaccine regimen, assuming 80 % efficacy against invasive GBS and stillbirth, could avert an

estimated 214,300 invasive GBS (iGBS) cases in infants annually (127,000 early-onset and 87,300 late-onset iGBS), and around 31,100 infant deaths, plus approximately 23,000 stillbirths [46]. A hexavalent capsular polysaccharide conjugate (GBS6) has shown robust immunogenicity in pregnancy with efficient transplacental antibody transfer in phase 2 studies supporting progression to late-phase evaluation [47]. If efficacious at scale, and implemented, maternal GBS vaccination would enable substantial scaling down of IAP. This programme would provide a direct antibiotic-sparing benefit in maternity care whilst preventing invasive neonatal infections [47].

5.2. *Klebsiella pneumoniae*

Klebsiella pneumoniae is a prominent cause of neonatal sepsis globally and often exhibits resistance to first-line (ampicillin/gentamicin), second-line (cephalosporins), and carbapenems, making infections difficult to treat and frequently fatal. Modelling using multi-country mortality and genomic data estimated that 22.4 % of neonatal sepsis deaths due to *Klebsiella pneumoniae* are caused by meropenem-resistant strains and projected that maternal vaccination could avert close to 80,000 neonatal deaths and 399,000 neonatal sepsis cases annually [12] with the largest impact in sub-Saharan Africa and South Asia, regions with the highest AMR burden [12]. Observational studies from diverse settings corroborate high case fatality for carbapenem-resistant Gram--negative neonatal sepsis and the rising prevalence of carbapenem-resistant *Klebsiella pneumoniae* colonisation and infection in NICUs [8,13,48–50]. By preventing infections frequently caused by multidrug-resistant strains, a maternal Klebsiella vaccine would directly reduce the need for last-line therapeutic agents in neonatal intensive care units [12]. Indeed, early-stage development of a maternal *Klebsiella pneumoniae* vaccine as well as monoclonal antibodies [51] are underway.

5.3. *Escherichia coli*

Escherichia coli is another major cause of neonatal sepsis and meningitis where resistance to third-generation cephalosporins and other classes is increasingly reported. As with GBS, a maternal *Escherichia coli* vaccine would aim to induce maternal IgG that is transferred transplacentally to neutralise invasive strains in the newborn. A maternal *Escherichia coli* vaccine candidate using a glycosylated surface-protein platform [52] demonstrates the growing investment in maternal vaccines targeting neonatal sepsis pathogens. If successful, such vaccines could reduce empiric broad-spectrum antibiotic use in the neonatal period by preventing substantial numbers of sepsis episodes.

6. Antimicrobial use versus antimicrobial resistance

Maternal vaccination can lower antimicrobial use (AMU) and AMR, but the effect depends on the pathogen. For viral targets, maternal RSV vaccination mainly reduces AMU. As mentioned previously, infants of vaccinated mothers received fewer antibiotic prescriptions in the first 90 days of life, showing an antibiotic-sparing effect without any direct impact on resistance in RSV itself [6]. For bacterial targets with little current resistance, a maternal GBS vaccine would likewise reduce AMU by avoiding IAP and empiric neonatal antimicrobial treatment. Since GBS remains susceptible to penicillin, the immediate effect on GBS AMR is likely to be modest [20,53,54].

In contrast, maternal vaccines against resistance-prone neonatal sepsis pathogens, especially *Klebsiella pneumoniae* and *Escherichia coli*, could reduce both AMU and AMR. Current routine maternal vaccines (Tdap, influenza) mainly lower AMU by preventing infant pertussis with the associated macrolide treatment and reducing influenza-related hospitalisations that often trigger empiric antibiotic use with an indirect impact on AMR [3,4]. Framing maternal immunisation in terms of AMU versus AMR may clarify the expected benefits and helps prioritise vaccines with the greatest resistance impact [43].

7. Challenges and barriers to maternal vaccination

Despite compelling evidence of benefit, scaling maternal immunisation faces scientific, regulatory, logistical, and behavioural barriers. Concerns about safety and vaccine hesitancy persist, trial design and licensure pathways in pregnancy remain complex, and implementation particularly in low and middle-income countries (LMICs) is limited by access, delivery platforms, and financing. Addressing these challenges is essential to realise the full public-health value of maternal vaccines.

Safety concerns and vaccine hesitancy. Hesitancy in pregnancy often stems from concerns about miscarriage, teratogenicity, and preterm birth, despite evidence of safety. For long-established vaccines, large studies show no increase in adverse maternal or neonatal outcomes, and healthcare professional recommendation remains a key predictor of uptake [55–57]. During the COVID-19 vaccine rollout, absence of initial trial data in pregnancy and misinformation reduced early coverage, but subsequent surveillance identified no new safety signals for mRNA vaccines, supporting broad use [42,57,58]. For RSVpreF, licensure followed robust efficacy data with real-world analyses showing no elevated preterm birth risk [59,60]. Persistent knowledge gaps highlight the need for clear, tailored communication for patients and healthcare professional [56,61].

Regulatory and ethical considerations. Historically, pregnant women were excluded from clinical trials, resulting in a ‘protection by exclusion’ model that delayed evidence collection in this population [62]. Ethical frameworks now call for fair inclusion with appropriate safeguards, and regulators have shown flexibility once pre-specified safety thresholds are met [62]. Demonstrating efficacy for maternal vaccines is difficult because infant endpoints are rare, requiring very large trials. Consequently, regulators increasingly use immunobridging and validated correlates of protection (CoP) to guide licensure and policy. This approach has been advanced by WHO GBS consultations and by multi-stakeholder consensus on CoP across pathogens [63,64]. The halted phase-3 trial of one maternal RSV candidate following an apparent preterm-birth signal and approval of RSVpreF with a restricted gestational window of vaccination and active safety monitoring illustrates the pregnancy risk–benefit sensitivity and the need for robust and transparent post-authorisation surveillance [59,60,65].

Access and implementation in LMICs. Delivery of maternal vaccines depends on antenatal care attendance, yet contact is wide-ranging amongst pregnant women where more than 1 visit is common, but completion of more than 4 or 8 varies widely [66,67]. The WHO Maternal Immunization and Antenatal Care Situation Analysis (MIACSA) highlights gaps in maternal vaccine delivery in LMICs such as limited cold chain in maternity settings, fragmented immunisation–maternal healthcare coordination, weak registry linkages, varied provider training for patient counselling [68,69], and routine monitoring of coverage and pregnancy safety is often inadequate. Community barriers such as gendered decision-making, low health literacy, and misinformation, further impede uptake. Here, provider knowledge, strong recommendations, and community engagement are key enablers [56,61,68].

Financing and value for money. Adoption of new maternal vaccines in resource-constrained settings depends on affordability and demonstrable value. While maternal tetanus programmes are highly cost-effective, financing for influenza and pertussis has been inconsistent. Growing evidence supports value for pertussis vaccine, where dynamic models in LMICs and country analyses report favourable cost-effectiveness under reasonable burden and coverage assumptions [70,71]. For GBS, global modelling projects show substantial health gains and broad economic benefits, guiding emerging investments, including the Global Alliance for Vaccines and Immunisation (Gavi) [53,72]. Policymakers also weigh the benefits of relieving health-system pressure and of antibiotic sparing, aligned with AMR strategies [53,56].

Data systems and pharmacovigilance. Sustained confidence requires routine measurement of coverage and outcomes. Many countries maintain separate antenatal care and immunisation information systems. Integrating these to capture maternal vaccine details, gestational timing of vaccination, and birth outcomes is feasible but under-resourced. Recommendations by WHO include strengthening passive and active safety surveillance in pregnancy, using perinatal registries and birth-defects monitoring where available, and harmonising definitions to enable signal detection and cross-region comparisons [53,68,69].

Path forward. Overcoming barriers will require (i) proactive, values-based communication by trusted antenatal care providers, (ii) fair inclusion of pregnant women in vaccine research with clear plans for safety oversight and CoP-based licensure when efficacy trials are not feasible, (iii) integration of maternal vaccines into routine antenatal care pathways, cold-chain and stock management in maternity settings, and integration of data exchange with immunisation registries, and (iv) sustainable financing that reflects full health and economic value. The approval and early rollout of maternal RSV vaccination, together with the collection of pregnancy-specific safety data for COVID-19 vaccines, show that rigorous evidence generation can go hand-in-hand with cautious, transparent policy. Public confidence builds when health systems deliver vaccines consistently and safely [42,58–60,68,69]. Closing this implementation gap, particularly in LMICs, is now the central challenge to achieving equitable maternal immunisation coverage.

8. Future directions and recommendations

Progress in maternal immunisation has supported the case for vaccines to control antimicrobial resistance (AMR), yet key scientific and policy gaps remain. First, immune CoPs that reliably predict infant benefit are incompletely defined for several priority pathogens (eg. GBS, *Escherichia coli, Bordetella pertussis*). Clarifying quantitative and functional antibody thresholds, supported by standardised assays, would enable immunobridging approaches and smaller, faster trials in pregnancy, accelerating development and licensure pathways for maternal vaccines [54,63]. At the same time, maternal-antibody and infant-vaccine interactions require investigation following evidence showing that higher maternally derived antibodies can 'blunt' infant serologic responses to their own routine priming doses without clear evidence of reduced clinical protection, which further drives the need to complete infant schedules [73,74].

Second, advancing maternal vaccine platforms should be a priority. Evidence from mRNA COVID-19 vaccines, including large pregnancy safety datasets, shows that nucleic-acid technologies and potentially other next-generation approaches with adjuvants can be adapted for use in pregnancy. Using these platforms for maternal vaccines targeting neonatal sepsis pathogens could improve effectiveness, simplify manufacturing, and enable rapid deployment [42]. Early evidence that maternal RSV vaccination lowers antibiotic prescribing in infants shows that pregnancy-targeted vaccines can spare antibiotic use. Future trials should predefine antibiotic-use outcomes and relate them to local AMR patterns to assist in quantifying this benefit [6].

Third, long-term consequences of maternal immunisation on infant immune growth remain unknown. Further vaccine research should assess whether preventing early infections, and therefore reducing early antibiotic exposure, alters the risk of immune-related conditions, for example allergy and asthma, or affects vaccine responses later in infancy and childhood [74]. Finally, more direct evidence connecting maternal vaccination during pregnancy to AMR outcome is needed. Comparative studies across hospitals and regions that link vaccine coverage, antibiotic use, and resistance patterns can quantify reductions in drug-resistant neonatal infections after maternal vaccine implementation, strengthening the case for including maternal vaccination during pregnancy in AMR strategies.

9. Conclusion

There are several ways in which maternal vaccination during pregnancy can reduce antibiotic resistance and reliance. First, fewer primary infections will mean fewer antibiotic treatments. Preventing infant infection, disease and hospital admissions will directly lower the number of antibiotic courses prescribed for confirmed or presumed bacterial disease [3–6,37,41,44,45]. Second, maternal vaccines reduce empiric antibiotic use driven by diagnostic uncertainty. For example, preventing infant COVID-19 and RSV admissions avoids many precautionary intravenous antibiotic courses commonly initiated while cultures are pending [6,41]. Third, there is a reduction of secondary bacterial infections that may complicate viral illness, further reducing the need for antibiotic treatment [4,44,45]. In short, the use of vaccines to prevent primary illness or downstream bacterial complications directly reduces antibiotic exposure, and eases selection pressure for resistance [75].

Routine maternal vaccines (Tdap, influenza, COVID-19, RSV) already deliver measurable antibiotic-sparing benefits by preventing infections that drive antibiotic use in mothers and neonates. Maternal vaccines in development (GBS, *K. pneumoniae, E. coli*) could further reduce the burden of neonatal sepsis and so diminish reliance on broad-spectrum AMU in NICUs to help to slow AMR progression. Alongside antibiotic stewardship and infection-prevention measures, maternal immunisation is a practical, scalable strategy to reduce antibiotic exposure in the perinatal period and beyond [43].

Realising this potential requires sustained action. We need to embed maternal vaccination within national AMR plans, strengthen antenatal care platforms for delivery, pharmacovigilance, and coverage monitoring, invest in research to define immune correlates and accelerate licensure, and ensure equitable financing for introduction in high-burden settings. If delivered successfully, maternal immunisation will continue to save lives today and help preserve antibiotic effectiveness for tomorrow.

Author statement

KLD conceived the idea for the review and EG coordinated the project. EG drafted the initial manuscript, which was critically reviewed and revised by all authors. All authors approved the final version of the manuscript and agree to be accountable for all aspects of the work. KLD is the guarantor of the review.

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