Bivalent prefusion F vaccination in pregnancy and protection against respiratory syncytial virus hospitalisation in infants until the age of six months: assessment of a United Kingdom-wide national vaccination programme using a multicentre, test-negative, case-control study

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Summary

Background In late summer 2024, the United Kingdom (UK) introduced the maternal bivalent respiratory syncytial virus (RSV) prefusion F (RSVpreF) vaccine for all pregnant individuals at a gestation of 28 weeks or more. After an initial catch-up phase, the maternal RSVpreF programme transitioned to year-round delivery, and in late summer 2025 nirsevimab replaced palivizumab for UK infants at high risk of severe RSV disease. We aimed to estimate the protection provided by maternal RSVpreF against hospitalisation with RSV in infants up to the age of 6 months, and to assess the overall performance of the UK RSV prevention programme, once this had entered a steady state.

Methods We conducted a prospective, consented, multi-centre, test-negative case-control study to analyse the effectiveness of maternal RSVpreF vaccination against the primary outcome of admission to hospital for RSV-associated acute lower respiratory tract infection (ALRI) in infants up to 6 months of age. Patient and public involvement from a group of parents informed study protocol design. Included patients were prospectively enrolled infants less than 6 months of age at the time of hospital admission, hospitalised with ALRI from September 2, 2025, to January 31, 2026, and tested for RSV. Infants were followed until hospital discharge or death whilst an inpatient. Primary vaccine effectiveness (VE) of maternal RSVpreF vaccination against RSV-associated hospitalisation for infants born at a gestation of 28 weeks or more, excluding nirsevimab recipients, was calculated with the use of a conditional logistic regression model adjusted by site, calendar month of attendance, gestational age at birth, socioeconomic status, age at admission and breastfeeding status.

Findings The primary analysis included 694 infants from 37 study sites in England, Scotland, Northern Ireland and Wales born at a gestation of 28 weeks or more who had not received nirsevimab: 429 RSV-positive cases (median age, 2.2 months, interquartile range 1.3-3.8 months) and 265 RSV-negative controls (median age, 1.7 months, interquartile range 1.0-3.3 months). Of recruited infants, 394/694 (57%) were male. Ethnicity data was available for 693 mothers; of these 538 (78%) identified as being of white ethnicity. The mothers of 161 RSV-positive case patients (38%) and 175 RSV-negative control patients (66%) had received the RSVpreF vaccine prior to delivery. The adjusted effectiveness of maternal RSVpreF vaccination for preventing infant hospitalisation was 61% (95% confidence interval [CI] 38-75) for infants up to 6 months of age, and 76% (95% CI 54-87) for infants up to 3 months of age. The overall effectiveness of the UK RSV prevention programme was 61% (95% CI 39-75) through to 6 months of age.

Interpretation In the real-world setting of the UK's maternal vaccination programme, RSVpreF vaccination was effective up until the age of 6 months in reducing the risk of hospital admission with RSV ALRI, as was the UK's infant RSV prevention programme as a whole. This data will help decision-

makers to evaluate whether RSVpreF or an anti-RSV infant monoclonal antibody best serves the needs of their infant population.

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Research in context

Evidence before this study

We previously evaluated RSVpreF maternal vaccine effectiveness (VE) to prevent RSV disease in infants during the first season of implementation in the United Kingdom (UK). However, low uptake within the recommended gestational window (28-31 weeks in the UK) and the relatively late timing of programme roll-out limited our ability to assess VE under optimal programme conditions, or to evaluate protection until 6 months of age.

We updated our previous review by searching PubMed using the terms “RSV AND maternal AND vaccin*” on February 2, 2026, restricting results to publications after our previous search on March 13, 2025, with no language restrictions. This search identified 202 citations. No new randomised controlled trials of RSV vaccination in pregnancy were published. We identified 9 non-randomised studies of RSVpreF VE conducted in Argentina (4), the USA (2), France (1), England and Scotland (1), and Scotland (1). Real-world studies report RSVpreF VE against RSV-related hospitalisation ranging from 58% to 82%, with higher effectiveness when vaccination occurs more than two weeks before delivery. Data on the durability of maternally-derived antibody protection is limited, with some evidence suggesting waning over time. The BERNI study (Argentina) reported RSVpreF VE of 78.6% (95% CI 62.1-87.9%) from birth to 3 months and 71.3% (95% CI 53.3-82.3%) from birth to 6 months. Notably, the generalisability of data from the US, Argentina, and France to the UK is limited by differences in maternal vaccination timing (32-36 weeks vs 28 weeks in the UK).

Added value of this study

Unlike our earlier evaluation conducted during programme roll-out, this study assesses maternal RSVpreF performance more than a year after implementation, when the vaccination programme had reached a steady-state. In addition, the timing of maternal vaccination in this cohort more closely reflects current UK recommendations (median gestational age at RSVpreF receipt 30 weeks) compared with season 1, enhancing the relevance of findings to routine clinical practice. Furthermore, by including infants born before 28 weeks’ gestation and those who received nirsevimab, we provide an overall estimate of the effectiveness of the UK infant RSV prevention programme as a whole. Finally, survey data from mothers who received pertussis vaccination but not RSVpreF (24% of recruits) suggest potential barriers related to perceptions of vaccine safety, necessity, and access highlighting opportunities for future public-health intervention.

Implications of all the available evidence

This study demonstrates that maternal RSVpreF vaccination at a gestation of 28-31 weeks, and the overall UK infant RSV prevention programme, are effective in reducing the risk of RSV-associated ALRI hospitalisation in

infants through to an age of 6 months. Decision-making around maternal RSVpreF vaccination appears to differ to that for pertussis, suggesting avenues to tackle low uptake. Our findings will inform decisions regarding the use of RSVpreF versus a monoclonal antibody when estimating likely uptake and impact, as well as decisions around the optimal timing of RSVpreF maternal vaccination at earlier (28–31 weeks) or later (32–36 weeks) gestational windows.

Introduction

Respiratory syncytial virus (RSV) is the most common cause of hospitalisation for respiratory disease in infants globally, with an estimated 1.4 million RSV-associated acute lower respiratory infection (ALRI) hospital admissions and 45,700 RSV-attributable deaths among infants of age 0-6 months every year.[1] In 2023, two population-level, anti-RSV prevention products were introduced: nirsevimab, a long-acting monoclonal antibody, and the maternal bivalent prefusion F protein-based (RSVpreF) vaccine (Abrysvo®). Both have been shown to be effective in a real-world setting.[2–9]

In late summer 2024, following a recommendation from the Joint Committee on Vaccination and Immunisation (JCVI), the United Kingdom (UK) introduced universal maternal RSVpreF vaccination from 28 weeks of gestation.[10] We previously showed in Season 1 of the BronchStop study,[3] using a test-negative design, a vaccine effectiveness (VE) of 58% (95% confidence interval [CI] 28–75) for this product in preventing hospital admission with RSV for all recruits to the study, and a higher estimated VE of 72% (95% CI 48-85) if given more than 2 weeks prior to delivery.

Introduction of the RSVpreF vaccination campaign in the UK began in late summer 2024 (August 12, 2024, in Scotland, and September 1, 2024, in England, Wales and Northern Ireland), shortly ahead of the 2024–25 RSV season peak in the week of 25 November 2024. The late roll-out and catch-up nature of the initial phases of this campaign meant that we could not assess RSVpreF protection until 6 months of age. Additionally, a high proportion of mothers recruited in Season 1 of the BronchStop study [3] were vaccinated later than the UK's currently recommended gestation of 28-31 weeks (median gestation at vaccination amongst BronchStop Season 1 recruits was 35 weeks, inter-quartile range [IQR] 32-37).This likely contributed to the lower VE (58%) for all study recruits, as nearly half of vaccinated RSV positive cases (34/73, 47%) were born within two weeks of maternal vaccination.

We therefore extended the BronchStop study into a second season to assess as a primary objective the effectiveness of the UK RSVpreF maternal vaccination programme whilst operating at a steady state, and to understand the protection provided to infants born after a gestation of 28 weeks through to 6 months of age. As secondary objectives we aimed to assess vaccine effectiveness for the subset of infants whose mothers had been vaccinated more than 14 days prior to delivery, compare in-hospital outcomes in RSV-positive infants of vaccinated and unvaccinated mothers, and understand whether VE was associated with infant age. We also sought to identify ongoing barriers to vaccine uptake: despite publicity campaigns to raise awareness of RSV and RSV vaccination,[11] uptake of maternal

RSVpreF remains low, with the latest estimates of 58% in England for births in August 2025,[12] and 62 % in Scotland for births in October 2025.[13]

In September 2025, nirsevimab was added to the UK immunisation schedule for high-risk infants (see details in Methods). We therefore also aimed to evaluate the *overall* effectiveness of the current UK infant RSV prevention programme by estimating VE in all infants, including those born before 28 weeks of gestation and those who had received nirsevimab.

Methods

Study design

We conducted a national multi-centre prospective, test-negative case control study to assess the effectiveness of maternal RSVpreF vaccination against hospital admission for RSV-associated ALRI amongst infants born to vaccine-eligible pregnant mothers (STROBE checklist available in appendix [pp 12-13]). A test-negative design was chosen as this reduces the chance of bias, including collider bias[14] due to differential healthcare seeking behaviours, as compared to a traditional case-control study.[15]

The BronchStop programme is delivered by PERUKI (Paediatric Emergency Research in the UK and Ireland) sites. The study-specific protocol, which included a pre-specified analysis plan, has previously been published.[16] Patient and public involvement was sought from a group of mothers of young children to inform data collection, consent procedures, and use of language in study publications. Further details on consent and ethical approvals are included in the appendix (pp 1-2)

United Kingdom infant RSV prevention programme

For the 2025-2026 season, all pregnant individuals in the United Kingdom were eligible for free RSVpreF vaccination, offered at a gestation of 28 weeks as part of the routine year-round maternal immunisation schedule, with gestational age determined based on an ultrasound scan conducted between 10-14 weeks of pregnancy.[17] Nirsevimab was made available free-of-charge to high-risk infants discharged from hospital after April 1, 2025: those born before 32 weeks' gestation, and those with bronchopulmonary dysplasia (BPD), congenital heart disease (CHD), or severe combined immunodeficiency (SCID).[10]

Study participants

In this study, which used a test-negative, case-control design, we recruited infants with a chronological age of 6 months or less admitted to 37 hospital sites across the United Kingdom from September 2, 2025, onwards. We prospectively recruited eligible infants during a hospital admission with a clinician-assigned diagnosis of bronchiolitis (cough, tachypnoea or chest recession, and wheeze or crackles on chest auscultation), lower respiratory tract infection (clinician diagnosis), or first episode of wheeze.[16] All participating sites had the capacity to undertake overnight paediatric admissions. Across all participating hospitals, infants admitted with one of

these diagnoses underwent RSV testing in line with their routine admission procedures and UK Royal College of Paediatrics and Child Health guidance,[18] in all instances using real-time reverse transcription polymerase chain reaction (rRT-PCR) or equivalent testing (for full details on testing by site see appendix [pp 5-6] . Test-positive infants were defined as those admitted with a positive RSV test. Test-negative infants were defined as those who tested negative for RSV.

For the primary outcome, infants born at a gestation of less than 28 weeks were excluded from the analysis, as they could not have benefitted from maternal vaccination. We also excluded infants who had previously received the licenced monoclonal antibodies palivizumab or nirsevimab as part of routine clinical care, or the long-acting monoclonal antibody clesrovimab as part of a clinical trial.

Procedures

We collected data on infant demographic characteristics including sex (as reported in the infant's medical records), Index of Multiple Deprivation (a marker of socioeconomic status) using home postcode, gestation at birth, and other co-morbidities known to be risk factors for severe RSV disease (BPD, CHD, and neuromuscular disease), length of hospital admission, highest level of care received, and respiratory support administered. Preterm birth was defined as birth at less than 37 weeks of gestation as per the World Health Organization (WHO) definition.[19] Paediatric intensive care, including access to invasive mechanical ventilation, is available free-of-charge to all children in the United Kingdom, either in-hospital (if this has a paediatric critical care unit) or via a paediatric critical care transfer team. Infants recruited were followed up until discharge from hospital or death, if this occurred as an inpatient. For participating mothers, self-reported gender identity was collected using a question asking whether it matched their sex assigned at birth (response options: yes; no [trans male]; no [non-binary]; other; prefer not to say). Self-reported maternal ethnicity, breast-feeding status, and maternal immunisation status, including gestation at time of vaccination, date of vaccination, and estimated due date, were collected. Additionally, consent was sought to access maternal vaccination records to ascertain RSVpreF and pertussis immunisation status (pertussis vaccination is offered at 20 weeks of gestation),[20] and for RSVpreF date of vaccination. Maternal vaccination status was verified using local hospital electronic health records (EHR) or primary care records. If local verification was not possible, the research team accessed central NHS Digital Spine records. Data was entered using the validated online data entry software REDCap (Research Electronic Data Capture) using the clinical report forms provided in the study protocol.[16] This software (REDCap) is hosted by Queen's University Belfast.

Outcome and exposure measures

The primary outcome was infant hospital admission with RSV-associated ALRI, in infants born at a gestation of 28 weeks or more who did not receive nirsevimab postnatally. The treatment exposure was defined as maternal RSVpreF receipt status prior to delivery amongst both case and control patients. To determine this, mothers were asked to recall whether they had received RSVpreF during pregnancy, and maternal medical records were accessed either locally by research staff or centrally when local access was not possible; for the primary analysis data from maternal medical records were used.

To compare gestational age at vaccination and the age of cases in Seasons 1 and 2 of the study, we compared our current dataset to that presented in our previous publication. In keeping with the analyses conducted in the MATISSE RCT [21] and our previous study[3] we conducted a prespecified VE analysis for the subgroup of infants whose mothers had received RSVpreF more than 14 days before delivery; this time period is considered sufficient for both maternal generation of anti RSV pre-F immunoglobulin G (IgG), and its transplacental transfer to the fetus.

We also performed pre-specified subgroup analyses comparing hospitalised vaccinated and unvaccinated RSV positive cases according to highest level of care afforded (high-dependency unit [HDU] or paediatric intensive care unit [PICU]), respiratory support administered (low-flow oxygen, high-flow oxygen, continuous positive airway pressure [CPAP] and invasive mechanical ventilation [IMV]).

Finally, we conducted a pre-specified analysis evaluating the overall performance of the UK infant RSV prevention programme, including infants born at a gestation of less than 28 weeks and those who received nirsevimab, with treatment exposure defined as maternal RSVpreF vaccination prior to delivery, receipt of nirsevimab, or both.

Statistical analysis

Effectiveness of the RSVpreF maternal vaccine against RSV-associated hospitalisation in infants born after 28 weeks of gestation was assessed using a test-negative design, comparing odds of vaccination among infants who were RSV-positive (case-patients) with those who were RSV-negative (control-patients). Sample size calculations were based on precision of the VE estimated by the test-negative design, as recommended by the WHO, and implemented using their VE calculator.[22] For full details of the statistical analysis please refer to the appendix (pp 1-2). **Role of the funding source**

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The authors vouch for

the accuracy and completeness of the data and for the fidelity of the study to the protocol.

Results

Recruitment commenced September 2, 2025, and continued until January 31, 2026. By this point the prespecified sample size was met for both cases and controls for the primary analysis. During the study period, 818 infants were recruited to the study across the 37 study sites (sites are detailed in the appendix pp 3-4) in the four UK Home Nations (England, Scotland, Wales and Northern Ireland). Of these, 108 were excluded from the study, and a further 16 from the primary analysis (13 because they had received nirsevimab,Figure)

In total, 429 RSV-positive infants (cases) and 265 RSV-negative infants (controls) were included in the primary analysis. None of the infants recruited died whilst an inpatient. The characteristics of the case and control patients for the primary analysis are shown in Table 1. Of recruited infants, 394/694 (57%) were male. The median age at hospitalisation was lower for controls than cases: 2.2 months for the RSV-positive cases (IQR 1.3-3.9) and 1.7 months for the RSV-negative controls (IQR 1.0-3.3) (p =0.0009). Of the 693 mothers for whom ethnicity data was available, 538 (78%) self-identified as being of white ethnicity: 341/429 (80%) mothers of cases, and 197/265 (74%) mothers of controls (p=0.30) (full ethnicity information provided in Table 1). All participating mothers reported that their gender identity matched their sex assigned at birth, except one mother who identified as non-binary. Disease was more severe in cases than controls: they were more likely to receive supplemental oxygen (288/429 [67%] of cases versus 87/265 [33%] of controls, p <0.0001) and to be admitted to paediatric intensive care (27/429 [6%] of cases versus 5/265 [2%] of controls, p=0.0072).

The mothers of 161 RSV-positive case patients (38%) and 175 RSV-negative control patients (66%) had received the RSVpreF vaccine prior to delivery. Of RSVpreF vaccinated mothers in Season 2 (this study), the median gestation of vaccine administration was 30 weeks (IQR 28-32), compared to 35 weeks (IQR 32-37) in Season 1.[3] The median age of all infant recruits to Season 2 of the study was 2.1 months (IQR 1.1-3.7) compared to 1.6 months in Season 1 (IQR 0.9-2.2) (appendix p 9).

The unadjusted vaccine effectiveness of RSVpreF for protecting against hospitalisation with RSV through to the age of 6 months was 69% (95% CI 57-78). Once adjusted for geographic site, month of admission, gestation, socioeconomic status, age at admission and breastfeeding status, the VE of maternal RSVpreF vaccination for infants born at a gestation of 28 weeks or more who had not received nirsevimab was 61% (95% CI 38-75). In a

prespecified analysis, we examined whether VE was affected by age, finding that the adjusted VE for protection against hospitalisation up until the age of 3 months was 76% (95% CI 54-87). A sensitivity analysis using maternal recall of RSVpreF receipt, rather than medical record documentation, which included 705 recruits, showed a similar estimate for protection through to 6 months of age: 61% (95% CI 39-76); the kappa statistic for the comparison of both methods was 0.71, indicating substantial agreement.[23]

We conducted a prespecified subgroup analysis to examine VE in infants whose mothers had received RSVpreF more than 14 days before delivery. In nine out of 161 RSV positive cases (6%) maternal RSVpreF vaccination had been received less than 14 days prior to delivery. This left 153/421 (36%) RSV positive cases and 168/258 (65%) RSV negative controls where maternal RSVpreF had been received more than 14 days prior to delivery. The estimated adjusted VE of maternal RSVpreF vaccination for protection until six months for this subgroup of cases and controls was the same as that for the primary analysis: 61% (95% CI 39-76). Within this subgroup, we also examined clinical outcomes for vaccinated and unvaccinated recipients (Table 2). Although RSVpreF vaccination more than 14 days before delivery was associated with a shorter overall length of stay (p=0.012), the difference between the groups was small, with an equal median length of admission for both groups (3 vs 3 days) and a just over half day reduction in the mean length of stay (3.5 vs 4.1 days). The risk of invasive mechanical ventilation (3% vs 3%, p=0.78) and PICU admission (7% vs 6%, p=0.74) did not appear to differ between the two groups.

As we had done previously,[3] we also examined the effectiveness of pertussis vaccination in preventing hospitalisation with RSV ALRI. Unlike our previous study, we found that in this analysis receipt of pertussis vaccination was also associated with the primary outcome of protection against RSV bronchiolitis, with a VE of 44 (95% CI 5-67). Examination of vaccination records for this cohort (appendix p 7) showed a strong correlation between RSVpreF and pertussis vaccination: 47% of mothers had received both vaccines, while only 2% had received RSVpreF without pertussis. The sensitivity of using pertussis vaccination to predict RSVpreF receipt was 95% (95% CI 92–97). Importantly however we identified 24% of participating mothers received pertussis but *not* RSVpreF during pregnancy. Analysis of survey responses from mothers who had received pertussis but not RSVpreF, a group who therefore appear not be opposed in principle to maternal vaccination, showed they were more likely to strongly disagree or disagree with statements regarding RSVpreF's safety, necessity, or ease of access, and more likely to hold neutral rather than positive views on its safety and necessity ($p < 0.001$ for all comparisons; appendix p 10). When we adjusted for maternal RSVpreF receipt when calculating the VE of

pertussis vaccination this showed no protection: adjusted VE was 0.08 (95% CI –73 to 51).The E-value for the primary outcome was 2.6.

Assessing the overall protection provided by the UK's infant RSV prevention programme, including infants born at any gestation, and using a combination of receipt of maternal RSVpreF at any time before delivery or nirsevimab, we found an overall effectiveness of 61% (95% CI 39-75) up until the age of 6 months. We also examined whether protection waned over time (appendix p 11), finding that the *unadjusted* protection afforded by maternal RSVpreF fell with infant age at bands of 0-1,2-3 and 3-4 months, albeit with wide confidence intervals.

Discussion

In this study we estimated effectiveness of the RSVpreF maternal vaccine against hospitalisation for RSV-associated ALRI in infants born at a gestation of 28 weeks or more whilst the UK RSV maternal vaccination programme was running at a steady state and found an overall effectiveness of 61% (95% CI 38-75). We found, unlike our previous study during the first season of RSVpreF rollout,[3] that excluding infants born less than 14 days after maternal receipt of RSVpreF did not affect the VE. This likely reflects the fact that, in Season 2, most RSVpreF recipients were vaccinated earlier in pregnancy than in Season 1 (median gestational age at administration: 30 vs 35 weeks). As a result, fewer RSV-positive cases had received RSVpreF shortly before delivery compared with our previous study (9/161 in Season 2, representing only 6 % of vaccinated cases). A recently published study from the 2024-2025 winter season in the US, where RSVpreF administration is recommended seasonally at 32-36 weeks' gestation, found an overall VE of 57% (95% CI 19-77) for protection against RSV-associated hospitalisation until the age of 6 months, with a median age of vaccination of 34 weeks.[5] Similarly to what we found in Season 1 of BronchStop, once the authors excluded infants born less than 14 days after maternal vaccination, the VE rose to 70% (95% CI 37-86). It is likely that earlier vaccination will be associated with a reduction in the number of infants who are born before they can benefit fully from the transplacental transfer of maternal anti-RSVpreF IgG. However, population level studies will be needed to understand the proportion of infants who would benefit from maternal vaccination at 28-31 weeks' gestation compared to vaccination at 32-36 weeks.

Infant protection against hospitalisation with RSV-ALRI was higher up until the age of 3 months (76%) than through to 6 months (61%). This is consistent with results from the MATISSE trial[24] and the BERNI study from Argentina,[4] and likely relates to the known gradual decrease over time in maternal IgG levels following birth. This finding is supported by our analysis of unadjusted VE for 2-month age bands, which shows evidence for waning

over time (appendix p 11). Our estimates for protection through to 6 months are in keeping with those from the US (57%), but lower than those from Argentina (71% for the BERNI study,[4] and 68% from another Argentinian study).[6] Differences between these high- and middle-income settings may relate to different severity thresholds for admission in these locations, or from a comparison of a seasonal campaign to a year-round one. In a seasonal campaign, the cohort of infants eligible for inclusion in a VE study is by definition younger than for a year-round campaign (see appendix p 9) and this may lead to a bias in results.

We found that pertussis and RSVpreF vaccination status were highly correlated, and that a substantial proportion (24%) of mothers in the study had received pertussis vaccination during pregnancy, but not RSVpreF. Survey responses suggest that this group, who do not appear fundamentally opposed to vaccination in pregnancy, could be more likely to accept RSVpreF if its safety and necessity were clearly communicated and access were made easier.

We found that once admitted, receipt of maternal RSV vaccination more than 14 days prior to delivery did appear to be associated with some evidence of protection against more severe disease. However, once hospitalised, there was no difference in the risk of admission to PICU or of IMV, similar to findings from the recently published US study.[5]

Our study has strengths and weaknesses. Strengths include the large number of recruiting sites (n=37), which means that we are likely to have captured a population that is representative of the United Kingdom as a whole, with a high proportion of recruited mothers self-identifying as not being of white ethnicity (22%), and with participants from all five socio-economic quintiles. Our results represent the effectiveness of the RSV maternal vaccine programme at a steady state and offer an example of what can be achieved to other countries considering introduction of a universal year-round RSVpreF vaccination programme.

Our study also has some limitations. The test-negative observational study design means that there is a risk of residual confounding and other biases such as collider bias. However, our calculated E-value of 2.6, the results from our pertussis negative control (once adjusted for maternal RSVpreF status) and concordance with final results from the MATISSE RCT[24] provide reassurance that the risk of such bias substantially affecting our estimate is low. We excluded high-risk infants born after 28 weeks' gestation who had received nirsevimab from our primary analysis, meaning our results cannot be extrapolated to understand the direct protection of RSVpreF to the infant population born after 28 weeks including those with high-risk conditions; equally our assessment of the effectiveness of the UK’s vaccination

programme was limited by the low numbers of recruited infants who received nirsevimab (13) and by a lack of population-level impact data. We were unable to explore the protection of RSVpreF beyond 6 months of age or against intensive care admission; larger studies will be needed to understand this. We were unable to access medical records for all maternal participants to establish RSVpreF status; however, a sensitivity analysis using maternal recall rather medical record documentation yielded a similar estimate for the primary outcome of 61% (95% CI 39-76)). Finally, the study was powered to analyse the effectiveness of RSVpreF maternal vaccination against RSV-associated hospitalisation with ALRI for our primary outcome; as such, all subgroup analyses should be considered exploratory.

Overall, our study provides important information for health systems to consider in relation to the introduction of either maternal vaccination or infant monoclonal antibodies (nirsevimab or clesrovimab) for protection of infants against RSV. These decisions are likely to be based on relative price and hence cost-effectiveness, however programme implementation and access are also important for overall public health benefit.

On an individual level, there is evidence that monoclonal antibodies administered at birth may provide greater effectiveness than maternal vaccination, possibly as antibody delivery is optimised at a critical time for risk reduction, and antibody waning begins from birth rather than in utero. A recent study from France, comparing a seasonal maternal RSVpreF vaccine strategy, similar to that reported in Bronchstart Season 1, to nirsevimab administration at birth, identified the latter was associated with a reduction in the risk of hospitalisation (HR 0.74, 95% CI 0.61 to 0.88).[7] Nirsevimab, if administered as result of a catch-up campaign, can also provide protection for infants up to a year of age.[8] The recent French study also demonstrated that nirsevimab was associated with reductions in requirement for PICU and mechanical ventilation when compared with maternal RSV vaccination; nirsevimab has been shown to be 80% effective against RSV-related PICU admission in the USA.[25] Greater volumes of comparative data will be required to fully understand the balance of benefit for the two approaches; a recently published French study for example suggests that if given at 28 weeks gestation, maternal RSVpreF infant protection may be similar to that from nirsevimab for the youngest infants (the impact on older infants was harder to assess, as RSVpreF is given seasonally in France)[26]RSVpreF vaccine, also potentially provides broader polyclonal protection, which will be more resilient to antigenic drift of RSV that have rendered monoclonal antibodies less active with time.[27]

Furthermore, at a population level there is increasing evidence in developed health settings that monoclonal antibodies may represent a better overall method of reducing the impact of RSV on infant populations. Our results demonstrate that uptake of maternal vaccination for RSV lags that of pertussis vaccination (Table S3) and identifies that vaccine safety concerns,

necessity and access were important factors creating this differential. In the UK, RSVpreF uptake stood at 58% for the latest estimate in England (births in August 2025),[12] and 62% in Scotland (births in October 2025).[13] Nirsevimab programs in general appear able to achieve greater coverage than maternal RSV vaccination. Although variable, many regions and countries have delivered highly impactful programmes for nirsevimab,[28,29]with the REACH study demonstrating a 78% reduction in RSV hospitalisation in Spain associated with nirsevimab use, compared with a corresponding 33% reduction in the UK associated with maternal RSV vaccine.[30] More data is required to enable healthcare systems in the global south to understand their optimal strategy, where vaccination delivery systems are established, with less capacity for adaptation to infant delivered monoclonals.

To have the greatest impact on infant health, and corresponding reduction in emergency care attendances, hospitalisations and potential need for paediatric intensive care, we believe our results should contribute to a re-evaluation of strategy, so that infant RSV outcomes in the UK more closely resemble those seen in countries that have adopted alternative implementation approaches.

Conclusion

This study evaluating the effectiveness of RSVpreF maternal vaccination programme, once in a steady state, indicates that it was effective against RSV-associated ALRI leading to hospital admission up until the age of 6 months. The UK RSV prevention programme, combining maternal RSVpreF for all, with nirsevimab for high-risk infants, also provided protection for all infants through to the age of 6 months. Our results can help inform healthcare systems in their evaluation of which RSV prevention product to introduce to protect infants from severe RSV disease and could contribute towards any re-evaluation of the UK's RSV prevention programme.

Figure legends

Figure: Study Population. Respiratory syncytial virus (RSV) test-positive case patients were infants of age less than 6 months hospitalised with a clinician-assigned diagnosis of bronchiolitis or lower respiratory tract infection between September 2, 2025, and January 31, 2026, at the BronchStop recruiting sites. RSV test-negative control patients were infants with the same diagnoses presenting to the same recruiting sites. Infants who had been admitted with these diagnoses underwent upper respiratory tract sampling for RSV testing by means of polymerase-chain-reaction assay or equivalent at admission (see Table S2 for list of testing modalities by site). LRTI denotes lower respiratory tract infection.

Competing interests

None of the authors declare any competing interests.

Author contributions

SC, SBD, DI, HG, ML, DM, SO, DR, TW and TCW conceived the study. SC, SBD, DI, HG, XL, ML, DM, SO, DR, TW and TCW made substantial contributions to the design of the work. CM and SH contributed towards acquisition of data for the work. RM and TCW performed the analysis and interpretation of the data. SC, SBD, RM, SO, DR and TCW drafted the manuscript. TCW, SOH and RM accessed and verified the data reported in the study, all the authors had access to data reported in the study, all authors revised the manuscript critically for important intellectual content and all authors approved the final manuscript prior to submission.

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Supporting data

The R code used to make the calculations for this paper is available on GitLab (https://git.ecdf.ed.ac.uk/twillia2/bronchstop/-/tree/main/maternal_VE_study_S2); the BronchStop dataset will be held for a minimum of 3 years and is available to be shared on reasonable request to the authors.

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