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A Critical Appraisal Of Economic Evaluations in RSV

Hudson R D A[1], Beuvelet M[2], Musci R[3], Aruffo E[3], Sardesai A[3], Kieffer A[2]

[1]Sanofi, Reading, UK, [2]Sanofi, Lyon, France, [3]Evidera Inc., USA

BACKGROUND

- Respiratory syncytial virus (RSV) is one of the primary causes of lower respiratory tract infections and hospitalisations among infants and children with an associated 3.6 million hospital admissions globally estimated for children <5 years of age in 2019.[1] In the UK, RSV is the leading cause of infant hospitalisation with roughly one in six paediatric admissions due to RSV every year.[2]
- Although roughly 85% of infants hospitalised due to RSV are otherwise healthy infants born at full term, no prophylactic treatments against RSV are reimbursed in the UK for healthy infants born late preterm or full term.[3]
- Health authorities are assessing the potential to introduce new RSV programmes to protect all infants.
- The Joint Committee on Vaccination and Immunisation (JCVI) in the UK advises authorities on immunisation, vaccination schedules and vaccine safety. Economic evaluations and modelling studies play a vital role in helping the JCVI assess the value of novel treatments to advise on changes to the UK's vaccination policy. Given the prominence of the JCVI, this advice further influences worldwide policy through National Immunisation Technical Advisory Groups (NITAGs). It is therefore critical that evaluations accurately reflect the clinical profile and licensed indication of immunisation products to ensure accurate decision making.

OBJECTIVES

- To explore the impact of alternate modelling approaches and the interpretation of published data on the results and conclusion of an economic evaluation.
- This study focuses on two evaluations for the use of nirsevimab (a long-acting monoclonal antibody) compared against no prophylaxis for preventing RSV-related lower respiratory tract disease in neonates and infants during their first RSV season in the UK.[4]

METHODS

The study compared two economic evaluations assessing the impact of nirsevimab on RSV health and cost outcomes; a dynamic transmission model by Hodgson et al. 2022,[5] and a static model by Kieffer et al. 2022 adapted for the UK perspective.[6]

Dynamic Model

UK population divided into 25 age groups, over a 10-year time horizon. Infants (<12 months in age) are further stratified based on eligibility to palivizumab and risk-status with respect to severe RSV infection.

Compartmental model structure following an extension of the Susceptible-Exposed-Infectious-Recovered framework also including asymptomatic infections, maternal-protective antibodies and treatment effectiveness waning.

Risk of infection dependent on contact between people in different age groups.

Prevention efficacy modelled using a parametric distribution with decay commencing at day one and occurring at an exponential rate over time.

Model outcomes include symptomatic infections, GP consultations, hospital admissions (including hospital bed days), deaths, QALY loss, cost outcomes, and optimal immunisation strategy (based on incremental cost-effectiveness ratio and purchasing price per dose).

Static Model

Infant only population aged 0 to 11 months, over a single RSV season based on gestational age and presence of high-risk comorbidities.

Static decision-analytic model following three key dimensions:

1. definition of the RSV season and infant age at the start of the season,
2. distribution of RSV cases over the year, and
3. rate of RSV-related healthcare resource use by age in months.

Risk of infection dependent on the age at time of infection and subpopulation.

Prevention efficacy modelled as a static value for the entire duration of protection (with flexibility to assess linear or exponential decay following the licensed period of protection of 150 days).

Model outcomes include total hospitalisations, ICU admissions, A&E and GP visits, outpatient follow-ups after an ICU admission, deaths, Economically Justifiable Price (EJP), QALY loss, and cost outcomes.

METHODS (Cont'd)

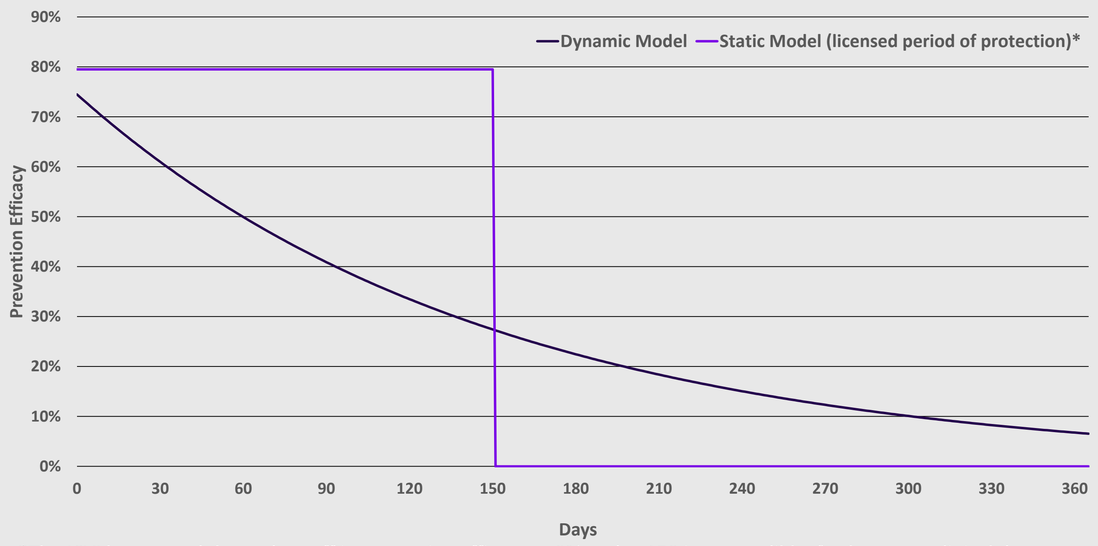
Key difference

- The dynamic model showed that as contact between infants <1 year of age and other individuals in a population is limited, the impact of reducing RSV incidence in infants is also expected to have a minimal impact on the transmission of RSV.[7] (This suggests that a dynamic model is less relevant in this age group[9] and a static model would sufficiently capture the impact of nirsevimab in infant RSV).
  - As both studies presented a similar conclusion the key difference was driven by the discrepancy in which protection against RSV-related health events was interpreted albeit from the same source.
  - The waning of prophylaxis-induced immunity follows an exponential decay in the dynamic model, with a reduction from 74.5% at day 1 to 27.4% at day 150. The static model follows the results of the clinical trials by maintaining protection at 79.5% over the licenced duration of protection (**Figure 1**; **Table 1**).

Calibration and Scenario Analysis

- To accurately compare both models (and highlight the differences), the static model was calibrated to align with the dynamic model on:
  - Risks of RSV-related health events
  - Coverage rates
  - Efficacy (including the approach used in the dynamic model surrounding duration of protection)
  - Population of interest
- Prevented hospitalizations and general practitioner visits (only for infants aged 0-11 months) were estimated under year-round and seasonal with National Immunisation Programme (NIP)-integrated catch-up immunisation strategies to compare the models.
- This exercise highlights that after the static model is parametrised in a similar way to the dynamic model the key differences arise from interpretation of the published data.

Figure 1. Decay of Prevention Efficacy for Nirsevimab Over Time



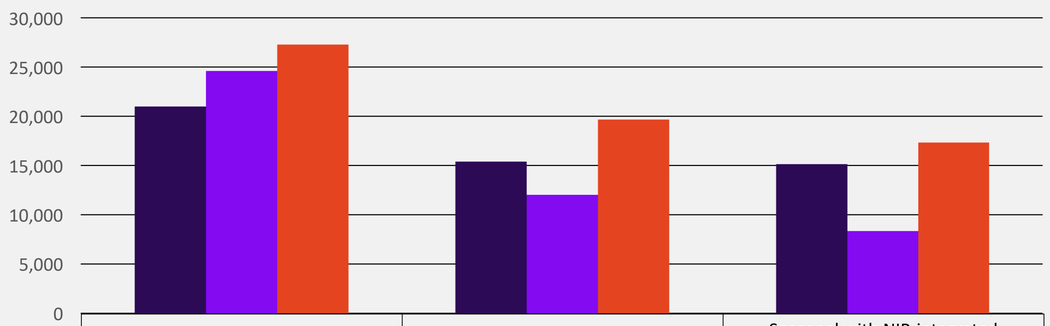
**The JCVI has agreed that a drop off in prevention efficacy to 0% at day 150 is not credible; furthermore, clinical data suggests that protection may continue with up to 50% efficacy through one year from administration.[9]*

Table 1. Decay of Prevention Efficacy for Nirsevimab by 30 Day Increments

Level of Protection Applied to Infants in:	Day 0	Day 30	Day 60	Day 90	Day 120	Day 150	Day 180
Dynamic Model	74.5%	61.0%	49.9%	40.9%	33.5%	27.4%	22.4%
Static Model	79.5%	79.5%	79.5%	79.5%	79.5%	79.5%	0.0%

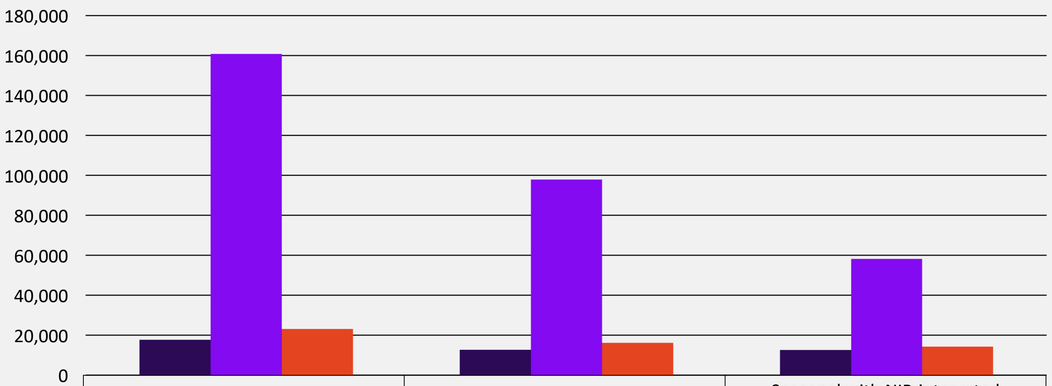
RESULTS

Total Inpatient Hospitalisations under No Prophylaxis and under Nirsevimab



	No Prophylaxis	Year Round*	Seasonal with NIP-integrated Catch-up*
Dynamic Model	20,989	15,390, [-27%]	15,137, [-28%]
Static Model	24,599	12,020, [-51%]	8,344, [-66%]
Calibrated Static Model	27,281	19,662, [-28%]	17,329, [-36%]

Total GP consultations under No Prophylaxis and under Nirsevimab



	No Prophylaxis	Year Round*	Seasonal with NIP-integrated Catch-up*
Dynamic Model	17,700	12,685, [-28%]	12,592, [-29%]
Static Model	160,793	97,902, [-39%]	58,160, [-64%]
Calibrated Static Model	23,093	16,166, [-30%]	14,260, [-38%]

**Values presented in these columns refer to: the number of total cases, [percent change relative to no prophylaxis].*

- Overall, the static model resulted in higher total and avoided hospitalizations and GP visits compared with the dynamic model under both immunization strategies. However, these differences can be primarily attributable to the parametrisation of each model and not differences in their structure, as post calibration both models produce similar results.
- The impact of parameterisation is most evident for GP visits, where the percentage difference in total and avoided GP consultations between both models reduced by 27% and 38% post calibration. A similar trend was observed for hospitalization where the percent difference between both models reduced by 28% and 36% in terms of total and avoided hospitalizations respectively, following calibration.

DISCUSSION

This study highlights the importance of appropriate interpretation and use of clinical data to estimate the value of new immunisation strategies to correctly inform recommending agencies for the purposes of decision making.

- The published dynamic model produced lower total and avoided hospitalisations, GP visits, and administered doses compared to the static model. This difference was driven by the choice of epidemiological data, leading to different estimates of RSV burden and the percentage of case reductions defined by prevention efficacy.
- Prevention efficacy is a critical component in modelling patient outcomes and an important driver of results. In this case the nirsevimab clinical evidence shows it to be sustained for a 150 days post-administration.[8,9]
- While both models use the same source to inform protection, implementation of an immediate exponential decay in efficacy applied in the dynamic model results in a loss in protection of 50% by day 104, and by the end of 5 months only 27% of infants remain protected. This approach is contrary to both the published nirsevimab data and license which significantly reduces the overall protection offered by nirsevimab, undervaluing the importance of the prophylaxis.
- In this case underestimating prevention efficacy significantly impacted the benefits and cost-effectiveness of nirsevimab reported by the dynamic model. This is important because HTA recommendations are based on cost-effectiveness as a whole or across varying subgroups of the overall eligible population.

This comparative analysis shows that differences in the use of key model parameters and assumptions drawn from the same source can have a significant impact on model results and their interpretations. Collaboration with manufacturers on key treatment parameters is vital to ensure validity of the analyses.

REFERENCES:

1. Li Y, Wang X, et al. *Lancet*. 2022 May 28;399(10340):2047-2064.
2. Oxford Vaccine Group. 2019. https://vk.ovg.ox.ac.uk/rsv
3. Murray J, Bottle A, Sharland M, et al. *PLoS One*. 2014;9(2):e89186. Published 2014 Feb 26.
4. AstraZeneca,. 2023 July. https://www.astrazeneca.com/media-centre/press-releases/2023/beyfortus-approved-in-the-us-for-the-prevention-of-rsv-lower-respiratory-tract-disease-in-infants.html
5. Hodgson et al. *Vaccine*. 2022 Nov 22;40(49):7151-7157.
6. Kieffer et al. *J Infect Dis*. 2022 Aug 15;226(Suppl 2):S282-S292.
7. Hodgson et al. *Vaccine*. 2022 Nov 22;40(49):7151-7157.
8. Griffin MP, et al. *N Engl J Med*. 2020 Aug 13;383(7):698. PMID: 32726528.
9. Hammitt LL, et al. *N Engl J Med*. 2022 Mar 3;386(9):837-846.

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