Ann Ig 2025 Sep-Oct; 37(5): 684-688. doi: 10.7416/ai.2025.2712. Epub 2025 Jun 12.

LETTER TO THE EDITOR

Nirsevimab: a change of paradigm in the prophylaxis of Respiratory Syncytial Virus disease among infants

Dear Editor,

In a recent paper (1), Garattini and Clavenna have suggested policy makers to be very cautious in introducing new immunization products in public health strategies for the prevention of Respiratory Syncytial Virus (RSV) infections, affirming that this risk is overestimated and the choices could be even driven by a bunch of powerful multinational companies. These considerations were published after several countries, including Italy, Spain, Luxemburg, France, Germany, and the United States, based on strong scientific evidence, included in their immunization schedules the administration of the monoclonal antibody (mAb) Nirsevimab for all newborns.

The RSV is a leading cause of respiratory illness in children under five, with the highest incidence in infants under one year of age in terms of morbidity, hospitalization, and mortality (2-7), accounting in 2019 for approximately 33 million cases of acute lower respiratory infections (ALRI) globally among children under five, resulting in about 3.6 million hospitalizations and an estimated 101,400 deaths (2,8). Most RSV-related deaths occur in low- and middle-income countries (LMICs), where access to healthcare is limited. In higher-income settings, while mortality rates are lower, RSV still contributes significantly to hospitalizations and healthcare costs. The burden is also consistent in the primary care context, and this should be taken into account in cost-benefit analysis of prevention strategies (9-10). To this regard it should be mentioned that RSV-associated bronchiolitis is a very serious disease in the first weeks of life, and often requiring oxygen and maintenance of a good nutritional status. More severe forms (requiring intensive care or fatal) affect, in over 90% of the cases, previously healthy children, often with long-term outcomes (11-13). In the 2023-2024 bronchiolitis season, RSV-associated disease has posed incredible challenges to the Italian National Health Service (NHS) in terms of hospitalizations and occupation of beds in intensive care units (14-16).

The availability of the new preventive drug Nirsevimab is going to change the paradigm of infants' immunization against RSV, since the prophylaxis of RSV disease requires the administration of only one dose of the drug. This implies that the drug can be fruitfully used through the universal "all-infant protection" strategy to reduce the burden of disease at the population level and the risk of hospitalization, with a reasonable cost-benefit ratio.

To this regard, data from Galicia (Spain), showed that universal use of Nirsevimab may substantially reduce infant hospitalizations for RSV-associated lower respiratory tract infection (LRTI), severe RSV-associated LRTI requiring oxygen, and all cause LRTI when provided in real-world conditions (17). Similar results were reported in Catalonia, with an overall reduction in the risk of bronchiolitis (18), as well as across the entire newborn population in Spain (19).

Further evidence on the effectiveness of RSV prevention through Nirsevimab administration came from other countries. In France, data showed an effectiveness of Nirsevimab bewteen 76% and 81% in preventing RSV-associated bronchiolitis among infants (20). The effectivness, safety, and impact of immunization with Nirsevimab in preventing severe RSV-associated disease among infants has been highlighted in recent literature reviews (21). Preliminary data on the real-world effectiveness of Nirsevimab against several RSV-associated end-points are also provided by a study conducted in the US (22). Similar results, including a dramatic reduction in hospital admissions, were obtained in the Italian Region of Valle d'Aosta in the 2023-24 season (23).

Annali di Igiene : Medicina Preventiva e di Comunità (Ann Ig)
ISSN (print) 1120-9135 ISSN (online) 3035-5559

https://www.annali-igiene.it

Cost benefit analyses should now take in to account the availability of a new effective product at a reasonable price and minimal additional organizational effort.

In fact, RSV infections in infants and children impose a substantial economic burden on the NHS, encompassing both direct healthcare costs - such as hospitalizations, diagnostics, and treatments - and indirect costs, including productivity losses for parents and caregivers of RSV-positive children. These costs are driven by frequent primary care visits, specialist consultations, emergency room visits, and hospitalizations in general wards and intensive care units.

A recent study evaluates the cost-effectiveness of interventions against RSV in infants, showing that mAb administration with a catch-up program was either cost-saving or cost-effective for various willingness-to-pay thresholds in multiple European countries, including Italy. Specifically, the seasonal mAb plus catch-up program provided significant reductions in RSV hospitalizations and quality-adjusted life years (QALYs) losses, proving to be cost-effective even at relatively conservative willingness-to-pay values (24).

Although some countries like Sweden and Ireland have not yet adopted an universal "all-infant protection" strategy, under the assumptions that targeting only preterm infants may be a satisfactory public health strategy, the Spanish National Immunization Technical Advisory Group (NITAG) and the US Centers for Disease Control and Prevention (CDC) have endorsed Nirsevimab for all infants entering their first RSV season. Similarly, the Germany's Standing Committee on Vaccination (STIKO) and the World Health Organization (WHO)'s Strategic Advisory Group of Experts on Immunization (SAGE) have similarly recommended broad RSV prophylaxis for infants. Moreover, the WHO has recently released a position paper recommending that all countries introduce products for the prevention of severe RSV disease in these infants (25).

In Italy, Health Authorities have allocated € 50 million to support the universal administration of Nirsevimab for newborns starting in November 2024 under the NHS. This decision, taken on the bases of public health needs and supported by the Italian NITAG (26), the National Institute of Health and the scientific associations, includes a strict monitoring plan to evaluate program adherence, regional implementation strategies, and overall effectiveness in reducing RSV cases, hospitalizations, and mortality. This evidence-based and equitable approach prioritizes the health of Italian newborns over economic interests, ensuring a public health decision made in the sole interest of the health of Italian newborns, to be included permanently in the National Immunization Preventive Plan (27-28).

Preliminary real-life data from several Italian regions show an unequivocal 70% to 88% reduction in bronchiolitis-related hospital admissions during the 2024/25 winter season, along with fewer accesses to emergency departments and neonatal intensive care units (29-32). In Lombardy Region, in particular, where the coverage rate of newborns was over 95% during winter season (November 2024 – March 2025) and 81% overall (65,049 over 80,670 born from January 2024 and March 2025), hospitalizations and Emergency Unit accesses decreased by 65-70%.

Despite its considerable investment, this preventive strategy has delivered unprecedented real life clinical results in a remarkably short time.

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References

1. Garattini L, Clavenna A. RSV prevention options for infants and older adults: A specific expanding competitive arena. Health Policy. 2024 Oct 20;**150**:105187. doi: 10.1016/j.healthpol.2024.105187. Epub ahead of print. PMID: 39442242.
2. Shi T, McAllister DA, O'Brien KL, Simoes EAF, Madhi SA, Gessner BD, et al. Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in young children in 2015: a systematic review and modelling study. Lancet 2017 Sep 2; **390**(10098):946-58. PMID: 28689664; PMCID: PMC5592248.
3. Hall CB, Weinberg GA, Iwane MK, Blumkin AK, Edwards KM, Staat MA, et al. The burden of respiratory syncytial virus infection in young children. N Engl J Med. 2009 Feb 5;**360**(6):588-98. doi: 10.1056/NEJMoa0804877. PMID: 19196675; PMCID: PMC4829966.
4. Geoghegan S, Erviti A, Caballero MT, Vallone F, Zanone SM, Losada JV, et al. Mortality due to Respiratory Syncytial Virus. Burden and Risk Factors. Am J Respir Crit Care Med. 2017 Jan 1;**195**(1):96-103. doi:10.1164/rccm.201603-0658OC. PMID: 27331632.
5. Hall CB, Weinberg GA, Blumkin AK, et al. Respiratory syncytial virus-associated hospitalizations among children less than 24 months of age. Pediatrics. 2013 Aug;**132**(2):e341-e348. doi: 10.1542/peds.2013-0303. Epub 2013 Jul 22. PMID: 23878043.
6. Meissner HC. Viral Bronchiolitis in Children. New Eng J Med. 2016 Jan 7;**374**(1):62-72. https://doi.org/10.1056/NEJMra1413456. PMID: 26735994.
7. Stein RT, Bont LJ, Zar H, Polack FP, Park C, Claxton A, et al. Respiratory syncytial virus hospitalization and mortality: Systematic review and meta-analysis. Pediatr Pulmonol. 2017 Apr;**52**(4):556-569. doi:10.1002/ppul.23570. Epub 2016 Oct 14. PMID: 27740723; PMCID: PMC5396299.
8. Li Y, Wang X, Blau DM, Caballero MT, Feikin DR, Gill CJ, et al. Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in children younger than 5 years in 2019: a systematic analysis. Lancet. 2022 May 28;**399**(10340):2047-2064. doi: 10.1016/S0140-6736(22)00478-0. Epub 2022 May 19. PMID: 35598608; PMCID: PMC7613574.
9. Thomas E, Mattila JM, Lehtinen P, Vuorinen T, Waris M, Heikkinen T. Burden of Respiratory Syncytial Virus Infection During the First Year of Life. J Infect Dis. 2021 Mar 3;**223**(5):811-817. doi: 10.1093/infdis/jiaa754. PMID: 33350450.
10. Scarpaci M, Bracaloni S, Esposito E, De Angelis L, Baglivo F, Casini B, et al. RSV Disease Burden in Primary Care in Italy: A Multi-Region Pediatric Study, Winter Season 2022-2023. Influenza Other Respir Viruses. 2024 Apr;**18**(4):e13282. doi: 10.1111/irv.13282. PMID: 38622776; PMCID: PMC11018906.
11. Vittucci AC, Antilici L, Russo C, Musolino AMC, Cristaldi S, Cutrera R, et al. Respiratory syncytial virus: can we still believe that after pandemic bronchiolitis is not a critical issue for public health?. Eur J Pediatr. 2023 Dec;**182**(12):5303-5313. doi: 10.1007/s00431-023-05201-y. Epub 2023 Sep 20. PMID: 37728752; PMCID: PMC10746572.
12. Bozzola E, Ciarlitto C, Guolo S, Brusco C, Cerone G, Antilici L, et al. Respiratory Syncytial Virus Bronchiolitis in Infancy: The Acute Hospitalization Cost. Front Pediatr. 2021 Jan 18;**8**:594898. doi: 10.3389/fped.2020.594898. PMID: 33537260; PMCID: PMC7848214.
13. Antilici L, Vittucci AC, Cristaldi S, Musolino AMC, Pisani M, Rotondi Aufiero L, et al. High-flow nasal cannulas versus standard oxygen therapy for moderate bronchiolitis: a quasi-experimental analysis. Pediatr Pulmonol. 2025 Jan; Epub 2024 Oct 25. doi: 10.1002/ppul.27358. PMID: 39451018; PMCID: PMC11740650.
14. Villani A, Vittucci AC, Antilici L, Pisani M, Scutari R, Di Maio VC, et al. Prevention of RSV Bronchiolitis: An Ethical Issue. Pediatr Infect Dis J. 2024 Aug;**43**(8):e296-e297. doi: 10.1097/INF.0000000000004354. Epub 2024 Apr 9. PMID: 38621157.
15. Sumsuzzman DM, Wang Z, Langley JM, Moghadas SM. Real-world effectiveness of nirsevimab against respiratory syncytial virus disease in infants: a systematic review and meta-analysis. Lancet Child Adolesc Health. 2025 Jun;**9**(6):393-403. doi: 10.1016/S2352-4642(25)00093-8. Epub 2025 May 1. PMID: 40319903.
16. Hak SF, Sankatsing VDV, Wildenbeest JG, Venekamp RP, Casini B, Rizzo C, et al; RSV ComNet Network.

Burden of RSV infections among young children in primary care: a prospective cohort study in five European countries (2021-23). Lancet Respir Med. 2025 Feb;**13**(2):153-165. doi: 10.1016/S2213-2600(24)00367-9. Epub 2025 Jan 9. PMID: 39799949.

17. Ares-Gómez S, Mallah N, Santiago-Pérez MI, Pardo-Seco J, Pérez-Martínez O, Otero-Barrós MT, et al. Effectiveness and impact of universal prophylaxis with nirsevimab in infants against hospitalisation for respiratory syncytial virus in Galicia, Spain: initial results of a population-based longitudinal study. Lancet Infect Dis. 2024 Aug;**24**(8):817-828. doi:10.1016/S1473-3099(24)00215-9. Epub 2024 Apr 30. PMID: 38701823.
18. Perramon-Malavez A, de Rioja VL, Coma E, Hermosilla E, Fina F, Martínez-Marcos M, et al. Introduction of nirsevimab in Catalonia, Spain: description of the incidence of bronchiolitis and respiratory syncytial virus in the 2023/2024 season. Eur J Pediatr. 2024 Dec;**183**(12):5181-5189. doi: 10.1007/s00431-024-05779-x. Epub 2024 Sep 28. PMID: 39340677; PMCID: PMC11527896.
19. Jimeno Ruiz S, Peláez A, Labourt A, Acuña FM, Linares L, Llana Martín I, et al. Evaluating the Effectiveness of Nirsevimab in Reducing Pediatric RSV Hospitalizations in Spain. Vaccines (Basel). 2024 Oct 11;**12**(10):1160. doi: 10.3390/vaccines12101160. PMID: 39460326; PMCID: PMC11510999.
20. Paireau J, Durand C, Raimbault S, Cazaubon J, Mortamet G, Viriot D, et al. Nirsevimab Effectiveness Against Cases of Respiratory Syncytial Virus Bronchiolitis Hospitalised in Paediatric Intensive Care Units in France, September 2023-January 2024. Influenza Other Respir Viruses. 2024 Jun;**18**(6):e13311. doi:10.1111/irv.13311. PMID: 38840301; PMCID: PMC11154801.
21. Orsi A, Scarpaleggia M, Baldo V, Barbone F, Chironna M, Giuffrida S, et al. First real-world data on universal respiratory syncytial virus prophylaxis with Nirsevimab in infants. J Prev Med Hyg. 2024 Aug 31;**65**(2):E172-E187. doi:10.15167/2421-4248/jpmh2024.65.2.3329. PMID: 39430977; PMCID: PMC11487721.
22. Xu H, Aparicio C, Wats A, Araujo BL, Pitzer VE, Warren JL, et al. Real-World Effectiveness of Nirsevimab Against Respiratory Syncytial Virus: A Test-Negative Case-Control Study (Preprint]. medRxiv. 2024 Sep 12:2024.09.12.24313545. doi: 10.1101/2024.09.12.24313545. PMID: 39314944; PMCID: PMC11419242.
23. Consolati A, Farinelli M, Serravalle P, Rollandin C, Apprato L, Esposito S, et al. Safety and Efficacy of Nirsevimab in a Universal Prevention Program of Respiratory Syncytial Virus Bronchiolitis in Newborns and Infants in the First Year of Life in the Valle d'Aosta Region, Italy, in the 2023-2024 Epidemic Season. Vaccines (Basel). 2024 May 17;**12**(5):549. doi:10.3390/vaccines12050549. PMID: 38793800; PMCID: PMC11125727.
24. Getaneh AM, Li X, Mao Z, Johannesen CK, Barbieri E, van Summeren J, et al. Cost-effectiveness of monoclonal antibody and maternal immunization against respiratory syncytial virus (RSV) in infants: Evaluation for six European countries. Vaccine. 2023 Feb 24;**41**(9):1623-1631. doi:10.1016/j.vaccine.2023.01.058. Epub 2023 Feb 1. PMID: 36737318.
25. Silenzi A, Siddu A, D'Amelio AC, Cataldi S, Fasano C, Maraglino F, et al. The new Italian National Immunization Technical Advisory Group (NITAG) and its commitment to endorse a new efficient National Immunization Plan in COVID-19 times. Ann Ist Super Sanita. 2023 Jan-Mar;**59**(1):26-30. doi: 10.4415/ANN_23_01_04. PMID: 36974701.
26. World Health Organization. WHO position paper on immunization to protect infants against respiratory syncytial virus disease, May 2025. Wkly Epidemiol Rec. 2025 May 30;**100**(22):193-218. Available from: https://iris.who.int/bitstream/handle/10665/381539/WER10022-eng-fre.pdf [Last accessed: 2025 Jun 9].
27. State-Regions Conference (Italy). 2024, Oct 17. Available from: https://www.statoregioni.it/media/lhnb3llv/p-fs-csr-atto-rep-n-188-17ott2024.pdf [Last accessed: 2025 Jun 9].
28. Signorelli C, Oleari F, Greco D, Ruocco G, Guerra R, Rezza G, et al. The Italian National Vaccine Prevention Plans, 1999/2020-2023/2025: challenges and obstacles to vaccine coverage goals. Commentary. Ann Ist Super Sanita. 2024 Oct-Dec;**60**(4):247-251. doi: 10.4415/ANN_24_04_02. PMID: 39699977.
29. MilanoToday. 2025, Jan 30. Così la Lombardia sta 'vincendo' contro il virus sinciziale (la bronchiolite). Available from: https://www.milanotoday.it/attualita/ricoveri-bronchiolite-virus-sinciziale.html [Last accessed: 2025 Jun 9].

30. TorinoCronaca. 2025, Jan 6. Influenza per 500 mila. Nei pronto soccorso 200 accessi al giorno. Available from: https://torinocronaca.it/news/torino/438189/influenza-per-500mila-nei-pronto-soccorso-200-accessi-al-giorno.html [Last accessed: 2025 Jun 9].
31. IVG. 2025, Mar 18. Bronchiolite in Liguria: 90% dei neonati vaccinato; casi diminuiti dell'88% in un anno. Available from: https://www.ivg.it/2025/03/bronchiolite-in-liguria-90-dei-neonati-vaccinato-casi-diminuiti-dell88-in-un-anno/ [Last accessed: 2025 Jun 9].
32. ANSA. 2025, Mar 18. Neonatologi Calabria, ok campagna vaccini contro virus sinciziale. Available from: https://www.ansa.it/calabria/notizie/2025/03/18/neonatologi-calabriaok-campagna-vaccini-contro-virus-sinciziale_0944c6ba-4c9c-490c-86fb-e5ae61d557ec.html [Last accessed: 2025 Jun 9].