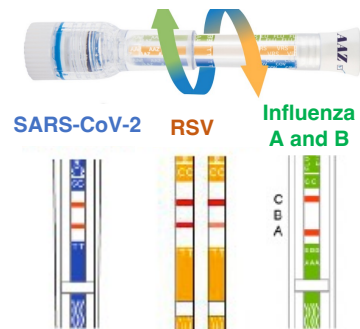


## Background

RSV causes a wide spectrum of respiratory diseases, including bronchiolitis and otitis media.

In the NIRSEGAL study, a negative effect of nirsevimab beyond one year was observed in the ambulatory setting, where an increased incidence of respiratory infections was reported. In outpatient care, these episodes consisted of non-specific respiratory infections potentially caused by RSV or by other respiratory viruses (influenza viruses, human metapneumovirus, rhinoviruses), without systematic virological sampling.

The aim of this work is to assess the effectiveness of nirsevimab during the first and second years of life in children with RSV-positive respiratory infections in ambulatory settings.



## Method

Multiplex antigen testing (SARS-CoV-2, influenza A and B, and RSV) was systematically performed in children presenting with clinical syndromes potentially related to respiratory viruses (bronchiolitis, influenza-like illness, otitis media...). A test-negative design was performed during the first and second years of life. Children whose mothers had received maternal vaccination were excluded.

## Results

- From October 15, 2024, to April 15, 2025 (season 1), 1,992 children younger than 13 months presenting with respiratory infections were enrolled, and 60.8% received nirsevimab.
- From October 15, 2025, to April 15, 2026 (season 2), 1,479 children younger than 13 months and 1,847 children aged 13–25 months presenting with respiratory infections were enrolled. 61.7% had received nirsevimab this season, and 65.7% had received nirsevimab the last season, respectively.

The Table on the right presents the effectiveness of nirsevimab during the first and second years of life. Estimated nirsevimab effectiveness was 85.7% (95% CI: 79.0–90.3) during the 2024–2025 season and 66.6% (95% CI: 50.3–77.5) during the 2025–2026 season, with a significant difference between seasons (p for interaction = 0.003).

Table. Effectiveness of Nirsevimab the first and second years of life according to symptoms

| Symptoms                                                                   | Age group<br>Season      | Nirsevimab | RSV- | RSV+ | Immunisation effectiveness<br>[95% CI] |
|----------------------------------------------------------------------------|--------------------------|------------|------|------|----------------------------------------|
| Bronchiolitis                                                              | <13 months<br>Season 2   | Nirse-     | 86   | 85   | 66.6% [50.3 ; 77.5]<br><b>p=0.003</b>  |
|                                                                            |                          | Nirse+     | 227  | 75   |                                        |
|                                                                            | <13 months<br>Season 1   | Nirse-     | 104  | 119  | 85.7% [79.0 ; 90.3]                    |
|                                                                            |                          | Nirse+     | 349  | 57   |                                        |
|                                                                            | 13-25 months<br>Season 2 | Nirse-     | 53   | 48   | -14.4% [-80.5 ; 27.4]                  |
|                                                                            |                          | Nirse+     | 137  | 142  |                                        |
| Other<br>respiratory<br>infections<br>(Otitis,<br>Flu-like<br>symptoms...) | <13 months<br>Season 2   | Nirse-     | 331  | 64   | 74.2% [59.2 ; 83.7]                    |
|                                                                            |                          | Nirse+     | 582  | 29   |                                        |
|                                                                            | <13 months<br>Season 1   | Nirse-     | 492  | 65   | 72.8% [57.0 ; 82.8]                    |
|                                                                            |                          | Nirse+     | 778  | 28   |                                        |
|                                                                            | 13-25 months<br>Season 2 | Nirse-     | 441  | 91   | 5.2% [-26.0 ; 28.7]                    |
|                                                                            |                          | Nirse+     | 782  | 153  |                                        |

Season 1:  
Oct. 15, 2024 to Apr. 15, 2025

Season 2:  
Oct. 15, 2025 to Apr. 15, 2026

## Conclusion

In ambulatory settings, the effectiveness could vary from one year to another, and according to the clinical syndromes.

No measurable effectiveness of nirsevimab against RSV-positive respiratory infections beyond the year of administration was observed.

Moreover, the effectiveness of nirsevimab was lower in season 2, especially for bronchiolitis. Those difference in effectiveness could be explain by a difference in circulating RSV clades: A.D.1 in 2024/2025 and A.D.3 in 2025/2026.