

Respiratory syncytial virus accounted for more than 100,000 deaths worldwide in children under five during 2019

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A new study published in *The Lancet* estimates that RSV-attributable acute lower respiratory infection was responsible for more than 100,000



deaths in children under five across the globe in 2019. The study is the first to examine RSV disease burden in narrow age brackets, reporting that there were over 45,000 deaths in infants under six months old in 2019, with one in five of the total global cases of RSV occurring in this age group.

"RSV is the predominant cause of acute lower respiratory infection in young children and our updated estimates reveal that children six months and younger are particularly vulnerable, especially with cases surging as COVID-19 restrictions are easing around the world and majority of the young children born in the last two years have never been exposed to RSV (and therefore have no immunity against this virus). With numerous RSV vaccine candidates in the pipeline, our estimates by narrower age ranges help to identify groups that should be prioritized, including pregnant people, so that children in the youngest age groups can be protected, similarly to current strategies which offer vaccines for whooping cough, typhoid, and tetanus to pregnant people," says Harish Nair, co-author of the paper, University of Edinburgh, UK.

This new study's findings are broadly consistent with previous estimates from a 2015 study, which placed the number of annual cases of RSV in children up to five years old at 33.1 million, resulting in a total of 118,200 overall deaths. However, these updated calculations of RSV mortality on global, regional, and national levels for the year 2019 include modeling data from over a hundred new studies, allowing researchers to provide estimates for narrower age groups—including from 28 days to six months old, which is known to be the age range with the highest RSV fatality rate—and community mortality rates (i.e., deaths that did not occur in a hospital).

Across the globe in 2019, there were 33 million RSV-associated acute lower respiratory infection episodes in children under five years old, leading to 3.6 million hospital admissions, 26,300 in-hospital deaths and



101,400 RSV-attributable deaths overall (including community deaths). This accounts for one in 50, or 2% of annual deaths from any cause in this age range.

For children under six months old, there were 6.6 million RSVassociated acute lower respiratory infection episodes globally in 2019. There were 1.4 million <u>hospital admissions</u>, 13,300 hospital deaths and 45,700 overall deaths attributable to RSV in this age range, accounting for one in 50, or 2.1% of annual deaths from any cause.

Based on estimates of in-hospital versus overall RSV mortality rates, globally only 26%, or approximately one in four RSV-associated deaths occur in a hospital. This is particularly apparent in low- and middle-income countries, where the in-hospital case-to-fatality ratio for children under five is 1.4%, compared to 0.1% in high income countries. Overall, 97% of RSV deaths in children under five occurred in low- and middle-income countries.

"Our study estimates that three-quarters of RSVs deaths are happening outside of a hospital setting. This gap is even greater in LMICs, especially in children under six months old, where more than 80% of deaths are occurring in the community. This reflects the fact that access and availability to hospital care are still limited in these regions. Early identification of cases in the community and referral for hospital admission of sick children (particularly those with low oxygen saturation in peripheral blood), and universal effective and affordable immunization programs will be vital going forward," says Xin Wang, coauthor of the study, Nanjing Medical University, China and University of Edinburgh, UK.

The authors acknowledge some limitations with this study. Variations in factors such as study setting, exact case definition for acute lower respiratory infection (ALRI), health-care access and seeking behavior,



and eligibility for RSV testing could affect estimates of mortality figures produced in the modeling. The breakdown by age bands was also limited by the data available for the study. In addition, all data were collected before the COVID-19 pandemic; it is unknown how the COVID-19 pandemic could affect RSV disease burden in the long term.

Writing in a linked comment, Tina Hartert, Vanderbilt School of Medicine, U.S., who wasn't involved in the research, said that "the influence of these data cannot be understated. There is a substantial RSV ALRI burden during the newborn period in LMICs, highlighting the potential for passive immunization strategies to meaningfully impact child health... Policy makers will benchmark benefits of RSV prevention against other priority public health interventions. Accurate estimates of prevention impact are critical to demonstrating the investment case for RSV prevention."

More information: 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, *The Lancet* (2022). DOI: 10.1016/S0140-6736(22)00478-0

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