



BACKGROUND

- Respiratory syncytial virus (RSV) is a leading cause of lower respiratory tract infections in young children, yet effective treatments remain unavailable.
- Maternal vaccination (MV) has recently emerged as a promising strategy to protect newborns from RSV and a increasing number of health economic evaluations (HEE).
- Accurate estimation of RSV disease burden is critical for developing robust decision models to guide healthcare planning but remains a challenge.

OBJECTIVES

- This systematic review aims to examine how HEE of RSV MV developed disease burden estimates, including methods and data sources to improve the understanding of RSV disease burden estimation and support further HEE.

METHODS

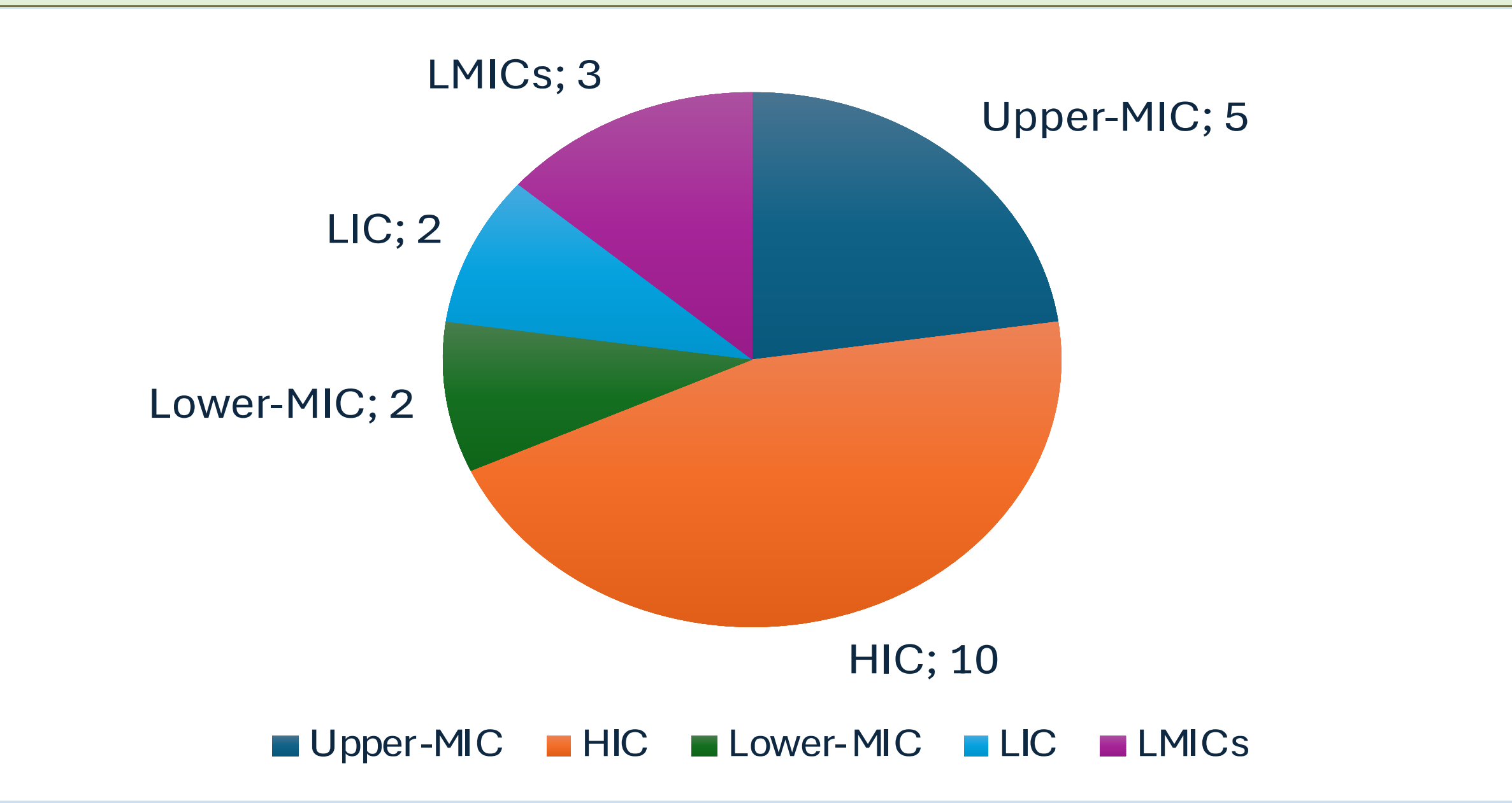
- A systematic search was conducted in MEDLINE, SCOPUS, EMBASE, NHS EED, HTA, Tufts CEA Registry, LILACS, and Web of Science since 2000.
- Search terms: (1) economic evaluation, (2) vaccine, and (3) respiratory syncytial virus (RSV) .
- Main outcomes of interest: incidence rates, mortality or case-fatality rates (CFRs), and inpatient and outpatient rates used as inputs in the studies, along with their respective calculation methods.
- Costs: 2024 U.S. dollars
- PROSPERO: CRD42024549989

RESULTS

Study	Location	MV	RSV incidence	RSV mortality	RSV hospitalization	Dose price	CEA results
Rey-Ares, 2024	Argentina	RSVPreF	GB-ALRI-RSV 2019, for UMIC. Distribution across months of age, relative risk of RSV-LRTI based on published US data.	Based on previous Argentinean studies. Due to data limitations, CFR was assumed to be invariant by age and term status	Local surveillance data adjusted by a multiplier of 1.56 (GB ALRI-RSV 2019)	NR	MV cost-effective at US\$141.18/dose
Gebretekle, 2024	Canada	RSVPreF	Retrospective study on RSV disease in Alberta, Canada, from 2010 to 2019	Based on previously published Canadian studies and Statistics Canada	Systematic review of the Canadian National Advisory Committee on Immunization (NACI)	US\$195.85	Nirsevimab programs are the most cost-effective option at current product prices
Ishiwada, 2024	Japan	RSVPreF	NR	Based on literature and US/CDC data	Japanese claims database for 2021	US\$59.03 to US\$590.32	MV cost-effective at US\$182/dose
Do, 2023	Vietnam	RSVPreF	Prospective surveillance and case-control study of hospitalized children with ARI in Vietnam combined with data from GB-ALRI-RSV 2019, for LMICs.	GB ALRI-RSV 2019 for LMICs	Several local published studies. The estimated RSV-ALRI admission rate was consistent with the GB ALRI-RSV 2019 for LMICs	US\$26.09	MV could be cost-effective at US\$5/dose.
Laufer, 2023	Mali	WHO PPC	Community-based study in Mali. Extrapolated out to 36 months based on the linear decline from Li et al 2020.	Data from a previous economic evaluation of RSV interventions in 72 GAVI eligible countries [Li, 2020] .	Community-based study conducted in Mali. For older children, a linear age-gradient based on data from the Gambia from (GB ALRI-RSV 2015.	US\$1.17 / US\$0.23 per dose (subsidized)	MV is not a cost-effective strategy, even assuming high vaccine efficacy
Mahmud, 2023	133 LMICs	RSVPreF	GB-ALRI-RSV 2019	Published data of Global burden of ALRI due to RSV in 2019	GB ALRI-RSV 2019	US\$3.71 per dose in Gavi countries; US\$7	MV at \$3.50/dose could be either cost-saving in all LMICs.
Koltai, 2023	Kenya and South Africa	RSVPreF	National data from Kenya Medical Research Institute and National Institute for Communicable Diseases of South Africa	Published national data. Out-of-hospital mortality the proportion of deaths that occurred outside of hospital (GB ALRI-RSV 2019 for LMICs and Laufer 2021)	K: Health and Demographic Surveillance System. Regional data were projected to the entire country adjusting for risk factors, using local data. SA: Sentinel surveillance of ILI and SARI in 3 public hospitals in 2 provinces	Kenya: US\$5.67 - 56.74; South Africa: US\$5.34 - 53.45	In Kenya and SA, MV at US\$40/dose is cost effective.
Getaneh, 2023	Denmark, Finland, England, Scotland, Italy,	WHO PPC and RSVPreF	Danish (2010-2017), Finnish (2006-2016), Scottish (2010-2016), Italian, and Dutch (2013-2016) patient registries; expert validation for missing data.	No preventable deaths was used in the base-case. In scenario analysis national registries from Denmark and Scotland.	Published time-series for all countries but Italy. ICD-9 coded RSV-hospitalizations for Italy, adjusted for underestimation.	US\$79.11	MV could be cost-effective at 50% lower price than nirsevimab and/or if higher protection is assumed.
Li, 2022	Norway	WHO PPC	NR	Norwegian Cause of Death Registry (2008-2017). Most deaths were of children with CHD or other	Norwegian Patient Registry. Monthly national data, over nine RSV seasons (2008-17), using ICD-10 codes.	US\$84.47	MV program is unlikely to be cost-effective, unless it reaches WHO PPC efficacy and has
Li, 2020	72 Gavi-eligible countries	WHO PPC and RSVPreF3	GB-ALRI-RSV 2015. Data from ten community-based studies in LMICs were pooled to estimate age-specific incidences. Data from LMIC was used for	Based on 19 studies from LMICs. Assumed that the numbers of community deaths are approximately equal to in-hospital deaths.	Cohort study in Kenya.	US\$3.83	MV need to be competitively priced to be relatively cost-effective.

- We included 21 HEE of RSV MV. The main outcomes were either QALY or DALY. 19 studies included MV, mAb, and no intervention in their comparative strategies
- Twelve studies primarily used national data from Health Information Systems, laboratory surveillance, and previous local studies to build epidemiological estimates, 9 from HICs. Seven studies utilized Global Burden of RSV-ALRI data for epidemiological estimates, with some using it as their primary source while used it to complement local surveillance data.
- Hospitalization data was the most frequently available. The use of ICD-codes might underestimate the number of admissions Outpatient estimation required various sources and methodologies, including WHO proxies, subtraction methods, and international data.
- Recent studies have adopted age-specific estimates for the first year of life, as opposed to aggregated incidence approach for children under five years old.
- Only studies conducted in LMICs considered out-of-hospital deaths, while some HIC studies excluded RSV-related mortality.
- Post-RSV complications (wheezing, asthma) included in only 3 HIC studies.

Figure 1: RSV MV HEE by Country Income Classification (n=21)



- Modeling approaches: 17 static models (including UNIVAC, McMarcel frameworks), 2 dynamic, 2 discrete event agent-based
- No studies included equity assessments or financial risk protection analyses
- 18/21 studies found MV potentially cost-effective at certain prices, with seasonal vaccination more cost-effective than year-round

CONCLUSION

- This review highlights methodological challenges in HEE of RSV MV strategies, particularly in LMICs, where the burden of disease is highest yet local data and HEE remain limited.
- Enhancing local data availability for RSV and strengthening the respiratory virus surveillance, are crucial steps to improve the reliability of HEE of RSV prevention strategies and enable more informed and effective policy decisions.



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