

Cost of childhood RSV management and cost-effectiveness of RSV interventions: a systematic review from a low- and middle- income country perspective

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BACKGROUND

Approximately 97% of global deaths due to RSV in children occur in low- and middle-income countries (LMICs).¹ Until recently, the only licensed preventive intervention has been a short-acting monoclonal antibody (mAb), palivizumab (PVZ) that is expensive and intensive to administer, making it poorly suited for low-resource settings.² Currently, new longer acting RSV mAbs and maternal vaccines are emerging from late-stage clinical development with promising clinical effectiveness.³ Evidence on the economic burden and value of interventions primarily is from high-income countries;^{4,5} however, evidence of economic value and affordability for patients in LMICs, where burden is greatest, must also be considered.

RESEARCH OBJECTIVE

Summarize existing evidence on cost-of-illness and cost-effectiveness of childhood RSV prevention interventions in LMICs.

KEY POINTS

- > RSV causes a substantial burden of illness and death among children, and 97% of these deaths occur LMICs
- > Until recently, the only preventive intervention for childhood RSV has been an expensive and complex mAb (PVZ) though several new technologies are emerging from late-stage clinical evaluation with promising results
- > We conducted a systematic review to identify cost estimates for the burden of childhood RSV and cost-effectiveness estimates of preventive interventions from LMICs
- > New technologies such as maternal immunization (MI) and mAbs may be more cost-effective in LMIC settings than PVZ, but existing evidence is too sparse and varied to draw conclusions about economic burden and tradeoffs
- > Further studies are needed to inform adoption of RSV prevention technologies specifically in LMICs



References: 1) Li Y, 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;399:2047–64; 2) Mac S, et al. Cost-effectiveness of Palivizumab for Respiratory Syncytial Virus: A systematic review. *Pediatrics* 2019;143:20184064; 3) Voirin N, et al. Potential Impact of Nirsevimab on RSV Transmission and Medically Attended Lower Respiratory Tract Illness Caused by RSV: A Disease Transmission Model. *Infect Dis Ther* 2021:2021:1–16; 4) Zhang S, et al. Cost of Respiratory Syncytial Virus-Associated Acute Lower Respiratory Infection Management in Young Children at the Regional and Global Level: A Systematic Review and Meta-Analysis. *J Infect Dis* 2020;222:S680–7; 5) Treskova M, et al. Assessment of the Effects of Active Immunisation against Respiratory Syncytial Virus (RSV) using Decision-Analytic Models: A Systematic Review with a Focus on Vaccination Strategies, Modelling Methods and Input Data. *Pharmacoeconomics* 2021;39:287

STUDY IDENTIFICATION

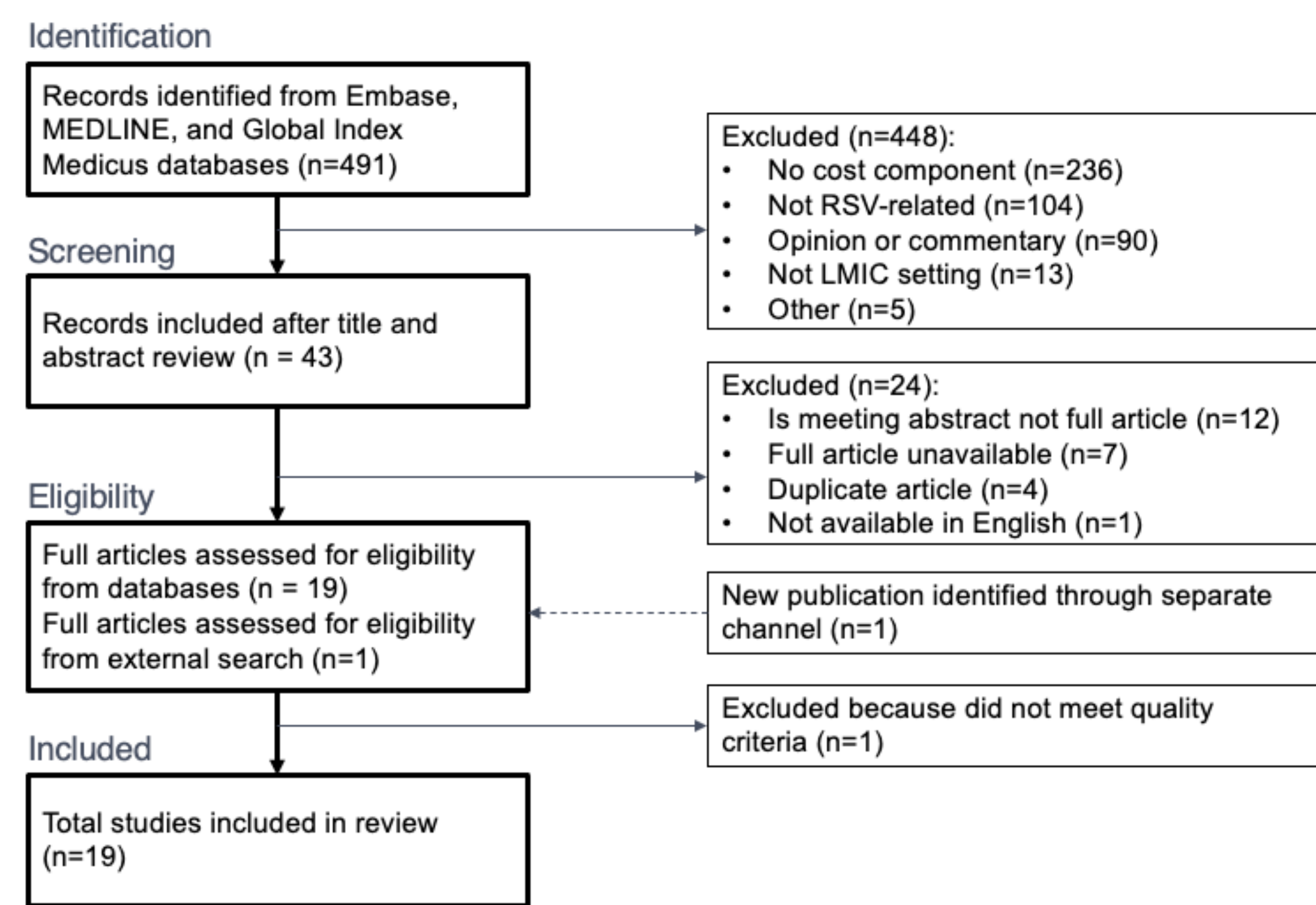


Figure 1. PRISMA flow chart of studies included in this systematic review. Across search results from 2000 – 2022, a total of 19 studies (9 CEA studies, 9 COI studies, and 1 study reporting both) were included for analysis.

METHODS

Study Identification

We conducted a systematic literature review adhering to PRISMA guidelines using the Embase, MEDLINE, and Global Index Medicus databases for publications between January 2000 and August 2022.

Study Selection

Two authors reviewed all titles and abstracts to identify studies that merited full article review. After reviewing all full-text articles for relevance, articles were evaluated for quality using the Drummond checklist. Of 491 articles reviewed, 19 met inclusion criteria. The 19 studies were analyzed in two groups based on the study objective: cost-effectiveness analysis (CEA) of an RSV intervention (n=10) or cost of illness (COI) estimation of RSV (n=10) (one study reported both).

Study Analysis

Data from each study were extracted into MS Excel for analysis. All cost estimates are presented in 2020 \$USD. To provide a willingness-to-pay (WTP) reference for contextualizing incremental cost-effectiveness ratios (ICERs) in the CEA analyses, the 2020 gross domestic product (GDP) per capita in \$USD is also included for each country.

RESULTS

COST-EFFECTIVENESS FINDINGS

CEA results varied widely. Study assumptions of intervention costs and effectiveness varied substantially, and their results often had wide confidence intervals. Evaluations of MI \$1,440 per disability-adjusted life year (DALY) averted (LMICs) to \$8,753/DALY averted (Mali) and \$118,845 per quality-adjusted life year (QALY) gained (Turkey); for long-acting mAbs found ICERs from \$462/DALY averted to \$2,971/DALY averted; and for PVZ \$4,671/DALY averted (Mali) to \$22,863/QALY gained (Mexico).

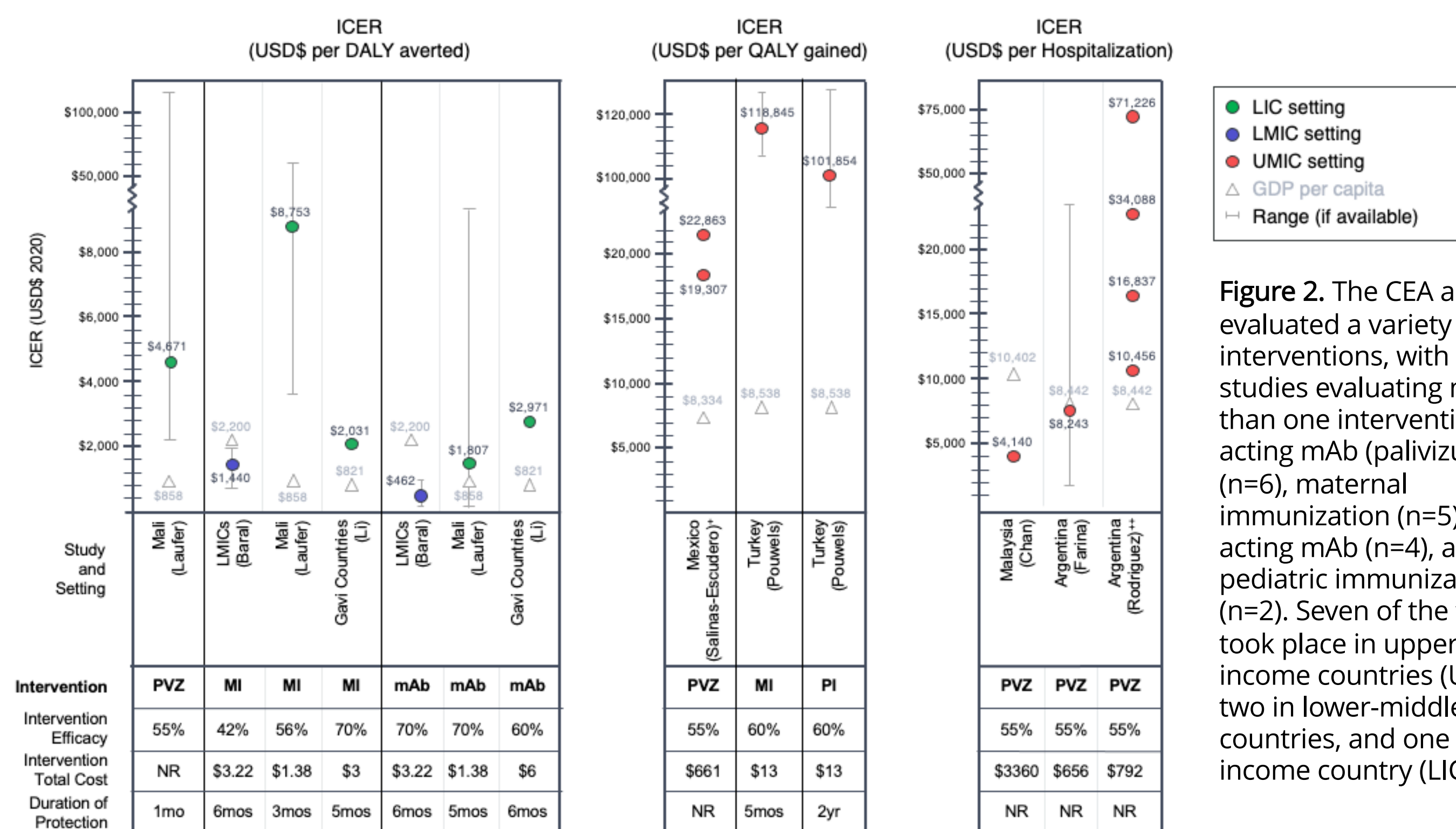


Figure 2. The CEA articles evaluated a variety of interventions, with most studies evaluating more than one intervention: short-acting mAb (palivizumab) (n=6), maternal immunization (n=5), long-acting mAb (n=4), and pediatric immunization (n=2). Seven of the ten CEAs took place in upper-middle-income countries (UMIC), two in lower-middle income countries, and one in a low-income country (LIC).

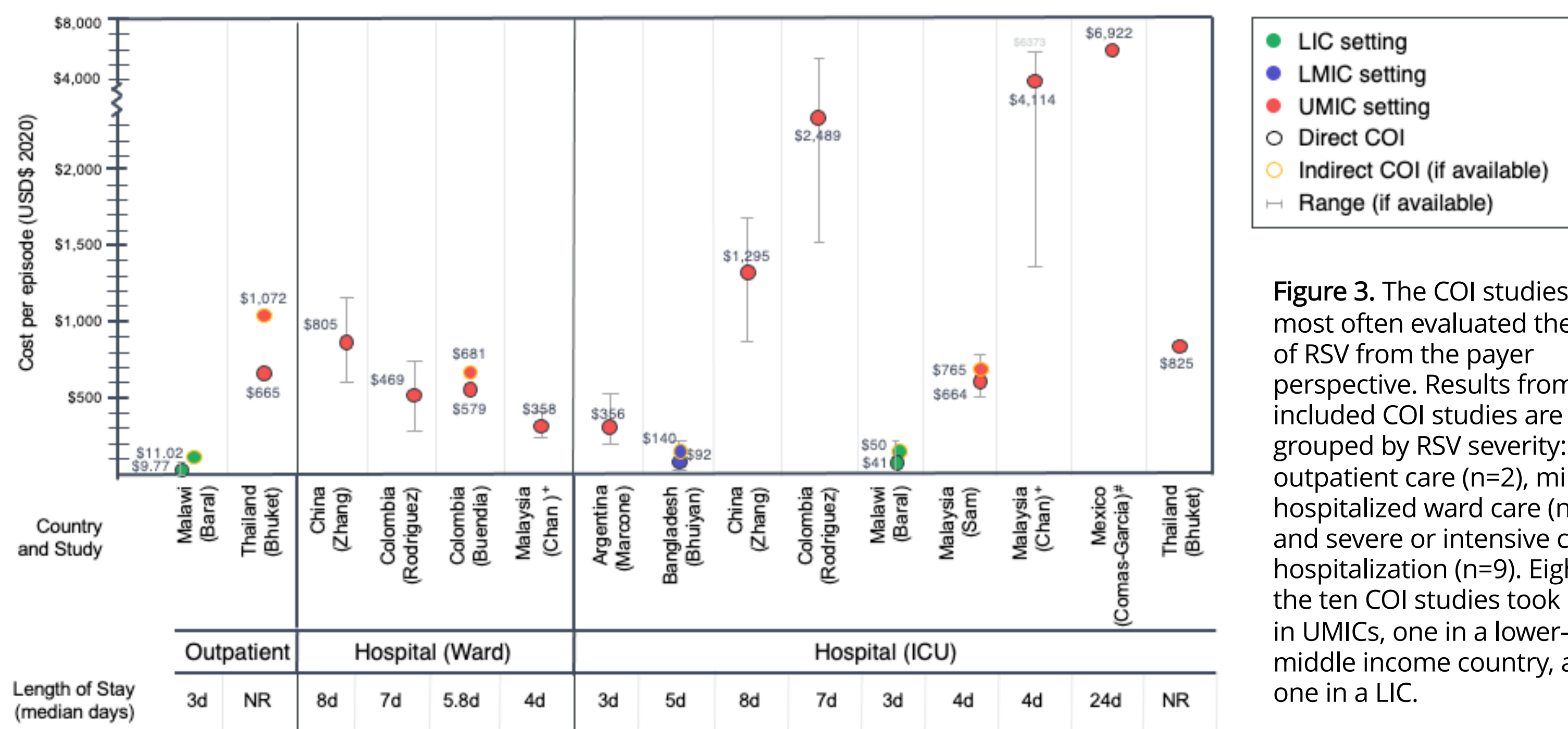


Figure 3. The COI studies most often evaluated the cost of RSV from the payer perspective. Results from the included COI studies are grouped by RSV severity: outpatient care (n=2), mild hospitalized ward care (n=4), and severe or intensive care hospitalization (n=9). Eight of the ten COI studies took place in UMICs, one in a lower-middle income country, and one in a LIC.

COST-OF-ILLNESS FINDINGS

COI estimates also ranged based on country and case severity. For severe RSV, cost per episode ranged from \$92 (Malawi) to \$4,114 (Malaysia). Five of the ten studies included indirect medical costs or non-medical costs. Two reported results in the context of total household costs and found that the cost per RSV episode accounted for 24% (Bangladesh) and 37% (Malawi) of monthly household income.

DISCUSSION

RSV represents a substantial disease burden in LMICs; however, evidence describing its economic burden is limited. CEAs to date rely heavily on intervention efficacy assumptions and implementation setting; as such the available estimates encompass a wide range of possible conclusions about the cost-effectiveness of RSV interventions. Generally, the ICERs for hypothetical MI or long-acting mAb are lower (more favorable) than for analyses of the existing short-acting mAb product PVZ. When comparing ICERs to the threshold of 1 GDP per capita in each study setting, however, whether MI or long-acting mAbs will be broadly cost-effective is unclear.

Further research is needed to understand the economic burden of childhood RSV in LMICs and reduce uncertainty about the relative value of anticipated RSV prevention interventions specifically in LMICs. Existing CEAs primarily quantify direct medical costs and near-term health effects; future studies should consider evaluating a lifetime horizon, including asthma and other sequelae, and a societal perspective of costs. As more precise data on intervention efficacy and duration of protection become available from ongoing clinical trials for new long-acting mAb and maternal vaccine products, those data will allow more accurate inputs for ICER estimation and relative value conclusions in future CEAs.