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Cost-Effectiveness of Respiratory Syncytial Virus Vaccines for Adults

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Abbreviations

ARI	acute respiratory illness
ED	emergency department
ICER	incremental cost-effectiveness ratio
ICU	intensive care unit
LRTD	lower respiratory tract illness
OECD	Organization for Economic Cooperation and Development
PPD	price per dose
QALY	quality-adjusted life-year
RSV	respiratory syncytial virus
UM-CDC	University of Michigan-Centers for Disease Control and Prevention
VE	vaccine efficacy
WTP	willingness to pay

Key Messages

- Three economic evaluations and 1 summary of economic evaluations were identified that assessed the cost-effectiveness of 2 respiratory syncytial virus (RSV) vaccines of interest (RSVPreF3 [Arexvy] and RSVpreF [Abrysvo]) compared with no intervention in older adults residing in high-income countries. No economic evaluations assessing mRNA-1345 were identified. No publications investigating RSV vaccination in adults aged 59 years or younger were identified.
  - In total, 5 economic evaluations for RSV vaccines in adults were identified.
  - Four economic evaluations were conducted in the US and 1 was conducted in Hong Kong. All results were presented in terms of incremental cost-utility ratios (i.e., incremental cost per quality-adjusted life-years gained). Net cost per outcome averted was reported for 1 economic evaluation, and cost per hospitalization averted was reported for 3 economic evaluations.
  - The results of all publications found that RSVPreF3 (Arexvy) and RSVpreF (Abrysvo) were more costly and more effective than no intervention for RSV-associated disease. All publications reported that vaccinating older adults against RSV disease was potentially cost-effective. All publications noted that the cost-effectiveness was dependent on vaccine cost, vaccine efficacy, the waning of vaccine protection, RSV hospitalization incidence, health care unit costs, and respective regional willingness-to-pay thresholds.
- The generalizability of the identified economic evaluations may be limited because the study settings were notably different from Canada. To estimate the cost-effectiveness of RSV vaccinations in Canada, a de novo economic evaluation conducted from a Canadian setting comparing RSVPreF3 (Arexvy), RSVpreF (Abrysvo), and mRNA-1345 is required.

Introduction and Rationale

Background and Rationale

Respiratory syncytial virus (RSV) is a significant cause of lower respiratory tract disease (LRTD) and hospitalization in Canada for older adults, immunocompromised individuals, and infants.[1,2] RSV infections predominantly occur during the fall to early spring, with the peak usually occurring from December to March in Canada.[1] RSV infections typically present with symptoms comparable to the common cold, and may include low-grade fever, cough, nasal congestion, and loss of appetite.[1] RSV infections can develop into severe pneumonia or bronchiolitis.[1] Recent literature from Canada has reported an increase in RSV-coded hospitalization rates among adults and that the rate of RSV-related hospitalizations increases with age.[2] Moreover, a higher rate of mortality has been observed in older individuals who are hospitalized for RSV than children.[1]

Three RSV vaccines have either been approved or are under review by Health Canada for the prevention of LRTD caused by RSV in adults aged 60 years and older. RSVPreF3 (Arexvy), an adjuvanted vaccine, and RSVpreF (Abrysvo), a bivalent vaccine, have both been approved for use by Health Canada for the prevention

of LRTD caused by RSV in adults aged 60 years and older.[3,4] mRNA-1345, an mRNA vaccine, is under review by Health Canda (as of January 2024) for the prevention of RSV in adults aged 60 years or older.[5] RSVPreF3 (Arexvy), RSVpreF (Abrysvo), and mRNA-1345 are all single-dose vaccines.[3,6,7]

Although multiple treatment options may be available for the prevention of RSV disease in older adults, the cost-effectiveness of the vaccines among adults in Canada remains unstudied.

Research Question

What is the cost-effectiveness of vaccination against RSV for healthy and/or high-risk adults aged 18 years and older compared to no vaccination or other RSV vaccines?

Methods

A review of the economic literature was undertaken to identify previously published economic evidence regarding the cost-effectiveness of the use of RSV vaccinations for adults (i.e., RSVPreF3 [Arexvy], RSVpreF [Abrysvo], mRNA-1345) in high-income countries.

Literature Search Methods

An information specialist conducted a literature search on key resources including MEDLINE, Embase, the Cochrane Database of Systematic Reviews, the International HTA Database, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search approach was customized to retrieve a limited set of results, balancing comprehensiveness with relevancy. The search strategy comprised both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. Search concepts were developed based on the elements of the research questions and selection criteria. The main search concept was respiratory syncytial virus vaccines. CADTH-developed search filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, or indirect treatment comparisons, economic evaluations, and citations related to health utilities or quality of life. The search was completed on December 6, 2023, and limited to English- and French-language documents published since January 1, 2013. Regular alerts updated the search until January 15, 2024.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Criteria	Description
Population	Adults aged 18 years and older
Intervention	RSV vaccinations for adults (i.e., RSVPreF3 [Arexvy], RSVpreF [Abrysvo], mRNA-1345)
Comparator	Any comparator (e.g., placebo, no intervention, alternative RSV prevention interventions)

Criteria	Description
Outcomes	Quality-adjusted life-years, disability-adjusted life-years, incremental costs, and incremental cost-effectiveness ratio (e.g., cost per QALY gained or incremental cost per event or event avoided), net monetary benefit, net health benefit
Study designs	Full economic evaluations (e.g., cost-minimization analysis, cost-consequence analyses, cost-effectiveness analyses, cost-utility analyses), health technology assessments, and systematic reviews

RSV = respiratory syncytial virus; QALY = quality-adjusted life-year.

Exclusion Criteria

Studies were excluded if they:

- did not meet the inclusion criteria outlined in Table 1
- were duplicate publications
- were published in languages other than English or French
- were not conducted in countries identified as high income by the World Bank[8]
- were systematic reviews whose primary cost-effectiveness studies were otherwise captured or excluded
- were published before 2013
- were conducted in a population solely consisting of people who are pregnant.

Data Extraction and Critical Appraisal

During data extraction, the following were collected: author, publication year, country, currency, source of funding, study design, modelling approach, study perspective, discounting, time horizon, outcomes, source of clinical efficacy, study population characteristics, and results. The quality of the included studies was critically appraised by 1 reviewer using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Economic Evaluations. Summary scores were not calculated for the included studies; rather, the strengths and limitations of each included publication were described narratively.

Cost-effectiveness outcomes were reported as unadjusted and adjusted. If adjusted, outcomes were adjusted to 2023 Canadian dollars using inflation rates from the Bank of Canada and Organization for Economic Cooperation and Development (OECD) purchasing power parity rates or average exchange rates from the Bank of Canada.[9-11]

Summary of Evidence

Quantity of Research Available

A total of 506 citations were identified in the literature search. Following the screening of titles and abstracts, 499 citations were excluded and 7 potentially relevant publications from the electronic search were retrieved for full-text review. In addition, 4 potentially relevant publications were retrieved from the grey literature search for full-text review. Of these potentially relevant publications, 7 were excluded for various reasons, leading to 4 publications that met the inclusion criteria and were included in this review. Two publications were identified from the published literature[12,13] and 2 publications were identified from the grey literature

search and were only available as presentation slides.[14,15] Appendix 1 (Figure 1) presents the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) flow chart of the publication selection and reasons for exclusions.

Of the 4 publications identified,[12-15] 3 were economic evaluations[12,13,15] and 1 was a summary of 3 economic evaluations.[14] The summary conducted by Ortega-Sanchez[14] compared 2 industry-funded economic evaluations (1 for RSVpreF [Abrysvo] and 1 for RSVPreF3 [Arexvy]), and a third economic evaluation, termed the University of Michigan-Centers for Disease Control and Prevention (UM-CDC) economic evaluation. The UM-CDC economic evaluation is the same model described in Hutton,[15] as confirmed by Hutton and Prosser.[16] The input parameters and results across the 2 publications were consistent when reported in both publications.[14,15] Both publications were included in this review because additional information was provided on the UM-CDC economic evaluation in the Ortega-Sanchez[14] summary and additional outcomes were reported in the Hutton[15] publication that were excluded from the Ortega-Sanchez summary.

Of the 5 unique economic evaluations included in this review, there were 2 decision tree models[13-15] and 1 discrete-event simulation model.[12] Ortega-Sanchez[14] did not provide sufficient details on the modelling approaches for all economic evaluations summarized. Three economic evaluations were set in the US[12,14,15] and 1 in Hong Kong.[13] All publications included RSVPreF3 (Arexvy) and RSVpreF (Abrysvo) as interventions. No identified publications included mRNA-1345 as an intervention or comparator. Table 2 in Appendix 1 provides an overview of the characteristics of the 5 included economic evaluations.

Summary of Critical Appraisal

The 4 publications of inclusion ranged from meeting 5 to 9 of the Joanna Briggs Institute (JBI) Critical Appraisal Checklist criteria (Appendix 1, Table 3) regarding study quality and applicability to adults aged 18 years or older. None of the publications included all issues of concern to users (e.g., none considered the cost-effectiveness of mRNA-1345, or adults between the ages of 18 and 59 years), and it was unclear whether the economic evaluations were generalizable to the Canadian population because they were set in the US[12,14,15] and Hong Kong.[13] Moreover, because 2 economic evaluations were published as presentation slides, limited details were reported for cost and utility inputs and it was unclear whether the results were presented for the health care payer perspective or societal perspective.[14,15]

Funding Sources of Examined Literature

The summary of 3 economic evaluations by Ortega-Sanchez[14] included 2 economic evaluations that were funded by the respective vaccine manufacturers (referred to as the industry-funded economic evaluations). Moghadas et al.[12] reported funding through the Natural Sciences and Engineering Research Council of Canada Discovery Grant and Alliance Grant, the National Institutes of Health, the National Science Foundation, and the Notsew Orm Sands Foundation; Wang et al.[13] reported funding from the Direct Grant for Research from The Chinese University of Hong Kong. Potential conflicts of interest were reported by Moghadas et al.[12] because an author disclosed their affiliation with Dalhousie University, which has previously received funds for clinical trials conducted by industry.

Summary of Findings

All publications reported analyses for adults aged 60 years or older[12-14] or adults aged 65 years or older (Appendix 1, Table 2).[14,15] The UM-CDC economic evaluation conducted a scenario analyses for adults aged 60 to 64 years.[14,15] No publications were identified that included adults aged 18 years to 59 years. All publications reported the results for RSVPreF3 (Arexvy) alone and RSVpreF (Abrysvo) alone versus no intervention. Moghadas et al.[12] also reported the results of a combined vaccination scenario in which the population intended for vaccination had a 50% probability of being administered either RSVPreF3 (Arexvy) or RSVpreF (Abrysvo) to achieve the desired vaccination coverage. No publications were identified that included mRNA-1345 as an intervention or comparator. A summary table of key RSV incidence and epidemiology inputs, vaccine efficacy, and the main findings of each identified economic evaluation, including original, unadjusted results, is available in Appendix 1, Table 4, Table 5, and Table 6, respectively.

Perspective

The UM-CDC[14,15] and Moghadas et al.[12] economic evaluations were conducted from the societal perspective (Appendix 1, Table 2). Wang et al.[13] was from the health care payer perspective. Although the perspective was not reported for the 2 industry-funded economic evaluations, email communications with the authors confirmed all results presented in the Ortega-Sanchez summary were from the societal perspective.[14]

Time Horizon, Discounting, and Reported Outcomes

Three economic evaluations (Wang et al.,[13] UM-CDC and the RSVPreF3 (Abrysvo) industry-funded economic evaluations[14,15]) had a time horizon of 2 years. The RSVpreF (Arexvy) industry-funded economic evaluation had a time horizon of 3 years.[14] Moghadas et al.[12] considered a single RSV season in base-case analyses and 2 RSV seasons in secondary analyses.

All economic evaluations applied a discount rate of 3%.[12-15] All publications reported cost-effectiveness as incremental cost-utility ratios using cost per quality-adjusted life-year (QALY) gained and/or cost per health outcome averted.[12-15]

Vaccination Coverage Rates

Vaccination coverage rates were reported by Moghadas et al.[12] and Wang et al.[13] (Appendix 1, Table 4). Moghadas et al.[12] presented results for 2 RSV vaccination coverages: 66%, which assumed similar coverage as the average influenza vaccination for adults aged 65 years or older residing in the US over the last 10 influenza seasons (i.e., 2010–2011 to 2020–2021), and 100% vaccination coverage.

Wang et al.[13] assumed 48.2% RSV vaccination coverage based on the most recent (i.e., 2022 to 2023) seasonal influenza vaccination rate of Hong Kong. Vaccination coverage was not reported in the UM-CDC and 2 industry-funded economic evaluations.[14,15]

Vaccine Efficacy Point Estimates

RSVpreF (Abrysvo)

Vaccine efficacy (VE) point estimates varied by vaccine and economic evaluation (Appendix 1, Table 5). For RSVpreF (Abrysvo), the UM-CDC and RSVpreF (Abrysvo) industry-funded economic evaluations used

the same estimates of VE against RSV hospitalization and emergency department (ED) visits (defined as medically attended LRTD) such that VE was 84.6% and 75% in seasons 1 and 2, respectively.[14,15] Estimates for RSVpreF (Abrysvo) VE against outpatient illness (defined as medically attended acute respiratory illness [ARI]) in season 1 were 65.2% and 65.1% in the UM-CDC economic evaluation and the RSVpreF (Abrysvo) industry-funded economic evaluation, respectively.[14,15] VE against outpatient illness in season 2 was 55% in both economic evaluations.[14,15]

The remaining 2 economic evaluations assessing RSVpreF (Abrysvo) reported different point estimates.[12,13] Moghadas et al.[12] used 65.1% and 48.9% in season 1 and season 2, respectively, for VE against medically attended RSV-related LRTD requiring outpatient care and 88.9% and 78.6% in season 1 and season 2, respectively, for VE against severe RSV-related LRTD requiring hospitalization.

Wang et al.[13] reported RSVpreF (Abrysvo) VE against LRTD as 84.6% and 75% in season 1 and season 2, respectively, and VE against RSV-related ARI as 65.2% and 55% in season 1 and season 2, respectively. Wang et al.[13] noted that LRTD could be treated via hospitalization or outpatient care and ARI could be treated via hospitalization, outpatient care, or self-managed care; therefore, VE was not specific to outpatient illness or hospitalization.

RSVPreF3 (Arexvy)

Point estimates for VE of RSVPreF3 (Arexvy) varied in all 4 economic evaluations (Appendix 1, Table 5). The UM-CDC economic evaluation used 79% and 27.8% for season 1 and season 2, respectively, for the VE of RSVPreF3 (Arexvy) against outpatient illness (defined as medically attended RSV-related ARI) and 87.5% and 52.9% in season 1 and season 2, respectively, for VE against hospitalization and ED visits due to RSV-related illness (defined as medically attended RSV-related LRTD).[14,15]

VE against RSV outpatient illness (defined as ARI, regardless of whether medically attended) in the RSVPreF3 (Arexvy) industry-funded economic evaluation assumed a season 1 peak of 74.2%.[14] VE against hospitalization and ED visits due to RSV-related illness (defined as LRTD, regardless of whether medically attended) in the RSVPreF3 (Arexvy) industry-funded economic evaluation assumed a season 1 peak of 88%.[14]

Moghadas et al.[12] reported point estimates of 82.6% and 67.2% in season 1 and season 2, respectively, for VE against medically attended RSV-related LRTD requiring outpatient care, and 94.1% and 78.8% in season 1 and season 2, respectively for severe RSV-related LRTD requiring hospitalization.

Wang et al.[13] reported VE against LRTD in season 1 and season 2 as 87.5% and 52.9%, respectively, and VE against RSV-related ARI as 79% and 27.8% in season 1 and season 2, respectively. Wang et al.[13] noted that LRTD could be treated via hospitalization or outpatient care and ARI could be treated via hospitalization, outpatient care, or self-managed care; therefore, VE was not specific to outpatient illness or hospitalization.

Modelling Approaches for Vaccine Efficacy

Modelling approaches for VE varied by economic evaluation (Appendix 1, Table 5). The industry-funded RSVPreF3 (Arexvy) economic evaluation assumed that VE against RSV-related LRTD and RSV-related ARI is

50% of its peak in month 1, and the peak (88% and 74.2%, respectively) is reached in the second month.[14] After reaching its peak, VE declines at a rate of 2.10% and 2.26% per month for 20 months for RSV-related LRTD and RSV-related ARI, respectively.[14] After 20 months, VE declines linearly until reaching 0% at 43 months for RSV-related LRTD and 34 months for RSV-related ARI.[14]

The industry-funded RSVpreF (Abrysvo) economic evaluation assumed that initial VE against RSV-related LRTD (84.6%) and RSV-related ARI (65.1%) would be stable for 7 months then decline to 75% and 55%, respectively, at month 14, further declining linearly to 0% at 24 months.[14]

The UM-CDC economic evaluation assumed that initial VE for RSV-related LRTD for RSVPreF3 (Arexvy) and RSVpreF (Abrysvo) would remain stable for 7 months (87.5% and 84.6%, respectively) at which point it would decline to 52.9% and 75%, respectively, in month 8 and remain flat until month 18 and month 14, respectively, then decline linearly to 0% at 24 months.[14,15]

Similarly, the UM-CDC economic evaluation assumed that initial VE for RSV-related ARI for RSVPreF3 (Arexvy) and RSVpreF (Abrysvo) would remain stable for 7 months (79% and 65.2%, respectively) at which point it would decline to 27.8% and 55%, respectively, in month 8 and remain flat until 18 months and 14 months, respectively, then decline linearly to 0% at 24 months.[14,15]

Moghadas et al.[12] considered 2 VE profiles to account for uncertainty in the waning of immunity. One VE profile was estimated by fitting a sigmoidal function over 24-months to obtain point estimates matching the mean efficacy determined in clinical trials and the other VE profile was estimated using point estimates from the clinical trials and assuming a linear reduction in VE starting 18 months after immunization, reaching 0% at 24 months.

Wang et al.[13] only reported the point estimates used to estimate VE in season 1 and season 2; assumptions pertaining to the waning of VE efficacy were not reported.

RSV Incidence

The incidence of RSV outpatient illness and RSV hospitalizations varied across economic evaluations (Table 4). Moghadas et al.[12] assumed a mean annual incidence of hospitalizations of 214 per 100,000 persons. Wang et al.[13] assumed that the RSV hospitalization rate varied by age and reported a rate of 10.54 per 100,000 persons for those aged 60 to 64 years, 20.9 per 100,000 persons for those aged 65 to 74 years, and 100.95 per 100,000 persons for those aged 75 years or older. The UM-CDC, RSVpreF (Abrysvo), and RSVPreF3 (Arexvy) industry-funded economic evaluations reported the annual incidence of RSV hospitalizations for their base case of adults aged 65 years and older as 162 per 100,000 persons, 256.3 per 100,000 persons, and 300 per 100,000 persons, respectively.[14]

The annual incidence of outpatient visits was reported for 4 economic evaluations.[12,14] The industry-funded economic evaluations for RSVpreF (Abrysvo), and RSVPreF3 (Arexvy) reported an annual incidence of outpatient visits of 1,348 per 100,000 persons and 2,430 per 100,000 persons, respectively.[14] The UM-CDC economic evaluation reported an annual incidence of outpatient visits of 2,278 per 100,000 for adults aged 65 years and older.[14,15] Moghadas et al.[12] reported an outpatient office visit annual incidence rate of 2,133 per 100,000 persons.

RSV Mortality

Two economic evaluations reported the RSV mortality rate (Table 4).[12,13] Based on the mortality of hospitalized patients ranging from to 6.6% to 11%, Moghadas et al.[12] estimated that 63% of deaths were attributed to those in an intensive care unit (ICU) and 37% were attributed to those in a general ward. Wang et al.[13] estimated age-dependent RSV mortality rates, which were 0.645 per 100,000 persons for patients aged 60 to 64 years, 1.423 per 100,000 persons for those aged 65 to 74 years, and 8.263 per 100,000 persons for those aged 75 years or older.

Utility Values

Two publications reported utility value inputs.[12,13] Moghadas et al.[12] applied utility weights sourced from the literature[17,18] associated with outcomes of interest (i.e., outpatient care [office or ED visit], hospitalized non-ICU patients, and hospitalized ICU patients), to age-dependent utility values, which ranged from 0.77 for patients aged 60 to 64 years to 0.51 for patients aged 85 years and older.

Wang et al.[13] obtained utility values from the literature, which were individuals without RSV (0.896),[19] self-managed care (0.82),[19] outpatient care (0.75),[19] and hospitalization (0.576),[19] and QALY loss for serious adverse events related to the vaccines (i.e., grade 3 reactogenicity [−0.000677]).[20] Wang et al.[13,] reported the incidence rate for serious adverse events of RSVpreF (Abrysvo) and RSVPreF3 (Arexvy) as 3.8% and 1%, respectively.[21]

Cost Inputs

Vaccine unit costs were consistent in 4 economic evaluations. Moghadas et al.[12] varied the cost of the RSV vaccines in their base-case analysis between US$50 and US$500 so that no reported ICERs have the same price per dose (PPD) (Appendix 1, Table 2). All other economic evaluations reported a vaccine cost for RSVpreF (Abrysvo) and RSVPreF3 (Arexvy) of US$200 and US$270, respectively.[13-15]

Unless otherwise stated, ICERs and costs are reported as 2023 Canadian dollars in this review. For publications reported in 2022 US dollars,[14,15] the reported dollar amounts were converted to Canadian dollars using OECD Purchasing Price Parity rates for 2022 and then inflated to 2023 Canadian dollars using the Bank of Canada inflation calculator. For publications reported in 2023 US dollars,[12,13] the reported dollar amounts were converted using the average US dollar exchange rate (1.3504) from January 1, 2023, to December 11, 2023, from the Bank of Canada.[11]

Limited details were provided for cost inputs and disaggregated costs in the Ortega-Sanchez summary,[14] but the author noted that direct medical costs per RSV hospitalization in the UM-CDC and RSVPreF3 (Arexvy) industry-funded economic evaluations were age-dependent whereas the RSVpreF (Abrysvo) industry-funded economic evaluation applied age- and comorbidity-dependent direct medical costs per RSV hospitalization. Accordingly, the range of direct medical costs per RSV hospitalization ranged from $27,055 to $28,329, $16,564 to $33,128, and $15,220 to $48,484 for the UM-CDC, RSVPreF3 (Arexvy) industry-funded, and RSVpreF (Abrysvo) industry-funded economic evaluations, respectively.[14,15] Although the 3 economic evaluations included in the summary by Ortega-Sanchez[14] were conducted from a societal perspective, specific details regarding the costs included in the societal perspective were not reported.

Hutton[15] reported the disease-specific medical costs for a hospitalization, ED visit, and outpatient visit; aggregated costs were not provided. Hutton[15] also noted that productivity costs were included in the model but did not provide further details.

Moghadas et al.[12] conducted analyses from the societal perspective and considered administration costs for vaccination ($34), vaccine costs, ED visits, office visits, and hospitalization costs in addition to indirect costs, which included productivity costs and lifetime income loss due to premature death.

Wang et al.[13] conducted analyses from the health care payer perspective and included direct costs for vaccine, hospitalization, outpatient care, self-managed care, and adverse events.

Population Intended for Vaccination: 60 Years and Older

Five economic evaluations evaluated the economic impact of providing RSVpreF (Abrysvo) or RSVPreF3 (Arexvy) relative to no intervention in adults aged 60 years and older.[12-14] The Ortega-Sanchez[14] summary reported both outdated results and updated results; from here forward, only the updated analyses and results are reported. Moghadas et al.[12] reported ICERs for RSVpreF (Abrysvo), relative to no intervention, in adults 60 years of age and older which ranged from $126,811 to $127,834 per QALY gained, depending on model time horizon, VE assumptions, and vaccine coverage assumptions (Appendix 1, Table 6). Wang et al.[13] reported the ICER for RSVpreF (Abrysvo) relative to no intervention as $186,230 per QALY gained. Wang et al.[13] also reported a sequential ICER in which RSVPreF3 (Arexvy) was dominated by RSVpreF (Abrysvo); however, it is unclear whether there is direct or indirect evidence to evaluate the treatment effect of RSVPreF3 (Arexvy) relative to RSVpreF (Abrysvo) or whether this estimate was naively derived. Finally, the summary publication reported 2 ICERs for RSVpreF (Abrysvo): 1 for the industry-funded economic evaluation and 1 for the UM-CDC economic evaluation.[14] The respective ICERs were $30,219 and $149,994 per QALY gained.[14] In the Moghadas et al.[12] analysis that assumed the population intended for vaccination would receive either RSVpreF (Abrysvo) or RSVPreF3 (Arexvy) (equal probability), the reported ICERs ranged from $127,047 to $128,293 per QALY gained depending on VE and vaccine coverage assumptions.

The reported ICERs for RSVPreF3 (Arexvy) relative to no intervention in adults aged 60 years and older were reported by Moghadas et al.[12] as ranging from $126,894 to $128,219 per QALY gained, depending on model time horizon, VE assumptions, and vaccination coverage (Appendix 1, Table 6). Wang et al.[13] reported an ICER of $219,299 per QALY gained for RSVPreF3 (Arexvy) versus no intervention. The summary by Ortega-Sanchez[14] reported ICERs of $81,288 and $259,597 per QALY gained for RSVPreF3 (Arexvy) versus no intervention for the industry-funded and UM-CDC economic evaluations, respectively. Ortega-Sanchez[14] also reported the cost per hospitalization averted. For RSVpreF (Abrysvo), it was reported to be $13,783 and $95,227 for the industry-funded model and UM-CDC model, respectively; for RSVPreF3 (Arexvy), it was $67,766 and $151,662 for the industry-funded model and UM-CDC model, respectively.[14]

One-way sensitivity analyses were reported for 3 of the 4 economic evaluations that evaluated the economic impact of providing RSVpreF (Abrysvo) or RSVPreF3 (Arexvy) relative to no intervention in adults aged 60 years and older.[13,14] Influential parameters for adults aged 60 years or older were not explicitly documented in the UM-CDC economic evaluation.[14] The 1-way sensitivity analysis for the industry-funded analysis of

RSVpreF (Abrysvo) only included vaccine price and RSV-associated hospitalization but both parameters were influential.[14] The 1-way sensitivity analysis for the industry-funded analysis of RSVPreF3 (Arexvy) identified the annual incidence of the first RSV-ARI event, the proportion of RSV-LRTD patients hospitalized, and VE as influential parameters. Additional influential parameters considered and identified by Wang et al.[13] included underdetection of RSV and the RSV attack rate.

Moghadas et al.[12] reported the maximum PPD and respective probabilities of being cost-effective at a willingness-to-pay (WTP) threshold of US$95,000 per QALY gained (i.e., $128,288 per QALY gained). Ranges presented are indicative of results varying depending on the VE modelling approach (i.e., sigmoidal versus linear). All ranges presented assumed 66% vaccination coverage and a WTP threshold of $128,288 per QALY gained. For RSVpreF (Abrysvo), the maximum PPD ranged from $158 to $159 over a time horizon of 1 RSV season and $266 to $331 over a time horizon of 2 RSV seasons.[12] The reported probabilities of RSVpreF (Abrysvo) being cost-effective relative to no vaccination at a WTP threshold of $128,288 per QALY gained were 61% to 62% over a time horizon of 1 RSV season and 67% to 72% over a time horizon of 2 RSV seasons.[12] Similarly, for RSVPreF3 (Arexvy), the maximum PPD ranged from $172 to $178 over a time horizon of 1 RSV season and $284 to $317 over a time horizon of 2 RSV seasons.[12] The reported probabilities of RSVpreF (Abrysvo) being cost-effective relative to no vaccination at a WTP threshold of $128,288 per QALY gained were 81% over a time horizon of 1 RSV season and 51% to 70% over a time horizon of 2 RSV seasons.[12] Assuming that population intended for vaccination can receive either RSVpreF (Abrysvo) or RSVPreF3 (Arexvy) (equal probability) and that 66% vaccination coverage is achieved, the maximum PPD ranged from $165 to $170 over a time horizon of 1 RSV season and $277 to $325 over a time horizon of 2 RSV seasons.[12] Relative to no intervention, the probabilities of a combined vaccination scenario being cost-effective at a WTP threshold of $128,288 per QALY gained were 55% to 74% over a time horizon of 1 RSV season and 53% to 67% over a time horizon of 2 RSV seasons.[12] Generally, the results assuming a sigmoidal VE profile had a lower maximum PPD and a lower probability of being cost-effective relative to the respective scenario assuming a linear VE profile. Moghadas et al.[12] also reported the maximum PPD and associated probability of RSVpreF (Abrysvo) being cost-effective relative to no vaccination assuming 100% vaccination coverage. The maximum PPD for each scenario was similar to the reciprocal scenario assuming 66% vaccination coverage. As well, the probability of being cost-effective assuming 100% vaccination coverage was generally higher than the reciprocal scenario which assumed 66% vaccination coverage.

Wang et al.[13] reported that RSVpreF (Abrysvo) and RSVPreF3 (Arexvy) had a 0% probability of being cost-effective at a WTP threshold of US$49,594 per QALY gained (i.e., $66,972 per QALY gained). Wang et al.[13] reported an increased probability of being cost-effective at a WTP threshold of $66,972 per QALY gained as the price of the vaccine decreased. Specifically, at a 75% price reduction for both vaccines, Wang et al.[13] reported that RSVpreF (Abrysvo) was the most cost-effective option at a WTP threshold of $66,972 per QALY relative to RSVPreF3 (Arexvy) and no intervention. The respective probabilities of RSVpreF (Abrysvo), RSVPreF3 (Arexvy), and no intervention being cost-effective were 97.68%, 0.1% ,and 2.2%.[13] As noted previously, it is unclear whether there is direct or indirect evidence to evaluate the treatment effect of RSVPreF3 (Arexvy) relative to RSVpreF (Abrysvo). Additionally, Wang et al.[13] reported that the maximum PPD would need to be $109 and $95 for RSVpreF (Abrysvo) and RSVPreF3 (Arexvy), respectively, for these

vaccines to be considered cost-effective at a WTP threshold of $66,972 per QALY gained. Ortega-Sanchez[14] and Hutton[15] did not report a WTP threshold.

Population Intended for Vaccination: 60 to 64 Years

One economic evaluation (i.e., UM-CDC) evaluated the economic impact of providing RSVpreF (Abrysvo) or RSVPreF3 (Arexvy) relative to no intervention in adults aged 60 to 64 years in scenario analyses.[14,15] Age-specific parameters such as the annual incidence of RSV-related hospitalizations, ED visits, and outpatient care visits, were lower for adults aged 60 to 64 years compared to adults aged 65 years and older (Table 4).[15] Conversely, outpatient visit costs were higher for adults aged 60 to 64 years than adults aged 65 years and older ($149 per visit versus $127 per visit).[15] Hospitalization costs for adults aged 60 to 74 years were less than those for adults aged 75 years and older (i.e., $27,055 per hospitalization versus $28,329).[15] VE was consistent for all age cohorts.[14,15]

The ICERs for RSVpreF (Abrysvo) and RSVPreF3 (Arexvy) were reported as $275,834 and $470,763 per QALY gained, respectively (Table 6).[14,15] Because the analysis was conducted as a scenario analysis, no parameters were identified as influential except for PPD. Hutton[15] presented a graph of the ICER relative to the PPD for the cohort aged 60 to 64 years. Ortega-Sanchez[14] and Hutton[15] did not report the probability of RSVpreF (Abrysvo) and RSVPreF3 (Arexvy) being cost-effective.

Hutton[15] reported the net cost per outcome avoided in adults aged 60 to 64 years. The net cost per avoided outcome for RSVpreF (Abrysvo) was $11,875 per outpatient visit avoided, $138,959 per ED visit avoided, $240,020 per hospitalization avoided, $1,174,835 per ICU stay avoided, and $6,063,664 per death avoided.[15] Similarly, for RSVPreF3 (Arexvy), the net cost per avoided outcome was $17,686 per outpatient visit avoided, $214,755 per ED visit avoided, $366,346 per hospitalization avoided, $1,768,569 per ICU stay avoided, and $9,221,822 per death avoided.[15]

Population Intended for Vaccination: 65 Years and Older

One economic evaluation (i.e., UM-CDC) evaluated the economic impact of providing RSVpreF (Abrysvo) or RSVPreF3 (Arexvy) relative to no intervention in adults aged 65 years or older.[14,15] As with the analyses for adults aged 60 to 64 years, VE was consistent for all age cohorts, the incidence of RSV-related hospitalizations and hospitalization costs increased with age, and the incidence of ED visits, the incidence of outpatient visits, outpatient visit costs, and ED visit costs were consistent across the cohorts aged 65 to 74 years and 75 years or older (Table 4).[15] The ICERs for RSVpreF (Abrysvo) and RSVPreF3 (Arexvy) were reported as $119,597 and $211,345 per QALY gained, respectively (Table 6).[14,15] Influential parameters identified via a 1-way sensitivity analysis for the UM-CDC economic evaluation included the incidence of RSV hospitalization, VE, vaccine cost, and duration of efficacy.[14,15]

Hutton[15] reported the net cost per outcome avoided in adults aged 60 years and older. The respective net costs per avoided outcome for RSVpreF (Abrysvo) were $7,074 for outpatient visits, $60,637 for ED visits, $72,006 for hospitalizations, $353,714 for ICU stays, and $1,389,590 for deaths.[15] Similarly, for RSVPreF3 (Arexvy), the net cost per avoided outcome was $11,748 per outpatient visit avoided, $101,061 per ED visit

avoided, $118,747 per hospitalization avoided, $593,734 per ICU stay avoided, and $2,273,874 per death avoided.[15]

Discussion

The review identified 5 economic evaluations conducted in high-income countries that assessed the cost-effectiveness of RSVpreF (Abrysvo) and RSVPreF3 (Arexvy) for the prevention of RSV disease in older adults in the US and Hong Kong.[12-15] All publications assessed and reported the cost-effectiveness associated with RSVpreF (Abrysvo) and RSVPreF3 (Arexvy) in older adult populations in terms of an ICER. Net cost per outcome averted was reported for 1 economic evaluation[15] and cost per hospitalization averted was reported for 3 economic evaluations.[14] All publications concluded that RSVpreF (Abrysvo) and RSVPreF3 (Arexvy) could be cost-effective,[12,14,15] with 1 publication specifying that RSV vaccines would be only be cost-effective at their regional threshold if the price of vaccines was reduced.[13] However, the reported ICERs ranged from $24,741 per QALY to $470,763 per QALY.[12-15] Based on commonly used thresholds, some of these ICERs would not be considered cost-effective. Across the economic evaluations, ICERs were significantly influenced by factors such as vaccine costs and the selection of input data.[12-15]

Limitations

None of publications included in this review (N = 4) assessed the cost-effectiveness of mRNA-1345, vaccinating adults under the age of 60 years, or vaccinating other high-risk populations (e.g., adults living in nursing homes or long-term care facilities, adults with weakened immune systems).[12-15] Moreover, the impact of dynamic RSV transmission (i.e., herd effects of RSV vaccination) was not explored by the 5 economic evaluations included in this review. A direct comparison of the cost-effectiveness of RSVPreF3 (Arexvy) relative to RSVpreF (Abrysvo) could not be made at the time of this review because there is no direct or indirect evidence evaluating the relative treatment effect of these 2 interventions. Thus, despite Wang et al.[13] stating that RSVpreF (Abrysvo) was dominated by RSVPreF3 (Arexvy), a statement of this nature cannot be made due to the lack of supporting clinical evidence. As such, the comparative cost-effectiveness of the 2 vaccines is unknown.

As noted in 3 publications, the results of the economic analyses are heavily dependent on the vaccine costs for RSVpreF (Abrysvo) and RSVPreF3 (Arexvy).[13-15] The 3 publications assumed the PPD of RSVpreF (Abrysvo) and RSVPreF3 (Arexvy) was US$200 and US$270, respectively.[13-15] At the time of this review, the list price of RSVpreF (Abrysvo) in Canada is unknown, and the list price of RSVPreF3 (Arexvy) is stated to vary by jurisdiction (ranging from $200 to $350) for patients paying out-of-pocket.[22] Moreover, VE is uncertain beyond the clinical trial length (i.e., approximately 14 months for RSVpreF [Abrysvo] and 18 months for RSVPreF3 [Arexvy]).[23,24] Given the lack of available long-term data, the modelling approach for initial VE and subsequent waning of protection varied across studies, highlighting uncertainty in VE. The summary publication by Ortega-Sanchez[14] highlighted the uncertainty of RSV incidence for hospitalization and outpatient disease and noted that the input was a key determinant of why the results differed across the 3 compared economic evaluations. Additionally, the cost-effectiveness of RSV vaccines may depend on the severity of the RSV season, as demonstrated by Wang et al.[13] To assess the long-term clinical efficacy across multiple seasons, a long-term modelling approach would be optimal, and only the RSVPreF3 (Arexvy)

industry-funded economic evaluation assessed efficacy beyond season 2.[14] Furthermore, although the economic evaluation by Wang et al.[13] was conducted from the health care payer perspective, it included over-the-counter care costs which typically would only be included from a societal perspective and may bias results in favour of RSVpreF (Abrysvo) and RSVPreF3 (Arexvy).

Two economic evaluations were funded by industry,[14] and 1 economic evaluation reported potential conflicts of interest,[12] which should be considered when assessing the results. The ICERs estimated by the industry-funded economic evaluations[14] were considerably lower than the ICERs produced by all other economic evaluations included in this review.[12-15] The summary of economic evaluations suggests that the differences between the UM-CDC and industry-funded economic evaluations were the result of initial VE and subsequent waning of VE, inputs costs, and the incidence of RSV outpatient disease and hospitalization.[14]

The Hutton[15] economic evaluation and Ortega-Sanchez[14] summary of economic evaluations were published as presentation slides and thus were not peer reviewed. Given the publishing format, limited information was available, and key information and assumptions were not reported (e.g., source of utility values, modelling approach, perspective).[14,15] The generalization of these results should be made with caution.

Generalizability

None of the included economic evaluations may be broadly applicable to the Canadian health care system despite being conducted in high-income countries, as defined by the World Bank.[8] No economic evaluations from a Canadian setting were identified to include in this review. Three economic evaluations were set in the US[12,14,15] and 1 was set in Hong Kong.[13] These economic evaluations may not be generalizable to a Canadian health care setting given differences in the structure of the health care systems, culture, access to health care services, mortality rates, and unit health care costs.[25,26] Specifically, unit cost parameters for health care resource use were specific to the study settings and may not reflect Canadian clinical practice or health care costs. As such, the model structures may be adaptable to the Canadian context, but the results reported by the publications may not be generalizable to the Canadian setting.

Conclusions

Three economic evaluations and 1 summary of economic evaluations (5 economic evaluations total) for RSVpreF (Abrysvo) and RSVPreF3 (Arexvy) as a preventive intervention for RSV disease in older adults (i.e., ≥ 60 years, 60 to 64 years, ≥ 65 years) were identified. All publications reported that RSVpreF (Abrysvo) and RSVPreF3 (Arexvy) were more costly and more effective than no intervention against RSV-associated disease. All publications reported that vaccinating older adults against RSV disease was potentially cost-effective. Notably, the summary of economic evaluations demonstrated that the cost per QALY is lower when vaccinating adults aged 65 years or older rather than adults aged 60 years or older.[14] After adjusting for currency and inflation, all ICERs, with the exception of the 2 industry-funded analyses, were greater than $100,000 per QALY.[12-15]

The 4 publications included in this review noted that the cost-effectiveness of RSV vaccination was dependent on vaccine cost, vaccine efficacy, the waning of vaccine protection, RSV hospitalization incidence, health care unit costs, and the respective regional WTP thresholds. At the time of this review, the list price

of RSVpreF (Abrysvo) in Canada is unknown, and the list price of RSVPreF3 (Arexvy) is stated to vary by jurisdiction (ranging from $200 to $350) for patients paying out-of-pocket.[22]

The generalizability of the economic evaluations to a Canadian health care setting is unknown. To understand the potential cost-effectiveness of RSV vaccinations, a de novo economic evaluation conducted from a Canadian setting comparing RSVpreF (Abrysvo), RSVPreF3 (Arexvy), and mRNA-1345 is required.

References

1. Health Canada. Respiratory syncytial virus (RSV): Canadian immunization guide. 2023; https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/respiratory-syncytial-virus.html. Accessed 2023 Dec 12.
2. Mac S, Shi S, Millson B, et al. Burden of illness associated with respiratory syncytial virus (RSV)-related hospitalizations among adults in Ontario, Canada: A retrospective population-based study. *Vaccine.* 2023;41(35):5141-5149. PubMed
3. AREXVY: Respiratory Syncytial Virus (RSV) Vaccine (recombinant, AS01E adjuvanted), 120 micrograms Respiratory Syncytial Virus glycoprotein F (RSVPreF3), Lyophilized Powder and Suspension for Reconstitution, Reconstituted Suspension for Intramuscular Injection [product monograph]. Mississauga (ON): GlaxoSmithKline Inc.; 2023 Aug 4.
4. ABRYSVO: Respiratory Syncytial Virus Stabilized Prefusion F Subunit Vaccine Lyophilized Powder for Solution, 120 mcg RSV stabilized prefusion F protein per 0.5 mL, Reconstituted Suspension for Intramuscular Injection [product monograph]. Kirkland (QC): Pfizer Canada ULC; 2023 Dec 1.
5. Moderna Biopharma Canada Corp. Moderna files for Health Canada review of its respiratory syncytial virus (RSV) vaccine, mRNA-1345. 2023; https://assets.modernatx.com/m/4f39eb758ef3acc/original/Health-Canada-mRNA-1345-Submission-FINAL.pdf. Accessed 2023 Dec 11.
6. Pfizer Inc. Prescribing information: ABRYSVO™ (Respiratory Syncytial Virus Vaccine) solution for intramuscular injection. Silver Spring (MD): U.S. Food and Drug Administration; 2023: https://www.fda.gov/media/168889/download?attachment. Accessed 2023 Dec 11.
7. Qiu X, Xu S, Lu Y, et al. Development of mRNA vaccines against respiratory syncytial virus (RSV). *Cytokine Growth Factor Rev.* 2022;68:37-53. PubMed
8. The World Bank. The world by income. 2022; https://datatopics.worldbank.org/world-development-indicators/the-world-by-income-and-region.html. Accessed 2023 Nov 8.
9. Bank of Canada. Inflation calculator. https://www.bankofcanada.ca/rates/related/inflation-calculator/. Accessed 2023 Dec 11.
10. Organisation for Economic Co-operation and Development. Purchasing power parities (PPP). https://data.oecd.org/conversion/purchasing-power-parities-ppp.htm. Accessed 2023 Dec 11.
11. Bank of Canada. Daily exchange rates: Lookup tool. https://www.bankofcanada.ca/rates/exchange/daily-exchange-rates-lookup/. Accessed 2023 Dec 11.
12. Moghadas SM, Shoukat A, Bawden CE, et al. Cost-effectiveness of prefusion F protein-based vaccines against respiratory syncytial virus disease for older adults in the United States. *Clin Infect Dis.* 2023:ciad658. PubMed
13. Wang Y, Fekadu G, You JHS. Comparative cost-effectiveness analysis of respiratory syncytial virus vaccines for older adults in Hong Kong. *Vaccines (Basel).* 2023;11(10):17. PubMed
14. Ortega-Sanchez IR. Economics of vaccinating U.S. adults ≥60 years-old against respiratory syncytial virus. 2023; https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-06-21-23/05-RSV-Adults-Ortega-Sanchez-508.pdf. Accessed 2023 Dec 4.
15. Hutton DW. Economic analysis of RSV vaccination in older adults. 2023; https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-06-21-23/04-RSV-Adults-Hutton-508.pdf. Accessed 2023 Nov 7.
16. Hutton DW, Prosser L. Expert Q&A: Exploring the cost-effectiveness of RSV vaccines in older adults. 2023; https://ihpi.umich.edu/news/expert-qa-exploring-cost-effectiveness-rsv-vaccines-older-adults. Accessed 2024 Jan 3.
17. Erickson P, Wilson R, Shannon I. Years of healthy life. *Healthy People 2000 Stat Notes.* 1995(7):1-15.
18. Gessner BD. The cost-effectiveness of a hypothetical respiratory syncytial virus vaccine in the elderly. *Vaccine.* 2000;18(15):1485-1494. PubMed
19. Mao Z, Li X, Korsten K, et al. Economic burden and health-related quality of life of respiratory syncytial virus and influenza infection in European community-dwelling older adults. *J Infect Dis.* 2022;226(Suppl 1):S87-s94. PubMed

20. Schmader KE, Levin MJ, Grupping K, et al. The impact of reactogenicity after the first dose of recombinant zoster vaccine on the physical functioning and quality of life of older adults: An open-label, phase III trial. *J Gerontol A Biol Sci Med Sci.* 2019;74(8):1217-1224. PubMed

21. Melgar M, Britton A, Roper LE, et al. Use of respiratory syncytial virus vaccines in older adults: Recommendations of the Advisory Committee on Immunization Practices - United States, 2023. *MMWR Morb Mortal Wkly Rep.* 2023;72(29):793-801. PubMed

22. Koshy CA, Pawar KM, Bloomfield T. How to access the new RSV vaccine, and how much will it cost? Your questions answered. 2023; https://www.cbc.ca/news/rsv-vaccine-questions-1.7052468. Accessed 2023 Dec 18.

23. Friedland L. GSK's RSVPreF3 OA vaccine (AREXVY). 2023; https://stacks.cdc.gov/view/cdc/129993. Accessed 2023 Sep 17.

24. Gurtman A. RSVpreF older adults: Clinical development program updates. 2023; https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-06-21-23/02-RSV-Adults-Gurtman-508.pdf. Accessed 2023 Jul 8.

25. Papanicolas I, Woskie LR, Jha AK. Health care spending in the United States and other high-income countries. *JAMA.* 2018;319(10):1024-1039. PubMed

26. Kong X, Yang Y, Gao J, et al. Overview of the health care system in Hong Kong and its referential significance to mainland China. *J Chin Med Assoc.* 2015;78(10):569-573. PubMed

27. Papi A, Ison MG, Langley JM, et al. Respiratory syncytial virus prefusion F protein vaccine in older adults. *N Engl J Med.* 2023;388(7):595-608. PubMed

28. Walsh EE, Polack F, Zareba A, et al. LB748. Efficacy and safety of bivalent respiratory syncytial virus (RSVpreF) vaccine in older adults. *Open Forum Infectious Diseases.* 2022;9(Supplement_2):S923. https://academic.oup.com/ofid/article/9/Supplement_2/ofac492.1871/6903998. Accessed 2023 Nov 3.

Appendix 1: Included Studies' Results

Note that this appendix has not been copy-edited.

Figure 1: Selection of Included Studies

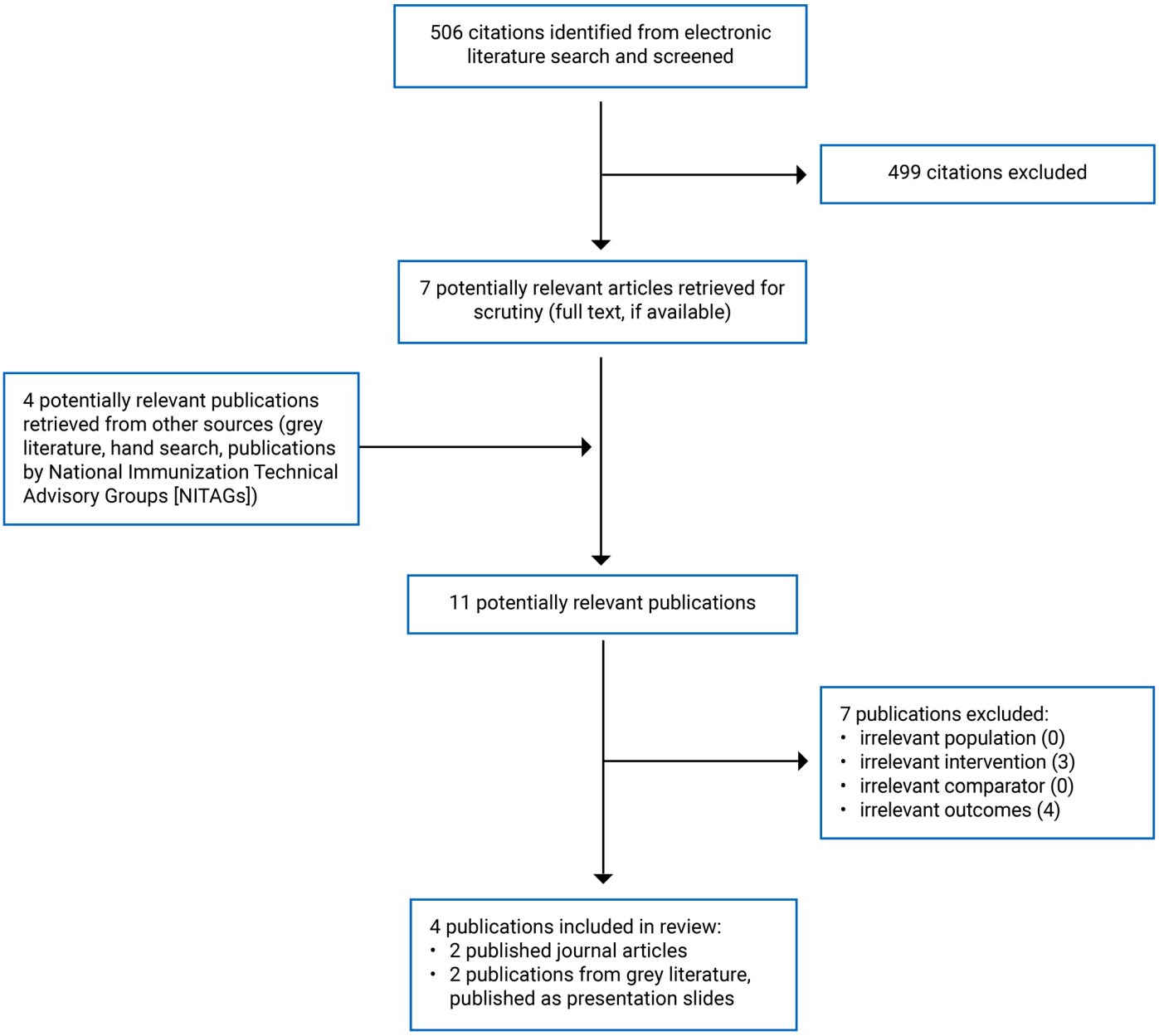

Table 2: Characteristics of Included Economic Evaluation

Characteristic	Hutton, 2023[15]	Moghadas et al., 2023[12]	Ortega-Sanchez,[a] 2023[14]	Ortega-Sanchez,[a] 2023[14]	Wang et al., 2023[13]
Economic evaluation name	UM-CDC[b]	NA	RSVpreF (Abrysvo) industry-funded	RSVPreF3 (Arexvy) industry-funded	NA
Publication type	Grey literature	Peer reviewed	Grey literature	Grey literature	Peer-Reviewed
Country	US	US	US	US	Hong Kong
Type of analysis	CUA and CEA[c]	CUA	CUA and CEA[d]	CUA and CEA[d]	CUA
Perspective	Societal (includes productivity costs)	Societal (includes productivity costs and lifetime income loss due to premature death)	Societal[e]	Societal[e]	Health care payer
Time horizon	2 years	Single RSV season[f]	2 years	3 years	2 years
Discount rate	3%	3%	3%	3%	3%
Population	≥ 65 years of age[g]	≥ 60 years of age	≥ 65 years of age[h]	≥ 65 years of age[h]	≥ 60 years of age
Intervention	• RSVpreF (Abrsyvo) • RSVPreF3 (Arexvy)	• RSVpreF (Abrysvo) • RSVPreF3 (Arexvy) • A combination of RSVpreF (Abrysvo) and RSVPreF3 (Arexvy)	• RSVpreF (Abrysvo)	• RSVPreF3 (Arexvy)	• RSVpreF (Abrysvo) • RSVPreF3 (Arexvy)
Comparator	No intervention	No intervention	No intervention	No intervention	No intervention
Modelling approach	Decision tree	Discrete-event simulation	Not reported	Not reported	Decision tree
Source of clinical efficacy	Not reported[i]	Phase III clinical trial data[23,24,27,28]	Phase III clinical trial data[j]	Phase III clinical trial data[j]	Phase III clinical trial data and data reported at the 2023 ACIP meeting[14,27,28]
Cost per dose	RSVpreF (Abrysvo) = US$200 RSVPreF3 (Arexvy) = US$270	Varied between US$50 and US$500	RSVpreF (Abrysvo) = US$200[k]	RSVPreF3 (Arexvy) = US$270	RSVpreF (Abrysvo) = US$200 RSVPreF3 (Arexvy) = US$270

Characteristic	Hutton, 2023[15]	Moghadas et al., 2023[12]	Ortega-Sanchez,[a] 2023[14]	Ortega-Sanchez,[a] 2023[14]	Wang et al., 2023[13]
Industry funding	None	None[l]	GlaxoSmithKline	Pfizer	None

ACIP = Advisory Committee on Immunization Practices; CEA = cost-effectiveness analysis; CUA = cost-utility analysis; NA = not applicable; RSV = Respiratory Syncytial Virus.

[a]The publication is a comparison of 3 economic evaluations, one of which is the same as Hutton.[15]

[b]The UM-CDC economic evaluation was also summarized by Ortega-Sanchez.[14]

[c]In addition to incremental costs per QALY gained, the publication reported net costs per outcome (outpatient, ED, hospitalizations, ICU stays, and deaths) averted.

[d]Costs per hospitalization averted are reported for the 3 economic evaluations compared.

[e]Specific details regarding the costs included in the societal perspective were not provided. While the publication was ambiguous as to whether results were presented for the health care payer perspective or the societal perspective, email communications with the authors confirmed that all results were from the societal perspective.

[f]Secondary analyses considering 2 RSV seasons were reported in a supplementary document and are not summarized in this review.

[g]Results were also presented for adults 60 to 64 years of age.

[h]Results were also presented for adults ≥ 60 years of age and 60 to 64 years of age.

[i]Hutton did not report clinical efficacy references.[15] However, the UM-CDC economic evaluation was one of 3 economic evaluations compared by Ortega-Sanchez and the author reports that all 3 economic evaluations as using phase III clinical trial data.[14]

[j]References for the phase III clinical trial data used were not provided in the study.

[k]An alternative price of US$140 is also reported based on an outdated analysis conducted in February 2023.

[l]Potential conflicts of interest were reported. One author disclosed their affiliation with Dalhousie University which has previously received funds for clinical trials conducted by GlaxoSmithKline and Pfizer, among others.

Table 3: Quality Appraisal Results

Author, year	Critical appraisal: Joanna Briggs Institute checklist[a]										
	1	2	3	4	5	6	7	8	9	10	11
Hutton, 2023[15]	Yes	Yes	Unclear[b]	Unclear[c]	No[b]	No[b]	Yes	Yes	Yes	No	No
Moghadas et al., 2023[12]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No
Ortega-Sanchez, 2023[14d]	Yes	Yes	Unclear[b]	Yes	No[b]	No[b]	Yes	Yes	Yes	No	No
Wang et al., 2023[13]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No

NA = not applicable.

[a]Questions:

Q1: Is there a well-defined question?

Q2: Is there comprehensive description of alternatives?

Q3: Are all important and relevant costs and outcomes for each alternative identified?

Q4: Has clinical effectiveness been established?

Q5: Are costs and outcomes measured accurately?

Q6: Are costs and outcomes valued credibly?

Q7: Are costs and outcomes adjusted for differential timing?

Q8: Is there an incremental analysis of costs and consequences?

Q9: Were sensitivity analyses conducted to investigate uncertainty in estimates of cost or consequences?

Q10: Do study results include all issues of concern to users?

Q11: Are the results generalizable to the setting of interest in the review?

[b]Limited details were reported for cost and utility inputs as the study was published as presentation slides.

[c]While clinical efficacy references were not reported, the economic evaluation from Hutton[15] was one of 3 economic evaluations compared by Ortega-Sanchez.[14] Ortega-Sanchez reports all 3 economic evaluations as using phase III clinical trial data.[14]

[d]This was a summary of 3 economic evaluations; critical appraisal is reflective of all economic evaluations included in the publication.

Table 4: Summary of RSV Incidence and Epidemiology Inputs From Included Economic Evaluations

Author, year	Economic evaluation name	Annual RSV incidence rates (per 100,000)			Mortality	Vaccination coverage
		Outpatient	Hospitalization	ED visits		
Hutton, 2023[15]	UM-CDC	60 to 64: 1,722 ≥ 65: 2,278	60 to 64: 65.5 65 to 69: 93.8	60 to 64: 110.4 ≥ 65: 200	NR	NR

Author, year	Economic evaluation name	Annual RSV incidence rates (per 100,000)			Mortality	Vaccination coverage
		Outpatient	Hospitalization	ED visits		
			70 to 74: 118.7 ≥ 75: 302.9			
Moghadas et al., 2023[12]	NA	≥ 60: 2,133	≥ 60: 214	≥ 60: 201	6.6% to 11%	66%; 100%[a]
Ortega-Sanchez, 2023[14]	RSVpreF (Abrysvo) industry-funded	1,348	≥ 65: 256.3	NR	NR	NR
Ortega-Sanchez, 2023[14]	RSVPreF3 (Arexvy) industry-funded	2,430	≥ 65: 300	NR	NR	NR
Wang et al., 2023[13]	NA	NR	60 to 64: 10.54 65 to 74: 20.90 ≥ 75: 100.95	NR	60 to 64: 0.645 per 100,000 65 to 74: 1.423 per 100,000 ≥ 75: 8.263 per 100,000	48.2%

ED = emergency department; NA = not applicable; NR = not reported; RSV = respiratory syncytial virus; UM-CDC = University of Michigan-Centers for Disease Control and Prevention

[a]Moghadas et al. presented results assuming 66% vaccination coverage and 100% vaccination coverage.[12]

Table 5: Summary of VE From Included Economic Evaluations

Author, year	Economic evaluation name	RSVpreF (Abrysvo) VE (%)		RSVPreF3 (Arexvy) VE (%)		Waning of vaccine immunity
		Outpatient care	Hospitalization	Outpatient care	Hospitalization	
Hutton, 2023[15]	UM-CDC	S1: 65.2[a] S2: 55[a]	S1: 84.6[b] S2: 75[b]	S1: 79[a] S2: 27.8[a]	S1: 87.5[b] S2: 52.9[b]	S1 VE remains stable for 7 months at which point it declines to S2 VE and remains flat from month 8 to 14 (RSVpreF [Abrysvo]) or month 8 to 18 [RSVPreF3 [Arexvy]) then declines linearly to 0% at 24 months.
Moghadas et al., 2023[12]	NA	S1: 65.1[c] S2: 48.9[c]	S1: 88.9[d] S2: 78.6[d]	S1: 82.6[c] S2: 67.2[c]	S1: 94.1[d] S2: 78.8[d]	Sigmoidal profile: Sigmoidal function was fit over 24-months to obtain point estimates matching the S1 and S2 estimates. Linear profile: S1 VE stable until 6.7 months after which VE declines linearly

Author, year	Economic evaluation name	RSVpreF (Abrysvo) VE (%)		RSVPreF3 (Arexvy) VE (%)		Waning of vaccine immunity
		Outpatient care	Hospitalization	Outpatient care	Hospitalization	
						to S2 VE and remains stable until 18 months, at which point it declines linearly to 0% at 24 months.
Ortega-Sanchez, 2023[14]	RSVpreF (Abrysvo) industry-funded	S1: 65.1[a] S2: 55[a]	S1: 84.6[b] S2: 75[b]	NR	NR	S1 VE remains stable for 7 months then declines to S2 VE at month 14, then declines linearly to 0% at 24 months
Ortega-Sanchez, 2023[14]	RSVPreF3 (Arexvy) industry-funded	NR	NR	74.2[e]	88[f]	50% of S1 VE in month 1 and S1 VE achieved in month 2 after which VE declines at a rate of 2.10% (LRTD) or 2.26% (ARI) for 20 months, then declines linearly to 0% at 43 months (LRTD) or 34 months (LRI).
Wang et al., 2023[13]	NA	ARI[g] S1: 65.2 S2: 55 LRTD[g] S1: 84.6 S2: 75		ARI[g] S1: 79 S2: 27.8 LRTD[g] S1: 87.5 S2: 52.9		NR

ARI = acute respiratory illness; LRTD = lower respiratory tract illness; NA = not applicable; NR = not reported; S1 = season 1; S2 = season 2; UM-CDC = University of Michigan-Centers for Disease Control and Prevention; VE = vaccine efficacy.

[a]VE estimate is specific to VE against medically attended RSV-related ARI requiring outpatient care.

[b]VE estimate is specific to VE against medically attended RSV-related LRTD requiring hospitalization or an emergency department visit.

[c]VE estimate is specific to VE against medically attended RSV-related LRTD requiring outpatient care.

[d]VE estimate is specific to VE against severe RSV-related LRTD requiring hospitalization.

[e]VE estimate is specific to VE against ARI, irrespective of whether ARI was medically attended.

[f]VE estimate is specific to VE against LRTD, irrespective of whether LRTD was medically attended.

[g]Wang et al. noted that ARI could be treated via hospitalization, outpatient care, or self-managed care and LRTD could be treated via hospitalization or outpatient care and ARI could be treated via hospitalization, outpatient care, or self-managed care; as such, VE was not specific to outpatient care or hospitalization.[13]

Table 6: Main Results of Included Economic Evaluations

Author, year	Country, currency[a]	RSVpreF (Abrysvo) vs no intervention		RSVPreF3 (Arexvy) vs no intervention	
		Original ICER (US$/QALY)	ICER (2023 CA$/QALY)[a]	Original ICER (US$/QALY)	ICER (2023 CA$/QALY)[a]
Hutton, 2023[15]	US, 2022 USD[b]	60 to 64 years: 218,350 ≥ 65 years: 94,673	60 to 64 years: 275,834 ≥ 65 years: 119,597	60 to 64 years: 372,656 ≥ 65 years: 167,301	60 to 64 years: 470,763 ≥ 65 years: 211,345
Moghadas et al., 2023[12]	US, 2023 USD	93,906 to 94,664[c]	126,811 to 127,834	93,968 to 94,949[c]	126,894 to 128,219
Ortega-Sanchez, 2023[14]	US, 2022 USD	Industry-funded model: ≥ 60 years: 23,921 ≥ 65 years: 19,585	Industry-funded model: ≥ 60 years: 30,219 ≥ 65 years: 24,741	Industry-funded model: ≥ 60 years: 64,348 ≥ 65 years: 55,088	Industry-funded model: ≥ 60 years: 81,288 ≥ 65 years: 69,591
		Hutton[15]/UM-CDC model: ≥ 60 years: 118,735 60 to 64 years[d]: 218,350 ≥ 65 years: 94,673	Hutton[15]/UM-CDC model: ≥ 60 years: 149,994 60 to 64 years: 275,834 ≥ 65 years: 119,597	Hutton[15]/UM-CDC model: ≥ 60 years: 205,638 60 to 64 years[d]: 372,656 ≥ 65 years: 167,301	Hutton[15]/UM-CDC model: ≥ 60 years: 259,597 60 to 64 years: 470,763 ≥ 65 years: 211,345
Wang et al., 2023[13]	Hong Kong, 2023 USD	137,907	186,230	219,299	296,141

CA = Canadian dollar; ICER = incremental cost-effectiveness ratio, QALY = quality-adjusted life-year; USD = US dollar; vs = vs.

Note: No evidence was found for third comparator (i.e., mRNA-1345) of interest.

[a]For studies reported in 2022 USD, the reported dollar amounts were converted to CAD using OECD Purchasing Price Parity rates for 2022[10] and then inflated to 2023 CAD using the Bank of Canada inflation calculator.[9] For studies reported in 2023 USD, the reported dollar amounts were converted using the average USD to CAD exchange rate (1.3504) from January 1, 2023 to December 11, 2023 from the Bank of Canada.[11]

[b]2022 USD was assumed as the model from Hutton[15] was one of 3 models summarized by Ortega-Sanchez[14] and Ortega-Sanchez specifies 2022 economic outcomes were measured.

[c]Range is based on the reported ICERs for 66% and 100% vaccination coverage, whether VE was modelled linearly or sigmoidally, and whether 1 RSV season or 2 RSV seasons were considered. ICERs for the combination scenarios in which the population can receive either RSVpreF or RSVPreF3 have reported ICERs of $127,047 to $128,293 (i.e., US$94,081 to US$95,004).

[d]Presented as a scenario analysis.

Appendix 2: Literature Search Strategy

Note that this appendix has not been copy-edited.

Economic Literature Search

Overview

Interface: Ovid

Databases:

- MEDLINE All (1946-present)
- Embase (1974-present)
- Note: Subject headings and search fields have been customized for each database.

Date of search: December 6, 2023

Alerts: Bi-weekly search updates until January 15, 2024

Search filters applied: Systematic reviews; meta-analyses; network meta-analyses; health technology assessments; economic evaluations; costs and cost analysis studies, and quality of life studies.

Limits:

- Publication date limit: 2013-present
- Language limit: English- and French-language

Table 7: Syntax Guide

Syntax	Description
/	At the end of a phrase, searches the phrase as a subject heading
MeSH	Medical Subject Heading
exp	Explode a subject heading
*	Before a word, indicates that the marked subject heading is a primary topic; or, after a word, a truncation symbol (wildcard) to retrieve plurals or varying endings
?	Truncation symbol for one or no characters only
adj#	Requires terms to be adjacent to each other within # number of words (in any order)
.ti	Title
.ab	Abstract
.hw	Heading word; usually includes subject headings and controlled vocabulary
.kf	Keyword heading word
.dq	Candidate term word (Embase)

Syntax	Description
.pt	Publication type
.mp	Mapped term
.yr	Publication year
.jw	Journal title word (MEDLINE)
freq = #	Requires terms to occur # number of times in the specified fields

MEDLINE Database Strategy

1. Respiratory Syncytial Virus Vaccines/
2. ("Respiratory syncytial virus prefusion F*" or RSVPreF* or RSV-PreF* or RSV-PRE-F*).ti,ab,kf.
3. ((Respiratory syncytial or RSV) adj5 ("prefusion F*" or "pre-fusion F*" or "PRE-F*" or PREF?)).ti,ab,kf.
4. (Ad26RSVpreF* or "Ad26 RSV preF*" or mRNA-1345* or mRNA1345* or "Ad26.RSV.preF*" or ABRYSVO* or AREXVY* or "PF-06928316*").ti,ab,kf.
5. ((Respiratory syncytial or RSV) and (vaccine? or vaccinat* or immunis* or immuniz*)).ti,kf.
6. or/1-5
7. Economics/
8. exp "Costs and Cost Analysis"/
9. Economics, Nursing/
10. Economics, Medical/
11. Economics, Pharmaceutical/
12. exp Economics, Hospital/
13. Economics, Dental/
14. exp "Fees and Charges"/
15. exp Budgets/
16. budget*.ti,ab,kf.
17. (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ti,kf.
18. (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ab. /freq=2
19. (cost* adj2 (effective* or utilit* or benefit* or minimi* or analy* or outcome or outcomes)).ab,kf.
20. (value adj2 (money or monetary)).ti,ab,kf.
21. exp models, economic/
22. economic model*.ab,kf.

23. markov chains/
24. markov.ti,ab,kf.
25. monte carlo method/
26. monte carlo.ti,ab,kf.
27. exp Decision Theory/
28. (decision* adj2 (tree* or analy* or model*)).ti,ab,kf.
29. or/7-28
30. "Value of Life"/
31. Quality of Life/
32. quality of life.ti,kf.
33. ((instrument or instruments) adj3 quality of life).ab.
34. Quality-Adjusted Life Years/
35. quality adjusted life.ti,ab,kf.
36. (qaly* or qald* or qale* or qtime* or life year or life years).ti,ab,kf.
37. Disability-Adjusted Life Years/
38. disability adjusted life.ti,ab,kf.
39. Healthy Life Expectancy/
40. (daly* or disability free life expectanc* or haly* or health* life expectanc*).ti,ab,kf.
41. (sf36 or sf 36 or short form 36 or shortform 36 or short form36 or shortform36 or sf thirtysix or sfthirtysix or sfthirty six or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).ti,ab,kf.
42. (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six or shortform6 or short form6).ti,ab,kf.
43. (sf8 or sf 8 or sf eight or sfeight or shortform 8 or shortform 8 or shortform8 or short form8 or shortform eight or short form eight).ti,ab,kf.
44. (sf12 or sf 12 or short form 12 or shortform 12 or short form12 or shortform12 or sf twelve or sftwelve or shortform twelve or short form twelve).ti,ab,kf.
45. (sf16 or sf 16 or short form 16 or shortform 16 or short form16 or shortform16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).ti,ab,kf.
46. (sf20 or sf 20 or short form 20 or shortform 20 or short form20 or shortform20 or sf twenty or sftwenty or shortform twenty or short form twenty).ti,ab,kf.
47. (hql or hqol or h qol or hrqol or hr qol).ti,ab,kf.
48. (hye or hyes).ti,ab,kf.
49. (health* adj2 year* adj2 equivalent*).ti,ab,kf.
50. (pqol or qls).ti,ab,kf.

51. (quality of wellbeing or quality of well being or index of wellbeing or index of well being or qwb).ti,ab,kf.
52. nottingham health profile*.ti,ab,kf.
53. sickness impact profile.ti,ab,kf.
54. exp health status indicators/
55. (health adj3 (utilit* or status)).ti,ab,kf.
56. (utilit* adj3 (valu* or measur* or health or life or estimat* or elicit* or disease or score* or weight)).ti,ab,kf.
57. (preference* adj3 (valu* or measur* or health or life or estimat* or elicit* or disease or score* or instrument or instruments)).ti,ab,kf.
58. disutilit*.ti,ab,kf.
59. rosser.ti,ab,kf.
60. willingness to pay.ti,ab,kf.
61. standard gamble*.ti,ab,kf.
62. (time trade off or time tradeoff).ti,ab,kf.
63. tto.ti,ab,kf.
64. (hui or hui1 or hui2 or hui3).ti,ab,kf.
65. (eq or euroqol or euro qol or eq5d or eq 5d or euroqual or euro qual).ti,ab,kf.
66. duke health profile.ti,ab,kf.
67. functional status questionnaire.ti,ab,kf.
68. dartmouth coop functional health assessment*.ti,ab,kf.
69. or/30-68
70. (systematic review or meta-analysis).pt.
71. meta-analysis/ or systematic review/ or systematic reviews as topic/ or meta-analysis as topic/ or “meta analysis (topic)”/ or “systematic review (topic)”/ or exp technology assessment, biomedical/ or network meta-analysis/
72. ((systematic* adj3 (review* or overview*)) or (methodologic* adj3 (review* or overview*))).ti,ab,kf.
73. ((quantitative adj3 (review* or overview* or synthes*)) or (research adj3 (integrati* or overview*))).ti,ab,kf.
74. ((integrative adj3 (review* or overview*)) or (collaborative adj3 (review* or overview*)) or (pool* adj3 analy*)).ti,ab,kf.
75. (data synthes* or data extraction* or data abstraction*).ti,ab,kf.
76. (handsearch* or hand search*).ti,ab,kf.
77. (mantel haenszel or peto or der simonian or dersimonian or fixed effect* or latin square*).ti,ab,kf.

78. (met analy* or metanaly* or technology assessment* or HTA or HTAs or technology overview* or technology appraisal*).ti,ab,kf.
79. (meta regression* or metaregression*).ti,ab,kf.
80. (meta-analy* or metaanaly* or systematic review* or biomedical technology assessment* or bio-medical technology assessment*).mp,hw.
81. (medline or cochrane or pubmed or medlars or embase or cinahl).ti,ab,hw.
82. (cochrane or (health adj2 technology assessment) or evidence report).jw.
83. (comparative adj3 (efficacy or effectiveness)).ti,ab,kf.
84. (outcomes research or relative effectiveness).ti,ab,kf.
85. ((indirect or indirect treatment or mixed-treatment or bayesian) adj3 comparison*).ti,ab,kf.
86. [(meta-analysis or systematic review).md.]
87. (multi* adj3 treatment adj3 comparison*).ti,ab,kf.
88. (mixed adj3 treatment adj3 (meta-analy* or metaanaly*)).ti,ab,kf.
89. umbrella review*.ti,ab,kf.
90. (multi* adj2 paramet* adj2 evidence adj2 synthesis).ti,ab,kf.
91. (multiparamet* adj2 evidence adj2 synthesis).ti,ab,kf.
92. (multi-paramet* adj2 evidence adj2 synthesis).ti,ab,kf.
93. or/70-92
94. 6 and preprint.pt.
95. 6 and (29 or 69 or 93)
96. 94 or 95
97. limit 96 to yr="2013-current"
98. limit 97 to (english or french)

Embase Database Strategy

1. *respiratory syncytial virus vaccine/
2. ("Respiratory syncytial virus prefusion F*" or RSVPreF* or RSV-PreF* or RSV-PRE-F*).ti,ab,kf,dq.
3. ((Respiratory syncytial or RSV) adj5 ("prefusion F*" or "pre-fusion F*" or "PRE-F*" or PREF?)).ti,ab,kf,dq.
4. (Ad26RSVpreF* or "Ad26 RSV preF*" or mRNA-1345* or mRNA1345* or "Ad26.RSV.preF*" or ABRYSVO* or AREXVY* or "PF-06928316*").ti,ab,kf,dq.
5. ((Respiratory syncytial or RSV) and (vaccine? or vaccinat* or immunis* or immuniz*)).ti,kf.
6. or/1-5
7. Economics/
8. Cost/

9. exp Health Economics/
10. Budget/
11. budget*.ti,ab,kf.
12. (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ti,kf.
13. (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ab. /freq=2
14. (cost* adj2 (effective* or utilit* or benefit* or minimi* or analy* or outcome or outcomes)).ab,kf.
15. (value adj2 (money or monetary)).ti,ab,kf.
16. Statistical Model/
17. exp economic model/
18. economic model*.ab,kf.
19. Probability/
20. markov.ti,ab,kf.
21. monte carlo method/
22. monte carlo.ti,ab,kf.
23. Decision Theory/
24. Decision Tree/
25. (decision* adj2 (tree* or analy* or model*)).ti,ab,kf.
26. or/7-25
27. socioeconomics/
28. exp Quality of Life/
29. quality of life.ti,kf.
30. ((instrument or instruments) adj3 quality of life).ab.
31. Quality-Adjusted Life Year/
32. quality adjusted life.ti,ab,kf.
33. (qaly* or qald* or qale* or qtime* or life year or life years).ti,ab,kf.
34. disability-adjusted life year/
35. disability adjusted life.ti,ab,kf.
36. healthy life expectancy/
37. (daly* or disability free life expectanc* or haly* or health* life expectanc*).ti,ab,kf.
38. exp Short form 36/

39. (sf36 or sf 36 or short form 36 or shortform 36 or short form36 or shortform36 or sf thirtysix or sfthirtysix or sfthirty six or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).ti,ab,kf.
40. (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six or shortform6 or short form6).ti,ab,kf.
41. (sf8 or sf 8 or sf eight or sfeight or shortform8 or short form8 or shortform 8 or short form 8 or shortform eight or short form eight).ti,ab,kf.
42. (sf12 or sf 12 or short form 12 or shortform 12 or short form12 or shortform12 or sf twelve or sftwelve or shortform twelve or short form twelve).ti,ab,kf.
43. (sf16 or sf 16 or short form 16 or shortform 16 or short form16 or shortform16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).ti,ab,kf.
44. (sf20 or sf 20 or short form 20 or shortform 20 or short form20 or shortform20 or sf twenty or sftwenty or shortform twenty or short form twenty).ti,ab,kf.
45. (hql or hqol or h qol or hrqol or hr qol).ti,ab,kf.
46. (hye or hyes).ti,ab,kf.
47. (health* adj2 year* adj2 equivalent*).ti,ab,kf.
48. (pqol or qls).ti,ab,kf.
49. (quality of wellbeing or quality of well being or index of wellbeing or index of well being or qwb).ti,ab,kf.
50. exp assessment of humans/
51. nottingham health profile*.ti,ab,kf.
52. sickness impact profile.ti,ab,kf.
53. health status indicator/
54. (health adj3 (utilit* or status)).ti,ab,kf.
55. (utilit* adj3 (valu* or measur* or health or life or estimat* or elicit* or disease or score* or weight)).ti,ab,kf.
56. (preference* adj3 (valu* or measur* or health or life or estimat* or elicit* or disease or score* or instrument or instruments)).ti,ab,kf.
57. disutilit*.ti,ab,kf.
58. rosser.ti,ab,kf.
59. Willingness To Pay/
60. willingness to pay.ti,ab,kf.
61. Standard Gamble/
62. standard gamble*.ti,ab,kf.
63. time trade-off method/

64. (time trade off or time tradeoff).ti,ab,kf.
65. tto.ti,ab,kf.
66. (hui or hui1 or hui2 or hui3).ti,ab,kf.
67. (eq or euroqol or euro qol or eq5d or eq 5d or euroqual or euro qual).ti,ab,kf.
68. duke health profile.ti,ab,kf.
69. functional status questionnaire.ti,ab,kf.
70. dartmouth coop functional health assessment*.ti,ab,kf.
71. or/27-70
72. (systematic review or meta-analysis).pt.
73. meta-analysis/ or systematic review/ or systematic reviews as topic/ or meta-analysis as topic/ or "meta analysis (topic)"/ or "systematic review (topic)"/ or exp technology assessment, biomedical/ or network meta-analysis/
74. ((systematic* adj3 (review* or overview*)) or (methodologic* adj3 (review* or overview*))).ti,ab,kf.
75. ((quantitative adj3 (review* or overview* or synthes*)) or (research adj3 (integrati* or overview*))).ti,ab,kf.
76. ((integrative adj3 (review* or overview*)) or (collaborative adj3 (review* or overview*)) or (pool* adj3 analy*)).ti,ab,kf.
77. (data synthes* or data extraction* or data abstraction*).ti,ab,kf.
78. (handsearch* or hand search*).ti,ab,kf.
79. (mantel haenszel or peto or der simonian or dersimonian or fixed effect* or latin square*).ti,ab,kf.
80. (met analy* or metanaly* or technology assessment* or HTA or HTAs or technology overview* or technology appraisal*).ti,ab,kf.
81. (meta regression* or metaregression*).ti,ab,kf.
82. (meta-analy* or metaanaly* or systematic review* or biomedical technology assessment* or bio-medical technology assessment*).mp,hw.
83. (medline or cochrane or pubmed or medlars or embase or cinahl).ti,ab,hw.
84. (cochrane or (health adj2 technology assessment) or evidence report).jw.
85. (comparative adj3 (efficacy or effectiveness)).ti,ab,kf.
86. (outcomes research or relative effectiveness).ti,ab,kf.
87. ((indirect or indirect treatment or mixed-treatment or bayesian) adj3 comparison*).ti,ab,kf.
88. [(meta-analysis or systematic review).md.]
89. (multi* adj3 treatment adj3 comparison*).ti,ab,kf.
90. (mixed adj3 treatment adj3 (meta-analy* or metaanaly*)).ti,ab,kf.
91. umbrella review*.ti,ab,kf.

92. (multi* adj2 paramet* adj2 evidence adj2 synthesis).ti,ab,kf.
93. (multiparamet* adj2 evidence adj2 synthesis).ti,ab,kf.
94. (multi-paramet* adj2 evidence adj2 synthesis).ti,ab,kf.
95. or/72-94
96. 6 and (conference abstract or conference review or preprint).pt.
97. 6 and (26 or 71 or 95)
98. 96 or 97
99. limit 98 to yr="2013 -Current"
100. limit 99 to (english or french)

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