The Hospital for Sick Children
Technology Assessment at SickKids (TASK)

APPENDICES

SYSTEMATIC REVIEW OF THE COST-EFFECTIVENESS OF INFLUENZA IMMUNIZATION PROGRAMS: A CANADIAN PERSPECTIVE

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The views expressed in the material are the views of the authors and do not necessarily reflect those of The Hospital for Sick Children, Public Health Ontario, or the province of Ontario.

CONFLICTS OF INTEREST

During the timing of writing this technical report, ET was an employee of AstraZeneca Canada.

Appendix 1: Search Strategies

MEDLINE (OvidSP) February 5, 2015

	#	Search	Results
MEDLINE	1	(orthomyxoviridae infections/ or influenza, human/ or expOrthomyxoviridae/ or (flu or flus or grippe* or influenza*).mp.) not haemophilisinfluenzae/ [****Influenza terms****]	102915
	2	immunotherapy/ or immunization/ or immunization, passive/ or immunization schedule/ or immunization, secondary/ or immunotherapy, active/ or vaccination/ or mass vaccination/ or Influenza Vaccines/ or (admune or aflunov or afluria or agriflu or agrippal* or alorbat or anflu or antiinfluenza* or "anti-influenza*" or "arepanrix b" or begrivac* or celtura or celvapan or chiromas or daronrix or "flu-vac" or fluad or fluarix or fluax or flublok or fluenz or flugen or flugene or fluinsure or flulaval or flumist or fluogen or flushield or flustat or fluvax or fluviral* or fluvirin* or fluviron or fluzone* or focetria* or gammaflu or grippovac or humenza or idflu or inflexal* or influject or influpozzi or influsplit or influvac* or intanza or "inviron-ol" or invivac or iradogen or mastaflu or "medi 3314" or "medi-3314" or medi3314 or munevan or mutagrip or nivgrip or optaflu or pandemrix or panenza or panvax or "pf 4522625" or "pf-4522625" or pf4522625 or prepandrix or previgrip or pumarix or "skf 106160" or "skf-106160" or skf106160 or vaxigrip or "x-flu").mp. or ((immunization or immunisation or vaccination) adj2 (campaign* or program*)).mp. [****Vaccine terms****]	172499
	3	immunotherapy/ec or immunization/ec or immunization, passive/ec or immunization schedule/ec or immunization, secondary/ec or immunotherapy, active/ec or vaccination/ec or mass vaccination/ec or Influenza Vaccines/ec or ((admune or aflunov or afluria or agriflu or agrippal* or alorbat or anflu or antiinfluenza* or "anti-influenza*" or "arepanrix b" or begrivac* or celtura or celvapan or chiromas or daronrix or "flu-vac" or fluad or fluarix or fluax or flublok or fluenz or flugen or flugene or fluinsure or flulaval or flumist or fluogen or flushield or flustat or fluvax or fluviral* or fluvirin* or fluviron or fluzone* or focetria* or gammaflu or grippovac or humenza or idflu or inflexal* or influject or influpozzi or influsplit or influvac* or intanza or "inviron-ol" or invivac or iradogen or mastaflu or "medi 3314" or "medi-3314" or medi3314 or munevan or mutagrip or nivgrip or optaflu or pandemrix or panenza or panvax or "pf 4522625" or "pf-4522625" or pf4522625 or prepandrix or previgrip or pumarix or "skf 106160" or "skf-106160" or skf106160 or vaxigrip or "x-flu" or ((immunization or immunisation or vaccination) adj2 (campaign* or program*))).mp. and ec.fs.) [****Vaccine terms and economics****]	4144
	4	1 and 3 [****Base set 4 economics as floating subheading without outbreaks *****]	891
	5	economics/ or exp "costs and cost analysis"/ or economics, behavioral/ or exp economics, hospital/ or hospital charges/ or hospital costs/ or exp economics, medical/ or fees, medical/ or economics, nursing/ or economics, pharmaceutical/ or "fees and charges"/ or fees, pharmaceutical/ or prescription fees/ or ("cost-effectiveness" or "cost-utilit*" or "cost-benefit*" or "cost-minimization*" or "cost-minimisation*" or ((value or net) adj2 benefit*)).mp.	254437
	6	1 and 2 and 5 [****Base set 3 economics or policy as subject headings without outbreaks*****]	765
	7	4 or 6 [****maximum universal results****]	1139
	8	limit 7 to humans	1109
	9	(orthomyxoviridae infections/ or influenza, human/ or expOrthomyxoviridae/ or (flu or flus or grippe*).mp. [****Influenza Terms****]	67784
	10	3 and 9 [****Base set 4 economics as floating subheading without outbreaks *****]	628
	11	9 and 2 and 5 [****Base set 3 economics or policy as subject headings without outbreaks*****]	529

	12	10 or 11 [****maximum universal results****]	800
	13	limit 12 to humans	783

EMBASE (Embase Classic+ Embase) 1947 to 2015 week 5

	#	Search	Results
EMBASE	1	exporthomyxovirus infection/ or exp Influenza virus/ or (flu or flus or grippe*).mp. [****Influenza Terms****]	113910
	2	immunization/ or active immunization/ or immunoprophylaxis/ or mass immunization/ or vaccination/ or preventive health service/ or influenza vaccination/ or influenza vaccine/ or (admune or aflunov or afluria or agriflu or agrippal* or alorbat or anflu or antiinfluenza* or "anti-influenza*" or "arepanrix b" or begrivac* or celtura or celvapan or chiromas or daronrix or "flu-vac" or fluad or fluarix or fluax or flublok or fluenz or flugen or flugene or fluinsure or flulaval or flumist or fluogen or flushield or flustat or fluvax or fluviral* or fluvirin* or fluviron or fluzone* or focetria* or gammaflu or grippovac or humenza or idflu or inflexal* or influject or influpozzi or influsplit or influvac* or intanza or "inviron-ol" or invivac or iradogen or mastaflu or "medi 3314" or "medi-3314" or medi3314 or munevan or mutagrip or nivgrip or optaflu or pandemrix or panenza or panvax or "pf 4522625" or "pf-4522625" or pf4522625 or prepandrix or previgrip or pumarix or "skf 106160" or "skf-106160" or skf106160 or vaxigrip or "x-flu" or ((immunization or immunisation or vaccination) adj2 (campaign* or program*))).mp. [****Vaccine Terms****]	245485
	3	immunization/ec or active immunization/ec or immunoprophylaxis/ec or mass immunization/ec or vaccination/ec or preventive health service/ec or influenza vaccination/ec or influenza vaccine/ec or ((admune or aflunov or afluria or agriflu or agrippal* or alorbat or anflu or antiinfluenza* or "anti-influenza*" or "arepanrix b" or begrivac* or celtura or celvapan or chiromas or daronrix or "flu-vac" or fluad or fluarix or fluax or flublok or fluenz or flugen or flugene or fluinsure or flulaval or flumist or fluogen or flushield or flustat or fluvax or fluviral* or fluvirin* or fluviron or fluzone* or focetria* or gammaflu or grippovac or humenza or idflu or inflexal* or influject or influpozzi or influsplit or influvac* or intanza or "inviron-ol" or invivac or iradogen or mastaflu or "medi 3314" or "medi-3314" or medi3314 or munevan or mutagrip or nivgrip or optaflu or pandemrix or panenza or panvax or "pf 4522625" or "pf-4522625" or pf4522625 or prepandrix or previgrip or pumarix or "skf 106160" or "skf-106160" or skf106160 or vaxigrip or "x-flu" or ((immunization or immunisation or vaccination) adj2 (campaign* or program*))).mp. and ec.fs.) [****Vaccine Terms****]	2659
	4	exp health economics/ or exp "health care cost"/ or ("cost-effectiveness" or "cost-utilit*" or "cost-benefit*" or "cost-minimization*" or "cost-minimisation*" or ((value or net) adj2 benefit*)).mp. [****Economics****]	653902
	5	1 and 3	1045
	6	1 and 2 and 4	2853
	7	5 or 6	3855
	8	limit 7 to human	3335

CINAHL (EBSCOHost) February 5, 2015

	#	Search	Results
CinAHL	S1	(MH "Influenza+") OR (MH "Influenza A Virus+") OR (MH "Influenza B Virus") OR (MH "Influenzavirus C") OR (MH "Influenza, Human") OR (MH "Influenza, Seasonal")	10844
	S2	(MH "Orthomyxoviridae+")	2438
	S3	(MH "Influenza, Seasonal")	205
	S4	(MH "Influenza, Pandemic (H1N1) 2009")	1195
	S5	(MH "Influenza+") OR (MH "Influenza, Human+") OR (MH "Influenza, Seasonal") OR (MH "Orthomyxoviridae+")	10960
	S6	S1 OR S2 OR S3 OR S4 OR S5	10960
	S7	(MH "Influenza Vaccine")	5803
	S8	(MH "Immunization Programs")	2855
	S9	(MH "Cost Benefit Analysis") OR (MH "Health Care Costs+") OR (MH "Costs and Cost Analysis+") OR (MH "Health Facility Costs") OR (MH "Cost Control+") OR (MH "Cost Savings") OR (MH "Nursing Costs")	56094
	S10	(MH "Economics, Pharmaceutical")	1320
	S11	(MH "Product Evaluation") OR (MH "Program Evaluation")	25438
	S12	(MH "Fees and Charges") OR (MH "Health Facility Charges")	6712
	S13	(MH "Health Systems Agencies") OR (MH "State Health Plans")	1503
	S14	(MH "Community Health Workers") OR (MH "Community Health Services+") OR (MH "Community Health Nursing+") OR (MH "Health Resource Utilization") OR (MH "Health Services Needs and Demand+")	251914
	S15	S7 OR S8	8168
	S16	"cost effectiveness"	7765
	S17	S9 OR S10 OR S11 OR S12 OR S13 OR S14	323411
	S18	(MH "Health Policy") OR (MH "Health Policy Studies")	27124
	S19	(MH "Insurance Coverage")	3505
	S20	(MH "Economics, Organizations, Control (Non-Cinahl)")	875488
	S21	S18 OR S19 OR S20	875519
	S22	S6 AND S15 AND S17 AND S21	425

EBM Review NHS EED/HTA (OvidSP) February 5, 2015

	#	Search	Results
NHS EED, HTA	1	ExpOrthomyxoviridae/ or orthomyxoviridae infections/ or influenza, human/ or (flu or flus or grippe* or influenza*).mp. [****Influenza Terms****]	243

Grey Matter List

Database	Keyword Search Term	Number of Hits	Results
CADTH	influenza	58	none relevant
Cochrane	influenza	92	none relevant
Health Quality Ontario	influenza	19	none relevant
Institute for Clinical Evaluative Services	influenza	62	none relevant
Institute of Health Economics	influenza	71	none relevant
McGill University Health Centre	influenza	2	none relevant
Newfoundland and Labrador Centre for Applied Research	influenza	4	none relevant
Ottawa Hospital Research Institute	influenza	26	none relevant
UBC Therapeutics Initiative	influenza	2	none relevant

Appendix 2: List of Provincial Influenza Information Websites (as of June 2015)

BC	http://www.immunizebc.ca/diseases-vaccinations/influenza
AB	http://www.albertahealthservices.ca/influenza.asp
SK	http://www.health.gov.sk.ca/influenza-flu
MB	http://www.gov.mb.ca/health/flu/
ON	https://www.ontario.ca/health-and-wellness/get-flu-shot/
QC	http://sante.gouv.qc.ca/en/programmes-et-mesures-daide/programme-de-vaccination-contre-la-grippe/
NS	http://www.cdha.nshealth.ca/public-health/immunization/flu-season-2014-2015
NB	http://www2.gnb.ca/content/gnb/en/departments/ocmoh/cdc/content/influenza/free_influenza_vaccine.html
PEI	http://www.healthpei.ca/fluclinics
NL	http://www.health.gov.nl.ca/health/publichealth/cdc/infoforpros_edu.html
YT	http://www.hss.gov.yk.ca/seasonal_flu_clinics.php
NWT	http://www.hss.gov.nt.ca/health/immunization-and-vaccines/nwt-immunization-schedule
NV	http://www.gov.nu.ca/health/information/influenza

Appendix 3: Data from Studies Rejected Based on Quality Appraisal

Author, Year	Relevant Target Population	Perspective	Analytical Technique	Country	Time Horizon	Currency, Costing Year, and Discounting	Model Type	Intervention	Comparator (Standard of Care)	Cost Items	Health Outcomes
Abellea (Brazil, TPP), 2007	Healthy adults 50 - 64 years old	Third Party Payer	CUA	Brazil	Single flu season	BRZ R$, 2003, 3%	Decision Tree/Analysis	Vaccination for all individuals in 50-64 years age group	Current policy of vaccination for high risk adults only	Vaccine, administration, physician visit, hospitalization, treatment/drugs, diagnostic tests	Cases of ILI, complications, hospitalizations death
Abellea (Brazil, Societal), 2007	Healthy adults, 50 - 64 years old	Societal	CUA	Brazil	Single flu season	BRZ R$, 2003, 3%	Decision Model	Vaccination for all adults	Vaccination for high risk adults only	Vaccine, administration, physician visit, hospitalization, treatment/drugs, diagnostic tests	Cases of ILI, complications, hospitalizations death
At'Kov, 2011	Healthy adults 18-64 years old	Employer	CBA	Russia	Single flu season	EUR 2006, no mention	Alongside non-RCT	Vaccination	No vaccination	Vaccine, administration, sick leave payments, absenteeism, presenteeism	Cases of ILI
Burckel, 1999	Healthy adults >18 years old	Employer	CBA	Brazil	Not reported	$USD, 1997, no mention	Mathematical equation	Vaccination	No vaccination	Vaccine, administration, physician visit, hospitalization, treatment/drugs, absenteeism	Cases of influenza
Campbell, 1997	Median age of 45. Exact ages not reported.	Employer	CEA	USA	Single flu season	USD, 1992, no mention	Mathematical equation	Vaccination	No vaccination	Vaccine, administration, absenteeism	Cases of ILI, cases of URI
Cicchetti, 2010	Healthy adults, 50 - 64 years old	Societal	CBA	Multiple	Not reported	EUR, not reported	Mathematical Equation	Vaccination for all adults	Vaccination for high risk adults only	Vaccine, administration, physician visit, hospitalization, treatment/drugs	Incidence of influenza

CUA = cost-utility analysis; CEA = cost-effectiveness analysis; CBA = cost-benefit analysis; QALYs = quality-adjusted life years; LCI = laboratory-confirmed influenza; ILI = influenza-like illness; AOM = acute otitis media; URI = upper respiratory infection; USD = US dollars; CAD= Canadian dollars; EUR = Euros

Author, Year	Relevant Target Population	Perspective	Analytical Technique	Country	Time Horizon	Currency, Costing Year, and Discounting	Model Type	Intervention	Comparator (Standard of Care)	Cost Items	Health Outcomes
Cohen P, 2003	Healthy adults, 18 - 64 years old	Employer	CBA	Australia	Not reported	Not reported	Alongside RCT	Vaccination	No vaccination	Vaccine, administration, absenteeism, worker replacement	Cases of ILI, cases of FI
Colombo, 2006	Healthy adults, 24 - 62 years old	Employer	CBA	Italy	5 months	EUR, no mention, no mention	Alongside non-RCT	Vaccination	No vaccination	Vaccine, administration, absenteeism	Cases of influenza
Hoshi 2007	Elderly adults >65 years old	Societal (incorrectly stated)	CUA	Japan	1 year	$USD, 2002, 3% on health outcomes, none on cost	Decision Tree/Analysis	Vaccination, full subsidy	No Vaccination and Vaccination at 71% subsidy	Vaccine, administration, physician visit, hospitalization, treatment/drugs	Years of life saved
Kumpulainen1997	Healthy municipal homemakers 18-62 years old	Not reported	CBA	Finland	Not reported	FIM, 1991, Not reported	Mathematical Equation	Vaccination	No vaccination	Vaccine, administration, physician visit, hospitalization, treatment/drugs, absenteeism	Cases of influenza
Lin, 2010	Cancer patients, 20-64 years old	Societal	CBA	Taiwan	1 year	$USD, 2007, 3%	Decision Tree/Analysis	Vaccination	No vaccination	Vaccine, administration, physician visit, hospitalization, absenteeism	Cases of influenza
Lin, 2010	Cancer patients, 20-64 years old	Health Care System	CBA	Taiwan	1 year	$USD, 2007, 3%	Decision Tree/Analysis	Vaccination	No vaccination	Vaccine, administration, physician visit, hospitalization, absenteeism	Cases of influenza

CUA = cost-utility analysis; CEA = cost-effectiveness analysis; CBA = cost-benefit analysis; QALYs = quality-adjusted life years; LCI = laboratory-confirmed influenza; ILI = influenza-like illness; AOM = acute otitis media; FI = febrile illness; USD = US dollars; CAD= Canadian dollars; EUR = Euros

Author, Year	Relevant Target Population	Perspective	Analytical Technique	Country	Time Horizon	Currency, Costing Year, and Discounting	Model Type	Intervention	Comparator (Standard of Care)	Costs Items	Health Outcomes
Mamma, 2013	Healthy employees, <65 years old	Not reported	CBA	Greece	Not reported	EUR, not reported	Decision Model	Vaccination	No vaccination	Vaccine, administration, absenteeism	Incidence of influenza
Martin, 2006	Working adults 15 - 64 years	Societal	CEA	Spain	Not reported	EUR, 2003, Not reported	Mathematical equation	Vaccination	Vaccination for high risk only	Vaccine, administration, physician visit, hospitalization, treatment/drugs, absenteeism	Incidence of influenza
Meltzer, 2005	Children aged 0-23 months, 6-59 months, 5 - 14 years; varying levels of risk	Societal	CBA	USA	1 year	$USD, 2000, No discounting except for lost future productivity, 3%	Monte Carlo model	Cohorts of children at varying risk are vaccinated	No vaccination	Vaccine, administration, physician visit, hospitalization, treatment/drugs, absenteeism	Cases of ILI, outpatient visits, hospitalizations death
Parlevliet, 2002	Employees at Academic Centre, no age stated	Employer	CBA	Netherlands	Not reported	EUR, 2002, not reported	Decision analysis	Vaccination	None stated	Vaccine, administration, absenteeism	Incidence of influenza
Teufel, 2008	Hospitalized children with asthma, no age stated	Not reported	CBA	USA	Not reported	USD, 2006, no discounting not specified	Decision Analysis	Increased assessment and vaccination	No increased assessment and vaccination	Vaccine, administration, physician visit, hospitalization, treatment/drugs, absenteeism	Incidence of influenza, physician visits, hospitalizations
Wang, C. 2002	Healthy adults >65 years old	Not reported	CBA	Taiwan	Not reported	USD, 1999, no mention of discounting	Mathematical equation	Vaccination campaign	No vaccination campaign	Vaccine, administration, physician visit, hospitalization, treatment/drugs	Cases of influenza, hospitalizations death

CUA = cost-utility analysis; CEA = cost-effectiveness analysis; CBA = cost-benefit analysis; QALYs = quality-adjusted life years; LCI = laboratory-confirmed influenza; ILI = influenza-like illness; AOM = acute otitis media; USD = US dollars; CAD= Canadian dollars; EUR = Euros

Author, Year	Relevant Target Population	Perspective	Analytical Technique	Country	Time Horizon	Currency, Costing Year, and Discounting	Model Type	Intervention	Comparator (Standard of Care)	Cost Items	Health Outcomes
Wang, S. 2005	Healthy adults >65 years old	Not reported	CUA	Taiwan	Single flu season	USD, 2001, 5% discounting	Mathematical equation	Vaccination	No vaccination	Vaccine, administration, outpatient visit, hospitalization, treatment/drugs	Hospitalizations, deaths
Scott, 1996	Healthy adults >65 years old	Individuals	CBA	New Zealand	1 year	USD, 1992, no discounting due to short time horizon	Mathematical equation	Vaccination	No vaccination	Vaccine, administration, physician visit, hospitalization, treatment/drugs	Cases of influenza, pneumonia, respiratory conditions, heart failure
Scott, 1996	Healthy adults >65 years old	Government	CBA	New Zealand	1 year	USD, 1992, no discounting due to short time horizon	Mathematical equation	Vaccination	No vaccination	Vaccine, administration, physician visit, hospitalization, treatment/drugs	Cases of influenza, pneumonia, respiratory conditions, heart failure
Scott, 1996	Healthy adults >65 years old	Society	CBA	New Zealand	1 year	USD, 1992, no discounting due to short time horizon	Mathematical equation	Vaccination	No vaccination	Vaccine, administration, physician visit, hospitalization, treatment/drugs	Cases of influenza, pneumonia, respiratory conditions, heart failure
Yoo, 2013	Children in elementary school	Societal	CUA	USA	Not reported	USD, 2009, no mention of discounting	Mathematical Equation	Vaccination	No vaccination	Vaccine, administration, physician visit, hospitalization, treatment/drugs, absenteeism	Receipt of first dose of immunization

CUA = cost-utility analysis; CEA = cost-effectiveness analysis; CBA = cost-benefit analysis; QALYs = quality-adjusted life years; LCI = laboratory-confirmed influenza; ILI = influenza-like illness; AOM = acute otitis media; USD = US dollars; CAD= Canadian dollars; EUR = Euros