Appendix

Cost-effectiveness of emergency preparedness measures in response to infectious respiratory disease outbreaks: a systematic review and econometric analysis: Supplementary Information

Appendix 1. Search concept construction

OVID MEDLINE

Date of	OVID	D Medline		
Search	#	Search Terms	Hits	
29/7/2019	1	Economics/	27061	
	2	"costs and cost analysis"/	47439	
	3	Cost allocation/	1997	
	4	Cost-benefit analysis/	77184	
	5	Cost control/	21373	
	6	Cost savings/	11287	
	7	Cost of illness/	25397	
	8	Cost sharing/	2443	
	9	"deductibles and coinsurance"/	1716	
	10	Medical savings accounts/	529	
	11	Health care costs/	37249	
	12	Direct service costs/	1171	
	13	Drug costs/	15395	
	14	Employer health costs/	1088	
	15	Hospital costs/	10427	
	16	Health expenditures/	18983	
	17	Capital expenditures/	1987	
	18	Value of life/	5653	
	19	exp economics, hospital/	23708	
	20	exp economics, medical/	14108	
	21	Economics, nursing/	3989	
	22	Economics, pharmaceutical/	2874	
	23	exp "fees and charges"/	29802	
	24	(low adj cost).mp.	51166	
	25	(high adj cost).mp.	13286	
	26	(health?care adj cost\$).mp.	10352	
	27	(fiscal or funding or financial or finance).tw.	136748	
	28	(cost adj estimate\$).mp.	2132	
	29	(cost adj variable).mp.	42	
	30	(unit adj cost\$).mp.	2368	
	31	(economic\$ or pharmacoeconomic\$ or price\$ or pricing).tw.	277405	
	32	Economic evaluation.mp.	9144	
	33	(Cost?effectiveness analysis or CEA).mp.	21933	
	34	(Cost?utility analysis or CUA).mp.	1153	
	35	(Cost?benefit analysis or CBA).mp.	26471	
	36	(Cost?consequence analysis or CCA).mp.	7687	
	37	(Cost?minimi?sation analysis or CMA).mp.	3583	
	38	(cost?outcome or marginal analysis).mp.	204	
	39	exp Cost benefit analysis/ or exp budgets/	90077	
	40	investment\$.mp. or investments/	39609	
	41	or/1-40	769608	
	42	exp Emergency Preparedness/	2678	
	43	exp Preparedness, Emergency/	2678	
	44	(Community Preparedness or Community Recovery or	2614	
		Emergency Operations Coordination or (Emergency Public Information and Warning) or Fatality Management or	2011	
		Information Sharing or Mass Care or Medical Countermeasure		
		Dispensing or (Medical Materiel Management and Distribution)		

1

	or Medical Surge or Non-Pharmaceutical Interventions or Public Health Laboratory Testing).mp.	
45	exp Public Health Surveillance/	2623
46	(Epidemiological Investigation or (Responder Safety adj Health) or Volunteer Management).mp.	2867
47	(disaster preparedness or public health emergencies).mp.	2012
48	((Detection adj assessment) or policy development or policy implementation or policy adaptation or health services or (coordination adj communication) or emergency risk communication or personal preparedness).mp.	393599
49	((state or local or national or legal or business or healthcare) and preparedness).mp.	4359
50	(vaccination or immuni?ation or anti?viral medication or personal hygiene or hand hygiene or household ventilation or ((food and safety) or storage) or food hygiene or respiratory etiquette or (washing and saniti?ing) or social distancing or triage or food security or (emergency adj3 food) or (school adj3 closure) or public gathering* or public meeting* or household isolation or quarantine or PPE or personal protective equipment or (environmental adj3 cleaning)).mp.	545475
51	or/42-50	940853
52	exp disease outbreak/ or exp communicable diseases/	119498
53	(disease outbreak or outbreak or epidemic or pandemic or public health emergency).mp.	150101
54	(avian flu or abola or EVD or H1N1 or H5N1 or infectious disease or influenza or swine flu or flu or MERS or Middle East Respiratory Syndrome).mp.	165207
55	(SARS or Severe Acute Respiratory syndrome or measles or zika or cholera or H7N9 or dengue or fever or plague or fever or malaria or polio).mp.	381260
56	(Bacillus cereus or Campylobacter jejuni or Clostridium or Cryptosporidium or Cyclospora cayetanensis or (E adj coli) or Hepatitis A or Listeria monocytogenes or Noroviruses or Salmonella or Shigella or Staphylococcus aureus or Staphylococcus or Vibrio parahaemolyticus or Vibrio vulnificus).mp.	493801
57	(Diphtheria or Haemophilus influenzae type b or Hib or Hepatitis B or Human Papillomavirus or HPV).mp.	165778
58	((Meningococcal adj Infection\$) or Mump\$ or Pertussis or Whooping Cough or Pneumococcal Infection\$ or Polio or Rotavirus or Rubella or German Measles or Tetanus or varicella or chicken pox or vectorbourne diseases or vector?bourne disease\$ or waterbourne diseases or water?bourne disease\$ or Cholera or Diarrhea or diarrhoea).mp.	255768
59	(Typhoid fever or Giardiasis or Schistosomiasis or Dracunculiasis or Dysentery or Cryptosporidiosis or amoebiasis or Traveler\$s diarrhea or travelers diarrhoea).mp.	68954
60	exp infectious disease medicine/ or exp malaria/ or exp influenza, human/ or SARS virus/ or exp norovirus/ or exp coronavirus infections/ or exp measles/ or exp poliomyelitis/ or exp chickenpox/	165698
61	(anthrax or botulism or brucellosis or campylobacter enteritis or chikungunya or chlamydia\$ or CJD or Creutzfeldt?Jakob).mp.	63613
62	(diptheria or echinococcosis or gonococcal or haemophilus influenzae or hepatitis or HIV or AIDS or human immunodeficiency virus or acquired immunodeficiency syndrome).mp.	714394
63	 (legionnaires?disease or leptospirosis or listeriosis or lyme or streptococcus pneumoniae or Q fever or rabies or congenital rubella or salmonella or shiga toxin or verocytotoxin?producing E?coli or STEC or VTEC or HUS or haemoltic?uraemic or hemoltic?uremic).mp. (shigellosis or smallpox or syphilis or congenital syphilis or 	182938
64		341238

2

VHF or viral hemorrhagic fever\$ or		trichinellosis or tuberculosis or TB or typhoid or paratyphoid or VHF or viral hemorrhagic fever\$ or viral haemorrhagic fever\$ or West Nile virus or Yellow fever or (enteritis adj3 yersinia)).mp.	
	65	or/52-64	2357602
	66	41 and 51 and 65 (studies before 2003 excluded)	18127

EMBASE

	EMBASE						
Date of Search	#	Search Terms	Hits				
29/7/2019	1	Socioeconomics/	133589				
	2	Cost benefit analysis/	81690				
	3	Cost effectiveness analysis/	143890				
	4	Cost of illness/	18428				
	5	Cost control/	65812				
	6	Economic aspect/	110246				
	7	Financial management/	110636				
	8	Health care cost/	181209				
	9	Health care financing/	13089				
	10	Health economics/	32080				
	11	Hospital cost/	20343				
	12	(fiscal or financial or finance or funding).tw.	178545				
	13	Cost minimization analysis/	3375				
	14	(cost adj estimate\$).mp.	3181				
	15	(cost adj variables\$).mp.	188				
	16	(unit adj cost\$).mp.	4210				
	17	investment\$.mp. or investments/	49607				
	18	or/1-17	906830				
	19	"Emergency Preparedness".tw.	1780				
	20	(Community Preparedness or Community Recovery	3358				
		or Emergency Operations Coordination or					
		(Emergency Public Information and Warning) or					
		Fatality Management or Information Sharing or					
		Mass Care or Medical Countermeasure Dispensing					
		or (Medical Materiel Management and Distribution)					
		or Medical Surge or Non-Pharmaceutical					
		Interventions or Public Health Laboratory					
		Testing).mp.					
	21	exp Public Health Surveillance/	210835				
	22	(Epidemiological Investigation or (Responder	3638				
		Safety adj Health) or Volunteer Management).mp.					
	23	(disaster preparedness or public health emergencies).mp.	2176				
	24	((Detection adj assessment) or policy development	124325				
		or policy implementation or policy adaptation or					
		health services or (coordination adj communication)					
		or emergency risk communication or personal					
		preparedness).mp.					
	25	((state or local or national or legal or business or healthcare) and preparedness).mp.	5302				
	26	(vaccination or immuni?ation or anti?viral	703894				
		medication or personal hygiene or hand hygiene or					
		household ventilation or ((food and safety) or					
		storage) or food hygiene or respiratory etiquette or					
		(washing and saniti?ing) or social distancing or					
		triage or food security or (emergency adj3 food) or					
		(school adj3 closure) or public gathering* or public					
		meeting* or household isolation or quarantine or					
		PPE or personal protective equipment or					
		(environmental adj3 cleaning)).mp.					
	27	or/19-26	1031364				

29 (diseases/ 207117 30 (disease outbreak or outbreak or epidemic or public health emergency).mp. 207717 30 (avian flu or abola or EVD or HIN1 or H5N1 or infectious disease or influenza or swine flu or flu or MERS or Middle East Respiratory Syndrome or fever or plague or fever or malaria or polio).mp. 198862 31 (SARS or Severe Acute Respiratory Syndrome or fever or plague or fever or malaria or polio).mp. 561066 32 (Bacillus cereus or Campylobacter jejuni or Clostridium or Cryclosporid ano or Stigella or Staphylococcus aureus or Staphylococcus or Vibrio parahaemolyticus or Vibrio vulnificus).mp. 579612 33 (Diphtheria or Haemophilus influenzae type b or HPV).mp. 241684 34 ((Meningococcal adj Infection\$) or Mump\$ or Perunoscocal Infection\$ or Notovirus or Nuterla or Nuterla or Nuterla or Closter 421975 34 ((Meningococcal adj Infection\$) or Mump\$ or German Measles or Tetanus or varicella or chicken pox or vectorbourne diseases or vector?bourne disease\$ or Octor?bourne diseases or vector?bourne disease\$ or Cholera or Diarthea or diarthoea).mp. 56723 35 (Typhoid fever or Giardiasis or Schistosomiasis or Taveler\$% diarthea or traveler\$% diarthea or traveler\$% 56723	r			
30 (avian flu or abola or EVD or H1N1 or H5N1 or infectious disease or influenza or swine flu or flu or flu or MERS or Middle East Respiratory Syndrome or measles or zika or cholera or H7N9 or dengue or fever or plague or fever or malaria or polio).mp. 561066 31 (SARS or Severe Acute Respiratory Syndrome or measles or zika or cholera or H7N9 or dengue or fever or plague or fever or malaria or polio).mp. 579612 32 (Bacillus cereus or Campylobacter jejuni or Cyclospora cayetanensis or (E adj coli) or Hepatitis A or Listeria monocytogenes or Noroviruses or Salmonella or Shigella or Staphylococcus aureus or Vibrio vulnificus).mp. 579612 33 (Diphtheria or Haemophilus influenzae type b or HPV).mp. 241684 34 ((Meningococcal adj Infection\$) or Mump\$ or Pertussis or Whooping Cough or Pneumococcal Infection\$ or Polio or Rotavirus or ravelela or disease\$ or vector?bourne diseases or vector?bourne diseases or waterbourne diseases or water?bourne diseases or waterbourne diseases or schoils or Schistosomiasis or Dracunculiasis or Dysentery or Cryptosporidiosis or amoebiasis or Traveler\$ diarrhoea).mp. 56723	-	28		119087
30 (avian flu or abola or EVD or H1N1 or H5N1 or infectious disease or influenza or swine flu or flu or meases or Middle East Respiratory Syndrome).mp. 198862 31 (SARS or Severe Acute Respiratory syndrome or measles or zika or cholera or H7N9 or dengue or fever or plague or fever or malaria or polio).mp. 561066 32 (Bacillus cereus or Campylobacter jejuni or Clostridium or Cryptosporidium or Cyclospora cayetanensis or (E adj coli) or Hepatitis A or Listeria monocytogenes or Noroviruses or Salmonella or Shigella or Staphylococcus aureus or Staphylococcus or Vibrio vulnificus).mp. 579612 33 (Diphtheria or Haemophilus influenzae type b or Hib or Hepatitis B or Human Papillomavirus or HPV).mp. 241684 34 ((Meningococcal adj Infection\$) or Mump\$ or Pertussis or Whooping Cough or Pneumococcal Infection\$ or Polio or Rotavirus or Rubella or German Measles or Tetanus or varicella or chicken pox or vectorbourne diseases or water?bourne disease\$ or waterbourne diseases or water?bourne disease\$ or topication or Garnanceliasis or Dysentery or Cryptosporidiosis or amoebiasis or Traveler\$% diarrhee or travelers 56723		29		207717
31 (SARS or Severe Acute Respiratory syndrome or measles or zika or cholera or H7N9 or dengue or fever or plague or fever or malaria or polio).mp. 561066 32 (Bacillus cereus or Campylobacter jejuni or Clostridium or Cryptosporidium or Cyclospora cayetanensis or (E adj coli) or Hepatitis A or Listeria monocytogenes or Noroviruses or Salmonella or Shigella or Staphylococcus aureus or Staphylococcus or Vibrio parahaemolyticus or Vibrio vulnificus).mp. 579612 33 (Diphtheria or Haemophilus influenzae type b or Hib or Hepatitis B or Human Papillomavirus or HPV).mp. 241684 34 ((Meningococcal adj Infection\$) or Mump\$ or Pertussis or Whooping Cough or Pneumococcal Infection\$ or Polio or Rotavirus or varicella or chicken pox or vectorbourne diseases or water?bourne disease\$ or waterbourne diseases or water?bourne disease\$ or Cholera or Diarthea or diarthoea).mp. 421975 35 (Typhoid fever or Giardiasis or Schistosomiasis or Dracunculiasis or Traveler\$ diarthea or travelers diarthoea).mp. 56723	-	30	(avian flu or abola or EVD or H1N1 or H5N1 or infectious disease or influenza or swine flu or flu or	198862
32 (Bacillus cereus or Campylobacter jejuni or Clostridium or Cryptosporidium or Cyclospora cayetanensis or (E adj coli) or Hepatitis A or Listeria monocytogenes or Noroviruses or Salmonella or Shigella or Staphylococcus aureus or Staphylococcus or Vibrio parahaemolyticus or Vibrio vulnificus).mp. 579612 33 (Diphtheria or Haemophilus influenzae type b or Hib or Hepatitis B or Human Papillomavirus or HPV).mp. 241684 34 ((Meningococcal adj Infection\$) or Mump\$ or Pertussis or Whooping Cough or Pneumococcal Infection\$ or Polio or Rotavirus or Rubella or German Measles or Tetanus or varicella or chicken pox or vectorbourne diseases or vector?bourne disease\$ or waterbourne diseases or water?bourne disease\$ or Cholera or Diarrhea or diarrhoea).mp. 56723 35 (Typhoid fever or Giardiasis or Dysentery or Cryptosporidiosis or amoebiasis or Traveler\$s diarrhea or travelers diarrhoea).mp. 56723	-	31	(SARS or Severe Acute Respiratory syndrome or measles or zika or cholera or H7N9 or dengue or	561066
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Pertussis or Whooping Cough or Pneumococcal Infection\$ or Polio or Rotavirus or Rubella or German Measles or Tetanus or varicella or chicken pox or vectorbourne diseases or vector?bourne disease\$ or waterbourne diseases or water?bourne disease\$ or Cholera or Diarrhea or diarrhoea).mp. 35 (Typhoid fever or Giardiasis or Schistosomiasis or Dracunculiasis or Dysentery or Cryptosporidiosis or amoebiasis or Traveler\$s diarrhea or travelers diarrhoea).mp. 56723		33	Hib or Hepatitis B or Human Papillomavirus or	241684
Dracunculiasis or Dysentery or Cryptosporidiosis or amoebiasis or Traveler\$s diarrhea or travelers diarrhoea).mp.		34	Pertussis or Whooping Cough or Pneumococcal Infection\$ or Polio or Rotavirus or Rubella or German Measles or Tetanus or varicella or chicken pox or vectorbourne diseases or vector?bourne disease\$ or waterbourne diseases or water?bourne	421975
		35	Dracunculiasis or Dysentery or Cryptosporidiosis or amoebiasis or Traveler\$s diarrhea or travelers	56723
36 exp inflectious disease medicine/ or exp malaria/ or 213621 exp influenza, human/ or SARS virus/ or exp norovirus/ or exp coronavirus infections/ or exp measles/ or exp poliomyelitis/ or exp chickenpox/	-	36	exp infectious disease medicine/ or exp malaria/ or exp influenza, human/ or SARS virus/ or exp norovirus/ or exp coronavirus infections/ or exp	213621
37 (anthrax or botulism or brucellosis or 78479 campylobacter enteritis or chikungunya or chlamydia\$ or CJD or Creutzfeldt?Jakob).mp.	-	37	(anthrax or botulism or brucellosis or campylobacter enteritis or chikungunya or	78479
38 (diptheria or echinococcosis or gonococcal or haemophilus influenzae or hepatitis or HIV or AIDS or human immunodeficiency virus or acquired immunodeficiency syndrome).mp.	-	38	haemophilus influenzae or hepatitis or HIV or AIDS or human immunodeficiency virus or acquired	938033
39 (legionnaires?disease or leptospirosis or listeriosis or lyme or streptococcus pneumoniae or Q fever or rabies or congenital rubella or salmonella or shiga toxin or verocytotoxin?producing E?coli or STEC or VTEC or HUS or haemoltic?uraemic or hemoltic?uremic).mp. 206207		39	(legionnaires?disease or leptospirosis or listeriosis or lyme or streptococcus pneumoniae or Q fever or rabies or congenital rubella or salmonella or shiga toxin or verocytotoxin?producing E?coli or STEC or VTEC or HUS or haemoltic?uraemic or hemoltic?uremic).mp.	206207
40(shigellosis or smallpox or syphilis or congenital syphilis or tick?borne viral encephalitis or congenital toxoplasmosis or trichinellosis or tuberculosis or TB or typhoid or paratyphoid or VHF or viral hemorrhagic fever\$ or viral haemorrhagic fever\$ or West Nile virus or Yellow fever or (enteritis adj3 yersinia)).mp.313309			(shigellosis or smallpox or syphilis or congenital syphilis or tick?borne viral encephalitis or congenital toxoplasmosis or trichinellosis or tuberculosis or TB or typhoid or paratyphoid or VHF or viral hemorrhagic fever\$ or viral haemorrhagic fever\$ or West Nile virus or Yellow fever or (enteritis adj3 yersinia)).mp.	
41 or/28-40 2651637	-			
42 18 and 27 and 41 (studies before 2003 excluded) 14223		42	18 and 27 and 41 (studies before 2003 excluded)	14223

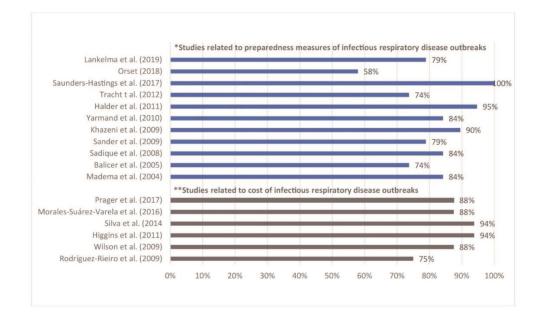
ECONLIT

Date of Search	Ec	EconLit					
	# Search Terms						
30/8/2019	1	cost OR (deductibles and coinsurance) OR Medical savings accounts OR health expenditure OR economic OR (fees and charges) OR Economic evaluation OR cost effectiveness analysis OR Cost utility analysis OR cost benefit analysis OR Cost consequence analysis OR Investment	1,344,466				
30/8/2019	2	(Emergency Preparedness) OR Preparedness OR emergency OR Surveillance OR disaster OR (detection or diagnosis or identification or early detection) OR screening OR vaccination OR hygiene OR school closure OR quarantine	48,619				
30/8/2019	3	disease outbreak OR disease OR infectious diseases OR communicable 9,194 diseases OR outbreak OR pandemic OR epidemic					
31/8/2019	4	S1 AND S2 AND S3 (limitation: from 2003 to 2019)	965				

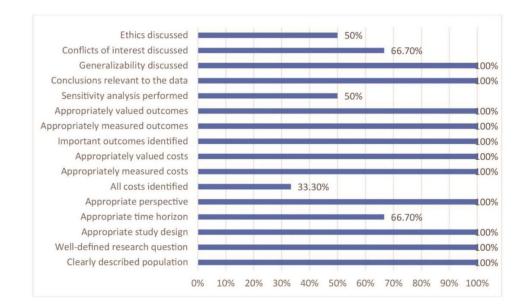
IDEAS REPEC

Date of	IDEAS REPEC						
Search	Search Term 1	Search Term 2	Search Term 3	Results (n)			
28/7/2019	cost-effective	infectious		139			
28/7/2020	Emergency Public Information and Warning	cost		8			
28/7/2021	Health Surveillance	infectious	cost	10			
30/7/2022	economics	health preparedness		39			
30/7/2023	cost-effectiveness	cost effectiveness	health preparedness	8			
30/7/2024	prevention	cost	disease outbreaks	42			
30/7/2025	economic evaluation	Public health surveillance		12			
30/7/2026	investment	Infectious disease	outbreak	16			
30/7/2027	economics	H1N1		16			
30/7/2028	economics	flu	outbreak	25			
1/8/2019	Cost-effectiveness	ebola		4			
1/8/2019	economics	disease threats		171			
1/8/2019	pandemic	economic	cost	42			

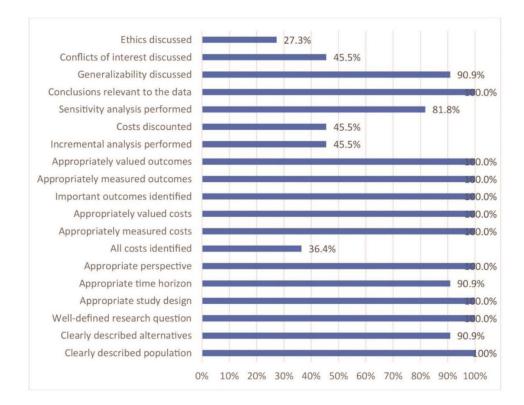
Appendix 2. Total quality appraisal score (in percentages) for all included studies (n=17)



Appendix 3. Quality appraisal score by item/question for the partial economic evaluation studies (n=6)



Appendix 4. Quality appraisal by item/question of the full evaluation studies (n=11)



Study, (Publication Year)	Setting, year	Study population (n)	Economic Evaluation	Approach	Perspective	Time Horizon	Type of Sensitivity analysis
Prager et al. (2017)	USA, n/a	The population of the USA	Cost of illness (although mentions about cost-effective of vaccination in the pandemic scenario, No CEA outcomes)	Simulation model	Healthcare system, Governmental, Societal	Not clearly stated	Performed, unclear
Morales-Suárez-Varela et al. (2016)	Spain, 2009-2010	Unvaccinated women of childbearing age with influenza A (H1N1)	Partial Economic Evaluation (Cost of illness)	Observational	Healthcare system, Societal	4 months	Not performed
Silva et al. (2014)	France, 2010-2011	Population with Influenza B (201)	Partial Economic Evaluation (cost of illness)	Observational	Payer, Societal	3 months	One-way sensitivity analysis and probabilistic analysis
Higgins et al. (2011)	Australia and New Zealand, 2009	All Influenza cases (H1N1) in New Zealand and Australia (762)	Partial Economic Evaluation Cost of illness	Observational	Healthcare system	3 months	Not performed
Wilson et al. (2009)	New Zealand, 2009	All Influenza hospitalisations in New Zealand) 1224 – 1122 hospitalizations and + 122 ICU	Partial Economic Evaluation, Cost of illness (incl. hypothetical cost- effectiveness analysis)	Observational	Healthcare system	12 months	Probabilistic sensitivity analysis
Rodríguez-Rieiro et al. (2009)	Spain, 2009	All Spanish patients with H1N1 (11,449)	Partial Economic Evaluation (Cost of illness)	Observational	Healthcare system	12 months	Not performed

Study, (Publication year)	, Setting, Population		Economic Evaluation	Perspective	Timeframe	Discount	Sensitivity analysis
(2 4.4.1.0000000, 5 000)	1		bservational studies		1		
Lankelma et al. (2019)	Netherlands, 2017-2018	Patients with acute RTI at the emergency department (1546 tests, 624 cases)	Partial Economic Evaluation	Healthcare system	4,5 months	N/A	Not performed
Sadique et al. (2008)	UK, 2005	Working parents with depending children	Partial Economic Evaluation	Societal	1 year	N/A	Scenarios
		Simulation	on or mathematical mode	els			
Orset (2018)	France, 2014	200 participants, data extrapolated	Both cost-benefit and cost-effectiveness analysis	Public health and societal	1 year	1% for costs	Not performed
Saunders-Hastings et al. (2017)	Canada, n/a	A simulation of Ottawa, Canada (1.2 million)	cost-effectiveness analysis	Healthcare system	Lifetime	1.5%	Multivariate sensitivity analyses
Halder et al. (2011)	Australia.A community in Western Australia2009(30,000)		cost-effectiveness analysis	Healthcare and Societal	Lifetime	3%	Scenarios
Tracht et al. (2012)	USA, (2009-2010 influenza season)	Simulation of the US (302 million people:73 million children, 191 million adults, and 38 million seniors)	cost-effectiveness analysis	Healthcare system and societal	1 year	N/A	Multivariate sensitivity analyses
Yarmand et al. (2010)	USA, (2009-2010 influenza season)	North Carolina State University undergraduate students (23,087)	cost-effectiveness analysis	Healthcare system	5 months	N/A	One-way and two-way sensitivity analyses
Sander et al. (2009)	USA, n/a	Residents of a 1 632-million-person city	Cost Utility Analysis	Societal	6 months	3%	Multivariate sensitivity analyses
Khazeni et al. (2009)	hazeni et al. USA, A U.S. metropolitan city		cost-effectiveness analysis	Societal	Lifetime	3% for benefits/ costs	Monte Carlo probabilistic sensitivity analysis
Balicer et al. (2005)	Israel, n/a	Population of Israel (1 618 200 cases)	Cost-benefit analysis	Healthcare system Societal	Lifetime	Not specified	Multivariate sensitivity analyses
Medema et al. (2004)	UK, Germany, Netherlands, (2004)	Developed Countries (1 Billion people)	Cost-effectiveness analysis	Healthcare system	Not clearly stated	5%	Performed unclear

Appendix 6. Characteristics of studies on preparedness and response measures of influenza outbreaks

RTI: Acute respiratory tract infection, N/A: Not applicable, UK: United Kingdom, US: United States

Study Intervention(s)/Screening methods vs. comparators **Outcomes/benefits** 1 vear Case 1: No Vaccination, Seasonal Outbreak Productivity loss and behavioural response Prage r et al. Case 2: No Vaccination, Pandemic Outbreak In the case of a pandemic influenza outbreak 2016 Vaccination: Vs. 1. Reduces illness-related workday losses from 83.3 million days to 61.1 million days (a reduction of 22.2 million days). 2. Causes 7.4 million days of workday losses due to the time that people spend on getting Case 3: Vaccination, Seasonal Outbreak Case 4: Vaccination, Pandemic Outbreak the vaccination doses. 3. Can reduce public avoidance behaviours by 25%. In the case of a seasonal influenza outbreak Vaccination: 1. Reduces illness-related workday losses from 18.7 million days to 13.9 million days (a reduction of 4.8 million days). 2. Causes 6.7 million days of workday losses due to the time that people spend obtaining vaccinations. 3. Can reduce public avoidance behaviours by 25%. Cases, PCP consultations and hospitalizations prevented Mede Cell culture-based intervention vs no intervention: 1. Egg-based vaccine manufacture ma et al. 2. Cell culture-based vaccine manufacture Cell culture-based intervention avoids 75 million influenza cases, 3.78 million PCP 2004 consultations for influenza treatment and, respectively, 5.81 million and 1.21 million Vs. influenza-related hospitalizations and excess deaths. No intervention Egg-based vaccine intervention vs no intervention: Egg-based vaccine intervention leads to vaccination of 17% of the population, which avoids 29.8 million influenza cases, 1.74 million PCP visits, 2.67 million hospitalizations and 556 000 deaths Cell culture-based intervention vs egg-based vaccine intervention with 17% vaccine coverage: Cell culture-based intervention strategy leads to vaccination of 37% of the population, avoiding an additional 35 million influenza cases, 2.04 million PCP consultations for influenza treatment, 3.14 million influenza-related hospitalizations and 654 500 excess deaths Years of life lost (YLL) Cell culture-based intervention strategy: 2.56 million

Appendix 7. Comparative analysis of health indexes when averting/responding to respiratory disease outbreaks

Supplemental material

Saund ers- Hasti ngs et al. 2017	 Vaccination and antiviral treatment Vaccination, antiviral treatment and antiviral prophylaxis Community-contact reduction, personal protective measures and voluntary isolation Community-contact reduction, personal protective measures, voluntary isolation and antiviral treatment School closure, community-contact reduction, personal protective measures, voluntary isolation and quarantine All interventions Vs. No intervention 	 Hospitalizations In case of no intervention, a total of 2 472 pandemic-associated hospitalizations have been estimated. Following no intervention, vaccination interventions (combined with other interventions) contributed to 765-815 hospitalizations. Last, school closure, combined with other interventions, contributed to 108-550 hospitalizations. YLL 3,026 2,2,801 1,767 1,607 1,393
		 6. 267 7. 9,421 Reductions of illness (H2N2 cases) Vaccination, personal protective measures, combined voluntary isolation and quarantine procedures resulted in the greatest reductions, producing attack rates of 50.0%, 45.5% and 33.9%, respectively. Antiviral treatment, antiviral prophylaxis, school closure and community-contact reduction produced only small reductions in illness attack rate, whether implemented alone or in combination with other interventions. Even in the absence of any pharmaceutical intervention, adherence to rigorous non-pharmaceutical protocols -school closure, community-contact reduction of the illness attack rate to 15.2%,
Khaze ni et al. 2009	 Vaccination and antiviral pharmacotherapy in quantities similar to those currently available in the U.S. stockpile (stockpiled strategy), Stockpiled strategy but with the expanded distribution of antiviral agents (expanded prophylaxis strategy), and Stockpiled strategy but with the adjuvanted vaccine (expanded vaccination strategy). Vs. no intervention 	 Clinical attack rate The clinical attack rate has been 11%, 17%, 19% and 33% for expanded adjuvanted vaccination, expanded antiviral prophylaxis, Stockpiled strategy and for no intervention, respectively. Deaths averted Expanded adjuvanted vaccination – 45 941 deaths averted Expanded antiviral prophylaxis – 32 745 deaths averted Stockpiled strategy – 29 761 deaths averted No intervention - No deaths averted
Sande r et al.	 HTAP25 with a stockpile for 25% of the population HTAP50 with a stockpile for 50% of the population HTAP with an unlimited stockpile 	QALYs gained, total Expanded adjuvanted vaccination – 404 030 total QALYs gained Expanded antiviral prophylaxis – 282 329 total QALYs gained

2009	4. School closure for 26 weeks	Stockpiled strategy – 258 342 total QALYs gained
2009	 School closure for 26 weeks Prevaccination 70% of the population with a low efficacy vaccine 	No intervention - No QALYs gained
		No intervention - No QAL 18 gamet
	7. HTAP50 + school closure:	QALYs per 1000 population, total
	8. HTAP + school closure:	All interventions gained a similar amount of QALYs, with some differences between
	9. Prevaccination + school closure: Prevaccinating 70% population with the low-	them (21,141 for no intervention to 21 403 for prevaccination and school closure).
	efficacy vaccine, plus closing all schools for 26 weeks	Compared to FTAP not involving school closure, FTAP plus school closure or
	10. Treatment only: Treating all cases with antivirals	prevaccination plus school closure gains 51 QALYs
	11. FTAP25 for household contacts and 60% of work/school contacts, stockpile for 25%	
	of the population	QALYs per 1000 population, incremental
	11. FTAP50 for household contacts and 60% of work/school contacts, stockpile for	FTAP and school closure and the intervention of prevaccination and school closure
	50% of population	contributed to the most incremental QALYs (262)
	12. FTAP for household contacts and 60% of work/school contacts, stockpile	
	unlimited	Deaths per 1000 population
	 14. FTAP25 + school closure 13. 15. FTAP50 + school closure 	Pre-vaccination intervention was the most effective strategy. Only 1 death/1000
	 13. 15. FTAP50 + school closure 14. 16. FTAP + school closure 	population occurred via this strategy.
	14. 10. $FTAP + school closure$	On the other side, most deaths have been seen in case of no intervention (13 deaths/1000 population) and FTAP25 with 12 deaths.
		population) and FTAF25 with 12 deaths.
		Number of cases
		Full TAP is the most effective single strategy, reducing the number of cases by 54%
		Pre-vaccination reduces the number of cases by 48%
		Adding school closure to full TAP or pre-vaccination further improves health outcomes
		Adding school closure to full TAT of pre-vacemation further improves health outcomes
Yarm	Self-isolation and mandatory quarantine	Effectiveness in low-levels of interventions
and	Vs.	Vaccination is more effective than self-isolation.
et al.		
2010	vaccination	Effectiveness in high-levels of interventions
		Self-isolation is more effective than vaccination. This has been shown due to
		weaknesses of vaccinations, such as delays in effectiveness.
Halde	Antiviral drugs combined with limited duration school closure	The illness attack rate of interventions (symptomatic)
	Antiviral drugs combined with mined duration school closure	
r et al.	Vs.	The illness attack rate ranges from 2.4% (SD 0.37) to 8.5% (SD 1.1) while that of the unmitigated attack rate is 13% (SD 0.9).
et al. 2011	¥ ð.	The individual school closure for 2 weeks along with the continuous -50% workplace
2011	1. School closure as a sole intervention alone and as dual, triple, quadruple strategy	closure, antiviral treatment, household antiviral prophylaxis and extended antiviral
	1. School closure as a sole intervention alone and as utal, utple, quadruple strategy	prophylaxis showed the lowest illness attack rate (2.4%). This combination is the most
	2. Other social distancing strategies, such as reduced workplace attendance	effective intervention.
	2. Oner soerar uistanening su aregies, such as reduced workplace anendance	Short-duration school closure is less effective (6.5 to 8.2 illness attack rate)
		Continuous school closure is more effective, with an attack rate of 3.2.
		Continuous school closure is more effective, with all attack rate of 5.2.

Orset 2018	Home confinement Vs. No intervention	 Incidence rate reduction by the home confinement intervention There are studies that indicate the higher the compliance rate regarding home confinement, the higher the reduction of the incidence rate of influenza will be. More particularly: In case of a 70% compliance rate: 83% reduction of incidence rate In the case of 80% compliance rate: 91% reduction of incidence rate The compliance rate with home confinement is between 75.90 and 94.44%, for this study. Rate reduction threshold in the incidence due to intervention The higher the proportion of all cases complying with home confinement, the higher the reduction rate of 49.24% of all cases complying with home confinement: €7.65 million Threshold for VSL
		million Threshold for VSL In case of 51.39% of all cases complying with home confinement: €5.06 million Threshold for VSL
Trach t t al. 2012	Mask wearing group Vs. No intervention	When there are no interventions (no masks worn) Cumulative number of cases/ based on three scenarios - R avg/unc [*] In the case of 1.25; A total of 101,424,384 cases. Most of them identified at 18-64 age group. In the case of 1.3; A total of 117 673 024 cases. Most of them identified at 18-64 age group. In the case of 1.35; A total of 130 043 351 cases. Most of them identified at 18-64 age group.
		 Hospitalizations Based on three different scenarios - R avg/unc: 1.25, 1.3, and 1.35 In the case of 1.25: For all age groups, a total of 3 275 616 hospitalizations have been estimated. 75.8% of them found to be in 18-64 ages In the case of 1.3: For all age groups, a total of 3 793 350 hospitalizations have been estimated. 74.8% of them found to be in 18-64 ages
		In the case of 1.35: For all age groups, a total of 4 184 352 hospitalizations have been estimated. 73.7% of them found to be in 18-64 ages
		Deaths More deaths have been found in ages 18-64, both in three scenarios, and more than 90% of the total deaths (281 319-349 578)

	As a result, the model showed that in case of 10% of the population wearing masks with an effectiveness of 20% in reducing susceptibility and infectivity, there is a large reduction in the cumulative number of cases.
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PCP: Primary care physician, YLL: Yearls of life lost, VSL: Value of statistical life, QALY: Quality-adjusted life year, FTAP: Full-targeted antiviral prophylaxis, SD: Standard deviation,

* Average effective reproduction number (uncontrolled)