Herd Immunity: Reviewing the impact of vaccinating children and healthcare workers to protect others

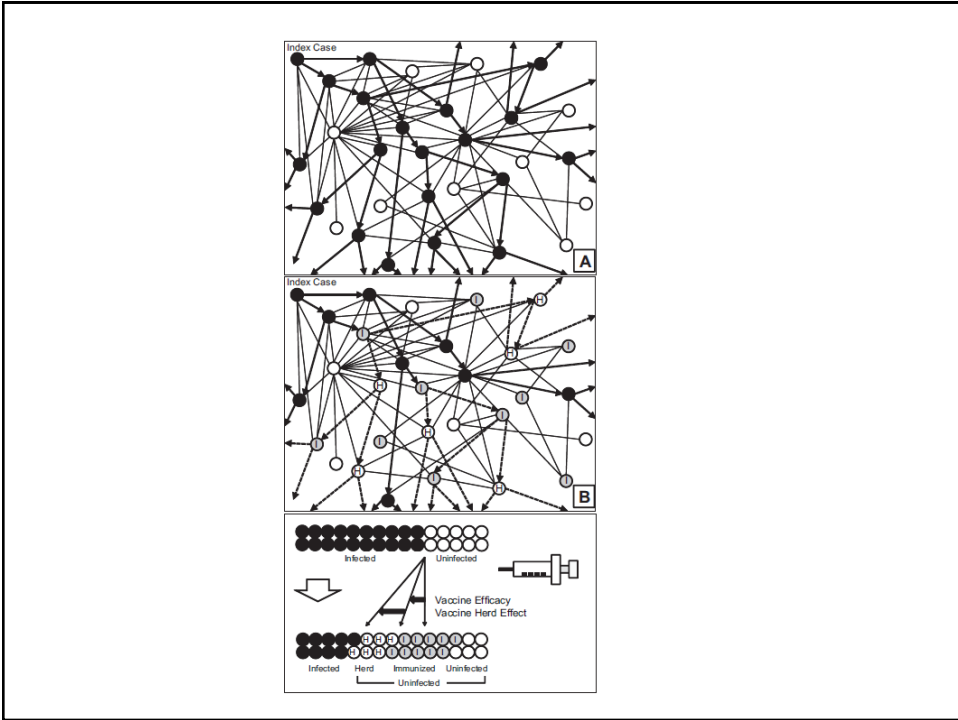Mark Loeb MD, MSc, FRCPC
McMaster University

NAIIS Summit, May 11, 2017, Atlanta

Herd Immunity

"The resistance of a group to attack by a disease to which a large proportion of the members are immune, thus lessening the likelihood of a patient with a disease coming into contact with a susceptible individual"

Fox JP et al, Am J Epidemiol 1971; 94:179-189

Herd immunity vs Community Protection?

Influenza Immunization Policy

- Adults and Children with selected chronic health conditions
- Residents of nursing homes and other chronic care facilities
- People ≥65 years of age
- Healthy children aged 6 to 23 months
- Women who will be pregnant
- Healthcare providers, household contacts of high risk individuals

National Advisory Committee on Immunization

Community Influenza Attack Rates and Complications by Age
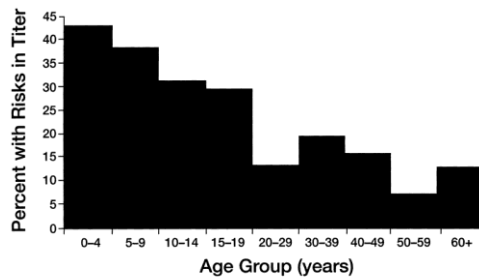
Monto, et al. *Epidemiol Infect*. 1993;110:145-60.
Study of the community of Tecumseh, MI, USA
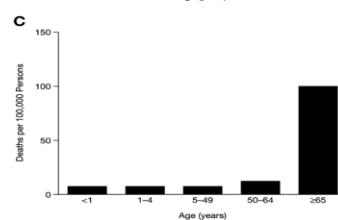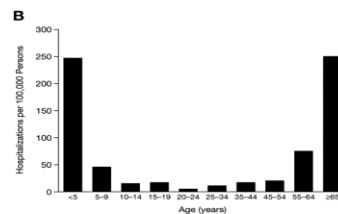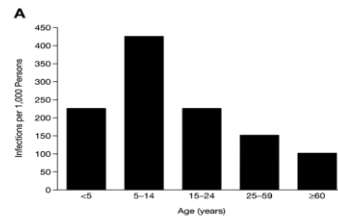
Immune Deficits in the Elderly
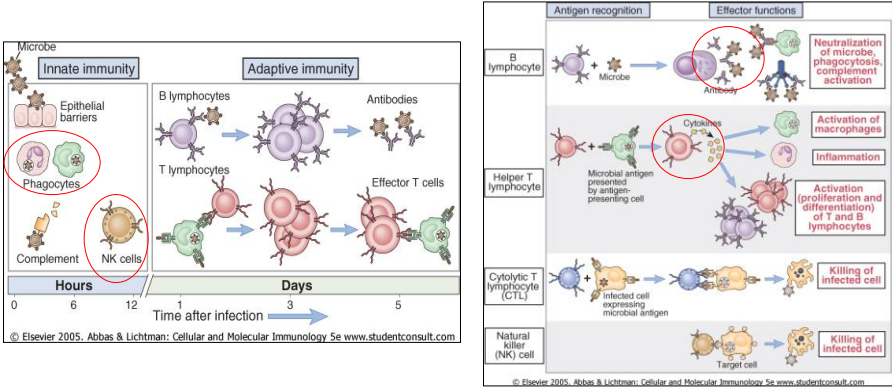
Figure 1-1 Innate and adaptive immunity.

Inflammaging: Theoretical Framework

↓CD4+ and CD8+Naïve T-cells (thymic inv.)

↓CD4+ T- cells (apoptosis)

Aging

↓ Ability to respond to pathogens

↑ CD8+ (accumulation of CD8+CD28- T-cells)

Chronic low grade inflammation due to IL-6 +TNF-α

CMV?
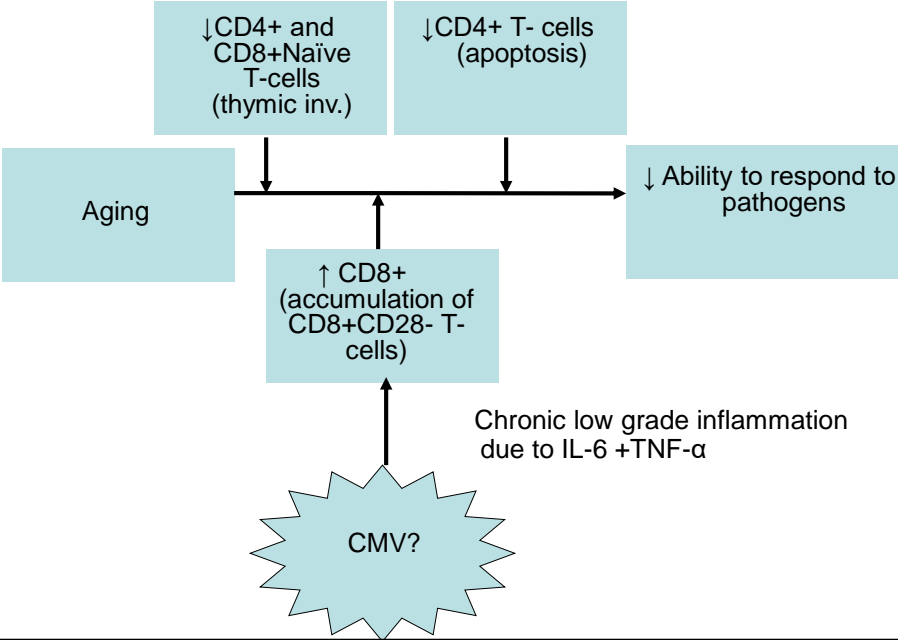
Evidence of bias in estimates of Influenza effectiveness in Seniors
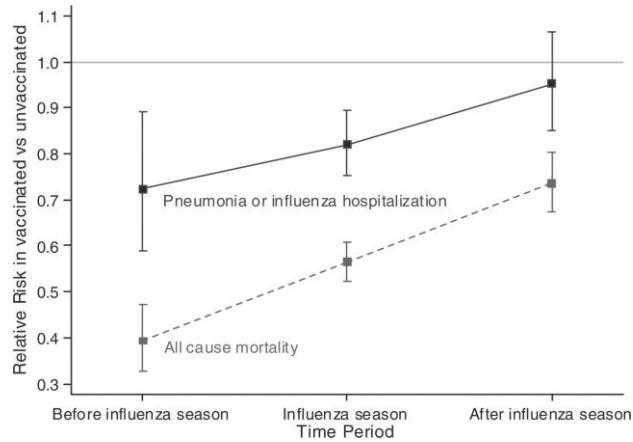
Jackson, L. A et al. Int. J. Epidemiol. 2006 35:337-344

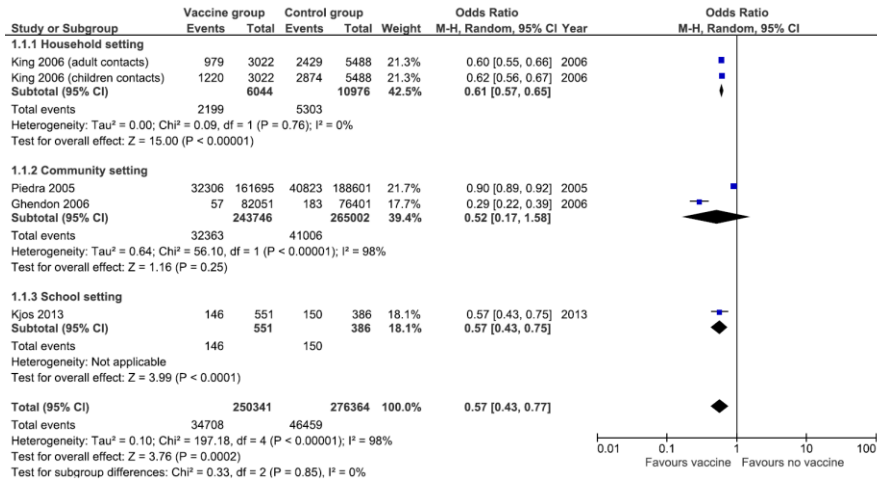# Influenza Vaccination of Schoolchildren in Japan Reduction in Excess Pneumonia and Influenza Mortality Among Older Adults

Reichert T et al. NEJM 2001;344:889-96.

Meta-analysis of Observational Studies for Herd effect in Influenza

Study or Subgroup	Vaccine group Events	Total	Control group Events	Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
1.1.1 Household setting							
King 2006 (adult contacts)	979	3022	2429	5488	21.3%	0.60 [0.55, 0.66]	2006
King 2006 (children contacts)	1220	3022	2874	5488	21.3%	0.62 [0.56, 0.67]	2006
Subtotal (95% CI)		6044		10976	42.5%	0.61 [0.57, 0.65]	
Total events	2199		5303				
Heterogeneity: Tau² = 0.00; Chi² = 0.09, df = 1 (P = 0.76); I² = 0%							
Test for overall effect: Z = 15.00 (P < 0.00001)							
1.1.2 Community setting							
Piedra 2005	32306	161695	40823	188601	21.7%	0.90 [0.89, 0.92]	2005
Ghendon 2006	57	82051	183	76401	17.7%	0.29 [0.22, 0.39]	2006
Subtotal (95% CI)		243746		265002	39.4%	0.52 [0.17, 1.58]	
Total events	32363		41006				
Heterogeneity: Tau² = 0.64; Chi² = 56.10, df = 1 (P < 0.00001); I² = 98%							
Test for overall effect: Z = 1.16 (P = 0.25)							
1.1.3 School setting							
Kjos 2013	146	551	150	386	18.1%	0.57 [0.43, 0.75]	2013
Subtotal (95% CI)		551		386	18.1%	0.57 [0.43, 0.75]	
Total events	146		150				
Heterogeneity: Not applicable							
Test for overall effect: Z = 3.99 (P < 0.0001)							
Total (95% CI)		250341		276364	100.0%	0.57 [0.43, 0.77]	
Total events	34708		46459				
Heterogeneity: Tau² = 0.10; Chi² = 197.18, df = 4 (P < 0.00001); I² = 98%							
Test for overall effect: Z = 3.76 (P = 0.0002)							
Test for subgroup differences: Chi² = 0.33, df = 2 (P = 0.85), I² = 0%							

Favours vaccine   Favours no vaccine

Flow Diagram of Trial: TIV vs Control

187 Hutterite colonies assessed for eligibility

138 Colonies excluded
- 31 Were ineligible
  - 15 Too geographically remote
  - 8 Participants were routinely vaccinated
  - 8 Do not allow childhood vaccinations
- 30 Were too busy
- 41 Were against influenza vaccination
- 1 Refused randomization to hepatitis vaccine
- 35 Had no interest

49 Colonies randomized

25 Colonies randomized to receive influenza vaccine (1895 individuals; median colony size, 78 [range 11-114])

24 Colonies randomized to receive hepatitis A vaccine (1500 individuals; median colony size, 62 [range 19-123])

593 Children and adolescents
502 Received the vaccine

528 Children and adolescents
445 Received the vaccine

3 Colonies withdrew prior to follow-up (122 individuals; median colony size, 51 [range 11-60])
4 Individuals were lost to follow-up
3 Were no longer interested
1 Left the colony

9 Individuals were lost to follow-up
5 Were no longer interested
1 Left the colony
1 Diagnosed with cancer
2 Died of cancer or myocardial infarction

1769 Completed follow-up

1491 Completed follow-up

1773 Included in the primary analysis

1500 Included in the primary analysis

Loeb, M. et al. JAMA 2010;303:943-950.

Indirect Protectiveness

Study Group	Influenza Vaccine	Hepatitis A Vaccine			P value
Participants who did not receive study vaccine	N=1271	N=1,055	Protective Effectiveness of Influenza Vaccine (95% CI)		
Participants with influenza detected by PCR- no. (%)	39 (3.1)	80 (7.6)			
Person days of follow up – no.	182,866	151,902			
Incidence of influenza – no. of cases/10,000 person-days	2.13	5.27	Simple	61 (8 - 83)	0.03
			Adjusted	61 (8 - 83)	0.03

Total Protectiveness

All participants	N=1773	N=1500		P Value
Participants with influenza detected by RT-PCR– no.(%)*	80 (4.5)	159 (10.6)	Protective Effectiveness of Influenza Vaccine (95% CI)	
Person days of follow up – no.	253,243	210,856		
Incidence of influenza – no. of cases/10,000 person-days	3.16	7.54	Simple 59 (5 - 82)	P=0.04
			Adjusted 59 (4 - 64)	P=0.04

Epidemic Curve of Influenza A and B in Enrolled Colonies
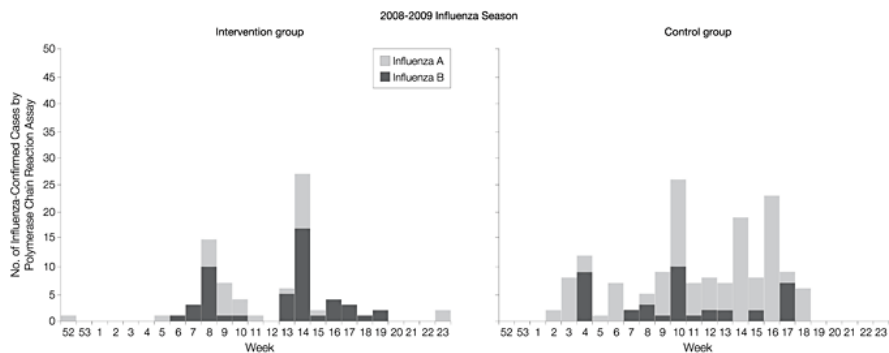

Loeb, M. et al. JAMA 2010;303:943-950.

Meta-analysis of RCTs for Herd effect in Influenza

Study or Subgroup	Vaccine group Events	Total	Control group Events	Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Gruber 1990	7	56	5	67	10.2%	1.77 [0.53, 5.92]	1990
Clover 1991	22	109	16	68	19.4%	0.82 [0.40, 1.71]	1991
Hurwitz 2000	11	113	21	115	18.1%	0.48 [0.22, 1.05]	2000
Principi 2003	22	729	16	370	21.6%	0.69 [0.36, 1.33]	2003
Loeb 2010	39	1271	80	1055	30.7%	0.39 [0.26, 0.57]	2010
Total (95% CI)		2278		1675	100.0%	0.62 [0.39, 0.96]	
Total events	101		138				

Heterogeneity: Tau² = 0.13; Chi² = 8.41, df = 4 (P = 0.08); I² = 52%
Test for overall effect: Z = 2.12 (P = 0.03)

Odds Ratio M-H, Random, 95% CI
0.01 0.1 1 10 100
Favours vaccine   Favours no vaccine

A Randomized Controlled Trial of Live Attenuated Vaccine versus Trivalent Inactivated Vaccine in Hutterite Children

M. Loeb, M. Russell, V. Manning, K. Fonseca, D. Earn, F. Aoki, G. Horsman, K. Chokani, M. Voight, L Schwartz, L. Babiuk, R. Goeree, E. Pullenayegum, S. Walter

McMaster University; University of Calgary; Provincial Laboratory for Public Health, Alberta; University of Manitoba; Saskatchewan Disease Control Laboratory; Saskatchewan Health; University of Alberta; St. Jude Children's Hospital and WHO Collaborating Center
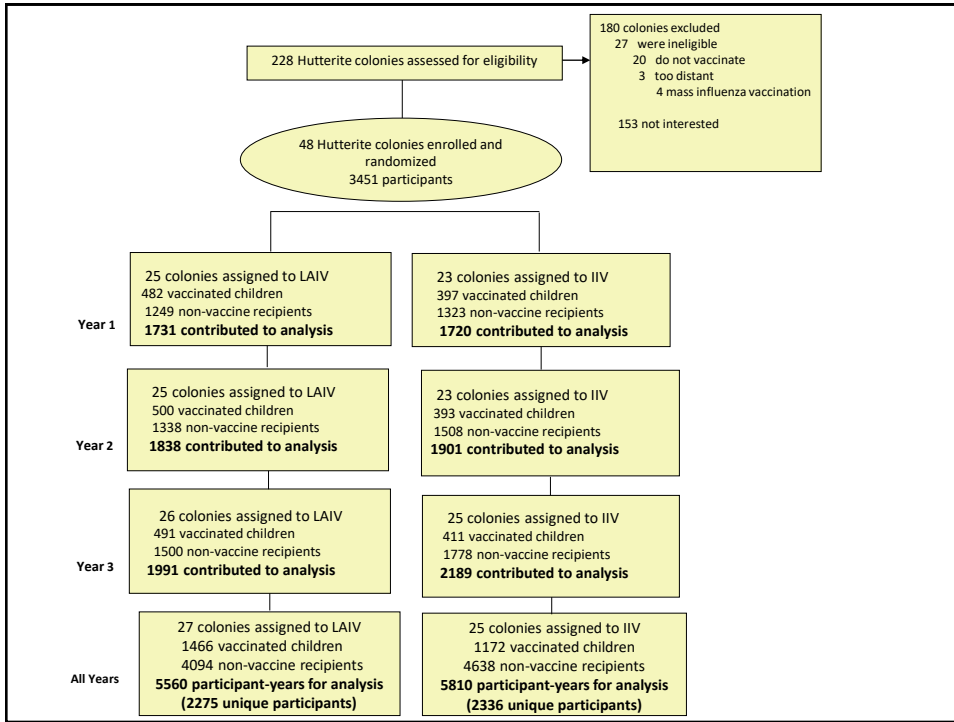
Effectiveness of LAIV compared to IIV at preventing RT-PCR confirmed influenza for all study participants

	LAIV	IIV	Hazard Ratio (95%CI)	P value
RT-PCR -confirmed Influenza				
Primary Outcome				
All Influenza				
All Years	295/5560 (5.3%)	304/5810(5.2%)	1.03 (0.85 to 1.24)	0.80
Year 1	119/1731 (6.9%)	74/1720 (4.3%)	1.61 (0.61 to 4.29)	0.34
Year 2	118/1838 (6.4%)	154/1901 (8.1%)	0.80 (0.39 to 1.64)	0.54
Year 3	58/1991 (2.9%)	76/2189 (3.5%)	0.85 (0.36 to 1.99)	0.70

Mandatory Influenza Vaccines for Healthcare Workers

PUBLIC HEALTH INTERVENTION

Mandatory seasonal influenza vaccination or masking of British Columbia health care workers: Year 1

Doran S. Ksienski, MD, FRCPC, MPH

ABSTRACT

OBJECTIVE: The Influenza Prevention Policy ("the Policy") aims to increase seasonal influenza vaccination coverage among British Columbia (BC) health care workers (HCWs).

PARTICIPANTS: HCWs who work in publicly funded facilities and attend patient care areas.

SETTING: The Policy was announced in August 2012 and took effect province-wide during the 2012/13 flu season.
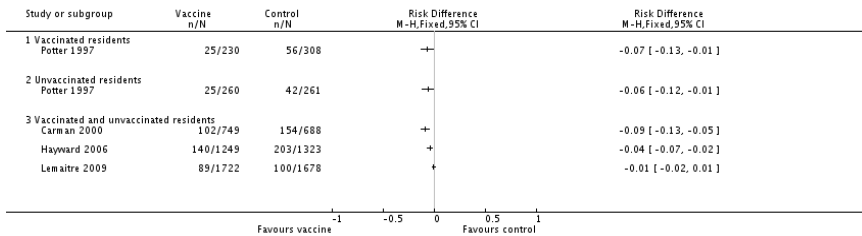
INTERVENTION: BC HCWs are required to receive seasonal influenza vaccination by the start of the flu season (December 1) or wear a mask while at work until the flu season ends (March 30). Vaccinated HCWs need to wear a green dot on their identification tag. HCWs are expected to report noncompliant coworkers. As initially proposed, continued noncompliance with the Policy could result in termination of employment (ultimately this component was put in abeyance).

OUTCOME: For the 2012/13 flu season, 74% of HCWs (35,889/48,818) at acute care facilities received influenza vaccination compared with 40% (23,375/58,212) in 2011/12 (difference in proportion=0.33, 95% confidence interval [CI]: 0.33-0.34, p<0.001). Similarly, staff vaccination rates at residential care facilities increased from 57% (21,535/37,700) for the 2011/12 flu season to 75% (27,617/36,620) in 2012/13 (difference in proportion=0.18, 95% CI: 0.18-0.19, p<0.001). Health care unions claimed that the Policy was coercive, and they launched an unsuccessful grievance with the BC Labour Relations Board.
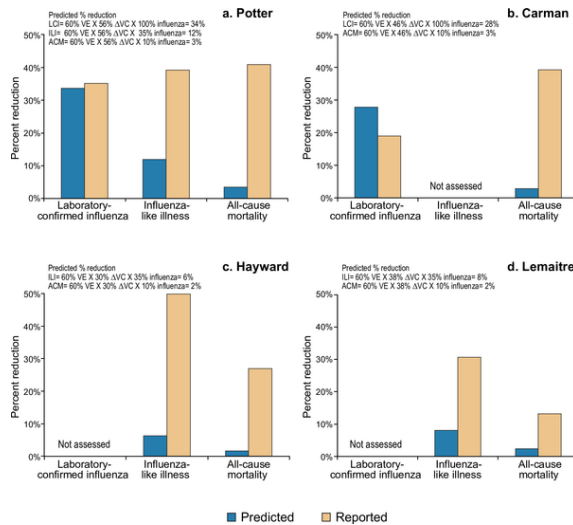
CONCLUSION: Implementation of the Policy was associated with increased HCW vaccination; the Policy was upheld by an independent arbitrator. Further research is required to correlate HCW vaccination coverage rates with changes in influenza incidence and its complications. Continued stakeholder engagement is vital to achieve a collaborative decision-making process.

Influenza vaccination for healthcare workers who care for people aged 60 or older living in long-term care institutions

Review: Influenza vaccination for healthcare workers who care for people aged 60 or older living in long-term care institutions
Comparison: 1 HCWs offered vaccination versus HCWs offered no vaccination: experimental design; data for periods of high influenza activity (three C-RCTs; Carman 2000 and Potter
Outcome: 5 Death from any cause

Study or subgroup	Vaccine n/N	Control n/N	Risk Difference M–H,Fixed,95% CI	Risk Difference M–H,Fixed,95% CI
1 Vaccinated residents				
Potter 1997	25/230	56/308		-0.07 [-0.13, -0.01]
2 Unvaccinated residents				
Potter 1997	25/260	42/261		-0.06 [-0.12, -0.01]
3 Vaccinated and unvaccinated residents				
Carman 2000	102/749	154/688		-0.09 [-0.13, -0.05]
Hayward 2006	140/1249	203/1323		-0.04 [-0.07, -0.02]
Lemaitre 2009	89/1722	100/1678		-0.01 [-0.02, 0.01]

-1 -0.5 0 0.5 1
Favours vaccine   Favours control

De Serres G, Skowronski DM, Ward BJ, Gardam M, Lemieux C, et al. (2017) Influenza Vaccination of Healthcare Workers: Critical Analysis of the Evidence for Patient Benefit Underpinning Policies of Enforcement. PLOS ONE 12(1): e0163586. https://doi.org/10.1371/journal.pone.0163586

Take Home Messages

- Vaccinating children is an important way, through herd immunity, to protect the elderly and others that cannot mount a robust response to influenza vaccine

- Healthcare workers should be vaccinated against influenza but the effect of protection on patients remains uncertain