Optimizing Influenza Vaccine Distribution

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Who Should Get Influenza Vaccine When Not All Can?

Rather than thinking only about saving the most lives when considering vaccine rationing strategies, a better approach would be to maximize individuals' life span and opportunity to reach life goals.

Ezekiel J. Emanuel* and Alan Wertheimer

The potential threat of pandemic influenza is staggering: 1.9 million deaths, 90 million people sick, and nearly 10 million people hospitalized, with almost 1.5 million production is just 425 million doses per annum, if all available factories would run at full capacity after a vaccine was developed. Under currently existing capabilities for manufacturing beds despite the presentation of another patient who is equally or even more sick; "Save the most quality life years" is central to cost-effectiveness rationing. "Save the worst-off"

Science 2006

- Should value people "on the basis of the amount the person invested in his or her life balanced by the amount left to live."
- Then vaccinate the most-valued people!
- Misses epidemiology: Transmission, Case mortality, Vaccine efficacy

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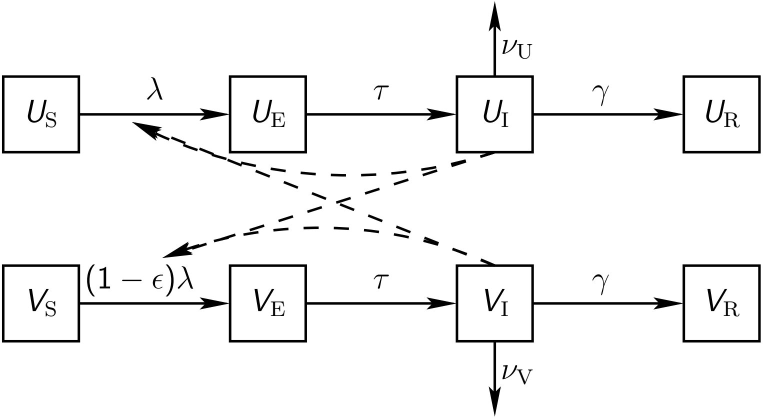
Problem Setup

- For influenza
- Age structure but not risk or occupation
- Given an outcome measure
- How to distribute limited vaccine doses?
- Nonlinear constrained optimization

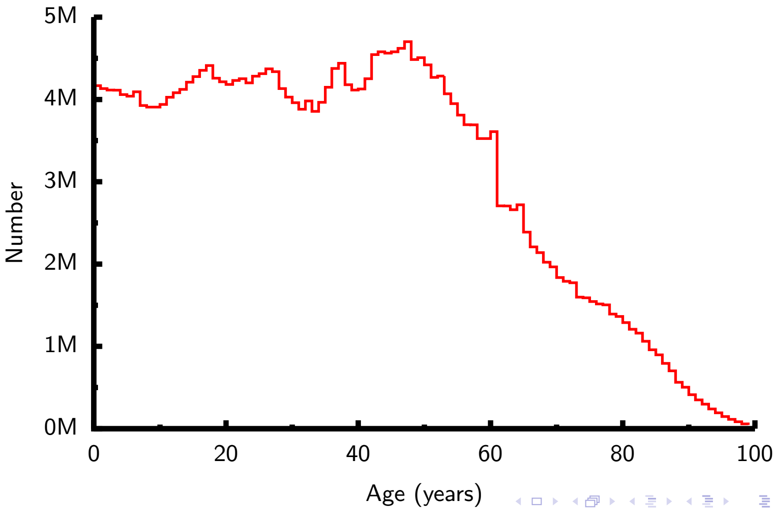
Model



Age structured $(0, 1\text{–}4, 5\text{–}9, 10\text{–}14, 15\text{–}19, \ldots, 70\text{–}74, 75+)$

No birth or natural death

2007 US Population Age Structure

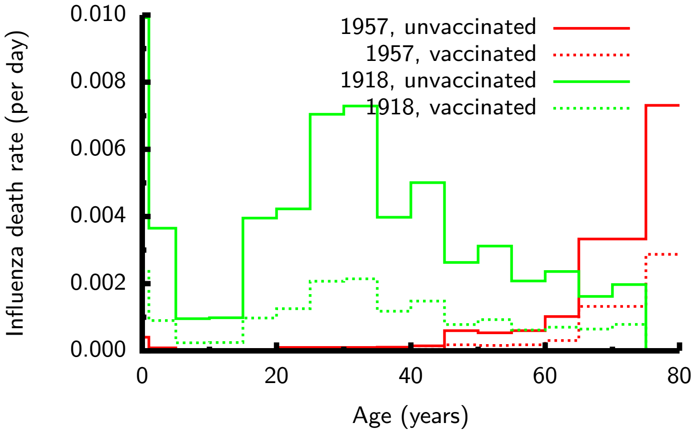


Parameters

Parameter	Ages	Value	Ref
Latent period, $1/\tau$	all	1.2 d	[1]
Infectious period, $1/\gamma$	all	4.1 d	[1]
Vaccine efficacy against infection, ϵ_a	0–64	0.80	[2, 3]
	65+	0.60	
Vaccine efficacy against death	0–19	0.75	[4, 2]
	20–64	0.70	
	65+	0.60	

[1] Longini et al, *Science*, 2005; [2] Galvani, Reluga, & Chapman, *PNAS*, 2007; [3] CDC, ACIP, 2007; [4] Meltzer, Cox, & Fukuda, *Emerg Infect Dis*, 1999.

Death Rate



Sources: Serfling, Sherman, & Houseworth, *Am J Epidemiol*, 1967; Luk, Gross, & Thompson, *Clin Infect Dis*, 2001; Glezen, *Epidemiol Rev*, 1996.

Contacts

OPEN ACCESS Freely available online PLoS MEDICINE

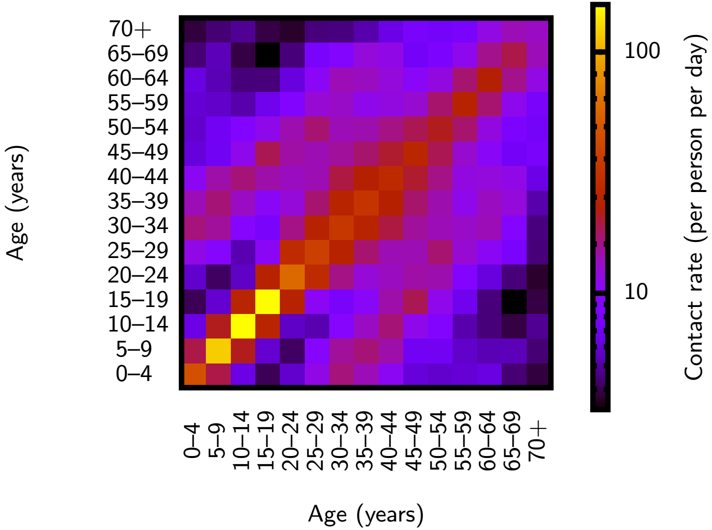
Social Contacts and Mixing Patterns Relevant to the Spread of Infectious Diseases

Joël Mossong[1,2*], Niel Hens[3], Mark Jit[4], Philippe Beutels[5], Kari Auranen[6], Rafael Mikolajczyk[7], Marco Massari[8], Stefania Salmaso[8], Gianpaolo Scalia Tomba[9], Jacco Wallinga[10], Janneke Heijne[10], Malgorzata Sadkowska-Todys[11], Magdalena Rosinska[11], W. John Edmunds[4]

PLoS Med 2008

Surveyed 7,290 Europeans for daily contacts

Contacts


70+
65–69
60–64
55–59
50–54
45–49
40–44
35–39
30–34
25–29
20–24
15–19
10–14
5–9
0–4
Age (years)
0–4
5–9
10–14
15–19
20–24
25–29
30–34
35–39
40–44
45–49
50–54
55–59
60–64
65–69
70+
Age (years)
100
10
Contact rate (per person per day)

R_0

- $R_0 = 1.4$ for Swine Flu (Fraser et al, *Science*, 2009)
- $R_0 = 2.0$ for 1918 Pandemic (Mills et al, *Nature*, 2004)
- We considered $R_0 = 1.4$ and also $R_0 = 1.2, 1.6, 1.8, 2.0$

Outcome Measures

Map outcome (number infected, dead, etc) to objective

- Total Infections
- Total Deaths
- Years of Life Lost: Using expectation of life (NCHS, US Life Tables, 2003)
- Contingent Valuation: Indirect assessment of value of lives of different ages
- Total Cost: Converts deaths, infections, etc into dollars

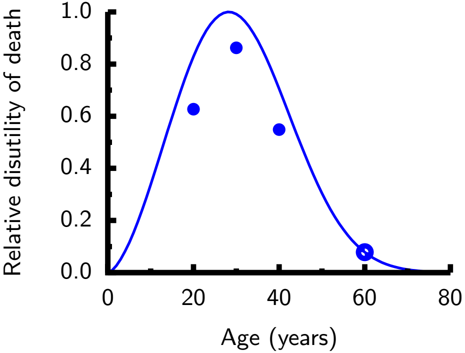
Contingent Valuation

- Survey asked about 20, 30, 40, 60 year olds and fit

$$v_a = a^{\omega-1}\exp\left(-\psi a^{\omega}\right)$$

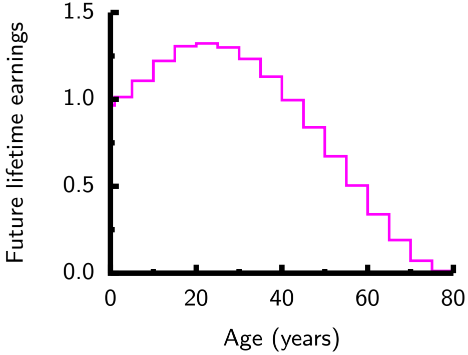
(Cropper et al, *J Risk Uncertain*, 1994)

- Alternative: wage–risk market data, but only for working-aged adults

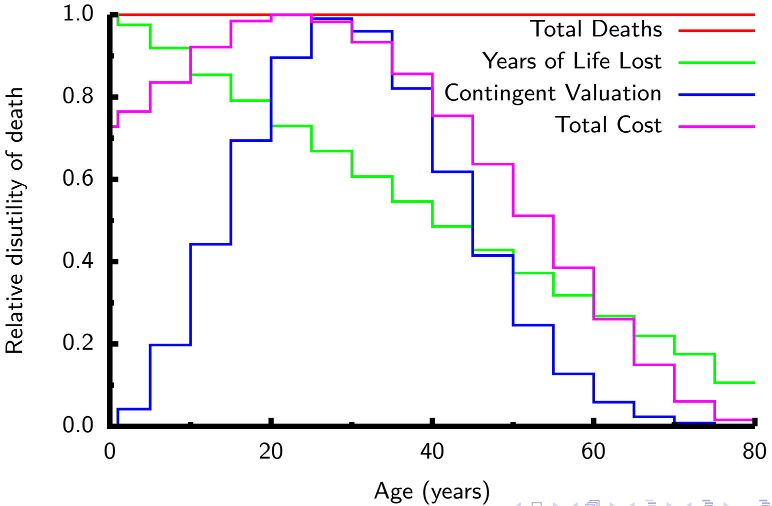


Total Cost

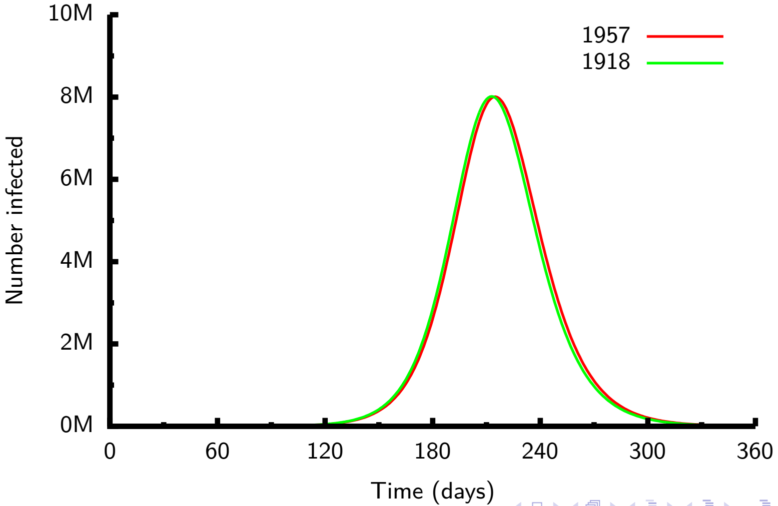
- Monetary cost of illness (Meltzer, Cox, & Fukuda, *Emerg Infect Dis*, 1999)
- Monetary cost of death
  - Future lifetime earnings (Haddix et al, 1996)
  - Alternatives: Include value of non-work time



Outcome Measures



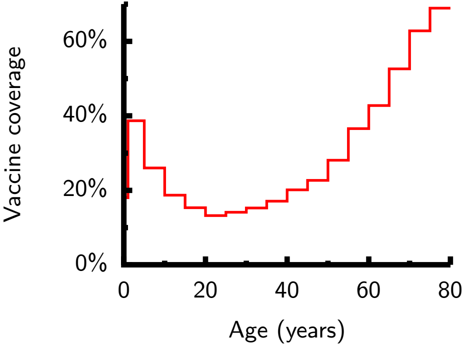
No Vaccination



Current Vaccination

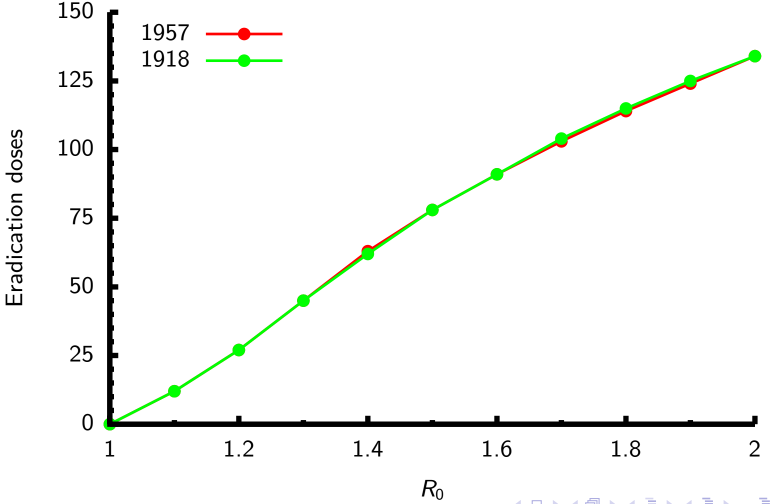
CDC estimate

- 84M doses used in 2007
- 100M+ doses annually
- 600M doses for Swine Flu

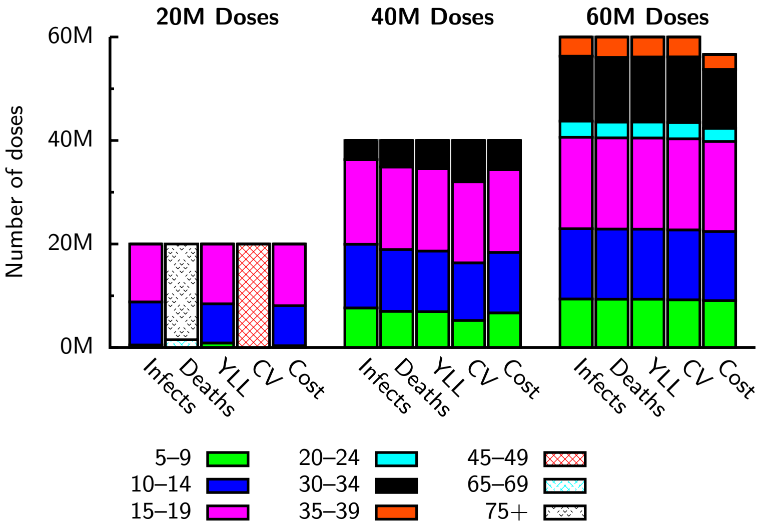


Sources: CDC, ACIP, 2008; NHIS, 2007.

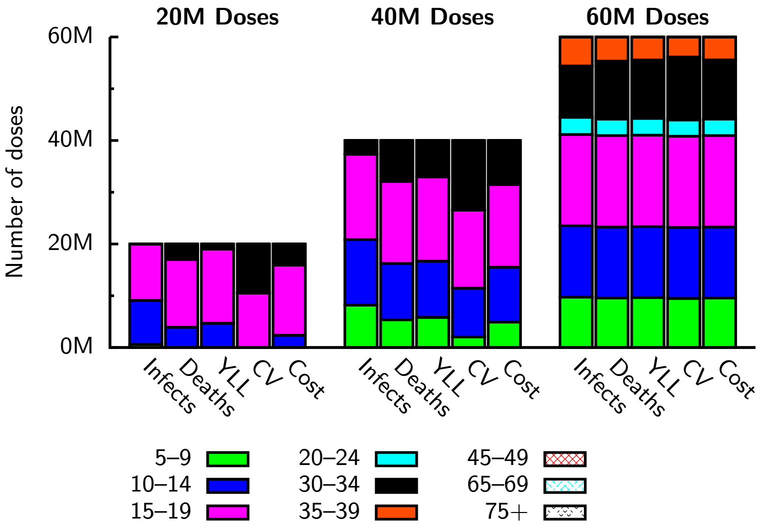
Eradication



1957-like Mortality



1918-like Mortality



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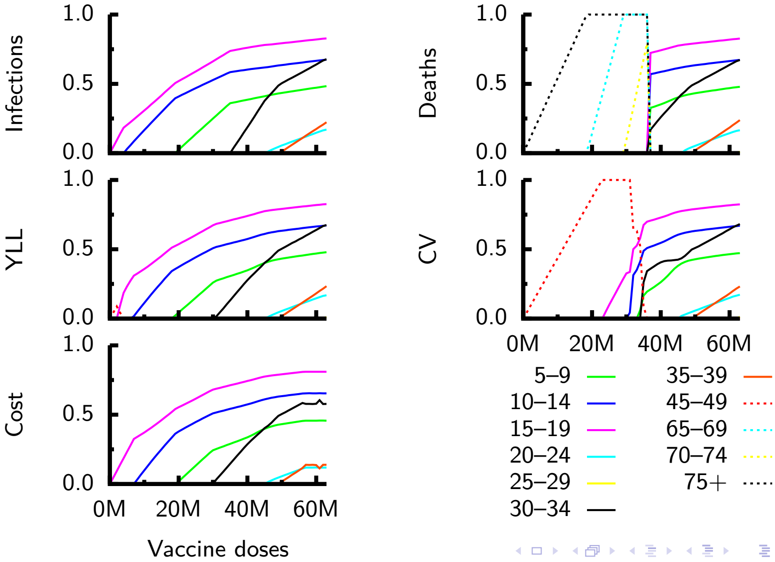

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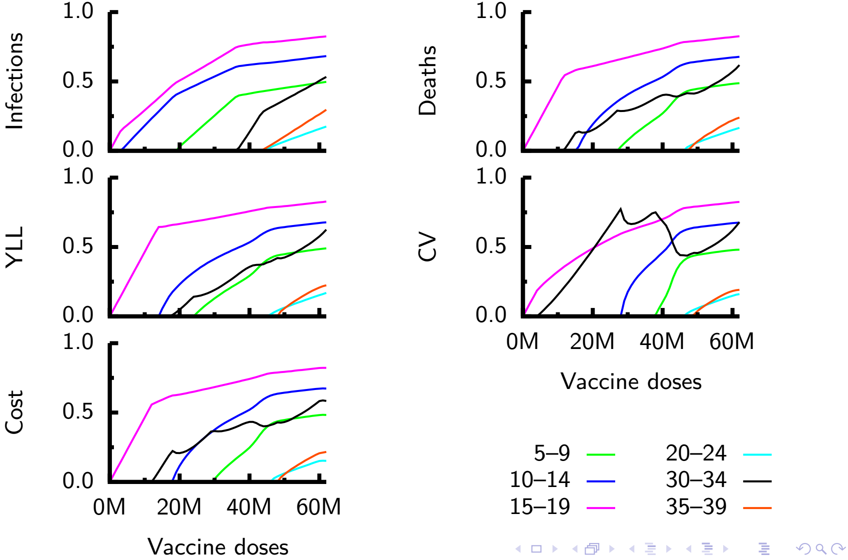
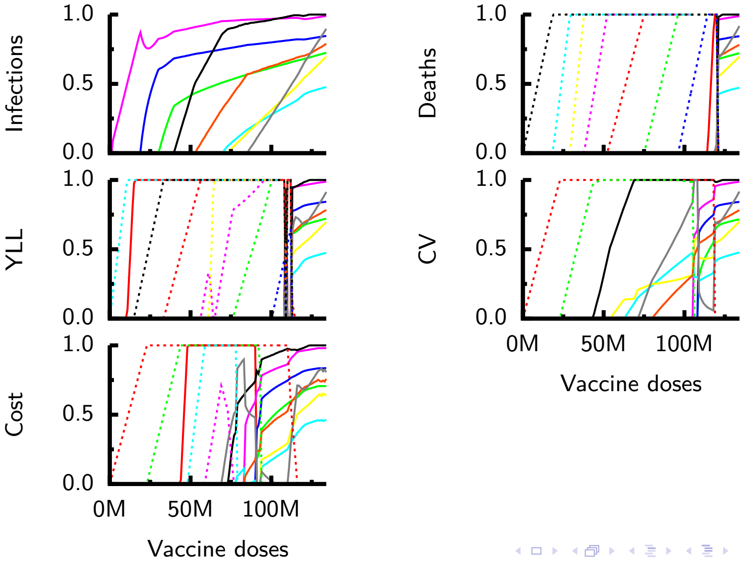


$R_0 = 2.0$, 1957-like Mortality



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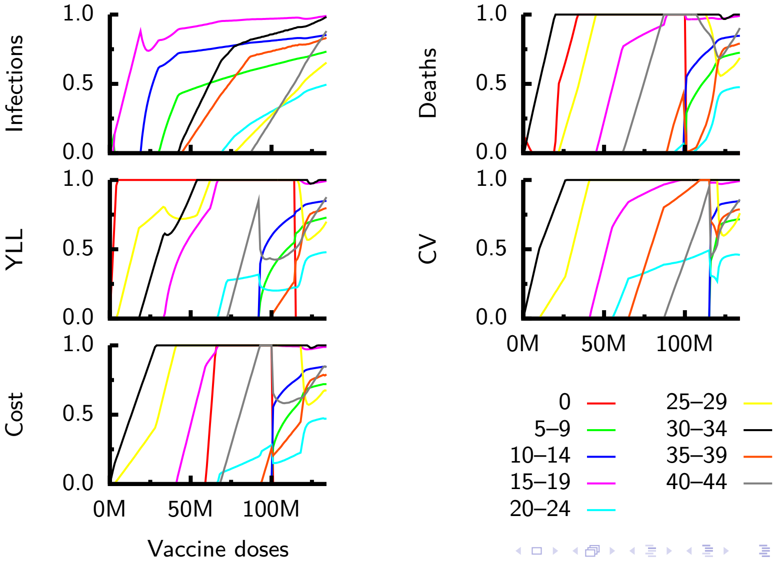
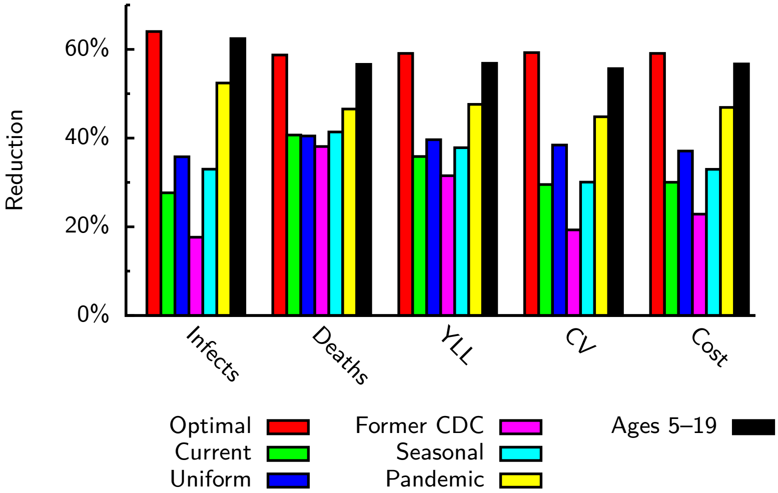


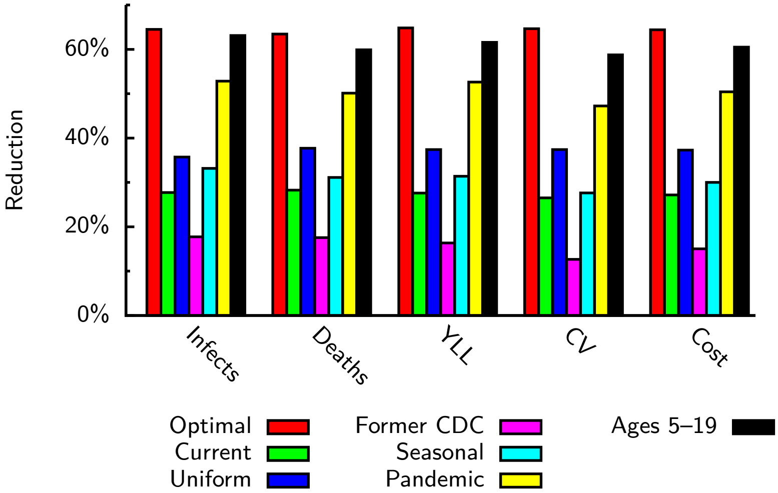
Sensitivity Analysis

- Reduced vaccine efficacy against infection
  Shifts to protecting at risk
- Reduced vaccine efficacy against death
  Reduced susceptibility in elderly
  Reduced infectious period for vaccinees
  Reduced infectiousness for vaccinees
  Little change for 50% reduction

1957-like Mortality, 40M Doses



1918-like Mortality, 40M Doses



Conclusions

- 65M doses prevents an $R_0 = 1.4$ epidemic
- 135M doses prevents an $R_0 = 2.0$ epidemic
- Can improve vaccination policies
- Infections: Vaccinate transmitters, children (5–19) & parents (30–39)
- Deaths, YLL, Contingent, & Cost:
  - When vaccine limited, vaccinate those at risk of death
  - When vaccine plentiful, vaccinate transmitters
  - Transition varies between outcome measures
  - Deaths averted transitions last
- Joint work with Alison Galvani
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