

Prof Maarten J Postma

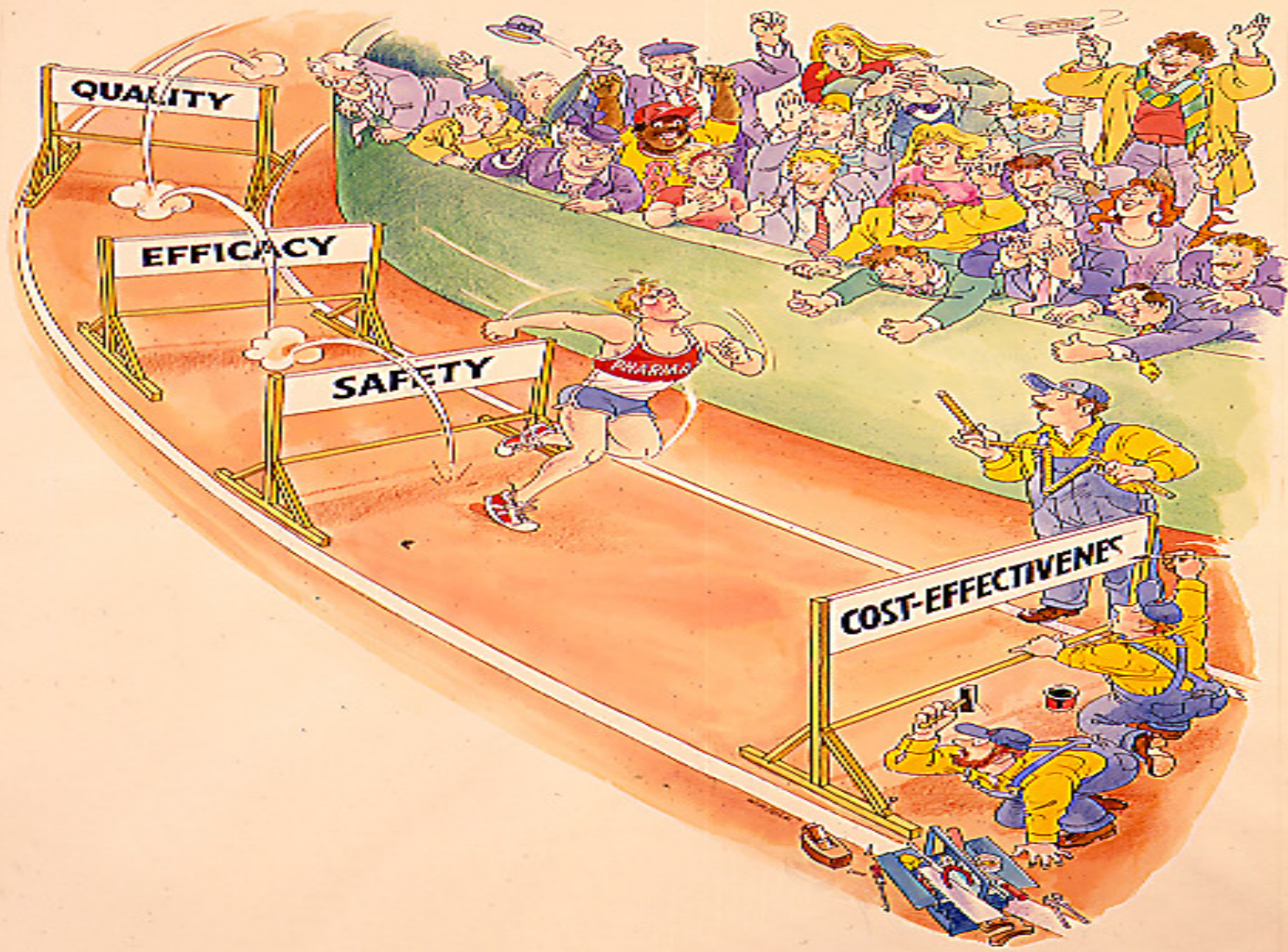
## Modeling for Optimization of Use of Limited Vaccine Quantities

Chair in Pharmacoeconomics

Department of Pharmacy  
University of Groningen  
Netherlands

# Modeling for Optimization of Use of Limited Vaccine Quantities

- Modeling
  - Epidemiology
  - Static vs. dynamic models ( $R_0$ )
- Limited vaccine quantities
  - Stockpiled pre-pandemic vaccine
  - Pandemic vaccines
- Optimization
  - # of deaths
  - Cost-effectiveness



## 4<sup>TH</sup> HURDLE NL

- HPV-vaccination; advice in April 2008
- HepB; discussions nearing finalization
- Pneumococcal; just started
- Influenza; age limit lowered to 60 years

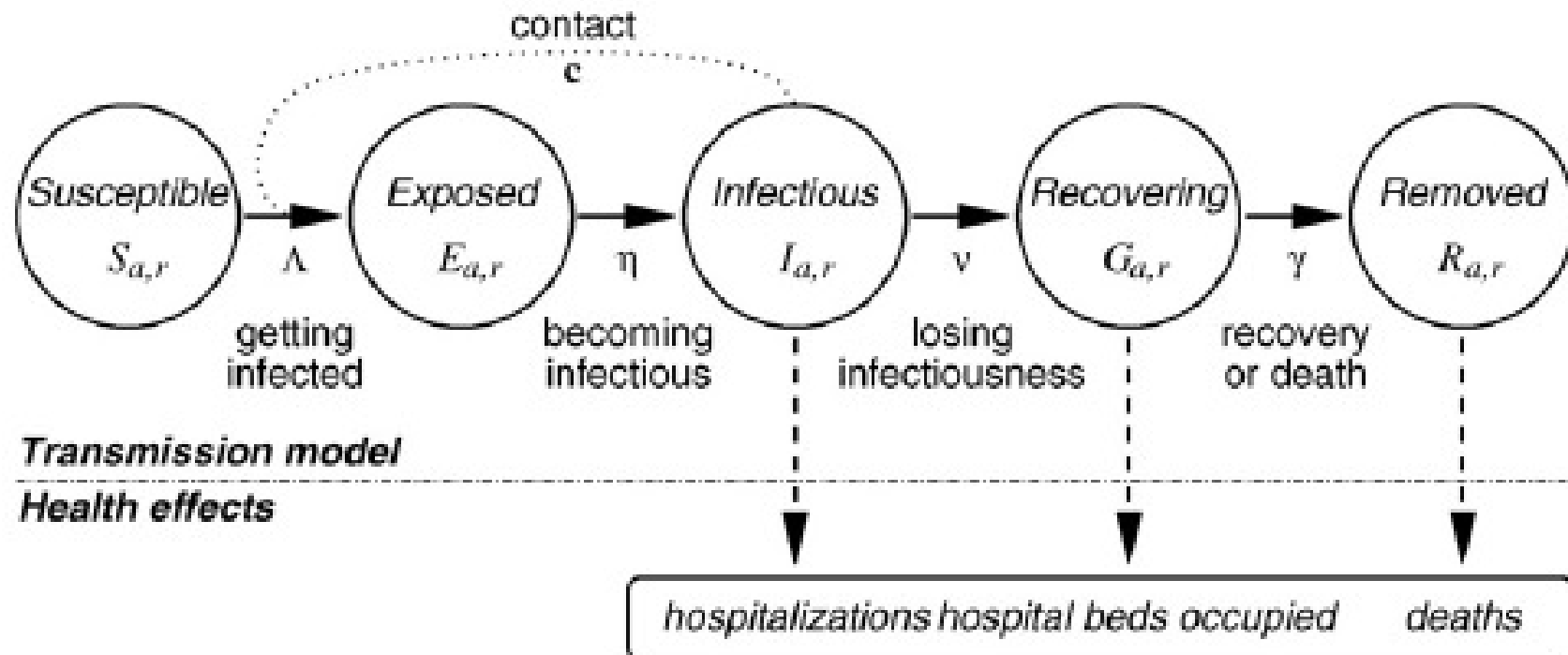


Fig. 1. Flow diagram of the transmission model and healthcare demand.

Calibration on the 1957/58 Infl A/H2N2 pandemic:  $R_0=1.73$

# MYLIUS ET AL

## ■ General

- Pandemic vaccine
- Prior or just after "uncontrolled peak"
- Overall attack rate 38%

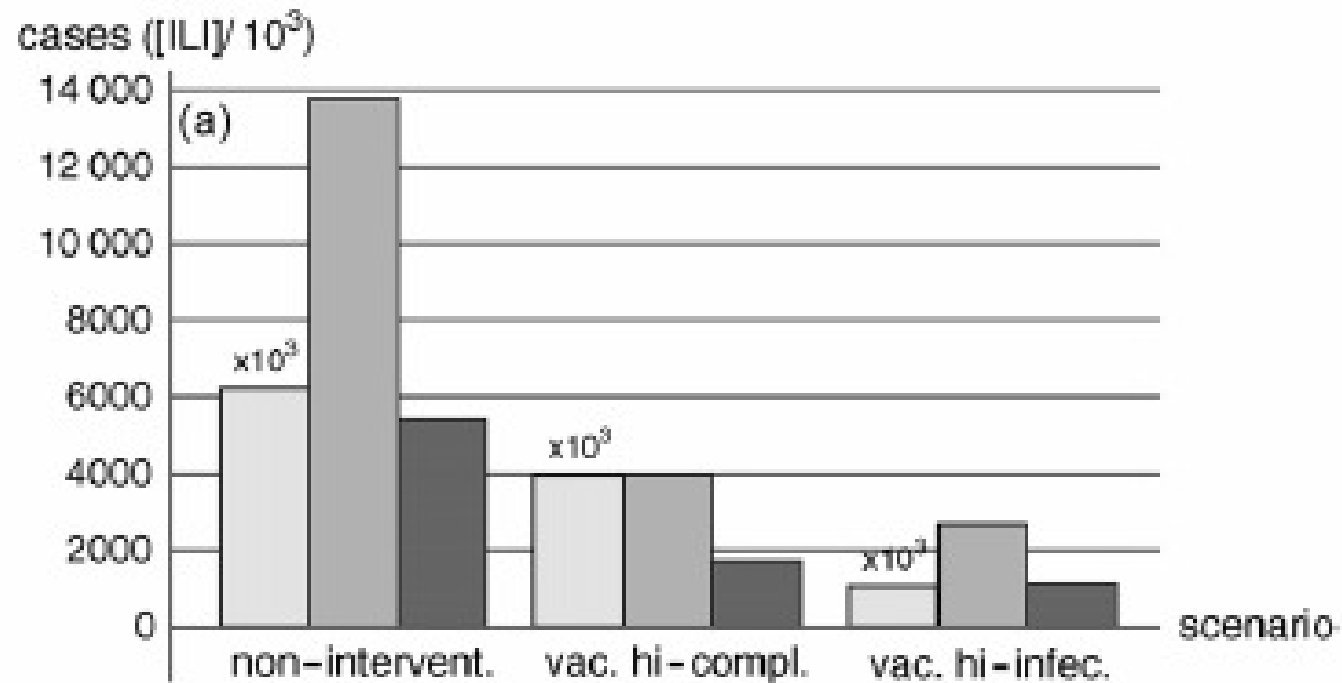
## ■ Vaccination

- 35 % coverage
- Prioritization for complications: 65+, ... , 13-19
- Prioritization for expected attack rates: 13-19, ... , 65+

## ■ Mortality (%)

	64-	65+
HR	0.034-0.051	1.69
LR	0.001-0.002	0.321

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f 60 days. Fig. 2a  
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influenza attack  
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## Vaccination implemented 20 days before the peak in the "uncontrolled pandemic"

Fig. 3. Predicted effects of interventions: cumulative number of patients with influenza-like illness (ILI) (light grey, numbers per  $10^3$ ), hospitalizations (medium grey) and fatalities (dark grey) for three scenarios: no intervention, allocation of vaccines to groups with a high-risk of developing complications, and allocation of vaccines to groups with a high-risk of infection. In the latter two scenarios, vacci-

# IMPLICATIONS

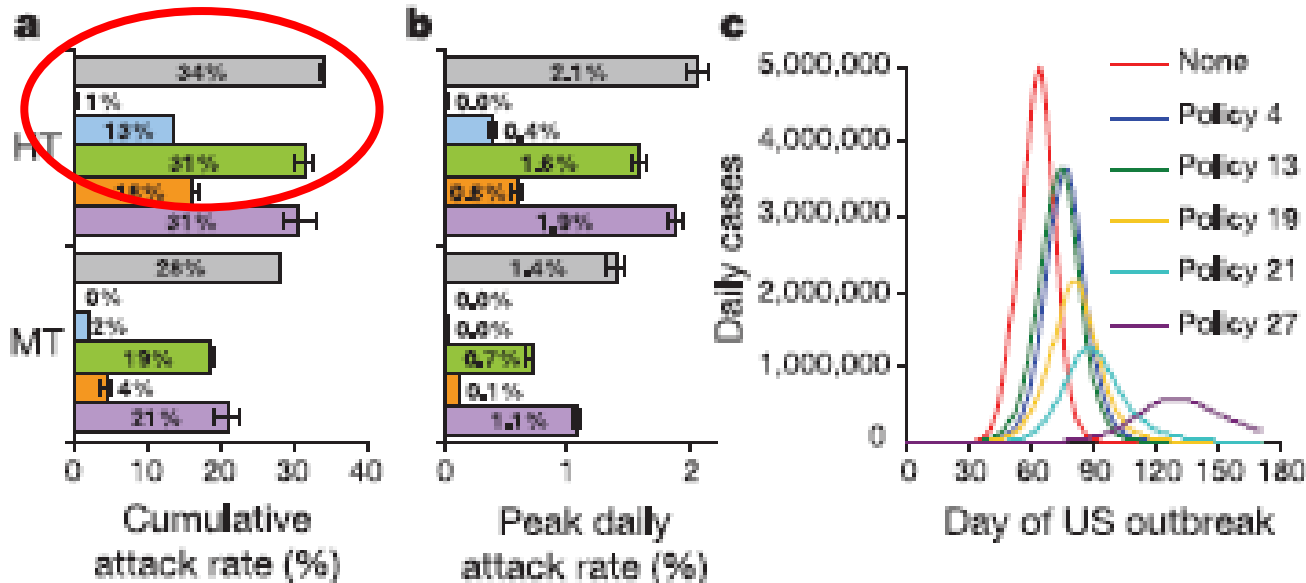
## ■ Prioritization

- High expected incidence if available before peak
- HR and 65+ if available later
- In line with reason
- In line with some other studies

# Strategies for mitigating an influenza pandemic

NATURE | Vol 442 | 27

Neil M. Ferguson<sup>1</sup>, Derek A. T. Cummings<sup>2</sup>, Christophe Fraser<sup>1</sup>, James C. Cajka<sup>3</sup>, Philip C. Cooley<sup>3</sup> & Donald S. Burke<sup>2</sup>



**Figure 4 | Impact of vaccination and combination strategies.** Results for the United States are shown. **a, b**, As Fig. 2a, b, but for a policy of mass vaccination assuming 1% of the population can be vaccinated per day from day 30 (red, second bar down), 60 (blue), 90 (green) after the first worldwide case, with 0–16 yr olds vaccinated first. Results for random (non-age prioritized) vaccination are also shown (orange), and for a policy of prioritizing those over 60 yr old (purple), both policies assuming that 1% of the population is vaccinated per day from day 60. Values in the absence of interventions are shown in grey. There is almost no effect of vaccination if started after 120 days. For comparison, the first US case is seen on day 47,

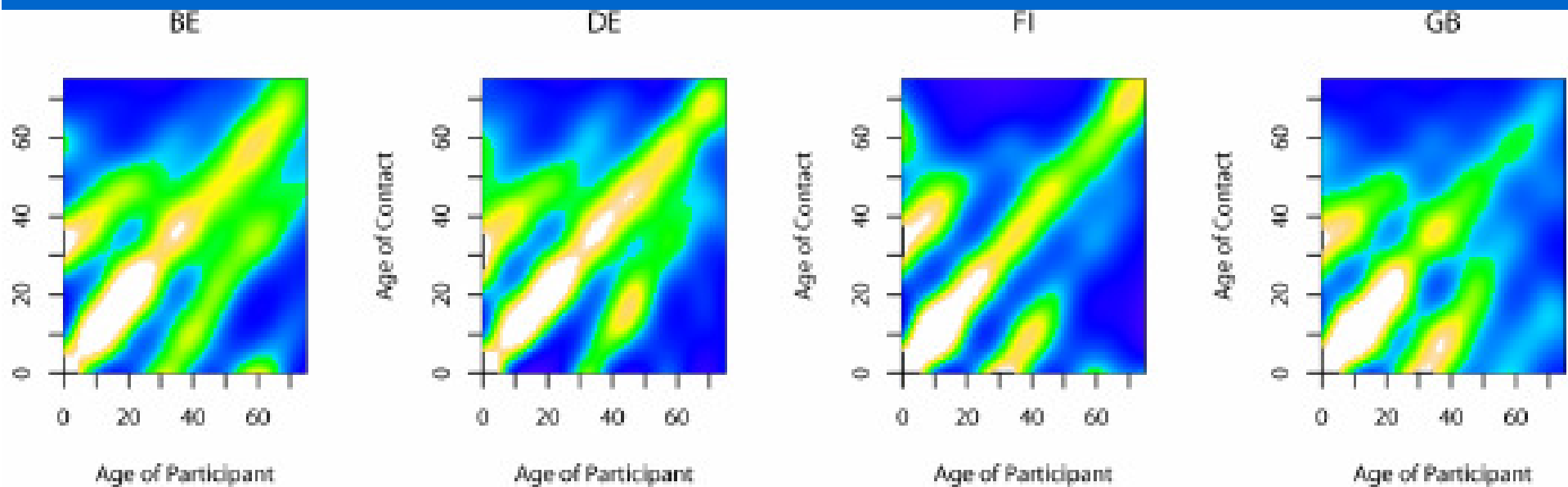
# IMPLICATIONS

## ■ Prioritization

- High expected incidence if available before peak
- HR and 65+ if available later
- In line with reason
- In line with some other studies

## ■ *Cost-effectiveness of Mylius et al/paper*

- ECHE Rome July 2008
- More countries
- Include stockpiling?
- Recent availability of contact patterns



## EU-POLYMOD Project

OPEN ACCESS Freely available online

PLOS MEDICINE

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

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

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## Containing Pandemic Influenza with Antiviral Agents

Ira M. Longini, Jr., M. Elizabeth Halloran, Azhar Nizam, and Yang Yang

From the Department of Biostatistics, The Rollins School of Public Health, Emory University, Atlanta, GA.

*Received for publication August 22, 2003; accepted for publication January 29, 2004.*

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For the first wave of pandemic influenza or a bioterrorist influenza attack, antiviral agents would be one of the few options to contain the epidemic in the United States until adequate supplies of vaccine were available. The authors use stochastic epidemic simulations to investigate the effectiveness of targeted antiviral prophylaxis to contain influenza. In this strategy, close contacts of suspected index influenza cases take antiviral agents prophylactically. The authors compare targeted antiviral prophylaxis with vaccination strategies. They model an influenza pandemic or bioterrorist attack for an agent similar to influenza A virus (H2N2) that caused the Asian influenza pandemic of 1957–1958. In the absence of intervention, the model predicts an influenza illness attack rate of 33% of the population (95% confidence interval (CI): 30, 37) and an influenza death rate of 0.58 deaths/1,000 persons (95% CI: 0.4, 0.8). With the use of targeted antiviral prophylaxis, if 80% of the exposed persons maintained prophylaxis for up to 8 weeks, the epidemic would be contained, and the model predicts a reduction to an illness attack rate of 2% (95% CI: 0.2, 16) and a death rate of 0.04 deaths/1,000 persons (95% CI: 0.0003, 0.25). Such antiviral prophylaxis is nearly as effective as vaccinating 80% of the population. Vaccinating 80% of the children aged less than 19 years is almost as effective as vaccinating 80% of the population. Targeted antiviral prophylaxis has potential as an effective measure for containing influenza until adequate quantities of vaccine are available.

American Journal of  
**EPIDEMIOLOGY**

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Bloomberg School of Public Health

# LONGINI ET AL

## ■ General

- Dynamic model
- Pre-pandemic vaccine
- $R_0=1.68$

## ■ Vaccination

- Of children vs. whole pop.
- In combination with stockpiling antivirals: treatment of index and TAP

## ■ Mortality

- 580 per million from 1957-58 pandemic
- 0.0580%

Table. Total NHS costs and QALY loss (discounted at 3.5%) resulting from an influenza pandemic occurring in 30 years assuming 1918 or 1957/69 CFR\*

Treatment program	Pandemic influenza cases (millions)	Pandemic influenza deaths (millions)	Discounted NHS costs (million £)	Discounted QALY loss (millions)	Incremental cost per QALY (£)
1918 scenario					
No intervention	15	0.344	113	2.23	
Treat only	15	0.236	1,361	1.56	1,861†
Test-treat	15	0.231	2,356	1.53	31,031‡
1957–69 scenario					
No intervention	15	0.044	113	0.395	
Treat only	15	0.030	1,361	0.303	13,668†
Test-treat	15	0.030	2,356	0.299	227,896‡

\*NHS, National Health Service; QALY, quality-adjusted life year; CFR, case-fatality ratio.

†Cost per QALY gained over no intervention program.

‡Cost per QALY gained over treat-only program.

## Cost-effectiveness of Antiviral Stockpiling and Near-Patient Testing for Potential Influenza Pandemic

M. Ruby Siddiqui\* and W. John Edmunds\*

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**TABLE 2. Simulated influenza case and death rates**

Intervention	Cases (no./1,000 persons)		Deaths (no./1,000 persons)	
	Mean	95% CI†	Mean	95% CI
None	334	297, 370	0.58	0.43, 0.75
80% targeted antiviral prophylaxis				
1 week	212	5, 265	0.33	0.01, 0.48
2 weeks	150	3, 238	0.23	0.00, 0.42
4 weeks	71	2, 204	0.11	0.00, 0.38
6 weeks	36	3, 182	0.06	0.00, 0.31
8 weeks	23	2, 162	0.04	0.00, 0.25
Vaccination (% of population)				
30	189	148, 231	0.25	0.14, 0.37
50	77	3, 134	0.08	0.00, 0.17
80	6	1, 20	0.01	0.00, 0.03
Vaccination (% of children)				
50	154	8, 227	0.28	0.01, 0.45
80	22	4, 62	0.05	0.00, 0.15

† Based on 200 simulations.

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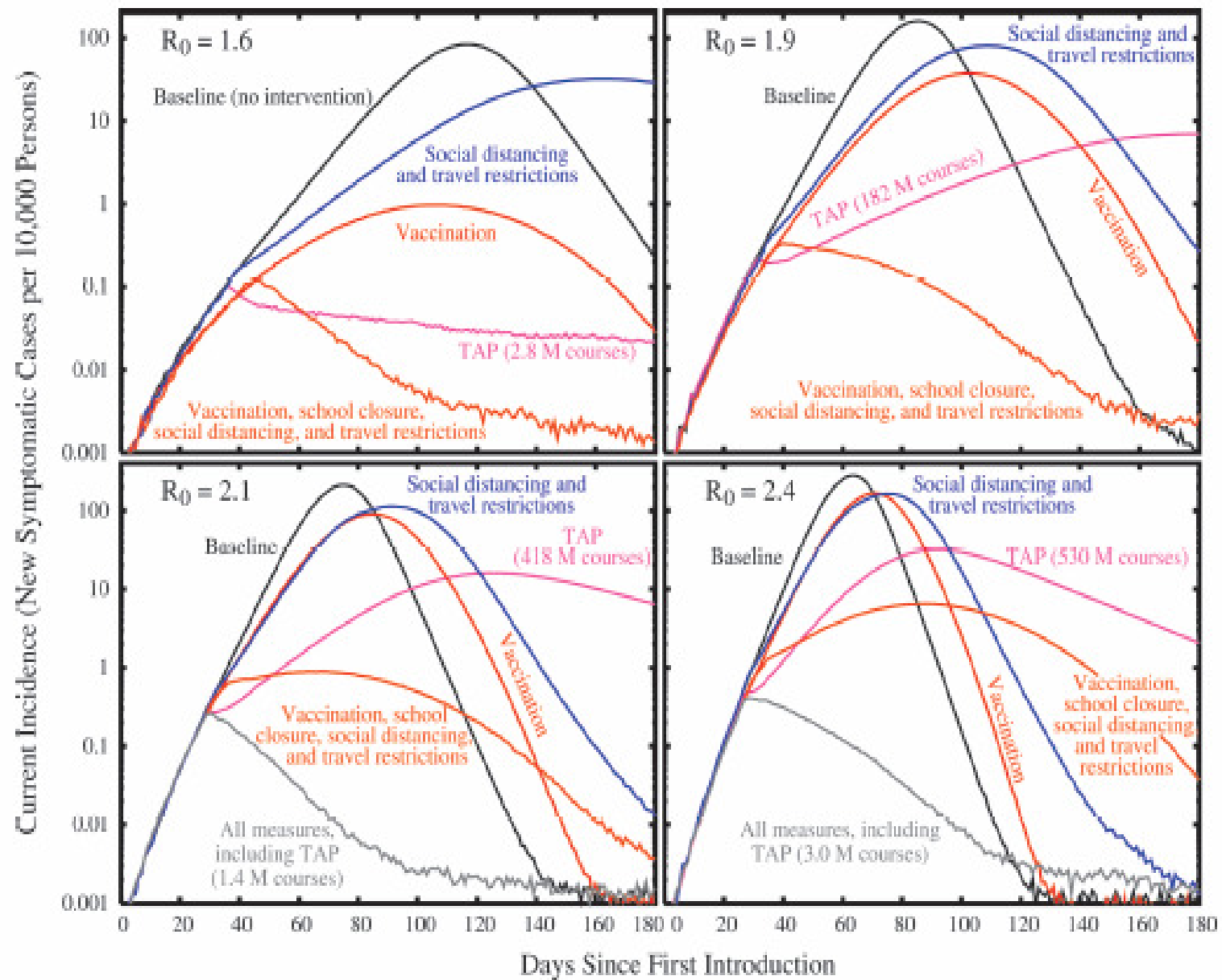
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# COST-EFFECTIVENESS

## ■ Cost-effectiveness

- Sander B, Nizam A, Garrison LP, Postma MJ, Halloran ME, Longini IM
- *Value in Health* accepted

## ■ Pre-vaccination

- Dominates do-nothing
- Dominates school closures alone if on top of school closure

## ■ TAP

- Also dominates do nothing
- At a lower ICER than pre-vaccination
- School closure combined with pre-vaccination provide more QALYs than TAP
- US\$51,000 / QALY

# COST-EFFECTIVENESS

- School closure
  - Involves high indirect costs
  - Some efficacy undisputed
  - Ferguson *et al*/paper advocating closure around peak

**BMC Public Health**



Research article

**Open Access**

**Estimating the costs of school closure for mitigating an influenza pandemic**

Md Z Sadique\*<sup>1,2</sup>, Elisabeth J Adams<sup>1</sup> and William J Edmunds<sup>1,2</sup>

# COST-EFFECTIVENESS ANALYSES

- *Meltzer et al*
  - Human capital method
  - 1999
- *Van Genugten et al*
  - Influenza & pneumococcal analysis
- *Siddiqui & Edmunds*
  - Antiviral stockpiling & near patient testing
- Static models

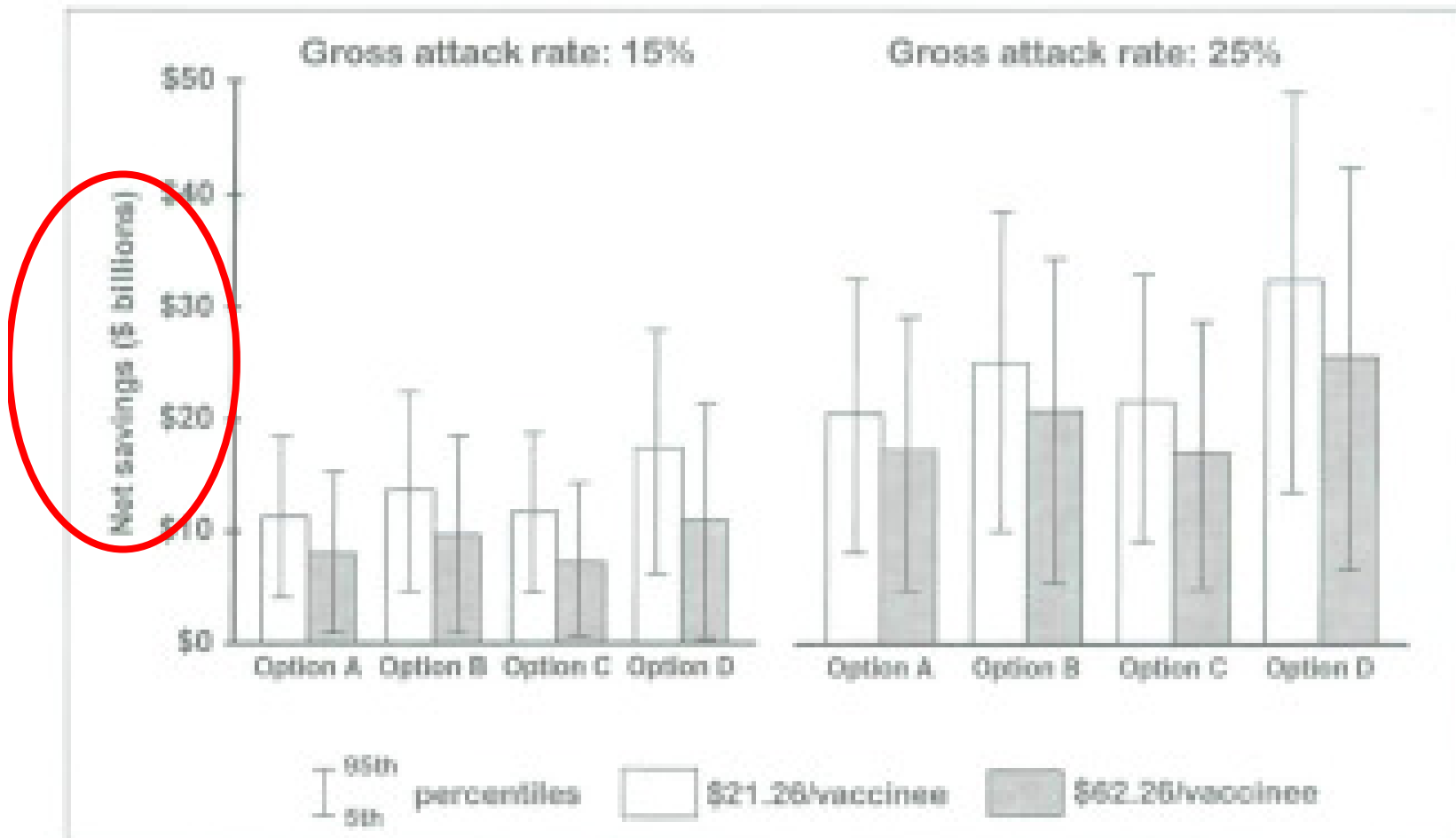


Figure 3: Four options for responding to an influenza pandemic: mean net economic returns. Notes: a) Bars show mean net returns for each option and assumed cost of vaccination. b) Option A: Similar to current Advisory Committee on Immunization Practices recommendations, with production and use similar to current, intra-pandemic recommendations (17). Assumed approximately 77 million vaccinees. Option B: Number of vaccinees as outlined in Scenario A plus 20 million essential service providers (5 million health-care workers + 15 million other service providers). Option C: Aim to achieve a 40% coverage of total U.S. population. Option D: Aim to achieve 60% coverage of total U.S. population (Appendix II).

# COST-EFFECTIVENESS ANALYSES

- *Meltzer et al*
  - Human capital method
  - 1999
- *Van Genugten et al*
  - Influenza & pneumococcal analysis
- *Siddiqui & Edmunds*
  - Antiviral stockpiling & near patient testing
- *Static models*

Table 3. Hospitalizations and deaths in the scenario analysis of influenza pandemic<sup>a</sup>

Scenario	No. of hospitalizations		
	Base case	Gross attack rate 10%	Gross attack rate 50%
Nonintervention	10,186	3,395	16,977
Influenza vaccination			
Total population	3,847	1,282	6,412
Risk groups	3,968	1,223	6,614
Pneumococcal vaccination	7,008	2,326	11,679
Neuraminidase inhibitors	5,093	1,698	8,489

<sup>a</sup>Assuming gross attack rates of 10% and 50%.

# DISCUSSION

- No ambition to comprise all studies
- Selected some for illustrative purposes
- Left out
  - Non-EU and non-US
  - Antivirals
  - Etcetera
- Abstracts/reports
  - Swiss Federal Office of Public Health
  - Influenza Vaccines for the World Conf

## "TAKE HOME"

- Certainly role for the vaccine in mitigating pandemic
- Of course
  - Efficacy is crucial
  - As early as possible
- Prioritizing
  - Early: those with expected high incidence
  - Late: those with high risk for complications
- Cost-effectiveness
  - Mortality uncertain but has profound impact on results
  - TAP considered as 1<sup>st</sup> choice
  - Vaccination does add and may be cost-effective
  - Combine with school closure
- Incremental analysis on antiviral stockpiles