H1N1pdm vaccination strategies: insights from modelling

Neil Ferguson

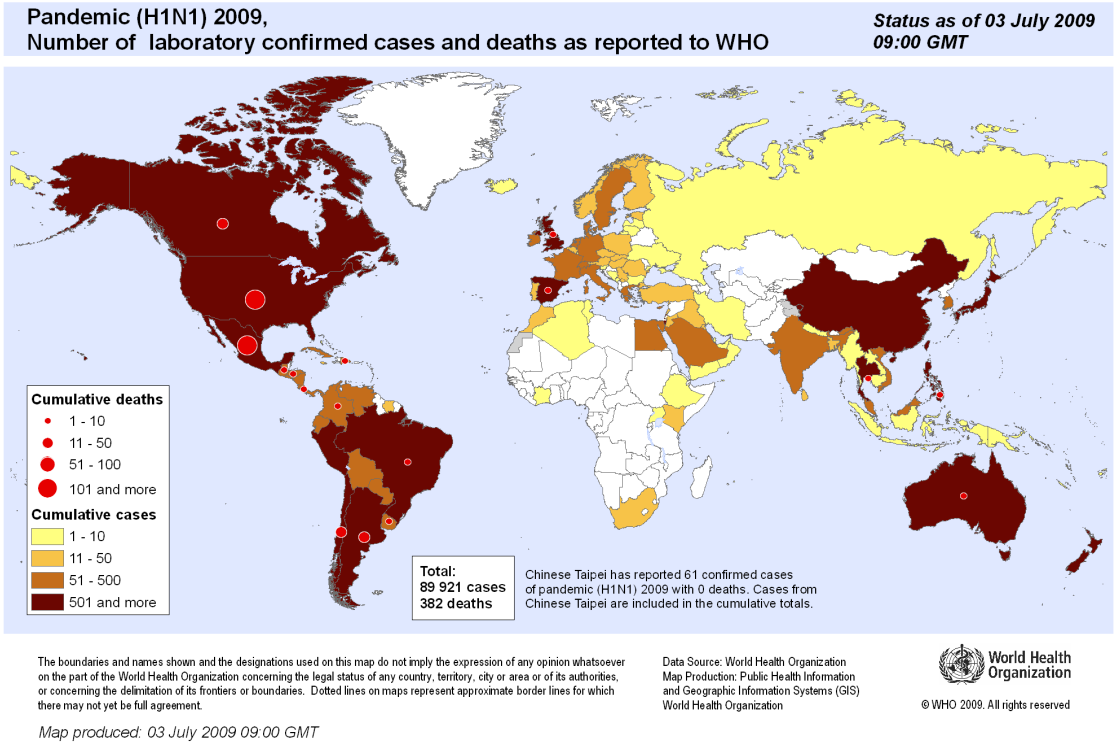
MRC Centre for Outbreak Analysis and Modelling
Imperial College London

Imperial College London

Key current issues

MRC Medical Research Council

- Severity of current pandemic:
  - What is likely health impact?
  - what interventions are justified/tolerable?
- Transmissibility:
  - How many have been infected so far?
  - How many (and who) will have been infected by the time vaccine is available?



Imperial College London

MRC Medical Research Council

The challenges in assessing severity

- Uncertain numerator (may be missing some deaths).
- Very uncertain denominator (surveillance missing large proportion of mild or asymptomatic infections).
- Lag between case onset (and report) and death.
- CFR for seasonal flu and 1957, 1968 pandemic also uncertain.
- Best guess – seasonal flu-like severity.
- But age groups affected v. different (so relative excess mortality may be higher).
- And severity in fall may differ…

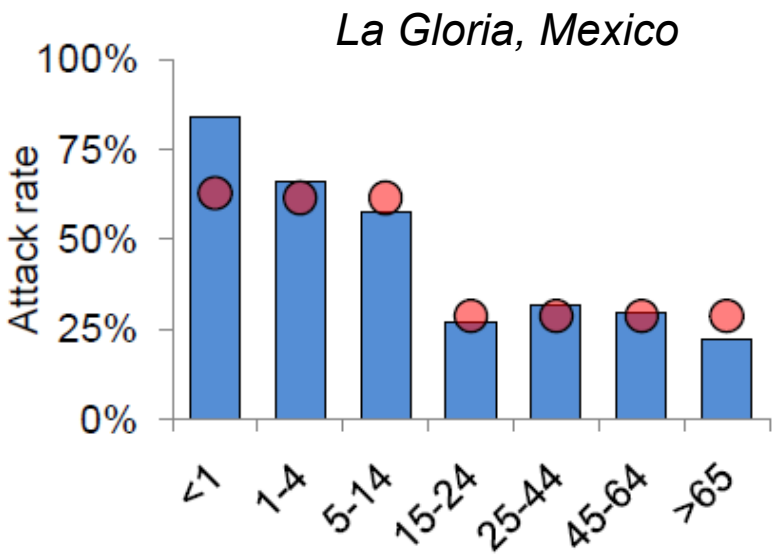
Decisions need to be made now, from available data, but on a precautionary basis

Imperial College London

MRC Medical Research Council

Who is most at risk?

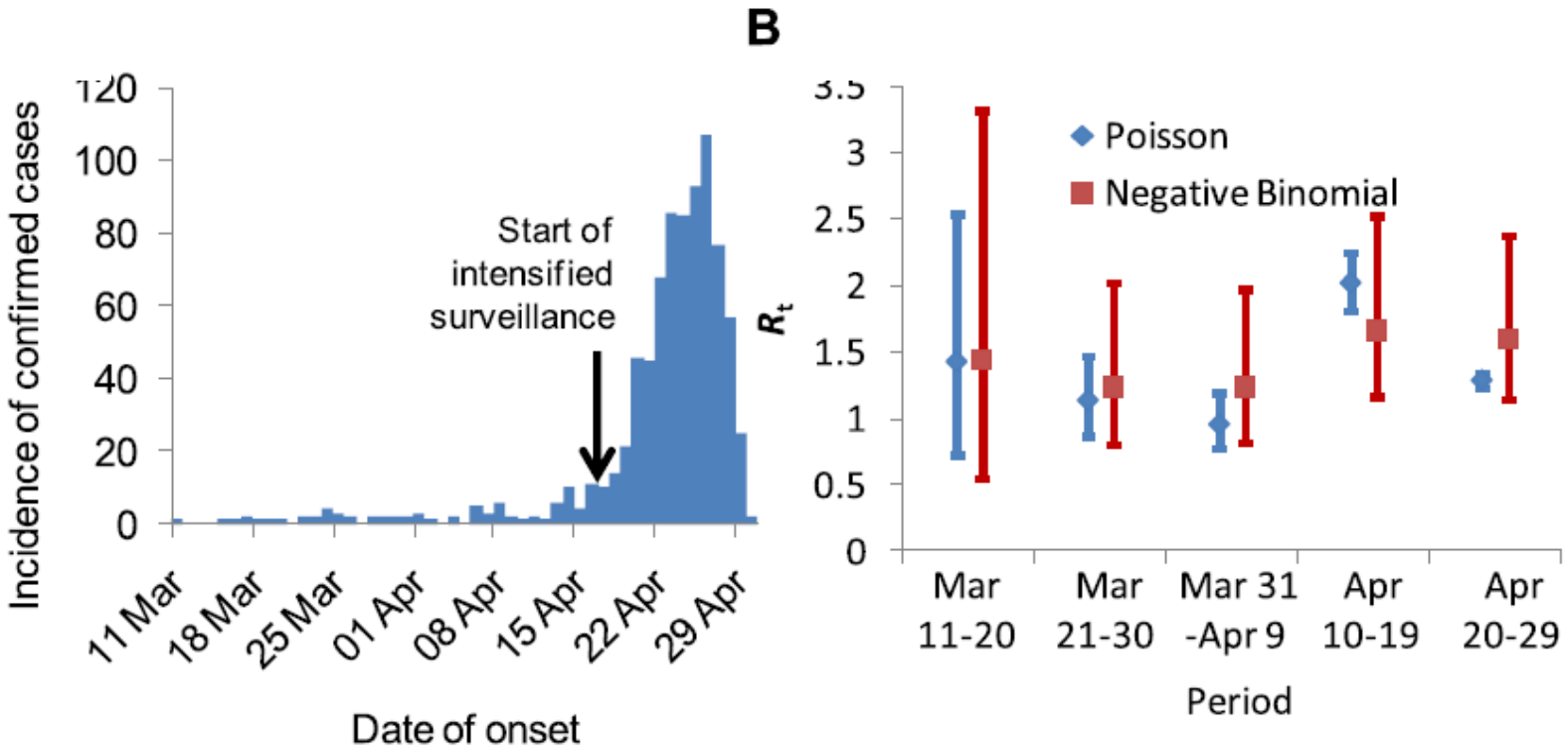
- Children are currently more at risk of getting infected (and probably transmit more).
- But illness nearly always mild.
- Most hospitalised cases are adults in the 20-50 age range.
- Elderly seem at low risk of hospitalisation.
- Majority of hospitalised cases have other health conditions – e.g. asthma.
- Data collected in the next few weeks will be critical to reduce uncertainty.



Imperial College London

R_0

MRC Medical Research Council



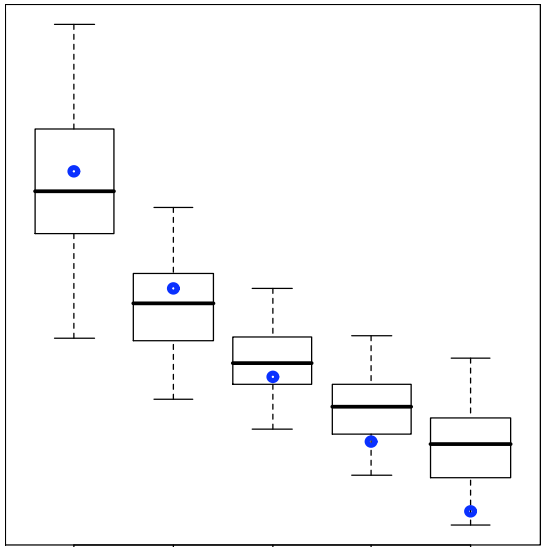
- **Mexico** - R_0=1.2-1.5 (95% Cr.I.:1.1-1.9) from 3 different approaches.
- **US** – difficult to evaluate, but perhaps 1.5-1.7 in late April.
- **UK** – 1.2-1.3 in June.
- **Chile & Argentina** – faster doubling time indicates 1.7+, but many uncertainties

Imperial College London

Analysis of household transmission in US

MRC Medical Research Council

- Collaboration with CDC (Lyn Finelli, Carrie Reed, Charlotte Kent , ...).
- Cases in household contacts more representative than index cases, due to ascertainment biases.
- 23% mean household contact secondary attack rate for ARI, 11% SAR for ILI - relatively low compared with previous pandemics.
- 2.7 day mean serial interval.
- Children (<18) >2-fold more susceptible than adults, under 5s more so.

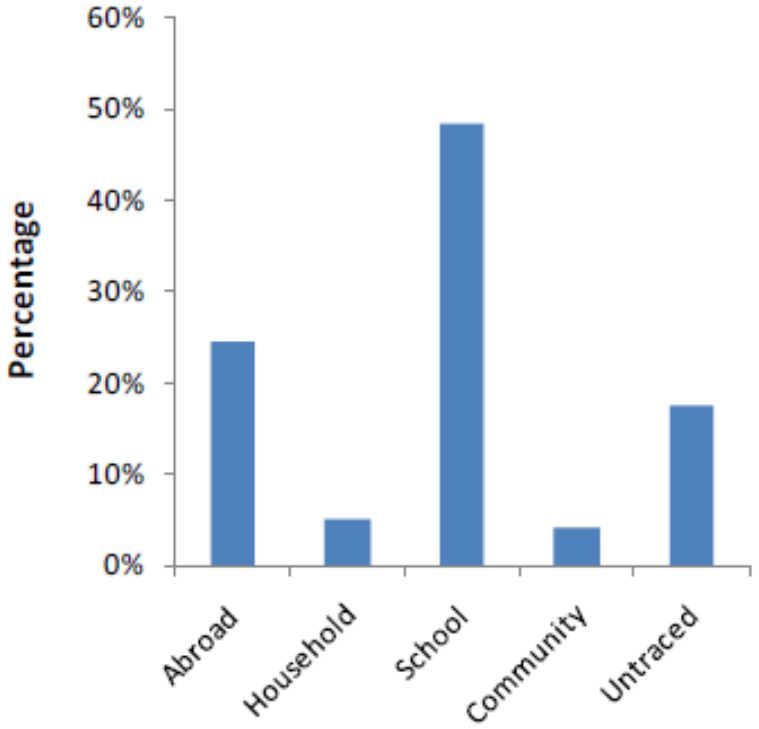


Imperial College London

Preliminary conclusions from UK

MRC Medical Research Council

- Household attack rates compatible with US estimates.
- Age-dependent patterns also similar.
- 3 day median serial interval in known index case-contact pairs.
- C-C transmission 2-fold larger than A-A, or A-C/C-A, with highly over-dispersed individual R.
- Significant reduction in illness in contacts from prophylaxis within 3 days of onset of index case (0% vs 13%).



Imperial College London

Vaccine strategy: country differences

MRC Medical Research Council

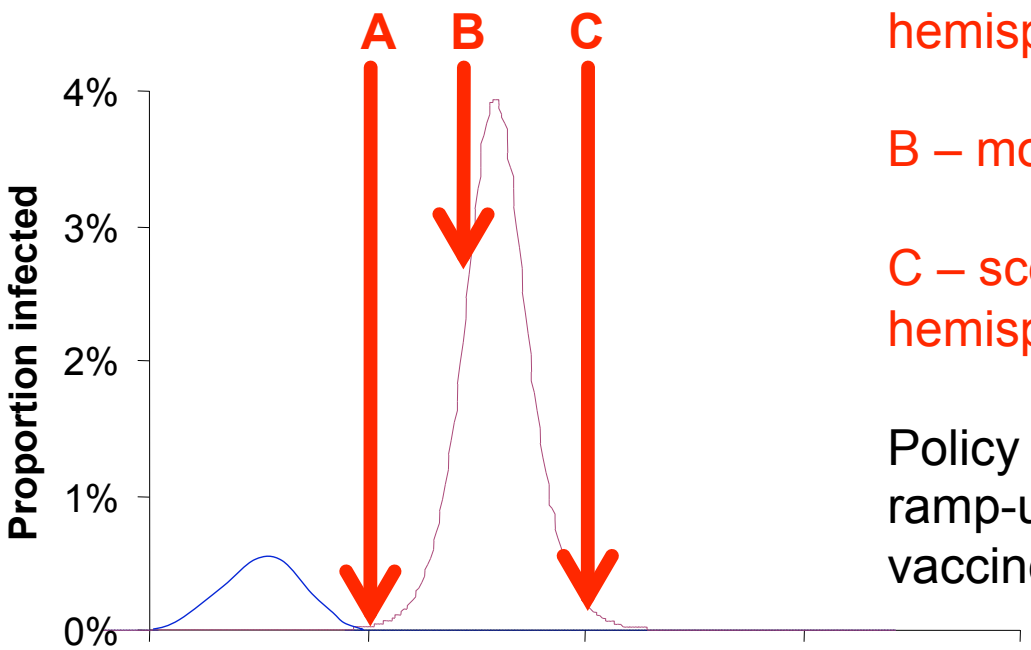
- Scale of vaccine delivery:
  - Large supplies early – target transmission?
  - Affects definition of risk groups, ability to vaccinate key workers.
- Timing of delivery relative to epidemic:
  - May affect prioritisation (HCWs/key workers, risk groups, key transmitters).
- Huge variation in capacity to delivery vaccine rapidly.
- And in availability of other countermeasures (e.g. antivirals).
- Universal guidance therefore probably not possible.

Imperial College London

Availability relative to epidemic timing

MRC Medical Research Council

- How does one best use vaccine in the face of a pandemic?
- If the main wave has passed, is it worth vaccinating? – perhaps, given only ~60% of population likely to be infected by then.



A – may be the situation in some N hemisphere develop countries.

B – more likely scenario, say in US.

C – scenario for many developing & S hemisphere countries.

Policy options also depend on scale of ramp-up and timescale over which vaccine order completed.

Imperial College London

Challenges of predicting impact of pandemic vaccines

MRC Medical Research Council

- Data from seasonal flu suggests protection against disease from matched vaccine will be high.
- Proxy immunological measures from trials do not give estimates of 3 key efficacy parameters:
  - ➢ Extent of true protection against infection given exposure (=reduction in susceptibility).
  - ➢ Therapeutic benefit (reduction in morbidity or mortality) for individuals who still get infected.
  - ➢ Epidemiological benefit – reduction in infectiousness for vaccinated individuals who still get infected.
- Breadth of response may also be important- adjuvant may help here.
- Response after one dose?

Modelling of vaccine strategies ongoing – results in next few weeks

Imperial College London

Summary

MRC Medical Research Council

- More questions than answers.
- Children more susceptible, contribute more to transmission.
- But overall risk of severe outcomes appears low, with most hospitalised cases have known risk factors.
- Modelling is looking at likely impact of a finite supply of vaccine targeted in a specific way (e.g. risk groups, children then adults).
- Results may be indicative of likely benefit - but prediction very difficult:
  - Timing of pandemic wave
  - Effectiveness of 1 vs 2 doses.
  - ...