Use of epidemic models in planning pandemic mitigation

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Introduction

- Modelling epidemic control – background.
- Likely timescale of a US pandemic.
- Pandemic mitigation.
- Combining measures.
- Conclusions about TLC.
Outbreak analysis & modelling: past examples

• SARS 2003 – estimates of transmissibility (R~3) and mortality (~15%).

• Smallpox modelling – mass vs ‘ring’ vaccination.

1. Containing the initial outbreak.

2. Slowing international spread.

3. Local mitigation:
   - Minimizing mortality/morbidity.
   - Slowing spread until vaccine avail.
   - Preserving societal resilience.
   - Minimizing economic impact.

_key question – is local control possible_?
Possible control measures

1. Vaccines – but take time to make.
3. Case isolation.
4. Household quarantine.
5. ‘Social distancing’ – e.g. school closure.
6. Infection control measures (e.g, masks).
7. Travel restrictions.

Controls need to be combined for best effect
What do we need to know to predict the effect of controls

• Overall, the effect of policies aiming to reduce transmission is (imperfectly) captured by their impact on $R_0$.

• Controls typically target one social context (e.g. households, schools etc), though effects may spill over (e.g. closing schools increases contacts elsewhere):
  ➢ Need to know (from data) how much transmission occurs in different social contexts (e.g. households, schools, workplaces, ‘community’).
  ➢ But only know split between households and ‘the rest’ (until now).

• Need to know how much transmission is reduced by a control in each context:
  ➢ Often easy to get an upper bound (= all transmission blocked).
  ➢ But what is likely compliance?
  ➢ And what are likely compensatory effects?
The reverse problem is more common – e.g. what is the impact of masks on community transmission? (Answer: we don’t know).

But for TLC, MIDAS groups asked to model arbitrary 50% reductions in transmission parameters, which were labelled ‘workplace social distancing’ and ‘generic social distancing’.

This is specifying a control by its effect on $R_0$. Not the same as modelling the mechanism of control (e.g. 50% workplace absenteeism).

Such reductions in transmission are, unsurprisingly, very effective control measures. But what practical measures can be employed to deliver such reductions, and what the evidence for their effectiveness?

Modelling cannot really address this issue – need data from past epidemics.
Simple vs complex models

- If we knew the effect of controls on $R_0$, then we do not need a (complex) model to say whether a particular combination of controls – such as TLC – will control transmission (i.e. achieve $R_0<1$).

- If $R_0<1$, then attack rates will be very low (depends on timing of policy start).

- Models allow one to be more quantitative – especially in estimating the impact of imperfect controls ($R_0$ reduced, but not to <1).

- Complex models (i.e. simulations or agent-based models) allow more ‘realistic detail’ (timing, logistics, behaviour etc) to be explored...

- …but the more complex the model, the more assumption-laden and difficult to validate.

- If simple and complex models agree, gives a degree of confidence!
• Computer simulation (up to 300 million people).

• Individuals reside in **households**, but go to **school** or a **workplace** during the day.

• Transmission specified separately for households and different place types.

• **Local movement/travel**: random contact between strangers, at a rate which depends on distance.

• **Air travel** incorporated.
Assumptions about transmission

• All the TLC models include households, schools, workplaces and community transmission.

• But the parameters governing the balance of school, workplace and community transmission are assumed – not estimated.

• Certain constraints from data exist (e.g. age-specific case incidence in past pandemics), but these do not allow school transmission rates to be estimated.

• Different assumptions about the importance of school/child transmission have been made in the models: Glass > Longini > Eubank > Ferguson.
Transmission parameters

• For US, estimated that 30% of transmission in a pandemic would be in the household.

• 33% then assumed to occur in schools and workplaces. Transmission coefficient in schools 2-fold larger than in workplaces.

• Distances between schools/workplaces and homes matched to data.

• 37% of transmission assumed to occur in the ‘community’.

• Community transmission is random, but localised – governed by a probability distribution of contact as a function of distance (=spatial kernel).

• Kernel parameterised to match data on journey distances.

• No modelling of other social contexts, due to lack of data on transmission.
Country-specific data

Using a data on all schools in US, plus data on workplace size/location.

- Data
- Model

Frequency vs. Size

Distance (km) vs. Probability

Number of workers vs. Workplace size category

Number of workers vs. Probability

Fit of Zipf model

Data vs. Model

Distance (km) vs. Probability
Influenza biology and treatment

- Analysis of best available data on pandemic and inter-pandemic flu.
- Short incubation period – 1-2 days.
- People most infectious very soon after symptoms.
- Antiviral drugs reduce symptoms and infectiousness (params as Longini)…
- …but also can be used in uninfected people to reduce chance of being infected (=prophylaxis).
Model validation

• Validation difficult – no pandemic for 40 years.
• Try and match past pandemics’ rate of spread, proportion affected etc.
• But data limited.
• Key result: $R_0$ for pandemic flu in 1.5-2.0 range.
• Also match to household study data.
Some uncertainties

- Nature of virus (avian- or human-like) – affects natural history and perhaps transmissibility.
- Proportion of transmission occurring in home, school, workplace, hospital, etc.
- Lethality/risk groups for severe illness.
- Effectiveness of ‘social distance measures’ and population compliance.
- Behaviour of population.
- Quality and timeliness of surveillance (ascertainment).
- Logistic constraints.
- .....
A US pandemic

- Large urban centres affected first, followed by spread to less densely populated areas.

\[ R_0 = 2.0/1.7 \]

Model parameterised with detailed data on US population

Up to 12% absenteeism at peak
If containment fails: global spread

- How fast, would travel restrictions have an effect?
• 80% drop in travel to affected countries seen in SARS epidemic – mostly spontaneous.

• Key problem – growth rate of flu pandemic – 10 fold in 7-14 days

• So stopping 90% of infections buys 1-2 weeks, 99% buys 2-4 weeks.

• So restrictions need to be >99% effective to buy significant time.
Masks/hygiene measures

No real data on effectiveness at a population level.
Mitigation strategies: conclusions from modelling

**Treatment**
Needs to be fast (within 12-24h of symptoms) to be very clinically effective, but then can also reduce infectiousness (and thus attack rates by ~1/8).

**Prophylaxis**
Treating everyone in household rather than just first case, can reduce illness rates by >1/3, but need ~50% stockpile.

**School closure**
Main effect is to reduce peak height (by ~40%), not total numbers infected.

**Vaccination**
Need to stockpile in advance – despite strain selection being a gamble. 20% stockpile of 30% efficacy vaccine targeted at kids could reduce total illness rates by 1/3.
Targeting measures

• Unclear whether super-spreaders exist for flu – and SARS tells us they would be difficult to target.

• Children more infectious - 2-fold more in households, but their contribution to transmission in schools and the community is unknown.

• Measures targeting different social contexts are additive in effect on $R_0$, while measures targeting same context can be antagonistic.

• Effect on attack rates always greater than reduction in $R_0$ – esp. close to $R_0=1$.

• Targeting in pandemic flu mitigation really involves moving down the hierarchy:

  ➢ case -> household -> school -> workplace -> community
Combinations of measures

- Nature paper looked at ~30 combinations of measures (see Supp Info.).
- Nearly all involved medical/pharmaceutical interventions.
- Combinations largely/entirely reliant on non-pharmaceutical interventions not examined, due to lack of data on effectiveness.
- Tightly defined ‘TLC’ scenario modelling commissioned early 2006.
- Nature paper had examined all TLC components in isolation and combination – except keeping children at home and generic and workplace ‘social distancing’.
- Conclusions: At $R_0=1.9$, TLC could achieve control ($R_0<1$, attack rate<4%), but only with >=50% social distancing and effective school closure (including 60% of households with children isolating children in the home).
Possible UK policy

Treatment of diagnosed cases
Cases stay home
Prophylaxis of household contacts
School closure
Pre-vaccination (stockpiling of H5N1 vaccine).

- Most reliance on pharmaceutical (inc. vaccine) interventions, less on social distancing.

- Backed by >>25% oseltamivir stockpile+large H5N1 vaccine stockpile.

- Modelling shows 66->90% reduction in attack rates. 1/3 reduction in attack rates even if not all arms of policy succeed.

- Key issues: Vaccine match, drug resistance, drug delivery.
Targeted layered containment

• UK policy minus vaccine, plus **household quarantine**, **keeping children home**, generic/workplace social distancing.

• Requirement for policy to achieve $R_0 \approx 1$, else stocks of antivirals insufficient.

• Policy achieves low (<4%) attack rates if:
  
  ➢ triggered early enough – i.e. before local attack rate reaches 1%.
  ➢ school closure has at least the effect predicted in my Nature paper.
  ➢ isolation of children in the home for the duration of the epidemic is possible with >50% of households complying.
  ➢ substantial reductions in community/workplace contact rates possible via ‘generic/workplace’ social distancing.
TLC: conclusions

• Bold and ambitious strategy – but essential to give realistic assessment of requirements for success, likely cost and policy robustness.

• To be a robust strategy, need:

  ➢ evidence of likely effectiveness of school closure.
  ➢ data on likely compliance with ‘voluntary’ NPIs for several months.
  ➢ evidence-based policies for achieving workplace/generic social distancing.
  ➢ logistics/stockpiles/pre-planning to support indirect effects of policy (e.g. liberal leave, childcare/nutrition, economic costs).
  ➢ policy designed to be ‘failsafe’ – i.e. stockpiles/public health resources sufficient to cope with 10-20%+ attack rates.
  ➢ consensus as to who pays – county/state/federal/business – both for implementation and indirect costs.
  ➢ consensus as to how severe a pandemic needs to be to invoke TLC.
This talk has sounded a cautious note.

Critical that TLC is not seen as an alternative to substantial antiviral/vaccine stockpiles.

BUT – faced with a 2%-30+% mortality pandemic, most countries would end up considering extreme public health measures, almost irrespective of likely success or economic cost.

Much better that the debate around the likely effectiveness of such measures happens now – and that implications thought through.

Pre-planning can only be positive.

But critical that we are honest with the public about the requirements and chances of success.

Building trust absolutely key – in the worst case, people will sacrifice a lot, so long as communication is clear and non-politicised.
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