Issues with prevailing COVID-19 impact models and considerations for policy

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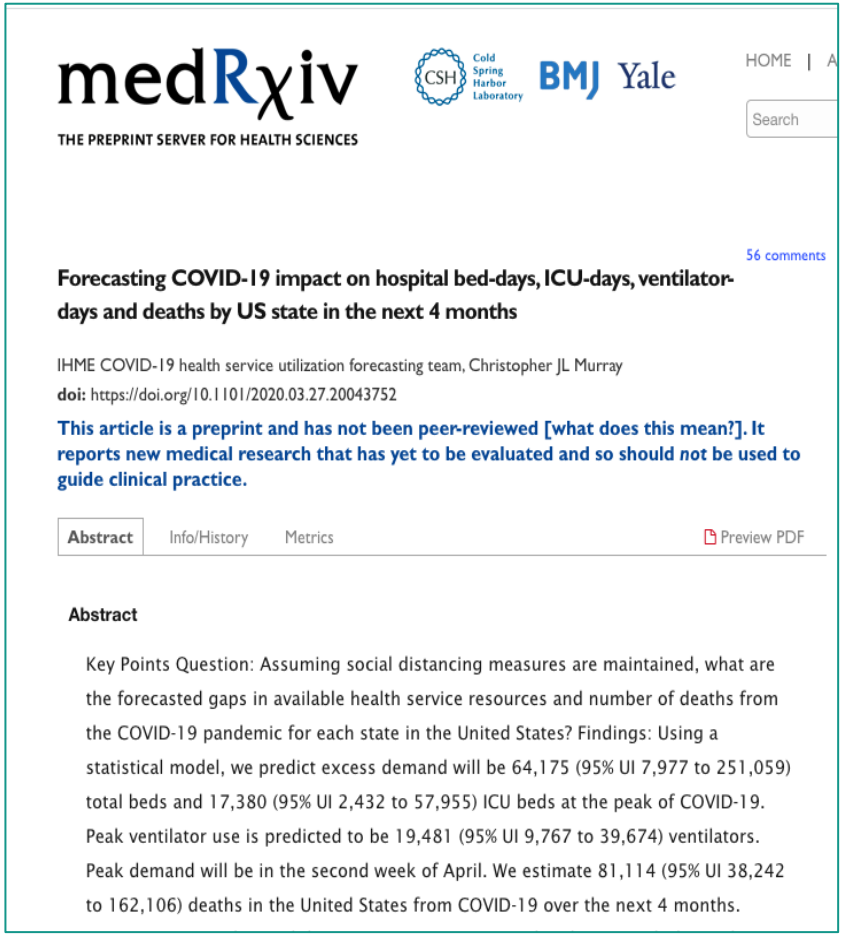
Key global updates – what has changed – a review of the evidence

- Downward revision of infection fatality rate
  - Lack of understanding of true denominator.
  - Frequently report based on those testing positive or cases presenting to hospital not population infection, much of which is believed to be asymptomatic.
- Upward revision in estimates of speed of infection (Re)
  - Originally considered 2.5 now up to 5.7.
  - Model includes ranges from 2.5 to 3.7
  - Suggests in contexts where population mixes the rates of underlying infection could be much higher than previously assumed (e.g. NYC may already have 40% infection)
- Objective of lockdown strategy unclear
  - "Flatten the curve" to prepare hospitals
  - In some settings "early" lockdown appears to have slowed spread, however, this may only delay fatalities
  - Vaccine development timeline estimated at 18 months
  - In high prevalence settings may have caused a mini-spike?

Current projections for most countries based on two dominant models



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Forecasting COVID-19 impact on hospital bed-days, ICU-days, ventilator-days and deaths by US state in the next 4 months

IHME COVID-19 health service utilization forecasting team, Christopher JL Murray

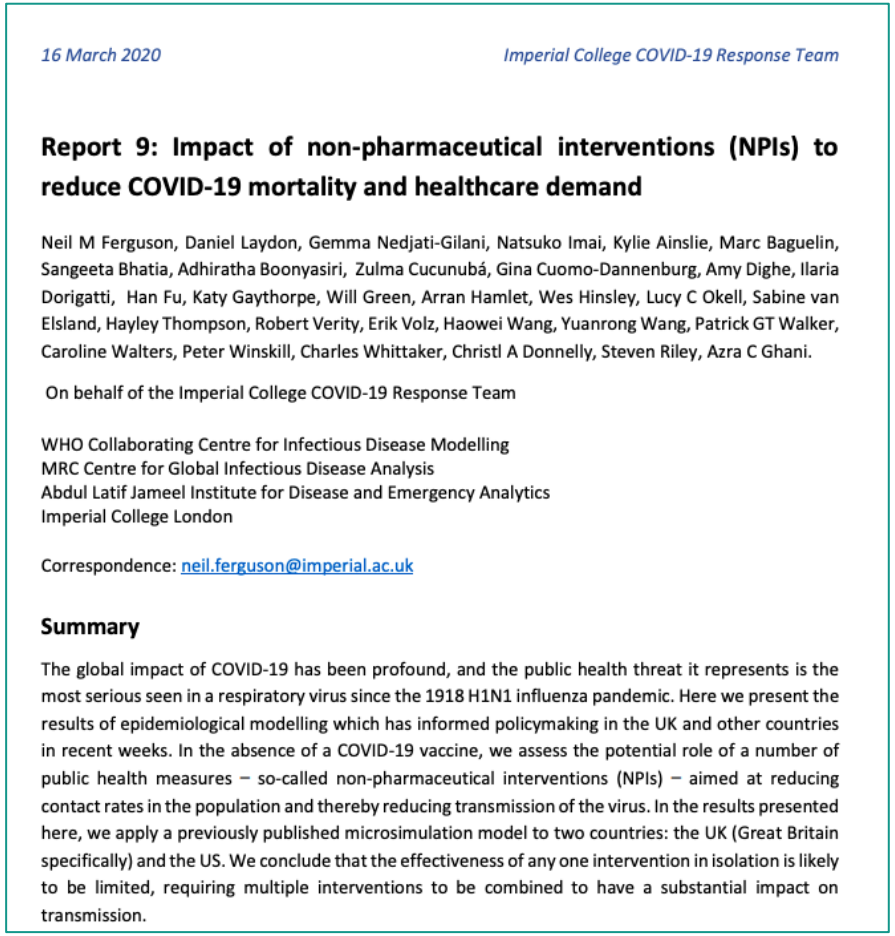
doi: https://doi.org/10.1101/2020.03.27.20043752

This article is a preprint and has not been peer-reviewed [what does this mean?]. It reports new medical research that has yet to be evaluated and so should *not* be used to guide clinical practice.

Abstract | Info/History | Metrics | Preview PDF

Abstract

Key Points Question: Assuming social distancing measures are maintained, what are the forecasted gaps in available health service resources and number of deaths from the COVID-19 pandemic for each state in the United States? Findings: Using a statistical model, we predict excess demand will be 64,175 (95% UI 7,977 to 251,059) total beds and 17,380 (95% UI 2,432 to 57,955) ICU beds at the peak of COVID-19. Peak ventilator use is predicted to be 19,481 (95% UI 9,767 to 39,674) ventilators. Peak demand will be in the second week of April. We estimate 81,114 (95% UI 38,242 to 162,106) deaths in the United States from COVID-19 over the next 4 months.



16 March 2020 *Imperial College COVID-19 Response Team*

Report 9: Impact of non-pharmaceutical interventions (NPIs) to reduce COVID-19 mortality and healthcare demand

Neil M Ferguson, Daniel Laydon, Gemma Nedjati-Gilani, Natsuko Imai, Kylie Ainslie, Marc Baguelin, Sangeeta Bhatia, Adhiratha Boonyasiri, Zulma Cucunubá, Gina Cuomo-Dannenburg, Amy Dighe, Ilaria Dorigatti, Han Fu, Katy Gaythorpe, Will Green, Arran Hamlet, Wes Hinsley, Lucy C Okell, Sabine van Elsland, Hayley Thompson, Robert Verity, Erik Volz, Haowei Wang, Yuanrong Wang, Patrick GT Walker, Caroline Walters, Peter Winskill, Charles Whittaker, Christl A Donnelly, Steven Riley, Azra C Ghani.

On behalf of the Imperial College COVID-19 Response Team

WHO Collaborating Centre for Infectious Disease Modelling
MRC Centre for Global Infectious Disease Analysis
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Summary

The global impact of COVID-19 has been profound, and the public health threat it represents is the most serious seen in a respiratory virus since the 1918 H1N1 influenza pandemic. Here we present the results of epidemiological modelling which has informed policymaking in the UK and other countries in recent weeks. In the absence of a COVID-19 vaccine, we assess the potential role of a number of public health measures – so-called non-pharmaceutical interventions (NPIs) – aimed at reducing contact rates in the population and thereby reducing transmission of the virus. In the results presented here, we apply a previously published microsimulation model to two countries: the UK (Great Britain specifically) and the US. We conclude that the effectiveness of any one intervention in isolation is likely to be limited, requiring multiple interventions to be combined to have a substantial impact on transmission.

Institute for Health Metrics and Evaluation. COVID-19 Projections. https://covid19.healthdata.org/projections. Published April 5, 2020. Accessed April 6, 2020.
Ferguson NM, Laydon D, Nedjati-Gilani G, Imai N, et al. *Imperial College COVID-19 Response Team. Impact of Non-Pharmaceutical Interventions (NPIs) to Reduce COVID19 Mortality and Healthcare Demand.*; 2020. https://www.imperial.ac.uk/media/imperial-college/medicine/sph/ide/gida-fellowships/Imperial-College-COVID19-NPI-modelling-16-03-2020.pdf.

Summary of models

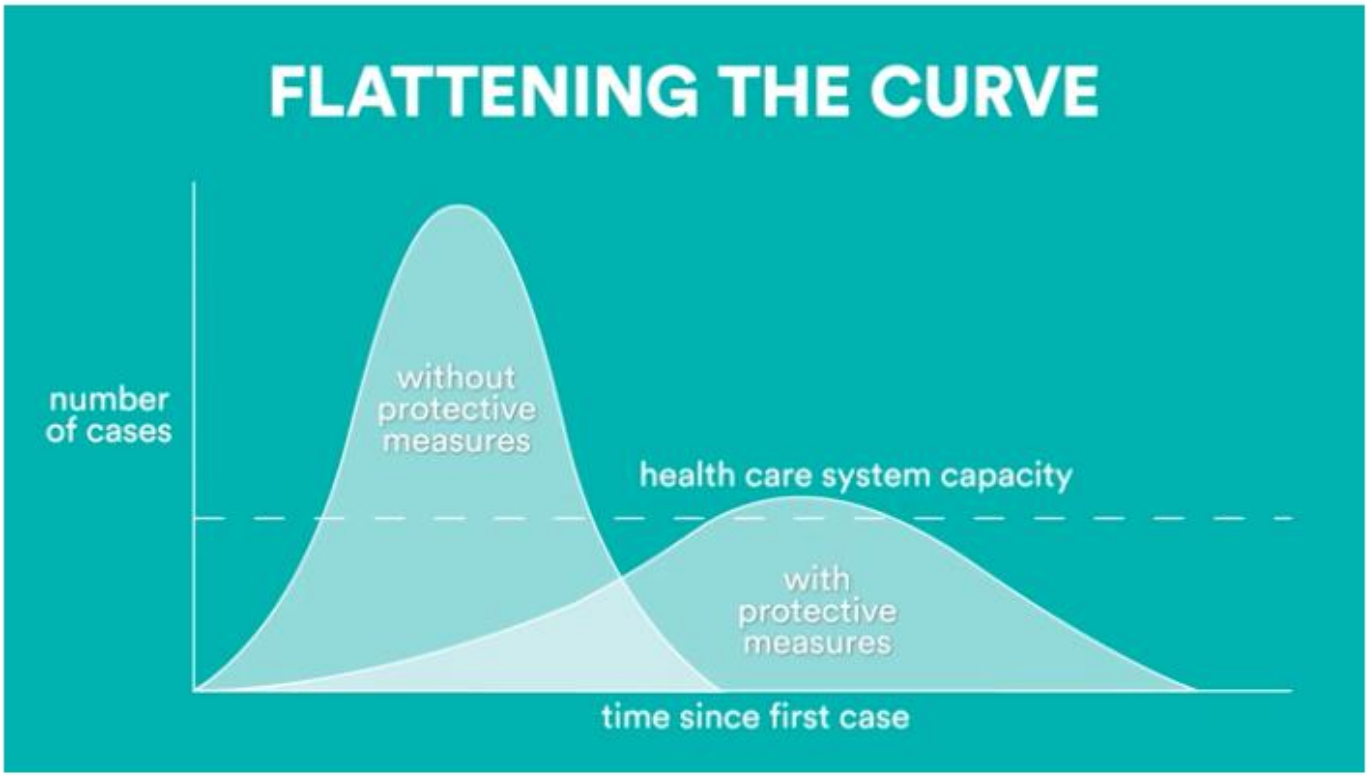
IHME

- Modelled Wuhan on rest of world
- Picture of what happened in Wuhan and says every outbreak will look like Wuhan. Therefore if we have certain number to day can project it out if it follows shape in Wuhan.
- ”Curve fitting tool” – not a dynamic model

Imperial college

- Picked up hotspots and extrapolated them
- Also assumption that larger fraction than people infected will come to hospital.
- Classic dynamic model - short comings of that class
- Potential for getting big numbers wrong (fraction requiring hospitalization/die)
- What to use as initial trajectory – homogeneity applied to heterogeneity – hot spots drove early epidemic modeling – but hotspots were in areas with underlying conditions

Strategies focus on "bending the curve" to preserve hospital capacity



Source: Carl Bergstrom, UW & Esther Kim
ALEX HOGAN/STAT

https://www.statnews.com/2020/03/11/flattening-curve-coronavirus/

Prevalence of certain conditions affect morbidity and mortality

US - CDC

High-Risk Conditions

COVID-19 is a new disease and there is limited information regarding risk factors for severe disease. Based on current available information and clinical expertise, **older adults** and **people of any age who have serious underlying medical conditions** might be at higher risk for severe illness from COVID-19.

Based upon available information to date, those at high-risk for severe illness from COVID-19 include:

- People 65 years and older
- People who live in a nursing home or long-term care facility

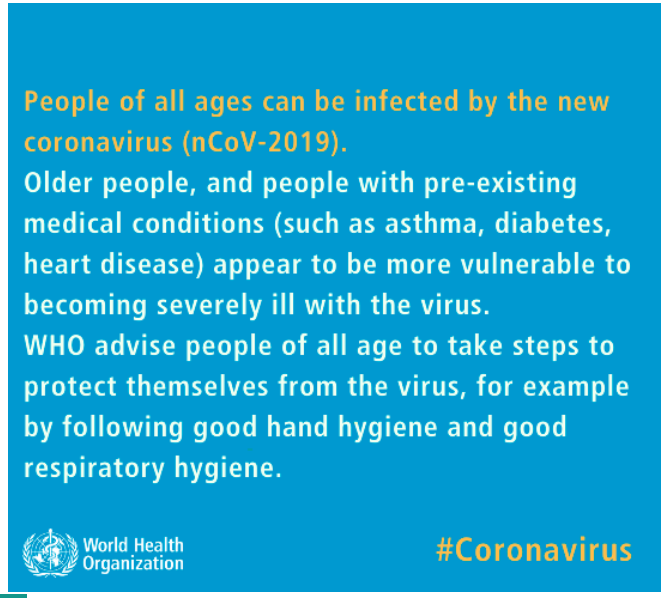
People of all ages with underlying medical conditions, particularly if not well controlled, including

- People with chronic lung disease or moderate to severe asthma
- People who have serious heart conditions
- People who are immunocompromised
  - Many conditions can cause a person to be immunocompromised, including cancer treatment, smoking, bone marrow or organ transplantation, immune deficiencies, poorly controlled HIV or AIDS, and prolonged use of corticosteroids and other immune weakening medications.
- People with severe obesity (body mass index [BMI] of 40 or higher)
- People with diabetes
- People with chronic kidney disease undergoing dialysis
- People with liver disease

https://www.cdc.gov/coronavirus/2019-ncov/hcp/underlying-conditions.html

In NYC, preliminary data show obesity has more significant impact than diabetes for ages 40 to 65

WHO



https://www.who.int/images/default-source/health-topics/coronavirus/myth-busters/mythbuster-2.png

Note: Recent Lancet study show that asthma and chronic lung data **are not risk factors,** despite mention by CDC and WHO. Scientific literature likely more up to date than CDC or WHO

Issue with dominant model projections

- Do not consider real-life conditions under which the virus transmits or heterogeneity of those conditions
  - In NYC, virus hits earliest and hardest in low income communities with medically vulnerable households (Queens and the Bronx). Still exploring potential explanations.
  - Incorrectly read these "signals" as representative of the entire City and assume rapid local onset of infection is actually occurring across the population as a whole.
  - Leads to erroneously high estimates of future infection.
- Do not correctly account for the number of already infected persons.
  - Much of the population it models as "virus naïve" may have already been infected with asymptomatic (totally subclinical) or mildly symptomatic (non-hospitalized) presentations.
  - As such they may overestimate the pool of people who remain susceptible, again contributing to overly large projections of future cases.
- Do not provide uncertainty ranges
- Have not been peer-reviewed
- Are focused on a single output (COVID deaths)
  - Do not consider morbidity or mortality which may happen as result of interventions proposed

Issue with proposed mitigation strategies

- Based on very limited evidence
  - Effect size of these measures are based primarily on modeling assumptions and early and rapid Cochraine review
- Make assumptions about effectiveness of proposed strategies and respective effect on transmission (e.g. school closures, social distancing).
  - Strategies have never been systematically evaluated
  - "Effect size" based on assumptions around reducing contact (and thus reducing spread) rather than evidence of effectiveness
- Do not consider other health affects of proposed interventions
  - Economic depravity (determinant of health)
  - Affects on education (determinant of health)
  - Violence, mental health, morbidity/mortality from shift in other care seeking behaviors

A new approach to modeling – the CoMO collaborative

- Shell that can be adapted based on real-time data
  - Template can be adapted as evidence changes
  - Easy to use interface that allows for "guesstimates" and input of local conditions" (e.g. ICU beds that can provide oxygen, hydration and meds)
- Calibrates curve based on start of epidemic and reported deaths.
  - Not clear in what direction this affects project
- Accounts for previous infections, so not based on endless pool of "infectables"
- Explicit about assumptions and evidence base
  - Updated daily by team at Oxford with latest inputs.
  - Currently developing background paper which documents assumptions.

https://comomodel.net/

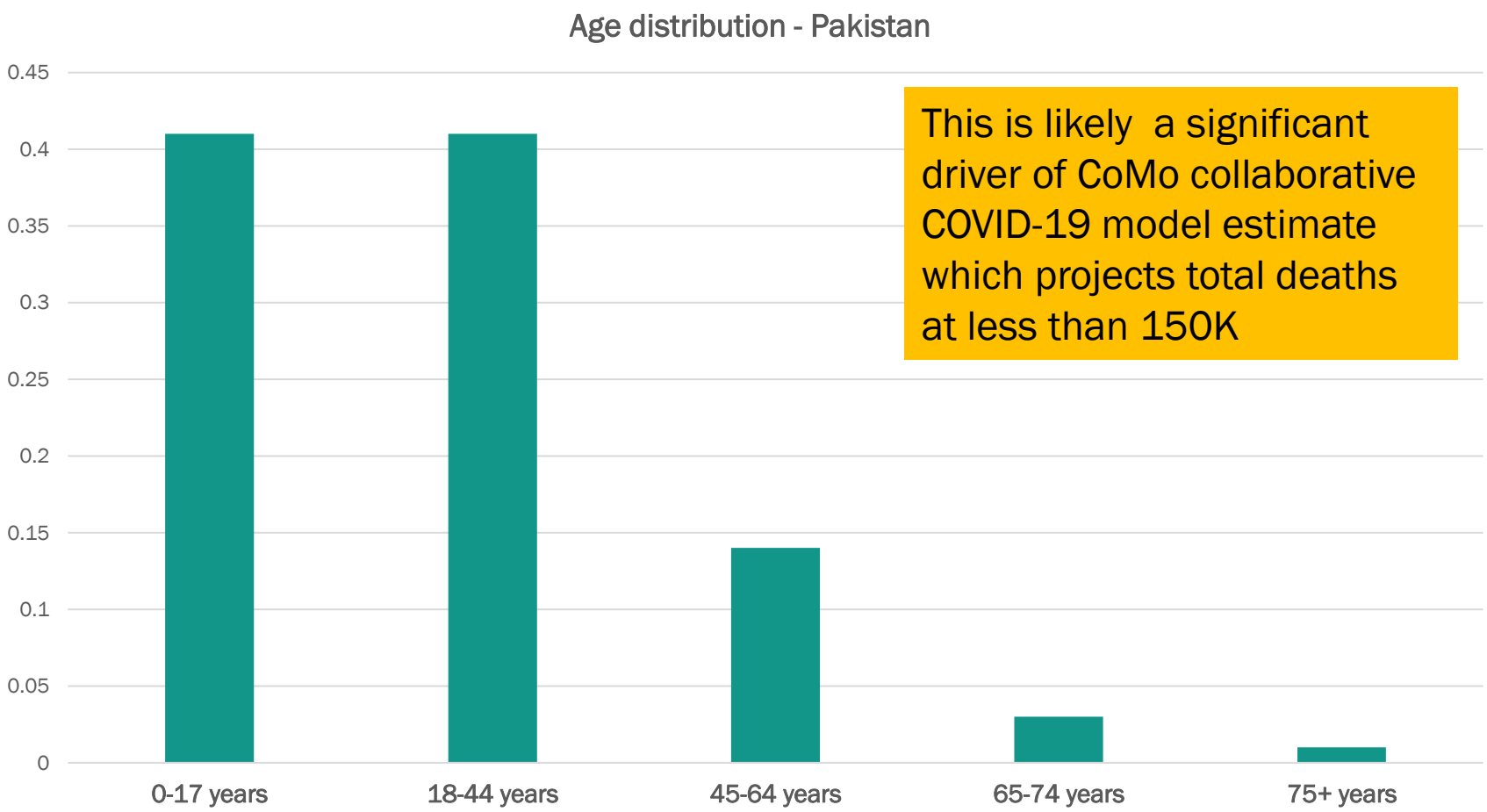
Without more specificity, this could still be an overestimate?

Even by CoMo collaborative model projection too high per current reports of dealths. This suggests IFR applied from HICs not relevant to LMICs

Potential reasons

- Virus already widespread before lock down
- Protective factors at play in LMICs
  - Age structure of population
  - Correlates of protection

Pakistan's population structure – 82% of population under the age of 45



This is likely a significant driver of CoMo collaborative COVID-19 model estimate which projects total deaths at less than 150K

https://population.un.org/wpp/Download/SpecialAggregates/EconomicTrading/

Key considerations

- Projections do not take into account how current measures have affected observed deaths or spread
  - Lockdown has been in place since 1 April and will be extended until 30 April. The effect will depend on how “strict” it was and may flatten the peak. Could result in result in “second wave”

- Model projections should always be considered with caution
  - Projected deaths will depend on a a range assumptions, which are subject to change
  - Provide point estimate rather than a range
  - Does not generate uncertainty estimates

- Idea ”bending the curve” was aimed at preserving hospital capacity with influx of COVID patients
  - By same logic, easing them should be dependent on this output
  - In some settings and where virus has spread rapidly, it may not be possible to prepare hospitals

- Mitigation strategies require evidenced based review before broad implementation
  - Based on mathematical assumptions with limited evidence base
  - Should consider impact on health of the strategy more broadly than COVID deaths alone
  - Have yet to be systematically evaluated with a proper study design, counterfactual, etc.

Policy implications

If infection fatality rates and projected numbers of deaths are overestimates **and** assumptions about current population infection rates are underestimates **and** potential for **asymptotic/presymtomatic** spread **then**, this has **significant implications** for policy response.

Policy response should consider current mitigation strategies through the lens of:

- **Feasibility** given underlying rationale for current mitigation strategies may have shifted
  - Contact tracing and boxing it if infection fast spreading with pre/asymptomatic spread?
  - ” Population based physical distancing if severe infection coming from household and hospital spread?
  - “Flattening the curve” based on potential for hospital readiness?

- **Health impacts** of currently current mitigation strategies
  - Lockdown effects on population health and non-Covid morbidity and mortality (direct and indirect) including through economic impact and effects on health?

- Age and condition specific mortality rates and how best to **engage with ‘‘at risk’’** populations around response
  - Precision public health as opposed to application of population wide measures

Next steps based on emerging evidence

- Communicate and contextualize individual risk
  - This will require a major effort given level of population fear
- Work with communities to identify those at risk and together finding solutions to engage with them about feasible and appropriate protection strategies.
- Reconsider mitigation strategies and weigh the cost and benefit of measures from a comprehensive health perspective looking more broadly than COVID-19 deaths as single focused endpoint

Additional slides

Resources on challenges with using models for decision making

- https://www.nature.com/articles/d41586-020-01003-6
- https://www.statnews.com/2020/04/17/influential-covid-19-model-uses-flawed-methods-shouldnt-guide-policies-critics-say/
- https://annals.org/aim/fullarticle/2764774/caution-warranted-using-institute-health-metrics-evaluation-model-predicting-course
- https://www.theatlantic.com/technology/archive/2020/04/coronavirus-models-arent-supposed-be-right/609271/