From:	Birx, Deborah L. EOP/NSC <(b)(6)
То:	Evaluation Only. Created with Aspose.HTML. Copyright 2013-2020 Aspose Pty Ltd.FYDIBOHF23SPDLT)/cn=Recipients/cn=a182eda693d040d3832bae6efcf7a255-Kadlec, Rob <robert.kadlec@hhs.gov>; Redfield, Robert R. (CDC/OD) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=9ab74a26317547b8a754285d9eaa847c-robert.redf </robert.kadlec@hhs.gov>
CC:	Redd, Stephen C. EOP/NSC (b)(6) @nsc.eop.gov>
Subject:	Fwd: Covid-19 modeling
Date:	2020/03/19 05:56:47
Priority:	Normal
Туре:	Note

The modeling study. You can see the assumptions. There was a modeling meeting yesterday and Steve will provide a summary. But you can see no country has crossed even 1000/1000000 yet but many models assume enormous attack rates and assume emergence in every fall. We will make time for everyone to discuss outside of the task force. Deb

Sent from my iPhone

Begin forwarded message:

From: "Birx, Deborah L. EOP/NSC" (b)(6) @nsc.eop.gov>
Date: March 16, 2020 at 7:58:47 AM EDT
To: "Moorhead, Quellie U. EOP/WHO" (b)(6) @who.eop.gov>
Subject: Fwd: Covid-19 modeling

For printing. The word document.

Sent from my iPhone

Begin forwarded message:

Subject: Fw: Covid-19 modeling

From: Ferguson, Neil M <neil.ferguson@imperial.ac.uk>

Sent: Sunday, March 15, 2020 10:48 PM

To: Zaidi, Irum F

Subject: RE: Covid-19 modeling

See attached for a slightly incomplete report on NPIs. It contains mostly UK modelling, but the results are very similar for the US. I will be including more US model runs in the next day or two, including locally triggered policies.

This report will (when tidied up) be released publicly tomorrow. Please keep this incomplete draft confidential for 24h, though it is fine to use the contents internally.

Also happy to share our estimates of CFR/IFR, healthcare demand needs (all in 5 year age bands):

	0 to 4	5 to 9	10 to 14	15 to 19	20 to 24	25 to 29	30 to 34	3.
Proportion of infections								
hospitalised	0.000744	0.000634	0.001171	0.002395	0.005346	0.01029	0.016235	0
Proportion of infections								
needing critical care	3.74E-05	3.18E-05	5.88E-05	0.00012	0.000269	0.000517	0.000815	0
Proportion of hospitalised								
cases needing critical care	0.050223	0.050223	0.050223	0.050223	0.050223	0.050223	0.050223	0
Proportion of critical cases								
dying	0.5	0.5	0.5	0.5	0.5	0.5	0.5	
Proportion of non-critical care								
cases dying	0.013448	0.013448	0.013448	0.013448	0.013448	0.013448	0.013448	0

This gives 4.4% of infections hospitalised, 30% of hospitalised cases needing ICUs.

IFR is 1% overall (we rounded up from the actual estimate of 0.97%!) in the UK population. Maybe different in France.

Most of these numbers will be in the final version of this

(>https://www.medrxiv.org/content/10.1101/2020.03.09.20033357v1<) which hopefully will come out in Lancet ID this week.

The 30% ICU figure comes from an observation in the UK and Italy that non-invasive ventilation is largely ineffective in COVID-19 cases.

Delays we have estimated:

- Mean time from hospital admission to discharge, non-ICU and non-lethal cases = 8 days
- • Mean time from hospital admission to death for lethal cases not admitted to ICU = 8 days
- • Mean time from hospital admission to ICU admission = 5 days

- • Mean time in ICU, non-lethal and lethal cases = 10 days
- Mean time remaining in hospital after discharge from ICU = 5 days
- • Mean time in ICU for lethal cases=10 days

Best,

Neil

Sender: Birx, Deborah L. EOP/NSC (b)(6) nsc.eop.gov> Kadlec, Robert (OS/ASPR/IO) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a182eda693d040d3832bae6efcf7a255-Kadlec, Rob <Robert.Kadlec@hhs.gov>; Redfield, Robert R. (CDC/OD) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=9ab74a26317547b8a754285d9eaa847c-robert.redf <olx1@cdc.gov>; Seema Verma (CMS/OA) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=user1acbd760 <Seema.Verma.OA@cms.hhs.gov>; Stephen Hahn <sh1@fda.hhs.gov>; Recipient: Fauci, Anthony (NIH/NIAID) [E] /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=826965b24a314ffca7eddcb6e8229aa7-anthony.fau <afauci@niaid.nih.gov>; Harrison, Brian (HHS/IOS) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=d145efc9c35c4865aca6e9d47786b204-Harrison, B <Brian.Harrison@hhs.gov>; Troye, Olivia (nsc.eop.gov) /o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ca87389c930143e68ae97cd3ff065113-Olivia.Troy @nsc.eop.gov> Redd, Stephen C. EOP/NSC (b)(6) nsc.eop.gov> Sent Date: 2020/03/19 05:55:53 **Delivered Date:** 2020/03/19 05:56:47

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

1. MRC Centre for Global Infectious Disease Analysis, J-IDEA; Department of Infectious Disease Epidemiology, Imperial College London

Summary

Introduction

The last time the world responded to a global emerging disease epidemic of the scale of the COVID-19 pandemic with no access to vaccines was the 1918-19 H1N1 influenza pandemic. In that pandemic, some communities, notably in the United States (US), responded with a variety of non-pharmaceutical interventions (NPIs) - measures intended to reduce transmission by reducing contact rates in the general population¹. Examples of the measures adopted during this time include closing schools, churches, bars and other social venues. Cities in which these interventions were implemented early in the epidemic were successful at reducing case numbers while the interventions remained in place. However, transmission rebounded once controls were lifted. Nevertheless, the cities in the US which adopted such measures early had overall lower mortality in 1918 than those which responded later-1.

Most of the countries of the world face the same challenge today with COVID-19, a virus with comparable lethality to H1N1 influenza in 1918. Two fundamental strategies are possible²:

- (a) **Suppression.** Here the aim is to reduce the reproduction number (the average number of secondary cases each case generates), R, to below 1 and hence to reduce case numbers to low levels or (as for SARS or Ebola) eliminate human-to-human transmission. The main challenge of this approach is that NPIs need to be maintained at least intermittently for as long as the virus is circulating in the human population, or until vaccine becomes available. In the case of COVID-19, it will be at least a 12-18 months before a vaccine is available³. Furthermore, there is no guarantee that initial vaccines will have high efficacy.
- (b) **Mitigation.** Here the aim is to use NPIs (and vaccines or drugs, if available) not to interrupt transmission completely, but to reduce the health impact of an epidemic, akin to the strategy adopted by some US cities in 1918, and by the world more generally in the 1957, 1968 and 2009 influenza pandemics. In the 2009 pandemic, for instance, early supplies of vaccine were targeted at individuals with pre-existing medical conditions which put them at risk of more severe disease⁴. In this scenario, population immunity builds up through the epidemic, leading to an eventual rapid decline in case numbers and transmission dropping to low levels.

The strategies differ in whether they aim to reduce the reproduction number (average number of secondary cases caused by each case), R, to below 1 (suppression) – and thus cause case numbers to decline – or to merely slow spread by reducing R, but not to below 1.

In this report, we consider the feasibility and implications of both strategies for COVID-19, looking at a range of NPI measures. It is important to note at the outset that given SARS-CoV-2 is a newly emergent virus, much remains to be understood about its transmission. In addition, the impact of many of the NPIs detailed here depends critically on how people respond to their introduction, which is highly likely to vary between countries and even communities. Last, it is highly likely that there would be significant spontaneous changes in population behaviour even in the absence of government-mandated interventions.

We do not consider the ethical implications of either strategy here, except to note that there is no easy policy decision to be made. Suppression, while successful to date in China, carries with it enormous social and economic costs which may themselves have significant impact on health and well-being in the short and longer—term. Mitigation will never be able to completely protect those at risk from severe disease or death and the resulting mortality may therefore still be high. Instead we

Commented [CD1]: Suggest delete "virus" here.

focus on feasibility, with a specific focus on what the likely healthcare system impact of the two approaches would be. We present results for the <u>United Kingdom (UK)Great Britain (GB)</u> and <u>the United States of America (US)</u>, but they are equally applicable to most high-income countries.

Most of the NPIs are suitable for either strategy, with one notable exception. For mitigation, a valid policy option is to attempt to "cocoon" those at greatest risk of severe outcomes from infection—such as those over 70 years of age or those with pre-existing health conditions. Whilst this could also be a short-term strategy to reduce risk under a suppression strategy, the duration for which this would need to remain in place (and hence the social, emotional and wider health impacts of such a strategy) would be different. We do not consider the ethical implications of either strategy here, except to note that there is no easy policy decision to be made. Suppression, while successful to date in China, carries with it enormous social and economic costs which may themselves have significant impact on health and well-being in the short and longer-term. Mitigation will never be able to completely protect those at risk from severe disease or death and the resulting mortality may therefore still be high. Instead we focus on feasibility, with a specific focus on what the likely healthcare system impact of the two approaches would be. We present results for the UK and US, but they are equally applicable to most high income countries.

Methods

Transmission Model

We modified an individual-based simulation model developed to support pandemic influenza planning^{5,6} to explore scenarios for COVID-19 in the United Kingdom (=UKGreat Britain (GB)). The basic structure of the model remains as previously published. In brief, individuals reside in areas defined by high-resolution population density data. Contacts with other individuals in the population are made within the household, at school, in the workplace and in the wider community. Census data were used to define the age and household distribution size. Data on average class sizes and staff-student ratios were used to generate a synthetic population of schools distributed proportional to local population density. Data on the distribution of workplace size was used to generate workplaces with commuting distance data used to locate workplaces appropriately across the population. Individuals are assigned to each of these locations at the start of the simulation.

Transmission events occur through contacts made between susceptible and infectious individuals in either the household, workplace, school or randomly in the community, with the latter depending on spatial distance between contacts. Per-capita contacts within schools were assumed to be double those elsewhere in order to reproduce the attack rates in children observed in past influenza pandemics⁷. With the parameterisation above, approximately one third of transmission occurs in the household, one third in schools and workplaces and the remaining third in the community. These contact patterns reproduce those reported in social mixing surveys⁸.

We assumed an incubation period of 5.1 days^{9,10}. For our baseline scenarios we use R_0 =2.2 and R_0 =2.4 based on fits to the early growth-rate of the epidemic in Wuhan^{10,+1}. Infectiousness is assumed to occur from 12 hours prior to the onset of symptoms for those that are symptomatic and from 4.6 days after infection in those that are asymptomatic with an infectiousness profile over <u>time</u> that results in a 6.5-day mean generation time. <u>For our baseline scenarios we useBased on fits to the early growth-</u>

Commented [GACH2]: Please check this part, it is not that easy to write when I don't really understand how it is implemented!

rate of the epidemic in Wuhan^{10,11}, we make a baseline assumption that R_0 =2.2 and R_0 =2.4 based on fits to the early growth-rate of the epidemic in Wuhan^{10,11} but examine values between 2.0 and 2.6... We assume that symptomatic individuals are 50% more infectious thant asymptomatic individuals. Individual infectiousness is assumed to be variable, described by a gamma distribution with mean 1 and shape parameter α =0.25. On recovery from infection, individuals are assumed to be immune to re-infection in the short_-term. Evidence from the Flu Watch cohort study suggests that re-infection with the same strain of seasonal circulating coronavirus is highly unlikely in the same or following season (Prof Andrew Hayward, personal communication).

Disease Progression and Healthcare Demand

Analyses of data from China suggest that 40-50% of infections were not identified as cases. This may include asymptomatic infections, mild disease and a level of under-ascertainment. We therefore assume that two-thirds of cases are sufficiently symptomatic to self-isolate (if required by policy) within 1 day of symptom onset, and seek care (or self-isolate) with a mean delay from onset of symptoms to care-seeking of 3 days and from a mean delay from onset of symptoms to hospitalisation of 5 days. The age-stratified proportion of infections that require hospitalisation and the infection fatality ratio (IFR) was-were obtained from an analysis of a subset of cases from China¹². These estimates were corrected for non-uniform attack rates by age and when applied to the UK-GB population result in an IFR of 0.9% with 4.4% of infections hospitalised (Table 1). We assume that 30% of those that are hospitalised will require critical care (invasive mechanical ventilation or ECMO) based on early reports from COVID-19 cases in the UK, China and Italy (Professor Nicholas Hart, personal communication), with a mean duration from hospital admission to admission to critical care of 6 days. Based on expert clinical opinion, we assume that 50% of those in critical care will die and an agedependent proportion of those that do not require critical care die (calculated to match the overall IFR). We calculate bed numbers assuming a total duration of stay in hospital of 8 days if critical care is not required and an additional 10 days if critical care is required. With 30% of hospitalised cases requiring critical, we obtain an overall mean of 11.5 days in hospital, slightly shorter than the duration from hospital admission to discharge observed for COVID-19 cases internationally¹³ (who will have remained in hospital slightly longer to ensure negative tests at discharge) but in-line with estimates for general pneumonia admissions14.

Table 1: Estimates of the severity of cases. The IFR estimates from Verity et al.12 have been adjusted to account for a non-uniform attack rate giving an overall IFR of 0.9% (95% credible interval 0.4-0.14). Hospitalisation estimates from Verity et al.12 were also adjusted in this way and scaled to match expected rates in the oldest age-group (80+ years) in a UKGB/US context. Note that we fixed the %-percentage of symptomatic cases requiring hospitalisation and critical care in the 80+ age-group and hence these do not include uncertainty-credible intervals.

A == ======	0/ summatamatic asses	0/ summatomatic asses	Infantian Fatality Batic
Age-group	% symptomatic cases	% symptomatic cases	Infection Fatality Ratio
(years)	requiring hospitalisation	requiring critical care	Median (95% credible
	Median (95% credible	Median (95% credible	interval)
	interval)	interval)	
0 to 9	3.8% (2.3-7.9)	0.01% (0.001-0.06)	0.006% (0.0002 – 0.03)
10 to 19	2.6% (1.6-5.5)	0.02% (0.003-0.08)	0.01% (0.001-0.04)
20 to 29	2.8% (1.7-5.8)	0.08% (0.04-0.15)	0.04% (0.01-0.09)
30 to 39	2.7% (1.7-5.7)	0.18% (0.11-0.28)	0.09% (0.04-0.17)
40 to 49	5.4% (3.8-7.6)	0.34% (0.23-0.48)	0.17% (0.07-0.30)

Commented [CD3]: Doesn't this need a reference?

Commented [FNM4R4]: May want to note that pneumonia was a key diagnostic criteria. Or switch to mentioning the repatriation flights or Diamond Princess instead – likely better

Commented [GACH5]: I don't see this in the parameters
– is this included? I must have taken this from your flu

50 to 59	12.6% (9.9-15.6)	1.5% (1.2-1.9)	0.75% (0.34-1.28)
60 to 69	19.7% (16.3-23.8)	5.4% (4.5-6.5)	2.7% (1.3-4.4)
70 to 79	28.7% (23.8-34.7)	12.4% (10.3-15.0)	6.1% (2.9-10.0)
80+	27.3%	19.3%	9.54% (4.53-15.8)

Non-Pharmaceutical Intervention Scenarios

We consider the impact of six different non-pharmaceutical interventions (NPI) alone and in combination (Table 2). Two of these interventions (case isolation and voluntary home quarantine) are triggered by the onset of symptoms and are implemented the same/next day. The other four (social distancing of those over 65 years, social distancing of the entire population, stopping mass gatherings and closure of schools and universities) are decisions made at the government level. For these interventions we therefore consider three-surveillance triggers based on testing of patients in critical careICUs: (a) the absolute number of cases diagnosed per week per county; (b) the cases per capita diagnosed per week per county; and (c) the cumulative number of cases diagnosed nationally. The first two trigger the intervention only in the affected county whilst the last triggers the policy nationally. We focus on cases diagnosed in intensive care units (ICUs), as testing is most complete for the most severely ill patients. For the main results we assume that the policy remains in place for 2-5When examining mitigation strategies, we assume policies are in force for 3 months, other than except for social distancing of those over the age of 65-70 which is assumed to remain in place for one month longer.

Table 2: Summary of NPI interventions considered.

Label	Policy	Description
CI	Case isolation in home	70%-of-sSymptomatic cases stay at home for 7 days, reducing non-household contacts by 75% for this period. Household contacts remain unchanged. Assume 70% of household comply with the policy.
HQ	Voluntary home quarantine	Following identification of a symptomatic case in the household, all household members remain at home for 14 days. Household contact rates double during this quarantine period, contacts in the community reduce by 75%. Assume 50% of household comply with the policy.
SDO	Social distancing of those over 70 years of age	Reduce contacts by 50% in schools or workplaces, increase household contacts by 25% and reduce other contacts by 75%. Assume 75% compliance with policy.
SD	Social distancing of entire population	All households reduce contact outside household, school or workplace by 75%. School contact rates unchanged, workplace contact rates reduced by 25%. Household contact rates assumed to increase by 25%.
MG	Stopping mass gatherings	In order of impact: shutting bars/pubs, restaurants, cinemas, night clubs, sporting fixtures, places of worship and theatres. These contacts represent 5% of all contact hours outside home, school or work. Assuming 3-fold higher transmission than other activities, we assume that this would reduce transmission in the community by 15%.
PC	Closure of schools & and	Closure of all schools, 25% of universities remain
	universities	open. Household contact rates for student families increase by 50% during closure. Contacts in the community increase by 25% during closure.

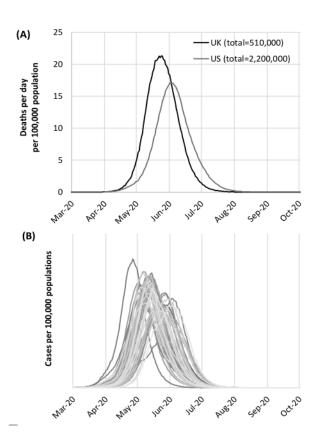
Results

Assuming that the virus was introduced in late-January with the first rise in cases occurring from March onwards, in an unmitigated scenariothe (unlikely) absence of any control measures or spontaneous changes in individual behaviour, we would expect a peak in mortality (daily deaths) to occur after approximately 3 months (Figure 1A). In such scenarios, given an estimated R₀ of 2.4, we predict 81~80% of the GB and US populations will-would be infected over the course of the epidemic, resulting in herd immunity in the population. Epidemic timings are approximate given the limitations of surveillance data in both countries: models were calibrated to reproduce the observed cumulative number of deaths in each country seen by 14th March 2020. The epidemic is predicted to be broader in the US as a whole compared to than in the UK-GB with a peak in deaths a few weeks later than the UK-and to peak slightly later. This is due to the larger geographic scale of the US, resulting in multiple more distinct localised epidemics across states (Figure 1B) than seen across GBthe UK. The higher peak

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Commented [FNM7R7]: "Place"

in mortality in the UKGB is due to the smaller size of the country and the its older population in the UK-compared to with the US. In total, in an unmitigated epidemic, we would predict approximately 510,000 deaths in the UKGB and 2.2 million in the US, not accounting for the potential negative effects of health systems being overwhelmed on mortality.



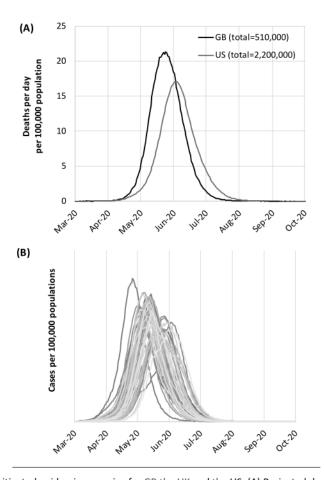


Figure 1: Unmitigated epidemic scenarios for <u>GB the UK and the US</u>. (A) Projected deaths per day per 100,000 population in the <u>UKGB</u> and US. (B) Case epidemic trajectories across the United States by state.

For <u>an uncontrolled epidemican unmitigated scenario</u>, we predict critical care bed capacity to-<u>would</u> be exceeded as early as the second week in April, with an <u>eventual</u>-peak that inin intensive care unit (ICU) bed demand-requirements that is approximately-over 305 times greater than the maximum supply in both countries (Figure 21).

Our projections show that to be able to reduce transmission sufficiently to contain the epidemic, a combination of case isolation and widescale social distancing are essential. If schools and universities are closed in addition to these interventions, we predict a reduction in critical care requirements from a peak in early to mid-April and a decline thereafter whilst the intervention policies remain in place. This is the only strategy in which critical care bed requirements would remain within surge capacity. Adding household quarantine to case isolation and widescale social distancing is the next best option, although we predict that surge capacity may be exceeded by nearly double under this policy. In either

scenario, once interventions are relaxed (in the example here, from September onwards), infections begin to rise, resulting in a predicted peak epidemic later in the year. In the most successful containment strategy, due to the lesser build-up of herd immunity, this is predicted to be larger than for the strategy which does not fully suppress transmission during the summer months. In order to be successful, such a strategy needs to be implemented as early as possible (results here are shown assuming this comes into place in April).

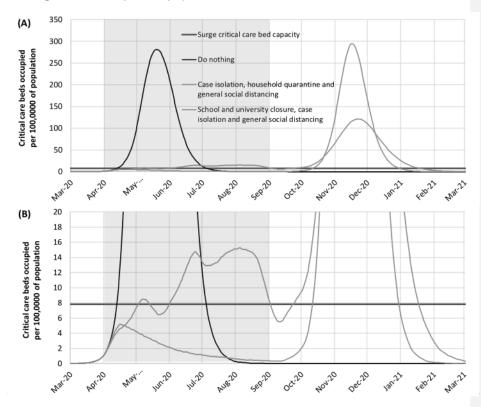


Figure 2: Containment strategy scenarios for the UK showing critical care bed requirements. The black line shows the unmitigated epidemic. Green shows a containment strategy incorporating closure of schools and universities, case isolation and widescale social distancing. The orange line shows a containment strategy incorporating case isolation, household quarantine and widescale social distancing. The red line is the estimated surge critical care capacity in the UK. The blue shading shows the period in which these interventions are assumed to remain in place. (B) shows the same data as in panel (A) but zoomed in on the lower levels of the graph. An equivalent figure for the US is shown in the Appendix.

of mitigation is to reduce the impact of the an epidemic by flattening the curve, and reducing the peak incidence and overall deaths (Figure 32). It is important to note that, because the aim here is to mitigate rather than suppress, the interventions need to be less intensive to ensure that a second wave of infection does not return once interventions are lifted. Furthermore, as tSince the aim of this strategy is to minimise mortality, the interventions need to remain in place for as much of the epidemic period as possible. Introducing too early risks allowing transmission to return once they are

lifted (if insufficient herd immunity has developed); it is therefore necessary to balance the timing of introduction with the scale of disruption imposed and the likely period over which the interventions can be maintained. In this scenario, interventions can limit transmission to the extent that little herd immunity is acquired — leading to interventions can be too successful at reducing transmission — leading to the possibility that a second wave of infection is seen once interventions are lifted

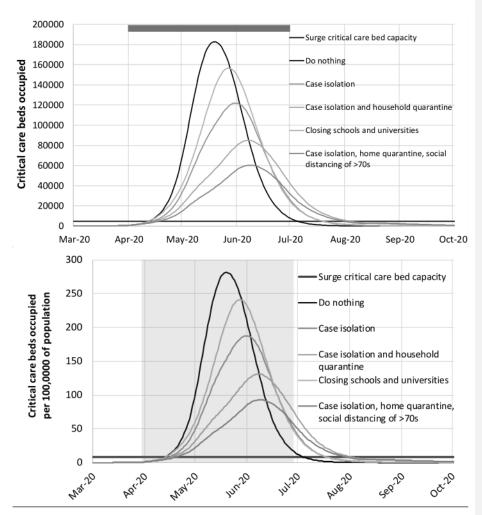


Figure 32: Mitigation strategy scenarios for the UKGB showing critical-ICUcare bed requirements. The black line shows the unmitigated epidemic. Green shows a mitigation strategy incorporating closure of schools and universities; orange case isolation; yellow case isolation and household quarantine; and blue case isolation, home quarantine and social distancing of those aged over 70. The blue shading barshading shows the 3-month period in which these interventions are assumed to remain in place.

Table 3 shows the predicted relative impact on both deaths and critical care ICU capacity of a range of different-single and combined NPI combinations-interventions applied nationally in the UKGB for a 3-month-period based on triggers of between 100 and 3000 critical care cases. The Conditional on that 3-months-duration, the most effective combination of interventions is predicted to be a combination of case isolation, home quarantine and social distancing of those most at risk (the over 70s). Whilst the latter has relatively less impact on transmission than other age groups, by-reducing morbidity and mortality in the highest risk groups, it is likely to-reduces both demand on critical care and overall mortality. In combination, this intervention strategy is predicted to reduce peak critical care demand by 67-69%two-thirds and reduce deaths by 49%half.

However, this <u>"optimal" mitigation</u> scenario would still <u>leave an result in an</u> 8-fold higher peak demand on critical care beds over and above the available surge capacity in both the <u>UKGB</u> and the <u>US</u>.

Stopping mass gatherings is predicted to have relatively little impact (results not shown) because the contact-time at such events is relatively small compared to the time spent at home, in school/the workplace and in other community locations such as bars and restaurants.

Overall, we find that the relative effectiveness of different policies is insensitive to the choice of local trigger (absolute numbers of cases compared to per-capita incidence), R_0 .a (in the range 2.0-2.6), and levels of severity within the varying IFR in the 0.25%-1.0% IFR-range.

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Table 3. Mitigation options for the UKGB. Relative impact of NPI combinations applied nationally for 3 months in the UKGB on total deaths and peak hospital ICU bed demand for different choices of cumulative ICU case count triggers. The cells show the percentage reduction in peak bed demand for a variety of NPI combinations and for triggers based on the absolute number of ICU cases diagnosed in a county per week. PC=school and university closure, CI=home isolation of cases, HQ=household quarantine, SD=large-scale general population social distancing of the entire population, SDOL70=social distancing of those over 70 years for 4 months (a month more than other interventions). Tables are colour-coded (green= higher effectiveness, red=lower). Absolute numbers are shown in Table A1.

	Trigger (cumulative ICU cases)	PC	CI	CI_HQ	CI_HQ_SD	CI_SD	CI HQ SDOL70	PC_CI_HQ_SDOL70
	100	14%	33%	53%	33%	53%	67%	69%
R ₀ =2.4	300	14%	33%	53%	34%	57%	67%	71%
Peak beds	1000	14%	33%	53%	39%	64%	67%	77%
	3000	12%	33%	53%	51%	75%	67%	81%
	100	23%	35%	57%	25%	39%	69%	48%
R ₀ =2.2	300	22%	35%	57%	28%	43%	69%	54%
Peak beds	1000	21%	35%	57%	34%	53%	69%	63%
	3000	18%	35%	57%	47%	68%	69%	75%
	100	2%	17%	31%	13%	20%	49%	29%
R ₀ =2.4	300	2%	17%	31%	14%	23%	49%	29%
Total deaths	1000	2%	17%	31%	15%	26%	50%	30%
	3000	2%	17%	31%	19%	30%	49%	32%
	100	3%	21%	34%	9%	15%	49%	19%
R ₀ =2.2	300	3%	21%	34%	9%	17%	49%	20%
Total deaths	1000	4%	21%	34%	11%	21%	49%	22%
	3000	4%	21%	34%	15%	27%	49%	24%

Given that mitigation is unlikely to a viable option without overwhelming healthcare systems, suppression is likely necessary in countries able to implement the intensive controls required. Our projections show that to be able to reduce R to close to 1 or belowtransmission sufficiently, a combination of case isolation, and widescale social distancing of the entire population and either school and university closure or household quarantine areare required essential (Figure 3, Table 4). If School closure is predicted to be more effective in achieving suppression than household quarantine (in addition to case isolation and social distancing). When policies include closure of schools and universities are closed in addition to these interventions, we predict a reduction in critical care requirements from a peak in early to mid-April approximately3 weeks after the interventions are introduced and a decline thereafter whilstwhile the intervention policies remain in place. While there are many uncertainties in policy effectiveness, this is the only strategy in which we predict that critical care bed requirements would remain within surge capacity.

Adding household quarantine to case isolation and widescale social distancing is the next best option, although we predict that there is a risk that surge capacity may be exceeded under this policy option. Combining large-scale social distancing, case isolation, household quarantine and school and university closure is predicted to have the largest impact, short of a complete lockdown which additionally prevents people going to work. In order to be successful, such a strategy needs to be implemented as early as possible (results here are shown assuming this comes into place in late March).

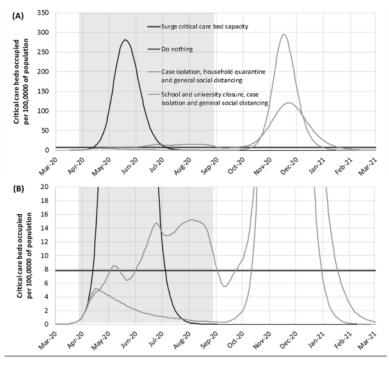


Figure 23: ContainmentSuppression strategy scenarios for the UKGB showing critical carelCU bed requirements. The black line shows the unmitigated epidemic. Green shows a containmentsuppression

strategy incorporating closure of schools and universities, case isolation and widescale social distancing beginning in late March 2020. The orange line shows a containment strategy incorporating case isolation, household quarantine and widescale social distancing of the entire population. The red line is the estimated surge critical carelCU bed capacity in the UKGB. The blue shading shows the 5-month period in which these interventions are assumed to remain in place. (B) shows the same data as in panel (A) but zoomed in on the lower levels of the graph. An equivalent figure for the US is shown in the Appendix.

Adding household quarantine to case isolation and widescale-social distancing is the next best option, although we predict that there is a risk that surge capacity may be exceeded under this policy option (Figure 3 and Table 4). Combining large-scale—all four interventions (social distancing of the entire population, case isolation, household quarantine and school and university closure) is predicted to have the largest impact, short of a complete lockdown which additionally prevents people going to work. In order to be successful, such a strategy needs to be implemented as early as possible (results here are shown assuming this comes into place in late March).

<u>In either scenario</u>, oOnce interventions are relaxed (in the example herein Figure 3, from September onwards), infections begin to rise, resulting in a predicted peak epidemic later in the year. The more <u>successful</u> a strategy is at suppression, the larger the later epidemic is predicted to be in the absence of vaccination, due to lesser build-up of herd immunity.

Given suppression policies may need to be maintained for many months, we examined the impact of an adaptive policy in which social distancing (and school+university closure, if used) is only initiated after weekly confirmed case incidence in ICU patients (a group of patients highly likely to be tested) exceeds a certain "on" threshold, and is relaxed when ICU case incidence falls below a certain "off" threshold (Figure 4). Case -based policies of home isolation of symptomatic cases and household quarantine (if adopted) are continued throughout.

Such policies are robust to uncertainty in both the reproduction number, R_0 (Table 4) and in the severity of the virus (i.e. the proportion of cases requiring ICU admission, not shown). Table 3 illustrates that suppression policies are best triggered early in the epidemic, with a cumulative total of 200 ICU cases per week being the latest point at which policies can be triggered and still keep peak ICU demand below GB surge limits in the case of a relatively high R_0 value of 2.6. Expected total deaths are also reduced for lower triggers, though deaths for all the policies considered are much lower than for an uncontrolled epidemic. The right panel of Table 4 shows that social distancing (and school+university closure, if used) need to be in force for the majority of the 2 years of the simulation, but that the proportion of time these measures are in force is reduced for more effective interventions and for lower values of R0. Table 5 shows that total deaths are reduced with lower "off" triggers; however, this also leads to longer periods during which social distancing is in place. Peak ICU demand and the proportion of time social distancing is in place are not affected by the choice of "off" trigger.

Commented [CD9]: This is not the term in the figure. It says "general social distancing". Table 2 says "Social distancing of the entire population" which is clearer.

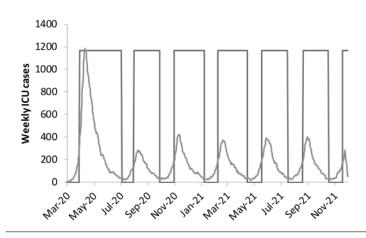


Figure 4: Illustration of adaptive triggering of suppression strategies in GB, for R_0 =2.2, a policy of all four interventions considered, an "on" trigger of 100 ICU cases in a week and an "off" trigger of 50 ICU cases. The policy is in force approximate 2/3 of the time. Only social distancing and school/university closure are triggered; other polices remain in force throughout. Weekly ICU incidence is shown in orange, policy triggering in blue.

Table 4. Suppression strategies for GB. Impact of three different policy option (case isolation+home quarantine+social distancing, school/university closure+case isolation+social distancing, and all four interventions) on the total number of deaths seen in a 2-year period (left panel) and peak demand for ICU beds (centre panel). Social distancing and school/university closure are triggered at a national level when weekly numbers of new COVID-19 cases diagnosed in ICUs exceed the thresholds listed under "On trigger" and are suspended when weekly ICU cases drop to 25% of that trigger value. Other policies are assumed to start in late March and remain in place. The right panel shows the proportion of time after policy start that social distancing is in place. Peak GB ICU surge capacity is approximately 5000 beds. Results are qualitatively similar for the US.

		<u>Total deaths</u>						
	<u>On</u>	<u>Do</u>						
<u>R</u> ₀	Trigger	nothing	CI HQ SD	PC_CI_SD	PC CI HQ SD			
2	<u>60</u>	<u>410,000</u>	<u>47,000</u>	<u>6,400</u>	<u>5,600</u>			
	<u>100</u>	410,000	<u>47,000</u>	<u>9,900</u>	<u>8,300</u>			
	<u>200</u>	410,000	<u>46,000</u>	<u>17,000</u>	<u>14,000</u>			
	<u>300</u>	410,000	<u>45,000</u>	<u>24,000</u>	<u>21,000</u>			
	<u>400</u>	410,000	<u>44,000</u>	<u>30,000</u>	<u>26,000</u>			
	<u>60</u>	460,000	<u>62,000</u>	<u>9,700</u>	<u>6,900</u>			
	<u>100</u>	<u>460,000</u>	<u>61,000</u>	<u>13,000</u>	<u>10,000</u>			
2.2	<u>200</u>	<u>460,000</u>	<u>64,000</u>	<u>23,000</u>	<u>17,000</u>			
	<u>300</u>	460,000	<u>65,000</u>	<u>32,000</u>	<u>26,000</u>			
	<u>400</u>	<u>460,000</u>	<u>68,000</u>	<u>39,000</u>	31,000			
	<u>60</u>	510,000	<u>85,000</u>	<u>12,000</u>	<u>8,700</u>			
	<u>100</u>	510,000	<u>87,000</u>	<u>19,000</u>	13,000			
2.4	<u>200</u>	510,000	90,000	30,000	<u>24,000</u>			
	300	510,000	94,000	<u>43,000</u>	34,000			
	<u>400</u>	510,000	<u>98,000</u>	53,000	39,000			
	<u>60</u>	550,000	110,000	20,000	<u>12,000</u>			
	<u>100</u>	<u>550,000</u>	110,000	<u>26,000</u>	<u>16,000</u>			
2.6	<u>200</u>	550,000	<u>120,000</u>	<u>39,000</u>	30,000			
	<u>300</u>	<u>550,000</u>	120,000	<u>56,000</u>	40,000			
	<u>400</u>	<u>550,000</u>	120,000	71,000	<u>48,000</u>			

	Peak	ICU beds	
<u>Do</u>			
<u>nothing</u>	CI_HQ_SD	PC_CI_SD	PC CI HQ SD
130,000	<u>3,300</u>	<u>930</u>	<u>920</u>
<u>130,000</u>	<u>3,500</u>	<u>1,300</u>	<u>1,300</u>
<u>130,000</u>	<u>3,500</u>	<u>1,900</u>	<u>1,900</u>
<u>130,000</u>	<u>3,500</u>	<u>2,200</u>	<u>2,200</u>
<u>130,000</u>	<u>3,800</u>	<u>2,900</u>	<u>2,700</u>
<u>160,000</u>	<u>7,600</u>	<u>1,200</u>	<u>1,100</u>
<u>160,000</u>	<u>7,700</u>	<u>1,600</u>	<u>1,600</u>
<u>160,000</u>	<u>7,700</u>	<u>2,600</u>	<u>2,300</u>
<u>160,000</u>	<u>7,300</u>	<u>3,500</u>	<u>3,000</u>
<u>160,000</u>	<u>7,300</u>	<u>3,700</u>	<u>3,400</u>
<u>180,000</u>	<u>11,000</u>	<u>1,200</u>	<u>1,200</u>
<u>180,000</u>	<u>11,000</u>	<u>2,000</u>	<u>1,800</u>
<u>180,000</u>	<u>9,700</u>	<u>3,500</u>	<u>3,200</u>
<u>180,000</u>	<u>9,900</u>	<u>4,400</u>	<u>4,000</u>
<u>180,000</u>	<u>10,000</u>	<u>5,700</u>	<u>4,900</u>
230,000	<u>15,000</u>	<u>1,500</u>	<u>1,400</u>
230,000	<u>16,000</u>	<u>1,900</u>	<u>1,800</u>
230,000	<u>16,000</u>	<u>3,600</u>	<u>3,400</u>
230,000	<u>17,000</u>	<u>5,500</u>	<u>4,700</u>
230,000	<u>17,000</u>	<u>7,100</u>	<u>5,600</u>

Proportio	n of time wi	th SD in place
CI HQ SD	PC_CI_SD	PC CI HQ SD
<u>96%</u>	<u>69%</u>	<u>58%</u>
<u>96%</u>	<u>67%</u>	61%
<u>95%</u>	<u>66%</u>	<u>57%</u>
<u>95%</u>	64%	<u>55%</u>
94%	<u>63%</u>	<u>55%</u>
<u>96%</u>	<u>82%</u>	<u>70%</u>
<u>96%</u>	80%	<u>66%</u>
<u>89%</u>	<u>76%</u>	64%
<u>89%</u>	<u>74%</u>	64%
<u>82%</u>	<u>72%</u>	<u>62%</u>
<u>87%</u>	<u>89%</u>	<u>78%</u>
<u>83%</u>	<u>88%</u>	<u>77%</u>
<u>77%</u>	<u>82%</u>	<u>74%</u>
<u>72%</u>	<u>81%</u>	<u>74%</u>
<u>68%</u>	<u>81%</u>	<u>71%</u>
<u>68%</u>	94%	<u>85%</u>
<u>67%</u>	<u>93%</u>	<u>84%</u>
<u>62%</u>	<u>88%</u>	<u>83%</u>
<u>59%</u>	<u>87%</u>	<u>80%</u>
<u>56%</u>	<u>82%</u>	<u>76%</u>

Table 5. As Table 4 but showing the effect of varying the 'off' trigger for social distancing and school/university closure on total deaths over 2 years, for R_0 =2.4.

			Total deat	<u>hs</u>
<u>On</u>	Off trigger as proportion of			
trigger	on trigger	CI_HQ_SD	PC_CI_SD	PC_CI_HQ_SD
	<u>0.25</u>	<u>85,000</u>	12,000	<u>8,700</u>
<u>60</u>	<u>0.5</u>	<u>85,000</u>	<u>15,000</u>	<u>10,000</u>
	<u>0.75</u>	<u>85,000</u>	14,000	<u>11,000</u>
	<u>0.25</u>	87,000	<u>19,000</u>	<u>13,000</u>
100	<u>0.5</u>	<u>87,000</u>	20,000	<u>15,000</u>
	<u>0.75</u>	<u>88,000</u>	<u>21,000</u>	<u>16,000</u>
<u>200</u>	<u>0.25</u>	90,000	<u>30,000</u>	24,000
	<u>0.5</u>	92,000	<u>36,000</u>	<u>27,000</u>
	<u>0.75</u>	94,000	<u>40,000</u>	30,000
	<u>0.25</u>	94,000	<u>43,000</u>	<u>34,000</u>
300	<u>0.5</u>	97,000	<u>48,000</u>	<u>37,000</u>
	<u>0.75</u>	99,000	<u>52,000</u>	<u>39,000</u>
	<u>0.25</u>	<u>98,000</u>	<u>53,000</u>	<u>39,000</u>
400	<u>0.5</u>	100,000	<u>61,000</u>	46,000
	<u>0.75</u>	100,000	<u>65,000</u>	<u>51,000</u>

Discussion

As the COVID-19 pandemic progresses, countries are increasingly implementing a broad range of responses. Our results demonstrate that it will be necessary to layer multiple interventions, regardless of whether suppression or mitigation is the overarching policy goal. However, suppression will require the layering of more intensive and socially disruptive measures than mitigation. The choice of interventions ultimately depends on the relative feasibility of their implementation and their likely effectiveness in different social contexts.

Disentangling the relative effectiveness of different interventions from the experience of countries to date is challenging because many have implemented multiple (or all) of these measures with varying degrees of success. Through the hospitalisation of all cases (not just those requiring hospital support), China in effect initiated a form of case isolation, reducing onward transmission from cases in the household and in other settings. At the same time, by implementing widescale social distancing, the opportunity for onward transmission in all locations was rapidly reduced. Several studies have estimated that these interventions reduced $R_{\rm t}$ to below 1^{15} . In recent days, these measures have begun to be relaxed. Close monitoring of the situation in China in the coming weeks will therefore help to inform strategies in other countries.

Overall, our results suggest that large_scale social distancing applied to the population as a whole would have the largest impact; and in combination with other interventions – notably home isolation of cases and school and university closure – has the potential to suppress transmission below the

threshold of R_t =1 required to rapidly reduce case incidence. A minimum policy for effective suppression is therefore population-wide social distancing combined with home isolation of cases and school and university closure.

To avoid a rebound in transmission, In principle-these policies would-will_need to be maintained until large stocks of vaccine were-are available to immunise the population — which could be 18 months or more. Adaptive hospital surveillance-based triggers for switching on and off largescale social distancing and school closure offer greater robustness to uncertainty than fixed duration interventions and can be adapted for regional use (e.g. at the state level in the US). Given local epidemics are not perfectly synchronised, local policies are also more efficient and can achieve comparable levels of suppression to national policies while being in force for a slightly smaller proportion of the time. However, welt may be possible to temporarily relax social distancing once case numbers are in decline, on the understanding that those measures would need to be reintroduced once when case numbers rebounded, but we estimate that for a national GB policy, intensive social distancing measures would need to be in force for at least 2/3.75% of the time (for R_0 =2.4, see Table 4) until a vaccine was available. However, the large uncertainties around the likely effectiveness of different policies — and the extent to which the population spontaneously adopts risk reducing behaviours — means it is difficult to be definitive about the likely initial duration of measures (except that it will be several months). Future decisions on when and for how long to relax policies will need to be informed by ongoing surveillance.

The measures used to achieve suppression might evolve over time. As case numbers fall, it becomes more feasible to adopt intensive testing, contact tracing and quarantine measures akin to the strategies being employed in South Korea today. Technology – such as mobile phone apps that track an individual's interactions with other people in society – might allow such a policy to be more effective and scalable if the associated privacy concerns can be overcome. However, if intensive NPI packages aimed at suppression are not maintained, our analysis suggests that transmission will rapidly rebound, potentially producing an epidemic comparable in scale to what would have been seen had no interventions been adopted.

The measures used to achieve suppression might evolve over time. As case numbers fall, it becomes more feasible to adopt intensive testing, contact tracing and quarantine measures akin to the strategies being employed in South Korea today. Technology — such as mobile phone apps that track an individual's interactions with other people in society — might allow such a policy to be more effective and scalable if the associated privacy concerns can be overcome. However, if intensive NPI packages aimed at suppression are not maintained, our analysis suggests that transmission will rapidly rebound, potentially producing an epidemic comparable in scale to what would have been seen had no interventions been adopted.

Long-term suppression may not be a feasible policy option in many countries. Our results show that the alternative relatively short-term (3—month) mitigation policy option might reduce deaths seen in the epidemic by up to half, and peak healthcare demand by two-thirds. In all scenarios, our results Our analysis suggests that show that the combinations of case isolation, household quarantine and social distancing of those at higher risk of severe outcomes (older individuals and those with other underlying health conditions) are the most effective policy combination for epidemic mitigation. Both case isolation and household quarantine are core epidemiological interventions for infectious disease

mitigation and act by reducing the potential for onward transmission through reducing the contact rates of those that are known to be infectious (cases) or may be harbouring infection (household contacts). The WHO China Joint Mission Report suggested that 80% of transmission occurred in the household¹⁶, although this was in a context where interpersonal contacts were drastically reduced by the interventions put in place. Social distancing of high-risk groups is predicted to be particularly effective at reducing severe outcomes given the strong evidence of an increased risk with age^{12,16} though we predict it would have less effect in reducing population transmission.

We predict that school and university closure will have an impact on the epidemic, under the assumption that children do transmit as much as adults, even if they rarely experience severe disease^{12,16}. We find that school and university closure is a more effective strategy for epidemic suppression than mitigation; when combined with large_scale social distancing, the effect of school closure is to further amplify the breaking of social contacts between households, and thus supress transmission. However, school closure is predicted to be insufficient to mitigate (never mind supress) an epidemic in isolation; this contrasts with the situation in seasonal flu epidemics, where children are the key drivers of transmission due to adults having higher immunity levels^{17,18}.

The optimal timing of interventions differs between containment—suppression and mitigation strategies, as well as depending on the definition of optimal. However, for mitigation, the majority of the effect of such a strategy can be achieved by targeting interventions in a three-month window around the peak of the epidemic. For suppression, early action is important important, and interventions need to be in place well before healthcare capacity is overwhelmed. Given the most systematic surveillance occurs in the hospital context, the typical delay from infection to hospitalisation means there is a 2- to 3—week lag between interventions being introduced and the impact being seen in hospitalised case numbers, depending on whether all hospital admissions are tested or only those entering critical care units. In the UK GB context, this means acting before COVID-19 admissions to intensive care units CUs exceed 200 per week (check).

Perhaps our most significant conclusion is that mitigation is unlikely to be feasible without emergency surge capacity limits of the UK and US health systems being exceeded many times over. In the most effective mitigation strategy examined, which leads to a single, relatively short epidemic (case isolation, household quarantine and social distancing of the elderly), the surge limits for both general ward and eritical-care|CU beds would be exceeded by at least 9 fold under the more optimistic scenario for critical care requirements that we examined. In addition, even if all patients were able to be treated, we predict there would still be in the order of 250,000 deaths in the-UKGB, and 1.1-???????
1.2 million in the US.

We therefore conclude that epidemic suppression is the only viable strategy at the current time. The social and economic effects of the measures which are needed to achieve this policy goal will be profound. Many countries have adopted such measures already, but even those countries at an earlier stage of their epidemic (such as the UK) will need to do so imminently. Our analysis informs the evaluation of both the nature of the measures required and the likely duration that these measures will need to be in place. However, it is not at all certain that suppression will succeed; no public health intervention with such disruptive effects on society has been previously attempted for such a long duration of time. How populations and societies will respond remains unclear.

Acknowledgements

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Appendix

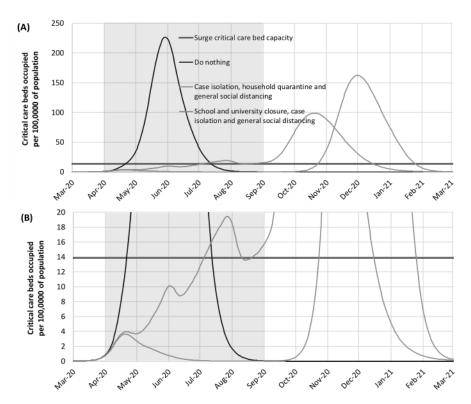


Figure A1: Containment strategy scenarios for the US showing critical care bed requirements. The black line shows the unmitigated epidemic. Green shows a containment strategy incorporating closure of schools and universities, case isolation and widescale social distancing. The orange line shows a containment strategy incorporating case isolation, household quarantine and widescale social distancing. The red line is the estimated surge critical care capacity in the UK. The blue shading shows the 5-month period in which these interventions are assumed to remain in place. (B) shows the same data as in panel (A) but zoomed in on the lower levels of the graph.

Commented [CD10]: This is not the term in the figure. It says "general social distancing". Table 2 says "Social distancing of the entire population" which is clearer.

Commented [CD11]: ICU?

Table A1. Mitigation options for the UK. Absolute impact of NPI combinations applied nationally for 3 months in the UK on total deaths and peak hospital ICU bed demand for different choices of cumulative ICU case count triggers. The cells show the absolute reduction in peak bed demand for a variety of NPI combinations and for triggers based on the absolute number of ICU cases diagnosed in a county per week. PC=school and university closure, Cl=home isolation of cases, HQ=household quarantine, SD=large-scale general population social distancing, SDOL70=social distancing of those over 70 years for 4 months (a month more than other interventions). Tables are colour-coded (green= higher effectiveness, red=lower).

	Trigger (cumulative ICU							
	cases)	PC	CI	CI_HQ	CI_HQ_SD	CI_SD	CI_HQ_SDOL70	PC_CI_HQ_SDOL70
	100	156	122	85	123	85	61	57
R0=2.4	300	157	122	85	121	78	60	53
Peak beds	1000	158	122	85	111	65	60	42
	3000	161	122	85	89	45	60	35
	100	125	105	70	120	98	50	83
R0=2.2	300	125	105	70	115	92	50	75
Peak beds	1000	126	105	70	106	76	49	59
	3000	132	105	70	86	51	49	40
	100	501	421	349	443	406	258	363
R0=2.4	300	499	421	349	440	393	259	360
Total deaths	1000	498	421	349	432	375	257	356
	3000	498	421	349	415	354	258	347
	100	451	367	308	423	395	238	373
R0=2.2	300	448	367	308	419	384	236	369
Total deaths	1000	445	367	308	412	366	234	360
	3000	445	367	308	396	340	234	351

Commented [CD12]: Not 5 months??

Commented [CD13]: Why not say "social distancing of the entire population" as in Table 2?

Commented [CD14]: This can't be right – Figure A1 shows a 5-month intervention so one month longer would be 6 months.