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Modelling to inform the COVID-19 response in Bangladesh

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13   **Abstract**

14   **Background:** Non-pharmaceutical interventions (NPIs) used to limit SARS-CoV-2 transmission vary in
15   their feasibility, appropriateness and effectiveness in different contexts. In Bangladesh a national
16   lockdown implemented in March 2020 exacerbated poverty and was untenable long-term, and a
17   resurgence in 2021 warranted renewed NPIs.

18   **Methods:** We developed an SEIR model for Dhaka District, parameterised from literature values and
19   calibrated to data from Bangladesh. We discussed scenarios and parameterisations with
20   policymakers with the aid of an interactive app. These discussions guided modelling of lockdown
21   and two post-lockdown measures considered feasible to deliver; symptoms-based household
22   quarantining and compulsory mask-wearing. We examined how testing capacity affects case
23   detection, and compared NPI scenarios on deaths, hospitalisations relative to capacity, working days
24   lost, and cost-effectiveness.

25   **Results:** Lockdowns alone were predicted to delay the first epidemic peak but could not prevent
26   overwhelming of the health service and were costly in lost working days. Impacts of post-lockdown
27   interventions depended heavily on compliance. Assuming 80% compliance, symptoms-based
28   household quarantining alone could not prevent hospitalisations exceeding capacity, whilst mask-
29   wearing prevented overwhelming health services and was cost-effective given masks of high
30   filtration efficiency. Combining masks with quarantine increased their impact. Even at maximum
31   testing capacity, confirmed cases far underestimate total cases. Recalibration to surging cases in
32   2021 suggests potential for another wave later in 2021, dependent on uncertainties in case
33   reporting and immunity.

34   **Conclusions:** Masks and symptoms-based household quarantining synergistically prevent
35   transmission, and are cost-effective in Bangladesh. Our interactive app was valuable in supporting
36   decision-making, with mask-wearing being mandated early, and community teams being deployed
37   to support quarantining across Dhaka. These measures likely contributed to averting the worst
38   public health impacts, but delivering an effective response at scale has been challenging. Messaging
39   to increase compliance with mask-wearing and quarantine is needed to reduce the risk and impacts
40   from another wave.

41

42   **Key words:** Coronavirus disease 2019 (COVID-19); Non-pharmaceutical interventions (NPIs); Low-
43   and middle- income countries (LMICS); Cost-effectiveness; Facemasks

Introduction

Human infections with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes the respiratory disease COVID-19, were first observed in China in December 2019 (Li et al., 2020). By the end of 2020, more than 80.3 million cases and 1.77 million associated deaths had been reported worldwide (European Centre for Disease Prevention and Control, 2021). With limited treatment options, countries turned to a range of non-pharmaceutical interventions (NPIs) to limit transmission. These measures include improved hygiene practices, social distancing, contact tracing, travel restrictions, quarantines, shielding of the vulnerable, lockdowns of differing severity, and facemasks. NPIs have been used by high-income countries (HICs) and low- and middle-income countries (LMICs) alike, but for a variety of reasons some of these measures may be less effective or more difficult to maintain in LMICs. Vaccines have come into play in 2021, but rollout has been almost exclusively in HICs. With negligible vaccination coverage and only NPIs to mitigate impacts, LMICs are now facing subsequent epidemic waves of faster-spreading variants and may have little protective immunity from prior infections (Cele et al., 2021; Planas et al., 2021).

Lockdowns can control COVID-19 epidemics by reducing the effective reproduction number, R_e, to below one (Flaxman et al., 2020). However, where many people live precariously without social support, lockdowns can exacerbate poverty (Amewu et al., 2020; Andam et al., 2020) and risk food security, whilst poor adherence limits their effectiveness. Social distancing may be impractical in densely populated areas (Anwar et al., 2020; Chowdhury et al., 2020; Gupta et al., 2020), hindered by larger household sizes and/or cramped conditions (Davies et al., 2020a). Urban slums and refugee camps, where rapid transmission and poor healthcare access co-occur, present a particular concern (Ahmed et al., 2020; Truelove et al., 2020). Shielding the most vulnerable, primarily older people and those with underlying health conditions (Clark et al., 2020), is also challenging in multi-generational households (Hodgins and Saad, 2020; Lloyd-Sherlock et al., 2020; United Nations, Department of Economic and Social Affairs, 2019a). Contact tracing is limited by testing capabilities (facilities, trained personnel, consumables, reagents and biosafety) (Anwar et al., 2020; Homaira et al., 2020; Rahaman et al., 2020) and information management capacity. Moreover, in settings where healthcare resources are already stretched, surge capacity is also low (Torres-Rueda et al., 2020).

Some features of LMICs may mitigate the health costs of any lowered efficiency of NPIs. The relatively younger populations in LMICs, with fewer underlying risk factors, means that a smaller proportion of cases are likely to be severe relative to HICs (Clark et al., 2020; Gupta et al., 2020; Hodgins and Saad, 2020). There has been speculation that the BCG (Bacillus Calmette-Guérin) vaccine, which is no longer routinely used in HICs, but is widely used in LMICs, may confer some protection from severe COVID-19, but evidence from trials is needed to confirm any association (Pereira et al., 2020). More generally, the wider social and economic consequences of NPIs may trade off against their impact on controlling disease, and the structure and underlying health of populations may impact the shape of this trade-off (Reidpath et al., 2020). Hence, there is an urgent need for the development and implementation of contextually appropriate interventions that take into account the population that they target and their needs (Hodgins and Saad, 2020).

During the pandemic, epidemiological models have received increased attention from governments and the public alike, and have influenced policy decisions worldwide (McBryde et al., 2020). However, a translational gap persists between policymakers and scientists working on models for disease forecasting and assessment of interventions. Early in the pandemic, this gap was exacerbated by uncertainties about the biology and transmission of SARS-CoV-2, and the limited information about its spread, given local testing and reporting capacities, not to mention people's behaviour. As a consequence, there is often simultaneously both overconfidence in, and mistrust of, models.

92 Ideally, policymakers, scientists and communities should work together to develop and implement
93 locally appropriate interventions. Models can play an important and overlooked role in facilitating
94 this process. By empowering decision-makers to better understand the mechanisms underpinning
95 the timescales and magnitude over which interventions lead to impact, as well as the uncertainties
96 and social and behavioural factors that affect their efficacy, co-created models can inform short- and
97 longer-term policies.

98 We investigate the potential impact of contextually appropriate NPI strategies to mitigate COVID-19
99 in Dhaka District, Bangladesh. High-density urban centres and refugee camps in Bangladesh led to
100 fears that strained health systems would be quickly overwhelmed (Anwar et al., 2020). Cases of
101 COVID-19 were first confirmed in Bangladesh on the 8th March 2020, and NPIs were subsequently
102 introduced, beginning with postponements to mass gatherings, followed by international travel
103 restrictions, and culminating in a national lockdown (announced as a 'general holiday') from 26th
104 March (Ahmed et al., 2020; Anwar et al., 2020). Rapid movement out of urban areas, particularly
105 from the capital city Dhaka, following the lockdown announcement led to virus spread across the
106 country (Anwar et al., 2020). The lockdown had swift economic repercussions: around 60% of
107 households lost their main income source, the majority of previously vulnerable non-poor
108 households slipped below the poverty line, and food security declined (Rahman et al., 2020). The
109 nationwide lockdown was quickly recognized as untenable long-term (ultimately ending on 1st June),
110 and considered only as a stop-gap measure.

111 With input from policymakers, we developed an SEIR model to compare the potential of NPIs
112 following the relaxation of lockdown. We designed an associated interactive app within which
113 policymakers could explore these scenarios to gain an understanding of how the model worked and
114 how uncertainties may influence outcomes. Here we compare scenarios based on projected 2020
115 COVID-19 deaths, and whether hospitalisations remain below capacity. We also explore associated
116 costs and the importance of having NPIs in place by the time lockdown ends. Finally, we examine
117 scenarios following resurgence of cases and a renewed lockdown in March 2021 and update our app
118 for ongoing policy use.

119

120 **Methods**

121 *Model description*

122 We developed a deterministic SEIR model comprising a set of ordinary differential equations (ODEs)
123 to describe SARS-CoV-2 transmission in Dhaka District, the most densely populated district in
124 Bangladesh. Dhaka District includes rural areas in addition to the city area itself, but, as case data
125 were resolved to district level, we consider the full district population, rather than restricting
126 analyses to the city population.

127 The model includes three infectious states, with latently infected individuals either becoming pre-
128 symptomatically infectious (I_p) before progressing to symptomatic infection (I_s), or becoming
129 asymptomatically infectious (I_a) until their recovery (Fig. 1). Susceptible individuals are exposed to
130 SARS-CoV-2 according to transmission rates specific to each infectious state (β^a , β^p and β^s).
131 These rates are based on: 1) asymptomatic individuals producing 65% of the secondary infections
132 produced by pre-symptomatic-to-symptomatic individuals (Yi et al., 2020); 2) 35% of secondary
133 infections from pre-symptomatic-to-symptomatic individuals happening in the pre-symptomatic
134 period (Liu et al., 2020); and 3) the value of R_0 :

135
$$R_0 = f^a \beta^a d^a + \left(1 - f^a\right)\left(\beta^p d^p + \beta^s d^s\right)$$

136 where $d^a = 7$, $d^p = 2$ and $d^s = 7$ are the mean durations (in days) of each infectious state (Byrne et
137 al., 2020; Hu et al., 2020), and f^a is the proportion of infections that are asymptomatic
138 (supplementary Table S4). Recovered individuals are considered to be immune.

139   We track numbers of both general and Intensive Care Unit (ICU) beds required by COVID-19
140 patients, and deaths due to COVID-19 (Fig. 1). A proportion of individuals $f^H \left(1 - f^{ICU} \right)$ that leave
141 the pre-symptomatic state join a holding category prior to progressing to general hospital beds,
142 while a second proportion $f^H f^{ICU}$ enters a holding category prior to entering ICU beds. Individuals
143 remain in these two holding categories from the first appearance of symptoms until the point at
144 which hospitalisation is required, on average 7 days (Liang et al., 2020; Linton et al., 2020). A third
145 holding category retains a proportion of individuals f^D from the first appearance of symptoms until
146 death, on average 20.2 days later (Linton et al., 2020; Verity et al., 2020). While we assume no
147 overlap between the groups in ICU versus general hospital beds, overlap between those that die and
148 the hospitalized groups is both permitted and expected. On leaving hospital, after a mean of 5 days
149 for general beds and 7 days for ICU (Rees et al., 2020), recovered individuals recuperate for an
150 average of 3 weeks before resuming work, if employed (Halpin et al., 2020). The number of
151 individuals in the seven health outcome states has no impact on transmission dynamics, and it is
152 assumed that there is no impact of a lack of hospital beds on the COVID-19 death rate. This
153 approach to modelling health outcomes is similar to that described in several other COVID-19
154 models (Davies et al., 2020b; Keeling et al., 2020).

155   We use data on the age structure of the Dhaka population (Bangladesh Bureau of Statistics,
156 2011) (supplementary Table S1) to inform parameters describing the risks of SARS-CoV-2 infections.
157 Previously estimated age-specific risk of death due to COVID-19, of hospitalisation for symptomatic
158 cases (Davies et al., 2020b), and of developing symptoms (Davies et al., 2020a) (supplementary Table
159 S2), were combined with the age distribution in Dhaka District, to estimate the overall proportions of
160 1) asymptomatic infections, $f^a = 0.701$, 2) symptomatic infections that lead to death, $f^D = 0.009$,
161 and 3) symptomatic infections requiring hospitalisation, $f^H = 0.073$. Of those hospitalised we
162 assume that the proportion requiring critical care in an ICU is $f^{ICU} = 0.31$ (World Health
163 Organisation (WHO), 2020a). We assumed no age-structure in contacts within our model.

164   The model was initially developed as an interactive epidemiological teaching tool
165 (http://boydorr.gla.ac.uk/BGD_Covid-19/CEEDS/), to allow policymakers to explore the impact of
166 interventions on health outcomes and working days lost. For speed and efficiency, and given the
167 large population (Dhaka District population in 2020 is around 13.8 million (Bangladesh Bureau of
168 Statistics, 2011; United Nations, Department of Economic and Social Affairs, 2019b)), the decision
169 was made to make the model deterministic rather than stochastic. We minimise computational
170 complexity by modelling transmission at the population level rather than at the level of the
171 individual or household. However, to more accurately model household quarantining, we further
172 subdivide the six disease states (Fig. 1) to track within-household transmission and account for
173 household-level susceptible depletion (Supplement A).

174   The ODEs comprising the model are provided in Supplement A and the model parameter
175 descriptions, values and sources, are listed in supplementary Table S4. Analyses were implemented
176 in R (R Core Team, 2019), with the ODEs numerically integrated using the package deSolve (Soetaert
177 et al., 2010). Code can be accessed from our Github repository
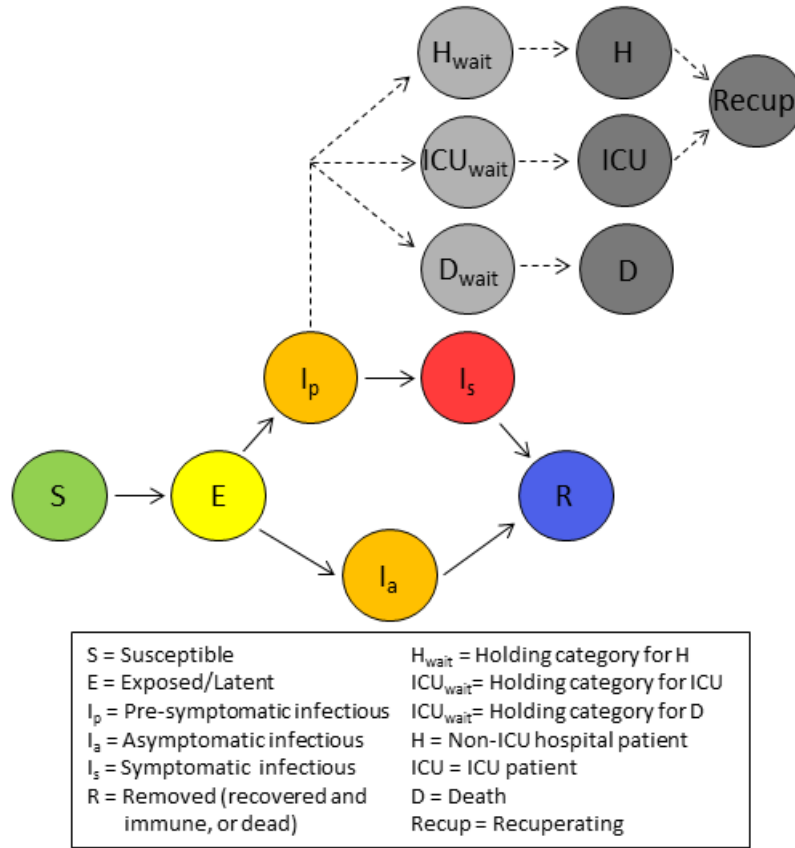178 (https://github.com/boydorr/BGD_Covid-19/BGD_NPI_model).

179

Figure 1: Model Schematic illustrating the movement of individuals between classes. Coloured circles indicate disease states that impact transmission. Grey circles describe health outcomes that are tracked but have no impact on disease transmission.

183

Interventions

We implemented three main NPIs – lockdown, household quarantining delivered through Community Support Teams (CSTs), and mask wearing – that were considered to be feasible by policymakers in Bangladesh. For each intervention we considered timing of implementation, scaling up and levels of compliance. In real-time we explored these interventions with policymakers including the lockdown duration, however here we model lockdown as implemented (26th March to 1st June 2020) and consider additional lockdown extensions, which, despite their impracticality, allow comparison to more feasible scenarios.

We define a lockdown as a scenario where all except essential workplaces are closed, including educational facilities, and people are asked to stay home where possible and practice social distancing. For compliant individuals and those that are not essential workers, this intervention is assumed to reduce contacts, and therefore transmission, outside of the household by the proportion ε^{ld}, while leaving within-household transmission unchanged. We achieve this by breaking down the transmission rates for the three infectious states into within- and between-household components using estimates of the SARS-CoV-2 household secondary attack rate, $\sigma = 0.166$ (Madewell et al., 2020), and the mean household size, $\eta = 4$ (Bangladesh Bureau of Statistics, 2016). We considered a scale-up period for the lockdown, during which compliance increased linearly from zero to a maximum. Following scale-up, we assume compliance starts to decline exponentially towards a minimum. Full details of implementation are given in Supplement A.

203   Under the household quarantine intervention, when a symptomatic individual occurs, that
204   individual's entire household is required to quarantine for 14 days. Those who develop symptoms
205   can self-report to a national COVID-19 hotline or are identified by word-of-mouth, triggering a visit
206   by CST, a volunteer workforce of community-based support workers trained by BRAC/FAO. The CST
207   confirm that symptoms are syndromically consistent with COVID-19, provide information on how to
208   limit spread, facilitate access to healthcare, and offer support to aid quarantine compliance, with
209   additional follow-up during the quarantine period.

210   Modelling household quarantine requires us to both identify both those individuals that
211   trigger quarantining (the first symptomatic individuals within households), and other individuals in
212   their households who also undergo quarantine. We subdivide the disease states to identify those
213   not currently in an infected household, those in a non-quarantined infected household, and those in
214   a quarantined household. When a susceptible individual in an uninfected household becomes
215   latently infected (through between-household transmission), $\eta - 1$ other individuals also move from
216   uninfected household categories into categories that identify them as being in a non-quarantined
217   infected household, making them vulnerable to both within-household and between-household
218   transmission. We track the group of individuals who were the first infected within a household
219   separately to those who subsequently became infected, allowing us to observe when household
220   index cases become symptomatic. A proportion of these symptomatic index cases comply with
221   quarantine, taking $\eta - 1$ individuals from non-quarantined infected households with them. We also
222   trigger quarantines when within-household cases resulting from index asymptomatic cases become
223   symptomatic. The equations generating these dynamics are described in Supplement A. Infectious
224   individuals within quarantined households are assumed to not cause any between-household
225   transmission. As with lockdown, household quarantining with CST support has defined start and end
226   times, and the proportion of households that comply increases linearly through a scale-up period,
227   after which compliance remains at a constant maximum (see Supplement A).

228   Finally, we considered compulsory mask-wearing outside of the household. Within the
229   model, masks are assumed to block a proportion, ε^m, of between-household transmission from
230   compliant individuals, while also blocking a proportion, $\varepsilon^m \rho^m$, of transmission to compliant
231   individuals, where $0 \le \rho^m \le 1$, i.e. masks protect others from the wearer, and the wearer from
232   others, to different degrees, with protection provided to the wearer never greater than that
233   provided to others (Howard et al., 2020; Stutt et al., 2020). The full description of mask wearing
234   effects, in relation to timing and compliance is provided in the Supplement A.

235   We model working days lost due to both illness and interventions. Based on the 2011
236   census (Bangladesh Bureau of Statistics, 2011), we assume 52% of the population is formally
237   employed, working five days a week. We model symptomatic and recuperating individuals to be off-
238   sick, and assume that deaths result in loss of all subsequent working days through 2020. During
239   lockdown, those workers that are both compliant and not essential workers lose their working days.
240   Those in quarantined households do not work, and, since household quarantine is based on
241   symptoms, we assume that, in addition to those quarantined due to COVID-19, a proportion of
242   households affected by non-COVID-19 influenza-like illnesses also undergo quarantine. Based on the
243   2011 census, 23% of the population is unemployed, but works within the household, e.g. with caring
244   responsibilities (Bangladesh Bureau of Statistics, 2011). When these individuals are hospitalised or
245   die, we assume another (possibly formally employed) household member replaces them, leading to
246   further loss of working days. Finally we assume that, in response to each death, a number of
247   grieving individuals (taken to be $\eta - 1$) do not work for a week. Details of the working days lost
248   calculation are provided in equations S.16-17.

Scenario comparison

With input from policy-makers, we explored 15 combinatorial scenarios for 2020, including a baseline with no interventions and unmitigated SARS-CoV-2 spread.

The first of four lockdown-only scenarios aimed to replicate the lockdown as implemented, from 26th March until 1st June 2020. The other three lockdown-only scenarios involved extending the lockdown by 1, 2 and 3 months. In all four scenarios we assume scale-up occurs over one week, with peak compliance of 80%, declining towards 30% (supplementary Fig. S1D); considered to be qualitatively similar to practice in Dhaka. The impact of lockdown on between-household transmission of compliant individuals ε^{ld} was estimated during model calibration (see below).

We also examined scenarios where lockdown, as implemented in Bangladesh, was followed by either CST interventions, compulsory mask-wearing or both, beginning a week before lockdown ended and continuing through 2020 with a 7-day scale-up period and 80% peak compliance with each intervention. The ability of masks both to protect others from transmission from the wearer and to protect the wearer from transmission from others depends on several variables, including the material used, the construction (e.g. layers of material), and the quality of fit (Aydin et al., 2020; Davies et al., 2013; Howard et al., 2020). Therefore, for mask-wearing we consider scenarios where there is low, medium, and high protection of others from the wearer ($\varepsilon^m = \{0.2, 0.5, 0.8\}$), and where the protection provided to the wearer is zero, half that provided to others, or equal to that provided to others ($\rho^m = \{0, 0.5, 1\}$), giving nine mask-wearing scenarios.

For the 2020 time horizon we compared the total: 1) hospitalisations, 2) deaths, 3) percentage of patient days exceeding hospital capacity (the sum of patients in excess of hospital beds each day, divided by the summed total patients over all days), 4) working days lost, 5) cost of implementing interventions and of healthcare for COVID-19 patients, 6) cost per death averted (relative to no intervention), and 7) the percentage return (in terms of healthcare savings) on investment (%ROI) in interventions. For estimating total cost we include healthcare provision for hospitalised COVID-10 patients, media campaigns, training and deployment of CSTs, and mask distribution, as detailed in Table 1. For each scenario, we used the total cost to estimate the cost per death averted. This was calculated by subtracting the cost of the baseline scenario from that of the focal scenario, then dividing by the reduction in deaths from the baseline. The %ROI for each scenario was calculated by subtracting the total cost of each scenario from the baseline, and dividing by the intervention implementation costs (i.e. the sum of all costs other than hospital care).

Given the heavy societal and economic costs of lockdowns, they are typically viewed as temporary measures to buy time for implementation of other less restrictive measures (e.g. mask wearing) or more targeted measures (e.g. household quarantines and contact tracing). To explore the impact of preparedness prior to lockdown ending, we examined the sensitivity of model outcomes (hospitalisations, deaths, working days lost, and exceeded hospital capacity) to the scale-up period and start date of post-lockdown interventions. Modelling lockdown as implemented in Bangladesh, we looked at scenarios where lockdown was followed by household quarantining only, mask-wearing only (assuming mask protectiveness parameters $\varepsilon^m = 0.5$ and $\rho^m = 0.5$), or both. We varied the start date of the post-lockdown intervention(s) from 30 days pre- to 30 days post-lockdown ending, while keeping the scale-up period constant at 7 days, and vice versa varying the scale-up period (zero to 30 days), while keeping the start constant (7 days prior to the lockdown end).

293 **Table 1: Costs associated with healthcare and interventions, derived from ongoing practices in Bangladesh.**

Item	Description of activities	Costs (USD)
Hospital care	Provision of hospital beds and associated care (mechanical ventilation, oxygen etc.) for severely ill COVID-19 patients.	$649/week/ICU patient $266/week/non-ICU patient
Community Support Team (CST) package	The CST package covers: - community health worker training and equipment - monthly per volunteer running costs, covering honorarium, phone credit, PPE for activities and management. Each volunteer can visit 20-40 quarantining households per day. Plans were to train 2000 volunteers, which was deemed sufficient to cover the Dhaka District population.	$200/volunteer trained and equipped $240/month/volunteer running cost $8,962/month advertising cost
Masks	An average of 5 re-usable cloth masks was provided to each household in Dhaka District. Mask wearing was promoted through a public awareness campaign.	$1/mask $8,962/month advertising cost
Lockdown	Public awareness campaign to encourage people to remain at home and practice social distancing.	$8,962/month advertising cost

294

295 *Model calibration*

296 We calibrated two parameters, R_0 and ε^{ld}, the proportion by which lockdown reduces between-
297 household transmission from compliant people, against daily COVID-19 death data in Bangladesh
298 (European Centre for Disease Prevention and Control, 2020). We chose to calibrate against reported
299 deaths rather than cases, since death data are less affected by testing and reporting capacity. To
300 obtain a time-series of deaths in Dhaka District, we extracted the proportion of district-resolved case
301 totals for Dhaka District from Bangladesh's COVID-19 dashboard ("Coronavirus COVID-19 Dashboard,
302 2020," 2020) and assumed this proportion remained constant. The first three cases in Bangladesh
303 were confirmed on 8th March 2020, but it is thought likely that infection began circulating
304 undetected prior to this, with genomic data indicating an introduction in mid-February and at least
305 eight introduced cases prior to the ban on international travel (Cowley et al., 2021). We therefore
306 initialise the model with eight infectious cases on 15th February 2020. The value of R_0 was
307 optimised to minimise the absolute difference between modelled and reported cumulative deaths
308 on the date lockdown started (26th March). Following this optimisation of R_0, the value of ε^{ld} was
309 similarly estimated by minimizing the difference between modelled deaths and data on the date
310 lockdown ended.

311   We recalibrated the model to data (Krispin and Byrnes, 2021) from the rapid resurgence
312 beginning in March 2021 to learn about the likely R_0 at that time, when B.1.351 increased in

9

313 frequency to become the dominant virus variant (Saha et al., 2021). In March 2021, levels of mask-
314 wearing and compliance with household quarantine were low, and there was no lockdown in place.
315 As cases increased, a loose lockdown was introduced on 5th April, with stronger restrictions applied
316 on 14th April and maintained until end May, with some relaxing of restrictions over this period. We
317 modelled this with a lockdown from 5th April to 1st June, with a 9 day scale-up period, maximum
318 compliance of 80%, and the same rate of declining compliance as in 2020 (supplementary Fig.S1C).
319 We also assume that from 5th April to 1st June there is an increase in both mask-wearing (with
320 $\varepsilon^m = 0.5$ and $\rho^m = 0.5$) and household quarantine, with a scale-up period of 9 days to reach a
321 compliance of 30%. Given considerable uncertainty around the number of infectious and immune
322 individuals in the population, we calibrated the model under a range of initialisation scenarios in
323 terms of immunity levels (0%, 25% and 50%) and circulating cases on 1st March. We assumed that
324 reported daily new cases represented around 10% of true cases (supplementary Fig. S1C), and that
325 prevalent infectious individuals were about eight times incident daily cases given the infectious
326 period duration. Dividing by two, assuming that these individuals are on average halfway through
327 their infectious period, we get an effective number of 11,451 infectious individuals for initialization
328 and an equivalent number of incubating individuals, but we also considered numbers 50% higher
329 and lower than this. We took two approaches to optimisation of R_0, minimizing the difference: 1)
330 between modelled and reported cumulative deaths over the period from 1st March-5th April 2021,
331 and 2) in the timing of the peaks in reported cases and modelled symptomatic cases (with the
332 constraint that modelled cumulative deaths from 1st March until 20th May had to be at least as high
333 as reported deaths over the same period).

334

335 *Sensitivity Analyses*

336 There is considerable uncertainty in the parameters governing SARS-CoV-2 transmission and health
337 impacts. We therefore undertook one-way sensitivity analyses across parameter value ranges for R_0
338 , the duration of disease states and health outcome stages, the introduction date, the household
339 secondary attack rate, the ratios of asymptomatic to symptomatic transmission, and of pre- versus
340 symptomatic transmission identified as plausible from the literature (supplementary Table S4). The
341 impact of changes in each of these parameters on the main model outputs was assessed individually,
342 while keeping other parameter values fixed. We ran this analysis over scenarios of: 1) no
343 interventions; 2) lockdown as implemented; 3) lockdown plus household quarantining; and 4)
344 lockdown plus compulsory mask wearing (with $\varepsilon^m = 0.5$ and $\rho^m = 0.5$).

345

346 **Results**

347 *Model calibration*

348 We estimated that $R_0 = 3.57$ for transmission of SARS-CoV-2 in Dhaka in 2020, and that the
349 lockdown reduced between-household transmission (ε^{ld}) by 97% for compliant individuals. The
350 match between modelled deaths and data during the early stages of the epidemic is illustrated in
351 supplementary Fig. S1A and B). Outputs from the calibrated model until the lockdown end indicate
352 that less than 10% of cases were recorded during this period (supplementary Fig. S1C). We further
353 explored how testing capacity might impact case detection within our interactive app, which
354 similarly indicated that the low, but increasing, testing capacity in Dhaka would fail to detect a high
355 proportion of cases given the high proportion of asymptomatic cases and distribution of tests to
356 individuals with other influenza-like illnesses.

357 Our estimates of R_0 in 2021 varied based on the initialisation scenario, with values increasing with
358 lower initial circulating cases and higher levels of immunity in the population (supplementary Table
359 S5). The approach used to optimise R_0 also impacted the estimates, with optimisation based on
360 matching to deaths in the early stages of the resurgence leading to lower values (range of 2.19-6.06)
361 compared to peak matching (range of 3.90-8.20). Our best guess initialisation scenario (11,451
362 initial infections and 25% prior immunity), led to an R_0 estimate of 3.32 when matching to deaths
363 and 5.30 when matching to peak timing, and corresponding death detection estimates of 32-75%
364 (matching to deaths), or 8-22% (peak matching). The peak in symptomatic cases obtained by
365 matching to deaths was always slightly later than the peak in reported cases, though never by more
366 than four days. When calibrated to the trajectory of deaths, the model predicted that while NPIs
367 controlled the resurgence, another peak will occur in the coming months following their relaxation
368 (supplementary Fig. S2C). In contrast, calibration by matching peak timing leads to the prediction
369 that the resurgence sufficiently spread through the remaining susceptible population to prevent
370 further waves (supplementary Fig. S2D).

371

372 *Impacts of scenarios on health outcomes and working days lost*

373 In the absence of interventions we predicted that COVID-19 patients would peak at 46,309 in late
374 May (Fig. 2A), greatly exceeding hospital bed capacity (estimated to be 10,947 in Dhaka District
375 (World Health Organisation (WHO), 2020b); supplementary Table S4). Under this scenario hospital
376 beds would have been unavailable for at least 55% of patient days (Fig. 3D) without accounting for
377 non-COVID-19 bed needs. Assuming unmitigated transmission, the epidemic would have likely led to
378 around 13.3 million cases (i.e. most of the Dhaka District population; supplementary Table S4) and
379 35,849 deaths (Figs. 3A, S2A & S3A). Although high relative to some of the mitigated scenarios,
380 these deaths represent 0.26% of the population, and would be expected to lead to a loss of <1% of
381 total working days (Fig. 3C).

382 We forecast that the lockdown as implemented in Bangladesh would delay the epidemic
383 (Figs 2A and S2A), with minor impacts on deaths and hospitalised cases (Fig. 3), while increasing
384 working days lost to 9.6%. Extensions were predicted to delay and widen the peak (Figs 2A and S2A,
385 extensions shown for up to three months, as further extensions had little impact on the epidemic
386 peak or total outcomes). Even with lockdown extensions, hospitalisations were still expected to
387 outstrip capacity (Fig.2A), with only modest reductions in deaths (Fig.3). Working days lost were
388 predicted to increase by 2.5-3.5% with each extra month of lockdown (Fig.3C).

389 We found that introducing household quarantining following lockdown led to the epidemic
390 peak being later, lower and wider than with lockdown alone (Figs 2A and S2A). Hospital capacity
391 was still exceeded, with deaths and hospitalisations reduced to levels similar to those achieved by a
392 three-month extension to lockdown. The additional working days lost by introducing and
393 maintaining household quarantines throughout 2020 were fewer than those lost by a one-month
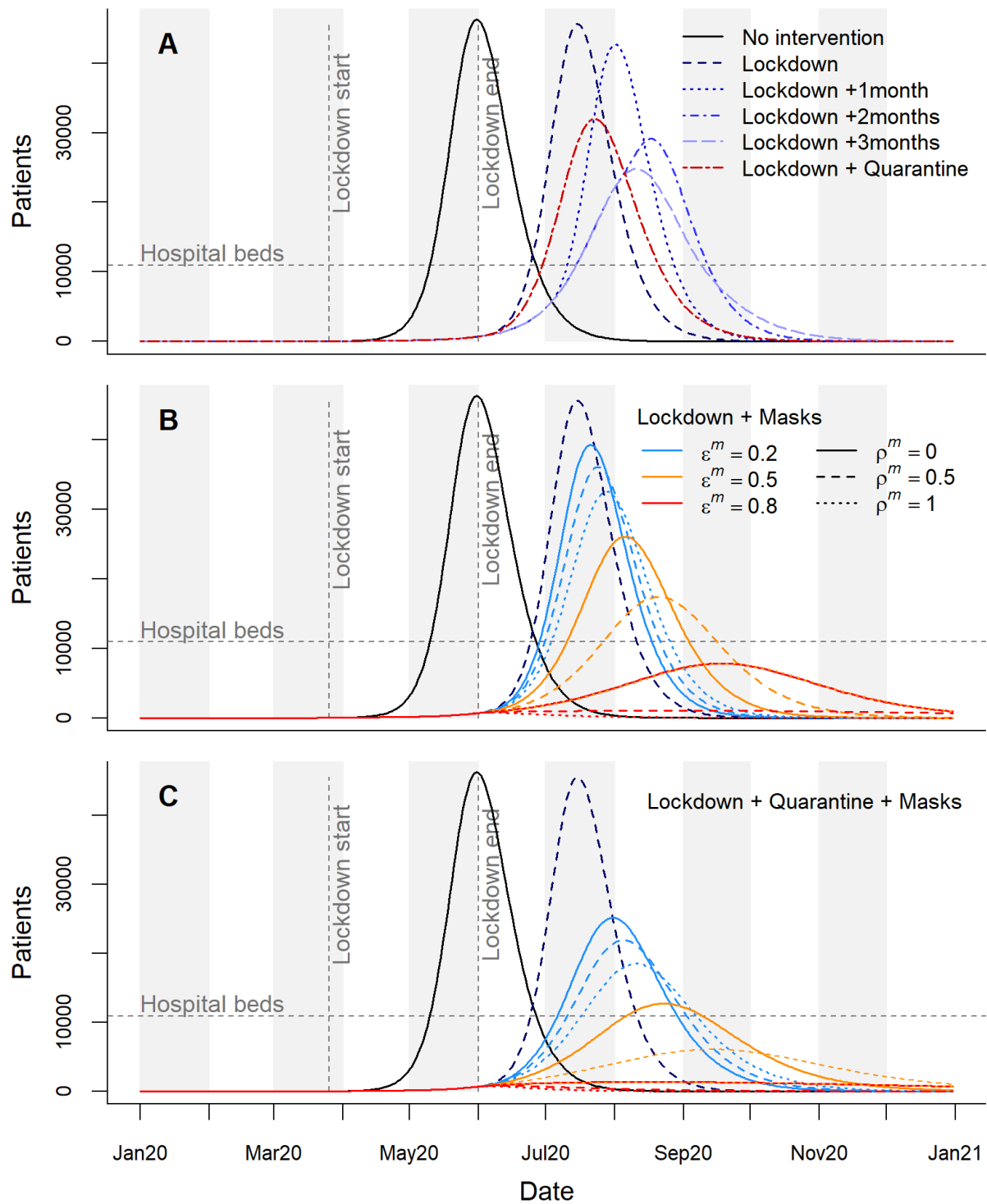394 lockdown extension (Fig. 3C).

11

Figure 2: Time series of hospital patients for intervention scenarios in 2020. Horizontal dashed lines indicate hospital bed capacity in Dhaka District. Vertical lines indicate the start and end points of lockdown as implemented in Bangladesh. A) Hospital patients in the absence of interventions, for the implemented lockdown plus extensions of up to 3 months, and for lockdown followed by household quarantine with community support teams. B) Lockdown as implemented followed by compulsory mask wearing, considering nine mask effectiveness scenarios; ε^m describes the proportion reduction in outward emissions by mask wearers, while $\rho^m \varepsilon^m$ describes the proportion protection to mask wearers from others' emissions. C) Combined impacts of the lockdown, household quarantine, and masks of different effectiveness.
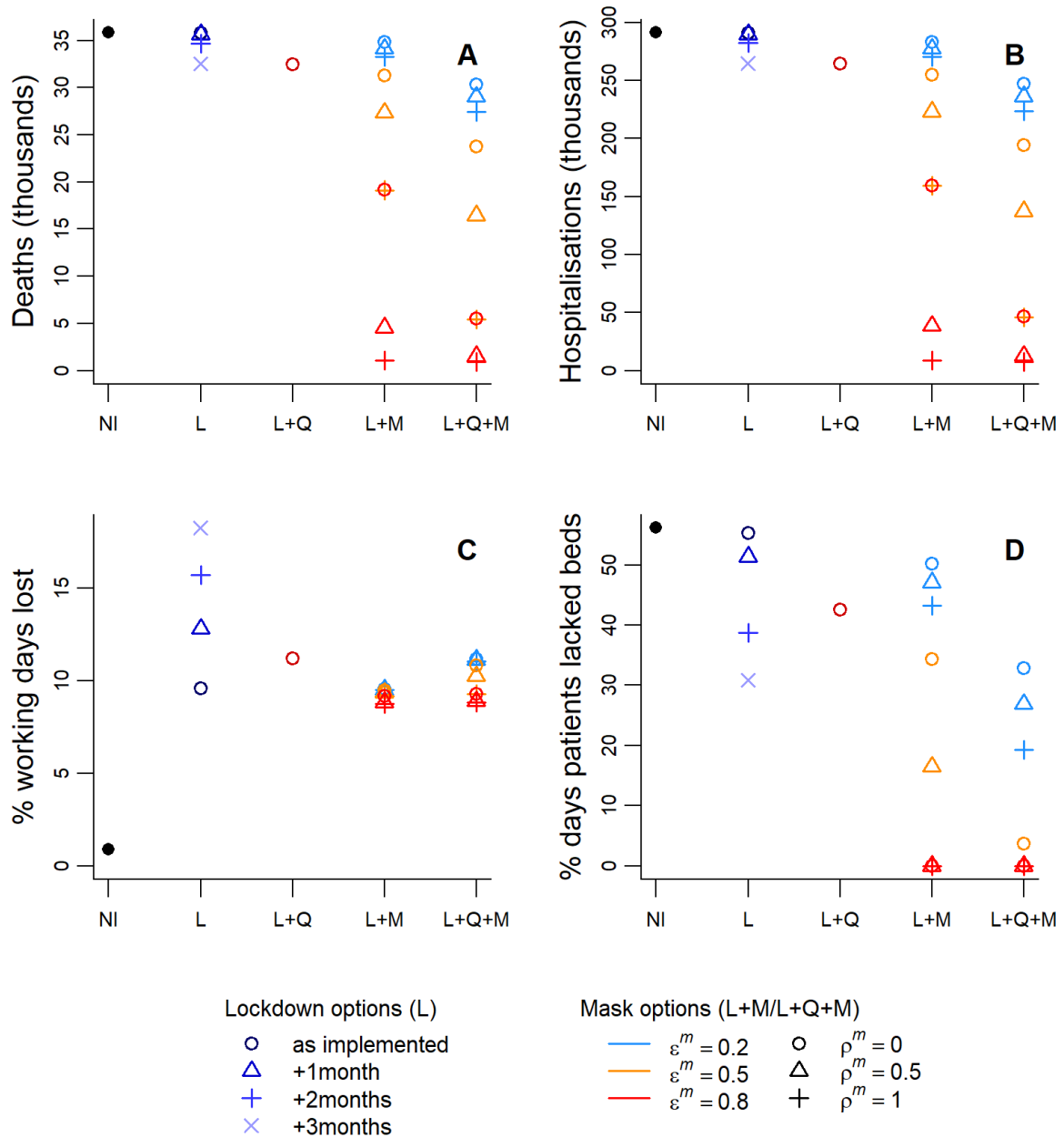
Figure 3: Summaries of health outcomes and working days lost for a range of interventions during 2020. NI=no intervention, L=lockdown, Q=household quarantine with community support teams, M=compulsory mask wearing. ε^m describes the proportional reduction in outward emissions by mask wearers, while $\rho^m \varepsilon^m$ describes the proportion protection provided to the mask wearer from others' emissions.

The impact of introducing compulsory mask-wearing following lockdown varied based on the effectiveness of the masks used (Figs 2B and 3). When $\varepsilon^m = 0.2$, i.e. low filtration efficiency, only relatively small reductions to the epidemic peak were predicted, with the decline increasing with mask effectiveness in terms of PPE (indicated by increasing ρ^m; Figs 2B and S2B). Masks with high filtration efficiency ($\varepsilon^m = 0.8$), or medium filtration efficiency combined with high PPE efficiency ($\varepsilon^m = 0.5$, $\rho^m = 1$) flattened the peak sufficiently to keep patient numbers below hospital capacity (Figs 2B and 3D). Effective masks also led to substantial drops in deaths and

13

417 hospitalisations, while slightly reducing working days lost relative to the lockdown-only scenario (Fig.
418 3).

419 Combining mask-wearing with household quarantine led to greater predicted reductions in
420 the epidemic peak and in both deaths and hospitalisations than either intervention alone (Figs 2C
421 and 3A-B). Percentages of working days lost increase as mask quality decreases, ranging from 8.8-
422 11.2%. A combined strategy of masks and quarantine following lockdown was strategized for
423 implementation in Dhaka District. In the end, mask provision was not directly funded despite
424 recommendations, but mask-wearing was promoted; by late 2020 mask use had largely declined to
425 normal levels. The data-based estimates of cumulative deaths in Dhaka District take a path similar to
426 those modelled by combining quarantining with either masks of high filtration effectiveness (
427 $\varepsilon^m = 0.8$) and low to medium PPE abilities (ρ^m of 0 or 0.5), or with masks of medium filtration
428 effectiveness ($\varepsilon^m = 0.5$) and $\rho^m = 1$ (supplementary Fig. S4C).

429

430 *Scenario costs*

431 Total costs of the scenarios explored ranged from $20.2.0-111.4 million (Fig. 4A). Despite requiring
432 no direct intervention costs, the baseline scenario is among the most expensive due to the
433 healthcare costs incurred by hospitalisations. Lockdown as implemented was predicted to be similar
434 in cost to the baseline (unmitigated transmission) with modest declines for lockdown extensions.
435 Incorporating household quarantine led to costs similar to extending lockdown for 2-3 months.
436 Combining lockdown with low effectiveness masks led to the highest costs due to the expense of
437 mask distribution, offset by only small reductions in healthcare costs. Masks of high effectiveness,
438 however, led to substantial cost reductions, which generally increased when masks and household
439 quarantine were modelled together.

440 Since most scenarios had a lower total cost than the baseline, the cost per death averted is
441 negative except in some of the lower effectiveness mask scenarios (Fig. 4B). Extended lockdowns,
442 and lockdowns combined with household quarantine and/or high effectiveness masks all provide
443 similar savings per death averted in the $1,500-$2,700 range.

444 The %ROI was generally positive, again with some exceptions where low effectiveness masks
445 were used (Fig. 4C). By far the highest %ROIs were given by extending lockdown by 2-3 months.
446 This is because, despite relatively small reductions in hospitalisations (Fig. 3B), the only costs to
447 lockdown extension are in advertising, and these costs are small relative to those of providing masks
448 to every household or maintaining CST (Table 1). Lockdown plus quarantining gave a %ROI of 127%.
449 The %ROI of all scenarios involving masks increased with the effectiveness of the masks in blocking
450 transmission. Interventions involving high effectiveness masks all had a higher %ROI than the
451 lockdown plus quarantine scenario.

452

453 *Intervention timing and scale-up*

454 Starting either household quarantining or compulsory mask-wearing prior to the end of lockdown
455 had little projected impact on health outcomes or the percentage of working days lost (Fig. 5A-D).
456 When masks and quarantining are combined, however, total deaths and hospitalisations are seen to

457 decline in response to moving their start dates further before the end of lockdown. This difference
458 occurs because the combined early start date of the two interventions pushes the epidemic peak
459 later (into 2021) than when considering either individually. Continuing interventions and calculating
460 outcomes over both 2020 and 2021, removes this apparent improvement in outcomes with start
461 dates prior to lockdown's end (supplementary Fig. S5A-D). As the start date of quarantining and
462 mask-wearing is delayed beyond the lockdown end date, their health benefits decline, with all
463 outcomes approaching those of the lockdown-only scenario. Similar consequences to delaying
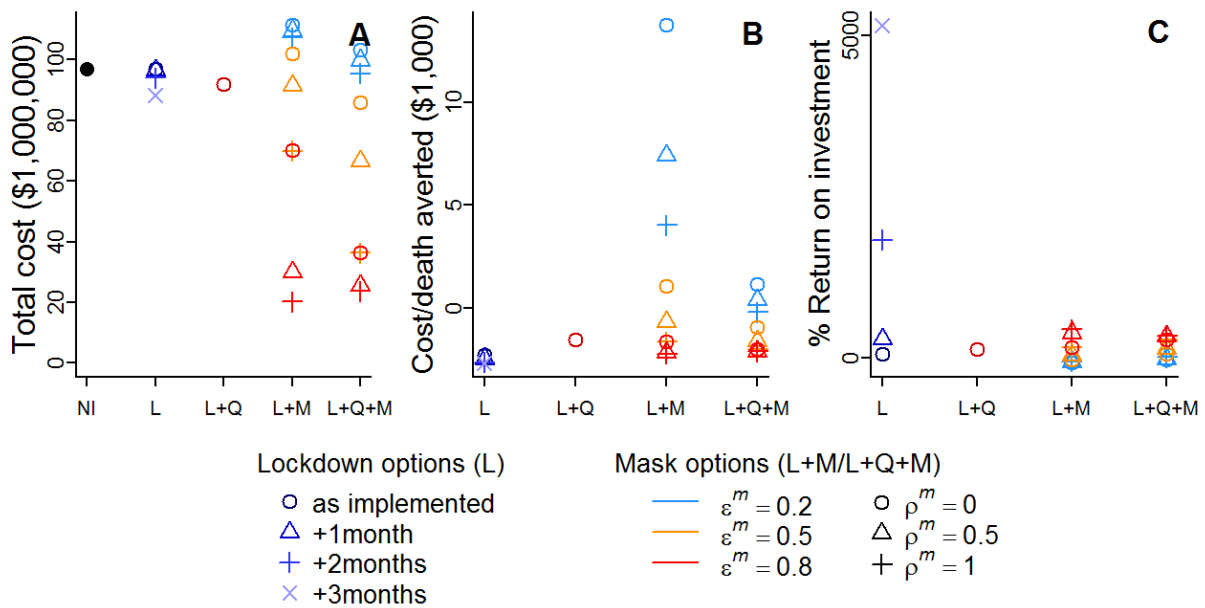464 intervention start dates result from lengthening the scale-up period (Fig. 5E-H).

465

466

467 **Figure 4: Costs of intervention scenarios.** NI=no intervention, L=lockdown, Q=household quarantine with
468 community support teams, M=compulsory mask wearing. ε^m describes the proportional reduction in
469 outward emissions by mask wearers, while $\rho^m\varepsilon^m$ describes the proportion protection provided to the mask
470 wearer themselves from others' emissions. A) Total cost of each intervention scenario to the government
471 based on costings in Table 1. B) Cost of each death averted relative to the baseline (NI) scenario. C)
472 Percentage return on investment in interventions in terms of healthcare savings.

473 *Sensitivity Analyses*

474 R_0 was among the top three most influential parameters for all five outcome measures reported
475 under all four baseline scenarios (Figs. S5-8). The duration of symptoms was among the top three
476 most influential parameters in determining working days lost (since symptomatic people are unable
477 to work) over all baselines, and, predictably, the mean lengths of stay in general hospital and ICU
478 beds were highly influential for the percentage of patient days that lacked beds. For all baselines,
479 other than that with no interventions, the introduction date of the disease ranked in the top three
480 most important parameters for all outcomes except the percentage of patient days lacking beds.
481 Some parameters only gained importance under specific baseline scenarios (for example, the level of
482 asymptomatic transmission becomes important under symptoms-based household quarantine); for
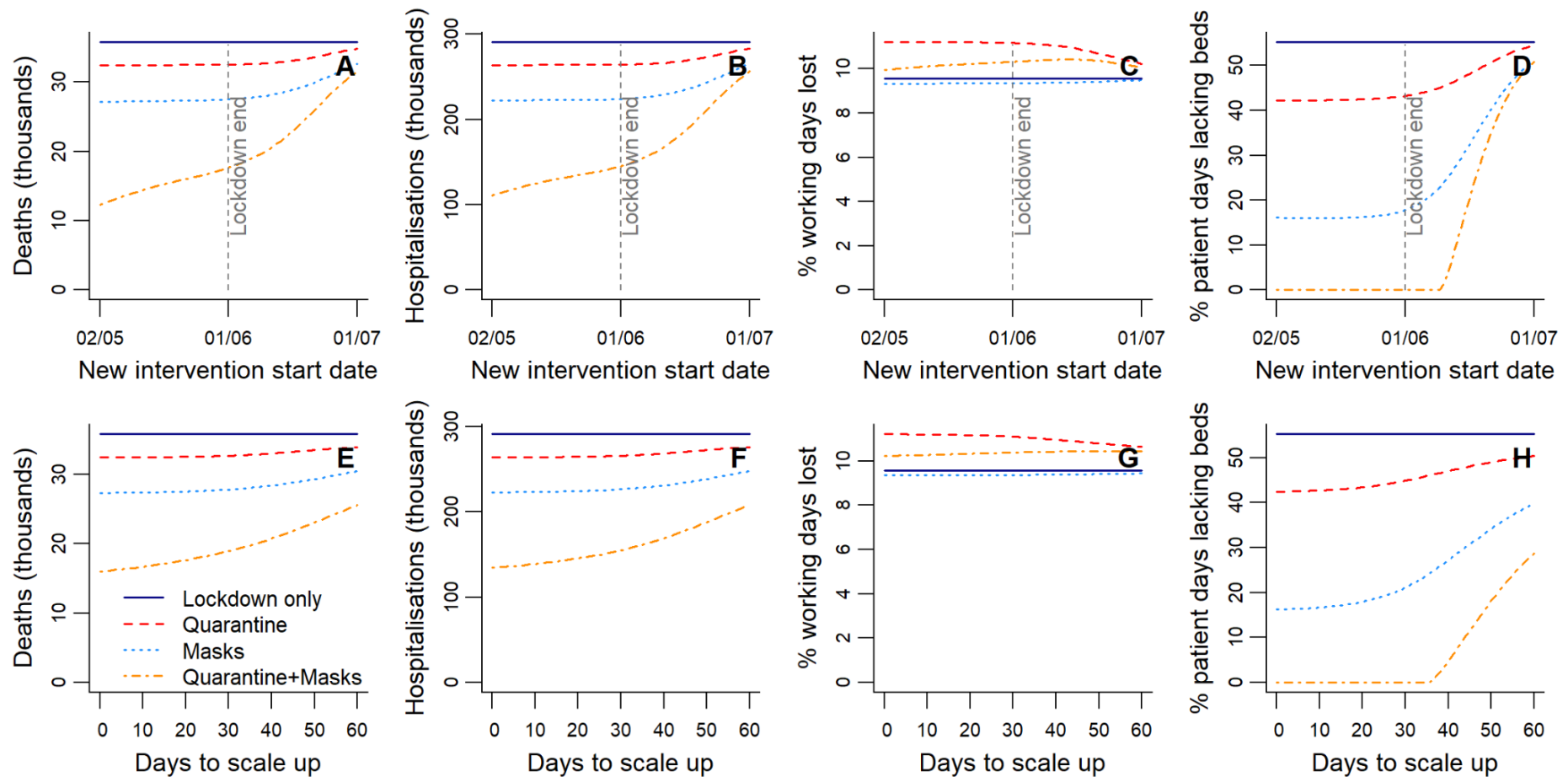483 more details see Supplement D.

Figure 5: Sensitivity to the start date and scale-up period of quarantine or mask wearing following lockdown. A-D) Changes in health outcomes and working days lost over 2020 when the start date of interventions (household quarantine, masks, or quarantine and masks) following lockdown is adjusted relative to the lockdown end date. The days taken to scale up interventions to their full effectiveness is held constant at seven days. E-H) Changes in the same outcomes when the time in days taken to scale up post-lockdown interventions is varied. The start date of the post-lockdown interventions is held constant at seven days prior to the lockdown end date.

Discussion

We modelled interventions for controlling COVID-19 transmission in Dhaka District, Bangladesh, comparing them based on their ability to prevent both deaths and overwhelming of the health system, as well as on their societal and health provider costs. We found that under expected compliance, lockdowns alone, regardless of duration, were both costly and unable to keep cases below hospital capacity, while preventing only a small proportion of deaths, confirming that they are not an appropriate long-term measure in this context (Amewu et al., 2020; Andam et al., 2020; Rahman et al., 2020). Additional quarantining of households with symptomatic individuals similarly was not predicted to prevent hospitalisations exceeding capacity. Modelling compulsory mask-wearing after the lockdown produced outcomes that varied widely depending on the effectiveness of masks in blocking transmission. Low-quality masks had limited impacts and were not cost-effective, whereas high-quality masks substantially reduced deaths, protected the healthcare system and were cost-effective. Combining mask-wearing and household quarantine led to further reductions in deaths and excess hospitalisations, and was cost effective when masks were of high quality. Simulations also suggest that early introductions of post-lockdown measures would have had negligible additional impact over the full course of the epidemic (though they may improve outcomes in the short-term), but gaps between lockdown ending and post-lockdown interventions (or long periods of scale-up) quickly dilute their impacts.

The inability of symptomatic household quarantining alone to prevent hospitalisations exceeding capacity is unsurprising. Even in HICs with greater healthcare capacity, lower R_0 estimates, and a lower proportion of asymptomatic transmission, other modelling studies have suggested that symptoms-based household quarantine would still overwhelm health systems (Aleta et al., 2020; Ferguson et al., 2020). Additional tracing and quarantine of non-household contacts of symptomatic individuals can improve the effectiveness of quarantine measures (Aleta et al., 2020). However capacity for extensive contact tracing is likely to be limited in high-density resource-constrained settings like Dhaka. The finding that combining symptomatic household quarantining with mask mandates (using mid- to high-quality masks) leads to effective control was crucial at the time, since both these NPIs were considered feasible. Given that household quarantining is triggered by a symptomatic case, and we estimate that most cases in Bangladesh are asymptomatic, a large proportion of infectious households are still likely missed by this measure, which will also have only limited impact on pre-symptomatic transmission. Since masks reduce transmission for all infections, irrespective of symptoms, masks work synergistically with household quarantine. While we consider scenarios where masks block only 20% of transmission, we note that this is a worst case scenario; experimental work suggests that our mid- to high-quality mask scenarios (blocking 50-80% of transmission) are more likely (Aydin et al., 2020; Davies et al., 2013). Observational (Hong et al., 2020; Wang et al., 2020) and other modelling (Stutt et al., 2020) studies provide further evidence for the effectiveness of masks in blocking transmission.

In reality, achieving the modelled effectiveness of household quarantining and mask-wearing depends on high compliance (we assumed 80% compliance in the main results presented here). A survey in Israel suggested that quarantining compliance is likely to be highly dependent on compensation for loss of work (Bodas and Peleg, 2020). However, such compensation may be unachievable in many LMICs. Reducing insecurity experienced by households under quarantine in other ways, for example by food provisioning and healthcare access, may help mitigate income loss

532 and boost compliance amongst poorer households. In Bangladesh, CSTs are already playing this role
533 in supporting quarantining households, and in LMICs more broadly, community health workers are
534 likely to prove invaluable in using the trust they have established to encourage compliance with NPIs
535 (Ballard et al., 2020).

536   Most of the NPIs we explored were very cost-effective, with savings per death averted and a
537 positive %ROI as a consequence of the high contribution of healthcare to overall costs. Note that
538 these returns occur despite the relatively young population in Bangladesh, which leads to a low
539 proportion of hospitalized cases (0.022). Furthermore, the societal costs (in terms of working days
540 lost) of the post-lockdown NPIs considered were small when compared with the initial lockdown
541 costs and potential extensions. These findings are in line with other work showing that the costs of
542 unmitigated transmission exceed those of implementing NPIs (Thunström et al., 2020; Torres-Rueda
543 et al., 2020). The costs we explore here are based on crude assumptions for mask purchase and
544 costs of training and rollout of CSTs in Dhaka where there is already a large community health
545 workforce that can be mobilized. However, we do not include food packages or additional support
546 for vulnerable communities that may increase NPI effectiveness but also costs.

547   Throughout the development of our model and interactive app, we incorporated
548 suggestions from policymakers on questions that most urgently needed answers, and on NPIs under
549 consideration and thought feasible to implement. This co-development allowed the investigation of
550 scenarios appropriate to the local context that addressed pressing policy concerns (McBryde et al.,
551 2020). The app, which allows a user-friendly exploration and visualisation of how scenarios impact
552 health outcomes and costs, proved to be an effective tool to support discussions with policymakers,
553 as the timing and combination of interventions, along with uncertainties in parameters, including
554 compliance, could be explored on the fly. This proved to be crucial in understanding the economic
555 and health trade-offs involved, as well as helping to demystify the model itself and the ensuing
556 epidemic.

557   Our study has a number of limitations. First, to ensure our model could run sufficiently
558 quickly within the interactive app, stochasticity and individual variation in transmission was not
559 incorporated. We expect only a minimal impact of these simplifications on disease trajectories and
560 key results due to the large population size considered and rapid epidemic growth observed.
561 However, they do limit the usefulness of the model for exploring elimination scenarios, since
562 stochasticity and superspreading, inherent to SARS-CoV-2 transmission (Adam et al., 2020), become
563 more influential under low levels of infection (Vespignani et al., 2020). Imported infections, which
564 may similarly become important near elimination, were also not considered. Age-structured models
565 have previously been proposed for studying COVID-19 (Davies et al., 2020b; Ferguson et al., 2020;
566 Keeling et al., 2020). We did not include age-structured transmission, which though not entirely
567 realistic, may be reasonable given the high degree of intergenerational mixing in Bangladesh
568 (United Nations, Department of Economic and Social Affairs, 2019a) and some other LMICs (Hodgins
569 and Saad, 2020). We also do not consider exacerbated mortality when hospital capacity is exceeded,
570 potentially underestimating mortality under some scenarios. Parameters used for case fatality, and
571 proportions of symptomatic and hospitalised infections, were based on age-dependent estimates
572 from HICs (Davies et al., 2020b, 2020a) and the age-distribution in Dhaka District. However, these
573 HIC-derived parameters may be less accurate when applied in this setting, as the incidence among
574 age classes of underlying conditions that increase COVID-19 risk likely differs in LMICs (Clark et al.,

575   2020). We also note that our estimates of working days lost make the assumption that employed
576   people cannot switch to working from home, possibly leading to overestimation.

577   More generally there remains considerable uncertainty around many of the model
578   parameters. Our sensitivity analyses indicated that R_0 was, predictably, very influential in
579   determining health outcomes, but is sensitive to the introduction date and number of imported
580   cases which are uncertain. In addition, prior to the lockdown in 2020, only 5 deaths due to COVID-
581   19 had been recorded in Bangladesh, and given the inherent stochasticity in these events, tuning R_0
582   to data in this time window is unlikely to be very accurate. Finally, prior to the 2020 lockdown, some
583   control measures, such as cancellations of large gatherings, had already been taken(Anwar et al.,
584   2020), potentially lowering our R_0 estimate. Our estimates of R_0 in 2021 similarly assumed no
585   interventions in the run-up to the 5th April lockdown, but low levels of mask-wearing and quarantine
586   may have led to underestimation. The 2020 R_0 estimate for Dhaka lies within the 90% confidence
587   interval estimated from a meta-analysis of pre-March 2020 estimates (Davies et al., 2020b). Many of
588   our 2021 estimates exceed this confidence interval, but none are in excess of the confidence interval
589   reported by Sanche et al. (2020). A possibly higher R_0 value for 2021 is also not unexpected, given
590   the dominant variant at the time (B.1.351) was known to be more transmissible than variants
591   prevalent in 2020. The effect of lockdown on between-household transmission rates was, like R_0,
592   tuned to reported death data, and proved to be higher than was anticipated in this high density
593   population; reducing transmission by 97%, suggesting that lockdown was very effective as a short-
594   term control measure. This high impact on compliant individuals might have been compensating for
595   our conservative assumption of no reduction in transmission from essential workers under lockdown
596   (unless off sick with symptomatic COVID-19), or underestimated lockdown compliance. An
597   overestimated R_0 (or indeed inaccuracies in other parameters) could also lead to overestimated
598   impacts of lockdown.

599   Our initial model assumed that recovered individuals remain immune through 2020.
600   Although immunity to SARS-CoV-2 is not permanent (Iwasaki, 2021), this assumption appeared
601   reasonable given effects of immunity loss were likely limited over this period. However, with
602   resurging cases in 2021 concomitant with relaxed NPIs and the emergence of the more transmissible
603   B.1.351 variant, the question of immunity became paramount (Saha et al., 2021). The level of
604   immunity in the population at the time of the resurgence was very uncertain, given only limited data
605   from which to infer case detection and laboratory evidence that prior COVID-19 infections elicit less
606   protection to the B1.351 variant (Planas et al., 2021).   These uncertainties translated into our
607   estimates of R_0 in 2021, which varied widely (2.19-8.2) under different assumptions, but with a best
608   guess of 3.32-5.30. The uncertainty in R_0 in turn leads to uncertainty in predictions, with some
609   suggesting a possible further wave later in 2021, while others preclude this.

610   We demonstrated the sensitivity of outcomes to the timing and scale-up of interventions,
611   but human behavioural responses most dramatically impact outcomes. For these reasons, our model
612   was primarily developed as a means to understand the potentially synergistic impact of
613   interventions, rather than to accurately forecast dynamics subject to unpredictable changing human
614   behaviours. We therefore considered compliance to interventions to be a crucial interactive element
615   of our app to build understanding and guidance on policy. Within the app, we also modelled the
616   degree to which the limited (but greatly increased) testing capacity would still under-detect

617 circulating cases, given some degree of cognitive dissonance and the considerable uncertainty in
618 pre- and asymptomatic transmission during the early months of the pandemic. Overall we found the
619 interactive app to be effective for communicating epidemiological modelling outcomes to
620 policymakers together with their caveats, and we recommend the use of such tools that can be
621 tailored to other settings and interventions.

622   In summary, we found that two NPIs combined, masks and symptoms-based household
623 quarantining, were capable of averting an anticipated public health crisis in Dhaka, while also being
624 good value for money. These measures were to a large extent rolled out in Bangladesh in 2020, and
625 appear to have contributed to limiting transmission, but the ensuing epidemic stretched the health
626 system. In practice, compliance with these interventions and fidelity of their implementation was
627 highly heterogeneous, with measures relaxing over the year as activity returned to levels
628 approaching normalcy. The surge in cases in 2021, apparently driven by the B.1.35 variant, has now
629 largely subsided. However, predictions about the risk of a further wave depend on, as yet,
630 unqualified assumptions and vaccination coverage remains low. NPIs therefore still have an
631 important role to play, particularly mask wearing, which is both very cost-effective and feasible, and
632 vaccine rollout needs to be pursued at pace.

633

637 **Data availability:** All data and code can be accessed via out Github repository
638 (https://github.com/boydorr/BGD_Covid-19/BGD_NPI_model). The interactive app is available at
639 http://boydorr.gla.ac.uk/BGD_Covid-19/CEEDS/.

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650

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