Modelling the impact of non-pharmaceutical interventions on COVID-19 transmission and healthcare demands in Cambodia: a scenario analysis

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Executive summary

Background
The current low numbers of confirmed COVID-19 cases in Cambodia suggest containment efforts have thus far been successful. However, as evident from the experience of other countries, there remains a risk that SARS-CoV-2 will begin to circulate widely in the population. In the event of transmission becoming widespread to the extent that containment is no longer feasible, the country may need to move to a mitigation or suppression phase, aiming to reduce transmission, minimise morbidity and mortality, and avoid healthcare systems becoming overwhelmed. This study assesses the impact of non-pharmaceutical interventions (NPIs), specifically those aimed at reducing social contacts, for mitigation and suppression of COVID-19 epidemic scenarios in Cambodia.

Approach
We conducted a scenario analysis using an age-structured transmission model to simulate COVID-19 epidemic trajectories over time. The model incorporates provincial-level demographic data, and age/setting-specific contact rates based on social mixing patterns data from Cambodia. Reductions in transmission and healthcare demands, as compared with unmitigated scenarios, were estimated under a range of NPI strategies (specifically: school, workplace and public space closures; reducing home visitors; self-isolation of symptomatic cases; and shielding of elderly people), implemented alone and in combination. We also evaluated strategies for suppression through triggering of intensive, lockdown-type phases involving more extreme reductions in contacts outside of home.

Key Findings

- Of the moderate NPIs assessed (i.e., excluding lockdowns), reducing contacts in public spaces was estimated to be the single most effective measure for mitigating peak healthcare demands. This was followed by reduced home visitors, self-isolation of symptomatic cases, and elderly shielding, which were all of comparable effectiveness.
- School closures and partial workplace closures were projected to have a relatively little impact on reducing transmission and peak healthcare demands.
- Even if used in combination, moderate social distancing interventions were insufficient to avoid healthcare, and in particular critical care, demands from far exceeding available capacity in most epidemic scenarios.
- More extreme reductions in social contacts, such as under lockdown-type interventions, were projected to reduce transmission by ~60-70%, and thus bring the effective reproduction number (R_{eff}) below or close to 1 in all scenarios.
- Suppression strategies, involving periodic triggering of lockdowns, were projected to dramatically reduce peak healthcare demands and cumulative numbers of severe/critical cases over a simulated 18-month period. However, in scenarios with moderate transmission potential (R_0=2.5), we estimated that lockdowns would need to be in place for over half of this period in order to keep critical care demands within national ICU bed capacity. There was a clear trade-off between the level of suppression achieved and the proportion of time under lockdown.
- In most scenarios, local triggering of lockdowns, at thresholds which consider provincial bed capacities, were projected to be more effective than national triggers for suppressing peak healthcare demands, particularly in later waves. However, this was also projected to increase the duration under lockdown in some provinces.
- Even under suppression strategies which keep peak healthcare demands within national capacity, we estimated that considerable numbers of critical COVID-19 cases would not receive appropriate care due to provincial shortages of critical care resources (e.g. ICUs, ventilators).

Public health implications

- Moderate social distancing measures which reduce contacts in public spaces and home visitors, along with self-isolation of symptomatic cases, could meaningfully reduce (but not control) widespread transmission and mitigate peak healthcare demands.
- Shielding of elderly and other vulnerable people, by limiting their contacts with non-household members, can also mitigate healthcare, and especially critical care, demands in the event of widespread transmission. However, the feasibility of this intervention, which may be difficult in multi-generational households, should be considered.
- School closures were estimated to have little impact on transmission potential or healthcare demands. This is consistent with modelling evidence from some other

settings. In light of this, and the adverse socio-economic impacts of this intervention, opening schools is assessed to be of relatively low risk, but should be monitored closely.

- In the event of widespread transmission, moderate social distancing NPIs, even if used in combination, are unlikely to prevent healthcare demands from exceeding available capacity, unless SARS-CoV-2 transmission potential in Cambodia is lower than has been estimated in most other settings.
- More extreme reductions in social contacts, such as in lockdown-type interventions, are likely to reverse epidemic growth, should this occur in Cambodia. Periodic triggering of lockdowns could dramatically reduce COVID-19 burden and pressure on healthcare systems. However, this type of suppression strategy would pose significant challenges:
    - It is likely that lockdowns would need to be triggered frequently, over a prolonged period, to keep healthcare demands within capacity, with severe socio-economic and health consequences;
    - Suppression through periodic lockdowns would require timely and accurate surveillance (e.g. of COVID-19 hospital admissions) across the country;
    - A suppression strategy which keeps healthcare demands within national capacity could still result in a disproportionate number of deaths in many provinces due to critical care shortages.
- Strengthening the capacity and resilience of existing healthcare resources, especially the workforce and critical care capacity, is crucial to ensure appropriate care for COVID-19 inpatients in any scenario of community transmission, even if suppressed. This might involve consideration of innovative safeguarding, resource mobilisation, and patient referral strategies.
- This analysis highlights the challenges of mitigation or suppression in the event of widespread SARS-CoV-2 transmission in Cambodia. If the main goal is to avert such challenges, sustaining and augmenting containment efforts is of utmost importance. Testing, contact tracing and isolation (TTI) strategies were beyond the scope of this study (see Limitations). However, evidence from other studies suggest that moderate social distancing measures can work synergistically with high-performance TTI systems, to both reduce strain on the latter, and increase prospects of containing SARS-CoV-2 outbreaks.

Study Limitations

- Due to low numbers of confirmed COVID-19 cases in Cambodia, most of which were imported, model calibration against case data from Cambodia was not possible. This study simulates scenarios of community transmission, which has yet to be observed in the country. The results are intended to provide evidence on the impact of mitigation and suppression strategies in plausible future scenarios, taking into account demographics, social mixing patterns and healthcare capacities in Cambodia, rather than model the current situation in the country.

- Absolute values of model outputs should be interpreted with caution. There remains wide uncertainty in a range of key epidemiological and clinical parameters for SARS-CoV-2/COVID-19, both in general, and in terms of their applicability in the Cambodia context. Projected impacts of different NPIs are estimates only. It was not possible to make very data-driven assumptions around how the interventions would affect contact rates.
- The model does not capture individual-level variation in transmission or super-spreader events. These could play an important role in determining epidemic dynamics and the success of different control measures, particularly during the early stages of an epidemic.
- The study focusses on NPIs which aim to reduce contact rates in the general population. We do not consider other NPIs such as testing, contact tracing and isolation (TTI) strategies, which cannot be robustly addressed using the types of data and compartmental models used for this analysis. Further evidence is needed to identify optimum TTI strategies, both alone and in combination with other NPIs, for control of SARS-CoV-2 in resource limited contexts.

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1. Background

The experience of many countries has demonstrated the extreme pressure that COVID-19, caused by SARS-CoV-2, can exert on healthcare systems. In countries of the lower Mekong region of Southeast Asia, confirmed cases to date have been substantially lower than many had anticipated, given their geographic proximity, travel links, and close socio-economic ties with China [1].

Clearly, caution is needed when interpreting and comparing reported case numbers, not least due to wide variation in surveillance strategies and capacities. Nonetheless, intensive contact tracing and isolation, along with other non-pharmaceutical interventions (NPIs) such as international border closures, travel restrictions, and physical distancing measures, are likely to have played an important role in reducing the spread of SARS-CoV-2 in these countries. Other contributing factors may include behavioural, cultural and environmental context, younger populations, and experience accrued from preparedness and response activities against other emerging infectious diseases, such as SARS and avian influenza A/H5N1. However, long-term implementation of more restrictive measures aimed at reducing social contacts is socially and economically unsustainable [2].

Cambodia confirmed its first imported case on 27th January and its first locally acquired case on 7th March. With only 139 confirmed cases as of 28th June 2020, and no confirmed deaths due to COVID-19, there is little evidence of community transmission in the country [3]. School and university closures, along with restrictions on international arrivals, were imposed swiftly after the first local confirmed case in March. Additional measures such as partial closure of public venues and offices, and temporary restrictions on within country movements, followed in April alongside intensive contact tracing and isolation. However, as highlighted by the experience of other countries, there remains a risk of transmission becoming widespread, particularly as more restrictive measures are lifted. In the event of widespread transmission, there is concern that containment strategies such as intensive testing, contact tracing and case isolation, may become less feasible and effective unless capacity for such measures can be scaled up dramatically [4].

In light of these risks, and difficult decisions around balancing restrictions with ongoing containment, we conducted a scenario analysis using mathematical modelling to assess the relative effectiveness of different NPI strategies for mitigation and suppression of COVID-19 in the event of widespread transmission in Cambodia. We focus here on NPIs which aim to reduce social contact rates in the general population. This study was conducted under the assumption that there is potential for widespread transmission to occur in Cambodia in future, at rates comparable to those estimated in a range of other settings.

2. Methods Summary

Methods are described in full in Appendix 1. In brief, we adapted a deterministic Susceptible-Exposed-Infectious-Removed (SEIR) model [5], stratified into 5-year age bands up to 65+, to simulate epidemic scenarios over time. Given the few reported cases in Cambodia to date, most of which were imported, it was not possible to calibrate simulations of generalised epidemic scenarios to existing case data from the country. We therefore accounted for uncertainty in the basic reproduction number, R_0, by drawing values from a normal distribution with mean 2.5 and standard deviation 0.5 (representing a 95% confidence interval of 1.5 - 3.5); thus we assume that unmitigated transmission potential in Cambodia would fall within the range estimated across other settings [6]. We also compared specific scenarios of “moderate”, “low” and “high” transmission potential, through simulations using R_0 values of 2.5, 1.5, and 3.5, respectively.

Projections of healthcare resource demands were implemented through a stochastic compartmental model [6], in which clinical cases have an age-dependent probability of developing severe illness (requiring general hospitalisation) or critical illness requiring intensive care.

The model incorporates age-specific contact rates in different settings (home, school, work, and other settings) based on a contact patterns survey conducted in rural and urban areas of Cambodia in 2012 (Appendix Figure A2). Provincial population sizes and demographic profiles were based on national census data. National and provincial healthcare resource capacities (numbers of beds, ICUs, and HCWs) were based on a survey conducted in 2009 [7,8], extrapolated to 2019 population sizes.

We considered a range of intervention strategies, consisting of one or more social distancing NPIs which are assumed to reduce contact rates in different settings, as summarised in Table 1. To evaluate the relative effectiveness of intervention strategies for mitigation of peak healthcare demands during a widespread epidemic, each intervention was simulated alone or in combination for a fixed four month period. We also evaluated suppression strategies which aim to keep healthcare demands within capacity, through intermittent triggering of lockdowns over an 18 month period. In these suppression scenarios, interventions alternated between a stringent lockdown phase, and a more ‘relaxed’ phase (during which reduced home visitors, elderly shielding, and self-isolation were maintained, but schools, workplaces and public spaces were fully open). Trigger thresholds were based on simulated numbers of COVID-19 hospital admissions per week relative to hospital bed capacity.

Table 1. Summary of NPIs considered

Intervention strategy	**Description**
1. School and university closure	Contacts in school and university settings reduced to zero.
2. Partial workplace closure	Workplace contacts reduced by 30%, 24%, and 16% in Phnom Penh, other urban, and rural areas, respectively. (Based on workplace contacts being reduced by 50% in industry and service sectors, and 0% in agricultural sector)
3. Partial public space closure (or general social distancing)	Contacts in 'other' settings (outside of home, school or work) reduced by 50%
4. Reduced home visitors	Contacts with non-household members at home reduced by 50%
5. Elderly shielding at home	Contacts among over 65s with non-household members reduced by 75%
6. Self-isolation of symptomatic cases at home	Symptomatic cases reduce their contacts with non-household members by 50%. (Modelled as a 35% reduction in the infectiousness of symptomatic cases, based on survey data showing that ~70% of social contacts are with non-household members).
7. Combined (1-6)	Simultaneous implementation of interventions 1 to 6 above
8. Lockdown/intensive interventions	Similar to 'Combined' strategy, but with more extreme reductions in contacts: ● Schools and universities closed ● Work contacts reduced by 79%,72% and 52% in Phnom Penh, other urban, and rural areas respectively (based on 80% reduction in industry and service sectors, 20% reduction in agricultural sector) ● Contacts with non-household members at home and in public spaces reduced by 90% ● Self-isolation of symptomatic cases

3. Results

3.1. Projections of an unmitigated epidemic in Cambodia

In an unmitigated epidemic (relating to the unlikely scenario of no control measures), the model projected a total of 5.7 million clinical cases (95% projection interval [PI]: 4.2 – 6.2 million) in Cambodia, with new clinical cases peaking at 0.12 million per day (0.05-0.18 million per day). We estimated that 86% (63- 94%) of the Cambodian population would be infected, with 43% of infected individuals showing clinical signs. At the peak of an unmitigated epidemic, the number of cases requiring hospitalization was projected to be ~48,000 (20,000 – 69,000), which is 2.5 (1.0- 3.5) times total bed supply in the country. The peak number of critical care beds required was 13,000 (5,300 – 19,000) at the national level, which is 13.2 (5.4- 19.2) times the total estimated capacity of 972 ICU beds in the country.

3.2. Impact of non-pharmaceutical interventions on transmission

The projected impact of each NPI scenario on transmission, based on percentage reduction in the basic reproduction number (R_0), is shown in Table 2. Results are shown for Phnom Penh and Takeo to illustrate differences between urban and rural areas. Among the six individual "moderate" interventions (#1-6), public space closures (or otherwise achieving a 50% reduction in contacts outside of home, school, and work), reducing home visitors, and self-isolation of symptomatic cases were each projected to reduce transmission by at least 11%. This was consistent in urban and rural areas, although public spaces closures reduced transmission to an even greater degree in Takeo (23%) compared with Phnom Penh (13%). This reflects the higher contact rates measured in 'other' settings (outside of home, school, or work) in rural areas compared to urban areas in the contact survey data (Appendix Figure A2). School and partial workplace closures were projected to achieve relatively small reductions in transmission (1 to 6%), with workplace closures more effective in urban compared to rural areas.

Combining these moderate interventions (#7) was projected to reduce transmission by more than 40%. However, for an epidemic with R_0=2.5, this combination would not be sufficient to bring the effective reproduction number (R_{eff}) below 1. The more extreme reduction in contacts in the lockdown scenario (#8) was projected to reduce transmission by around 62% in Phnom Penh, and 71% Takeo, which would be sufficient to control transmission with R_0 values of up to 2.6 and 3.4, respectively.

Table 2. Projected impact of physical distancing NPIs on transmission. Values represent the percentage reduction in the basic reproduction number, R_0, relative to an unmitigated scenario. Estimates are shown for Phnom Penh and Takeo to illustrate the difference between the most urban and most rural provinces. Interventions are described in Table 1. Cells are colour coded: **Blue = higher effectiveness; red = lower effectiveness**.

Geographic Area	1. School closure	2. Partial workplace closure	3. Partial public space closure	4. Reduce home visitors	5. Elderly shielding	6. Self-isolation	7. All combined (1-6)	8. Lockdown
Phnom Penh	3%	6%	13%	11%	1%	13%	42%	62%
Takeo	2%	1%	22%	13%	2%	13%	46%	71%

3.3. Impact of non-pharmaceutical interventions on peak healthcare demands

To assess the relative effectiveness of NPIs for mitigating peak bed demands, we conducted simulations in which each intervention was implemented nationwide for a 4 month period, timed to centre on the peak of an unmitigated epidemic. (In reality, it is unlikely that peak timing would be precisely known, or indeed that many of these NPIs would be implemented alone; however, the main objective here was to compare their potential for mitigating peak healthcare demands).

The projected number of critical care beds required over time are shown in Figure 1. Projected reductions in peak bed demands during the 4 month intervention period for individual and combined interventions, in epidemic scenarios with low, moderate, and high transmission potential are summarised in Table 3.

In most scenarios, none of the moderate NPIs, even if used in combination, were projected to keep critical care demands from far exceeding the national ICU bed capacity (Figure 1). While the large reduction in transmission under a lockdown would prevent epidemic growth during its implementation, completely releasing this measure and returning to normal contact rates results in a rapid surge in cases, with peaks of comparable size to the unmitigated scenarios.

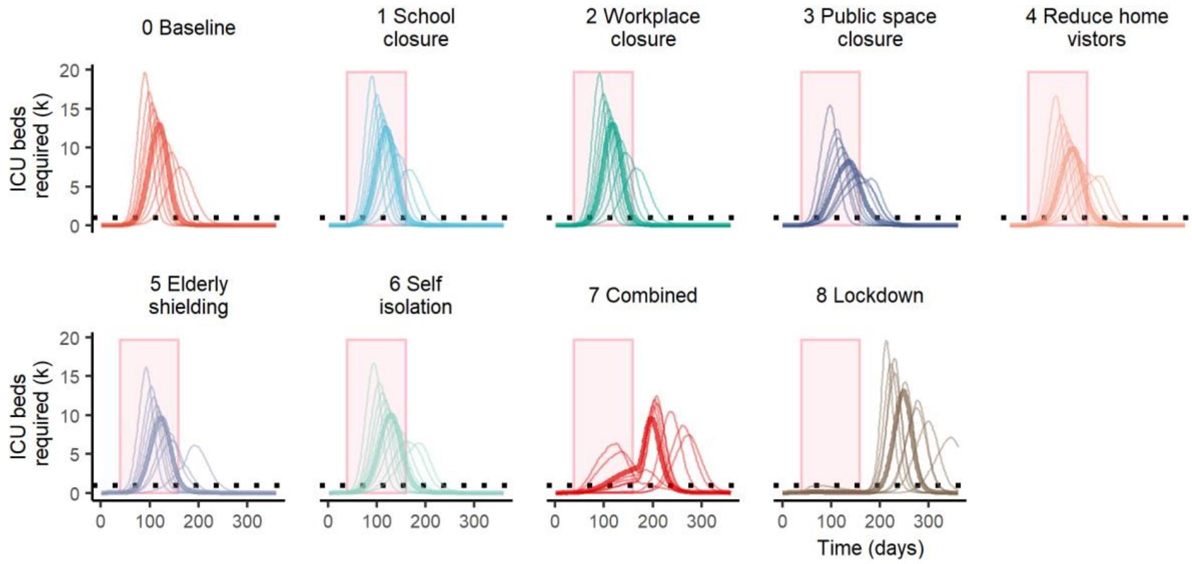

Figure 1. Projected impact of 4 month interventions on daily critical care bed requirements. "Baseline" = unmitigated scenario. Plotted lines represent deciles from 100 simulations (R_0 sampled from a normal distribution with mean=2.5, sd=0.5); projections R_0=2.5 shown in bold. Dotted horizontal lines indicate the estimated total number of ICU beds in the country. The shaded pink area represents the 4 month intervention period.

The relative reductions in peak healthcare demands under different NPIs followed a pattern broadly similar to their effectiveness for reducing transmission. Compared with an unmitigated scenario with R_0=2.5, a 50% reduction in contacts in public spaces was projected to reduce peak bed demands by over a third, while reduced home visitors and self-isolation of symptomatic cases each reduced these peaks by over 20% (Table 3). Elderly shielding was projected to have a similar impact on critical care demands, despite having little impact on transmission, highlighting the importance of shielding groups at high risk of severe disease. The relative effectiveness of different NPIs for mitigation was robust to uncertainty around R_0, although the percentage reductions compared with unmitigated transmission were generally larger for low R_0 values (Table 3).

Table 3. Projected impact of NPIs for mitigating peak bed demands when implemented nationwide, alone or in combination, over a 4 month period. Values show the percentage reduction in national peak bed demands during the intervention period (compared with an unmitigated scenario). Intervention scenarios are described in Table 1. Cells are colour coded: **Blue = higher effectiveness, red = lower effectiveness**.

Transmission scenario	Variable	1. School closure	2. Partial workplace closure	3. Public space closure	4. Reduced home visitors	5. Elderly shielding	6. Self-isolation	7. Combined	8. Lockdown
Moderate (R_0=2.5)	Reduction in peak non-ICU beds	3%	<1%	32%	21%	12%	21%	81%	98%
	Reduction in peak ICU beds	4%	<1%	32%	22%	23%	22%	83%	98%
Low (R_0=1.5)	Reduction in peak non-ICU beds	8%	5%	50%	40%	18%	44%	59%	60%
	Reduction in peak ICU beds	8%	4%	49%	41%	33%	44%	60%	61%
High (R_0=3.5)	Reduction in peak non-ICU beds	2%	<1%	21%	14%	10%	13%	58%	97%
	Reduction in peak ICU beds	2%	<1%	21%	15%	18%	14%	60%	97%

3.4. Suppression through adaptive triggering of lockdowns

Although lockdowns were projected to reduce R_{eff} below or close to 1, this intervention cannot be implemented indefinitely. Therefore, we simulated the impact of suppression strategies involving intermittent triggering of lockdowns at different thresholds over an 18-month period. The impact of a suppression strategy on bed demands over time for R_0=2.5 is shown in Figure 2, illustrating the reversal and resurgence of epidemic growth as lockdowns are triggered and relaxed. Local triggering of lockdowns, when the weekly number of COVID-19 admissions in each province reach a certain threshold relative to the provincial bed capacity, was projected to be more effective at suppressing peaks in bed demands, compared with nationwide triggering according to national admissions and bed capacities, particularly for later waves. This finding was broadly consistent across R_0 values and trigger thresholds explored, except in the high transmission scenario (R_0=3.5), in which national triggers were more effective than local triggers at suppressing the initial peak (Table 4, Figure A6).

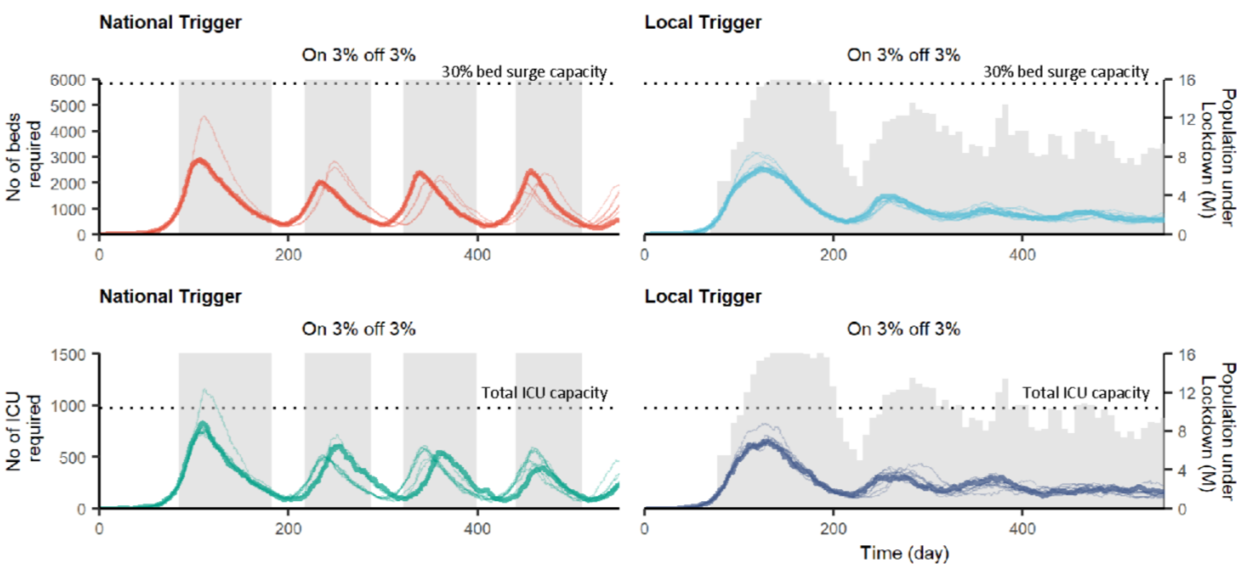

Figure 2. Projected impact of suppression strategies on total hospital bed demands (upper) and ICU bed demands (lower) over an 18 month period, for R_0=2.5. In the national trigger scenario, nationwide lockdown is implemented when weekly COVID-19 hospital admissions reached 3% of the total number of beds in the country, and relaxed after falling below the same threshold. In the local trigger scenario, lockdowns are triggered independently in each province according to provincial COVID-19 admissions and bed capacities. Plotted lines represent 10 model realisations, with the median simulation in bold. Lockdown periods are shown in the shaded areas, with heights representing the number of people under lockdown. Results for other trigger thresholds and R_0 values are shown in Table 4 and Figure A6.

All trigger strategies explored (with thresholds ranging between 0.5% to 5% of the total national or provincial hospital bed supply) were projected to dramatically reduce both cumulative and peak numbers of severe and critical cases compared with the unmitigated scenarios (Table 4). However, there was a clear trade-off: more stringent (i.e. lower) trigger thresholds resulted in more effective suppression at the cost of a higher proportion of time spent under lockdown.

For a scenario with R_0=2.5, we estimate that national triggering of lockdowns when weekly COVID-19 admissions exceeded 3% of the maximum bed capacity (>600 admissions per week) would result in peak non-ICU and ICU bed occupancies of around 12% and 80%, respectively (not accounting for non-COVID-19 patients). However, this threshold required lockdowns to be in place for over half of the 18-month simulation period. It also assumes that some moderate interventions (reduced home visitors, elderly shielding, and self-isolation) are maintained throughout. Furthermore, the estimated occupancy rates assume referral of critical patients to hospitals where ICU beds are available (largely concentrated in Phnom Penh). If critically ill patients remain within their home provinces, we estimate that, over an 18 month period, thousands would not receive appropriate care due to provincial ICU bed shortages, even if peak critical cases are suppressed below national ICU capacity. Local triggering based on provincial hospital bed capacities, and/or more conservative trigger thresholds, could help mitigate but not avert the burden associated with provincial ICU bed shortages (Table 4). Geographic disparities are explored further in the next section.

The potential for suppression strategies to keep healthcare demands within national capacity was highly dependent on R_0. In the low transmission scenario (R_0=1.5), all trigger thresholds maintained peak critical care demands within national ICU bed capacity, with minimal time spent under lockdown. In the high transmission scenario (R_0=3.5) none of the trigger thresholds prevented peak ICU bed demands from far exceeding national capacity, and even non-ICU bed capacities would be severely strained (Table 4). (Although we acknowledge that an R_0 value this high may be unrealistic for Cambodia, given that community transmission has yet to be observed).

3.5. Impact of suppression strategies at provincial level

Finally, we compared the impact of national and local triggering of lockdowns on mitigating critical care shortages and duration under lockdown at the provincial level. Figure 3 illustrates the results for a scenario with R_0=2.5, and trigger thresholds at 3% of national or provincial hospital bed capacity. In the national trigger scenario, we estimate that in many provinces, hundreds of critically ill cases (in some provinces over a thousand) may not receive necessary care if they are not referred to provinces with available ICU capacity. Provincial ICU shortages were projected to be particularly severe in south-central Cambodia (surrounding Phnom Penh), and in the northwest. Local triggering, at thresholds based on provincial hospital bed capacity, was projected to reduce, but not avert this burden associated with provincial ICU shortages (Figure 3A). In most provinces, the projected duration under lockdown was comparable between the national and local triggers. However, some provinces (including Phnom Penh) were projected to benefit from shorter durations under lockdown in the local trigger strategy, while others might spend significantly longer under lockdown (Figure 3B).

Table 4. Projected impact of suppression strategies through adaptive triggering of lockdowns over an 18 month period. In the national trigger scenarios, nationwide lockdown was implemented when national weekly COVID-19 hospital admissions (that require ICU or non-ICU) reached 0.5%, 1%, 3%, or 5% of the total number of beds in the country, and relaxed after falling below the same threshold. In the local trigger scenario, lockdowns were triggered independently in each province according to provincial COVID-19 admissions and bed capacities. Elderly shielding, reduced home visitors, and self-isolation were maintained throughout. Cells are colour coded: **Blue = higher effectiveness, red = lower effectiveness**. (Projections over time, and additional model outputs, are provided in Appendix Table A2 and Figures A6-A8).

Transmission scenario	Variable	Unmitigated (Do nothing)	Lockdown strategy and threshold							
			National 0.5%	Local 0.5%	National 1%	Local 1%	National 3%	Local 3%	National 5%	Local 5%
Moderate (R0=2.5)	Total critical cases	70,888	3,735	4,207	7,111	6,636	15,813	14,272	22,077	19,108
	Critical cases not admitted to ICU[a]	68,529	224	706	1,678	1,308	7,991	4,833	13,736	8,569
	Peak non-ICU beds required	35,330	509	502	849	825	2,190	1,955	3,363	2,881
	Peak ICU beds required	13,010	187	179	309	286	766	674	1,141	991
	Peak bed occupancy[b]	191%	3%	3%	5%	4%	12%	11%	18%	16%
	Peak ICU bed occupancy[b]	1336%	19%	18%	32%	29%	79%	69%	117%	102%
	Proportion of time under lockdown	0%	74%	72%	68%	69%	57%	58%	49%	50%
Low (R0=1.5)	Total critical cases	44,224	759	464	1,335	889	2,672	2,218	5,404	3,333
	Critical cases not admitted to ICU[a]	36,715	8	20	39	53	318	243	1,843	422
	Peak non-ICU beds required	10,670	122	68	225	129	550	323	858	498
	Peak ICU beds required	3,804	42	23	72	44	175	101	267	160
	Peak bed occupancy[b]	58%	1%	0.4%	1%	1%	3%	2%	5%	3%
	Peak ICU bed occupancy[b]	391%	4%	2%	7%	5%	18%	10%	27%	16%
	Proportion of time under lockdown	0%	11%	12%	10%	10%	5%	6%	2%	4%
High (R0=3.5)	Total critical cases	78,030	27,354	28,369	29,564	30,422	36,720	36,440	40,701	40,239
	Critical cases not admitted to ICU[a]	76,350	20,784	19,658	23,779	23,750	30,693	29,925	34,774	34,556
	Peak non-ICU beds required	52,259	3,703	4,811	5,421	6,003	8,766	9,549	8,735	12,319
	Peak ICU beds required	19,437	1,405	1,761	2,040	2,219	3,201	3,406	3,201	4,342
	Peak bed occupancy[b]	283%	20%	26%	29%	33%	47%	52%	47%	67%
	Peak ICU bed occupancy[b]	1996%	144%	181%	209%	228%	329%	350%	329%	446%
	Proportion of time under lockdown	0%	86%	77%	80%	72%	67%	57%	64%	47%

[a] Critical cases not admitted to ICU = the projected number of critical cases who do not receive ICU treatment due to provincial ICU shortages (i.e. if patients are not referred between provinces)

[b] Peak bed/ICU bed occupancy = the projected peak number of hospital beds/ICU beds needed for COVID-19 patients as percentage of the total number of beds/ICU beds in the country (if patients are referred between provinces when needed)

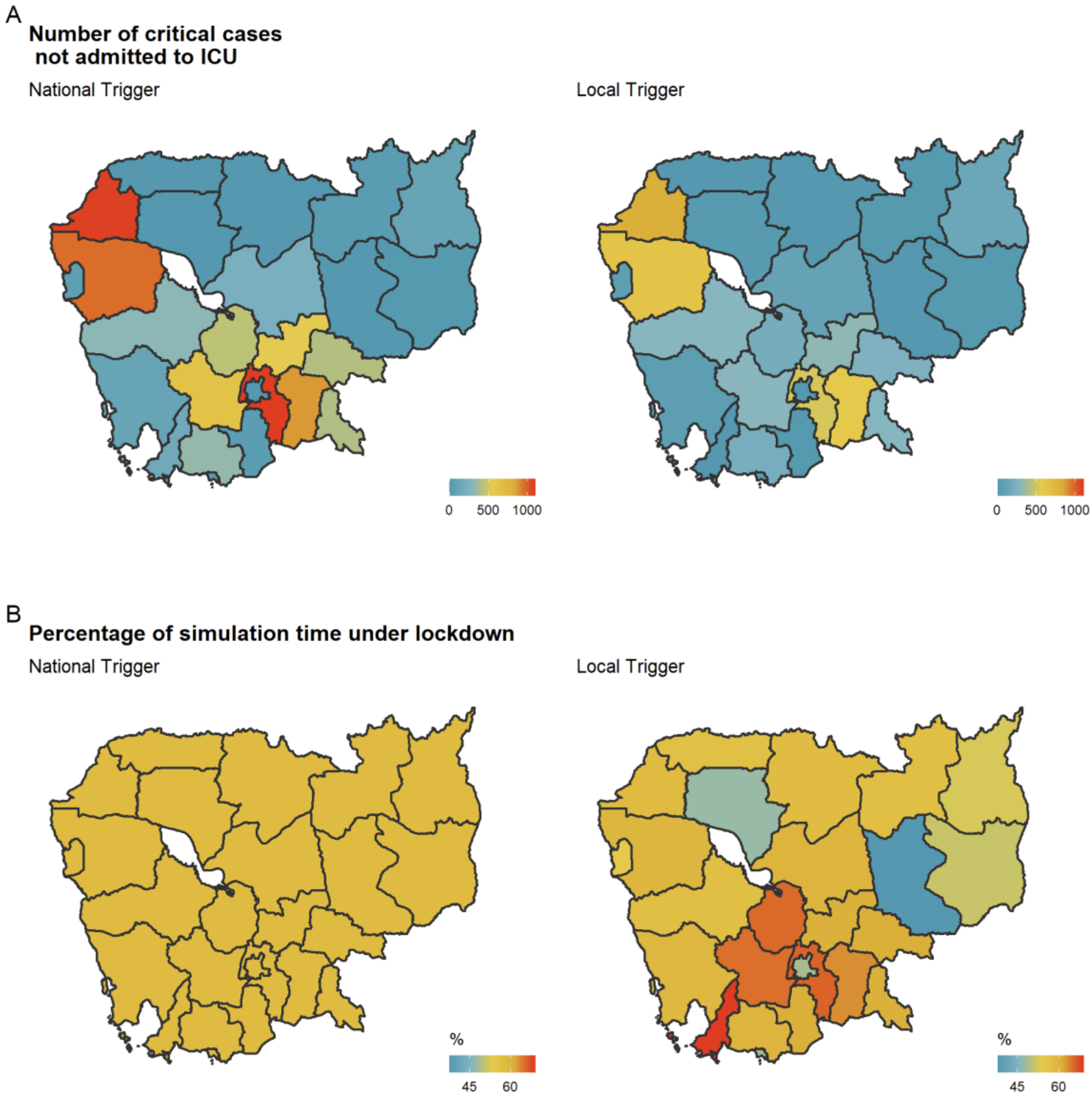

Figure 3. Comparison of national and local triggering of lockdowns on provincial critical care shortages and proportion of time under lockdown, for R_0=2.5. In the national trigger scenario, nationwide lockdown is implemented when national weekly COVID-19 hospital admissions (that require ICU or non-ICU) reached 3% of the total number of beds in the country, and relaxed after falling below the same threshold. In the local trigger scenario, lockdowns are triggered independently in each province according to provincial COVID-19 admissions and bed capacities. (A) The cumulative number of critical cases which do not receive ICU due to provincial shortages (if they remain within home province), over the 18 month simulation period. (B) The percentage of the 18-month period spent under lockdown.

4. Discussion

The current low numbers of confirmed COVID-19 cases in Cambodia suggest containment efforts have been successful, and may also point to lower transmissibility of the virus in this setting. However, as the country seeks to lift more restrictive measures, there remains a risk that SARS-CoV-2 will begin to circulate widely in the population. In the event of transmission becoming widespread to the extent that containment is no longer feasible, the country may need to move to a mitigation or suppression phase, aiming to reduce and delay transmission, minimise morbidity and mortality, and avoid healthcare systems becoming overwhelmed.

Our modelled scenarios suggest that, even if used in combination, moderate social distancing interventions and self-isolation of symptomatic cases would be unlikely to maintain health resource demand below capacity in the event of widespread transmission in Cambodia, unless transmission potential is lower than has been observed in most other settings. In particular, school and partial workplace closures were projected to have minimal impact on peak healthcare demands when implemented alone. This is broadly consistent with projections in other countries using similar modelling approaches [6,9], and a recent review of evidence on the impact of school closures [10].

Schools have been closed in many countries, including Cambodia. In light of wide uncertainties around the role of children in transmission of COVID-19, and the detrimental social and health impacts of school closures, the value of this intervention has been the subject of much debate [11]. Recent evidence suggests that children are less susceptible not only to severe clinical illness, but also to infection [12], and both of these factors were incorporated into our model. However, even when relaxing assumptions around reduced infectiousness of subclinical cases, and age-varying susceptibility to infection, school closures were projected to have a relatively small impact. We caution that our model may underestimate the impact of this intervention if, for example, contacts at school were under-reported in our contact survey data compared with contacts in other types of settings. Furthermore, the model results should not be interpreted as suggesting that risk of transmission clusters associated with schools, or indeed workplaces, is necessarily low. But they do suggest that contacts in these settings might contribute relatively little to overall transmission during a generalised epidemic in Cambodia.

Although unlikely to avoid healthcare, and particularly critical care, demands from far exceeding capacities in Cambodia, our findings show that moderate social distancing measures which reduce contacts in public spaces and home visitors, along with self-isolation of symptomatic cases, could still meaningfully reduce transmission and peak healthcare demands during a mitigation phase. Shielding of elderly and other vulnerable people, by limiting their contacts with non-household members, is also important to reduce healthcare, and especially critical care, demands. However, the feasibility of, and public compliance with, these measures should be considered. For example, while elderly shielding has the potential to significantly reduce health service pressure and mortality, it would require high levels of adherence and may be difficult to implement in multi-generational households [13].

If an epidemic takes off in Cambodia, we estimate that more extreme reductions in contacts, such as under a lockdown scenario, may be necessary to reduce the reproduction number below or close to 1 in most scenarios. This is consistent with experience and analyses in many countries with community transmission, where the effective reproduction number only fell below 1 following the implementation of intensive interventions [14,15]. Because such extreme measures impose profound socio-economic burdens and secondary adverse effects on health, and may lead to a rebound in cases when lifted, suppression strategies, involving periodic triggering of intensive interventions have been proposed as an alternative strategy [16,17].

Our results show that suppression via periodic lockdowns could substantially reduce the health burden of COVID-19 in scenarios of community transmission in Cambodia. However, this strategy would likely require frequent triggering of lockdowns, over a prolonged period, if it is to reliably maintain healthcare demand below national capacities. Furthermore, due to wide geographic disparities in healthcare resources in Cambodia, many provinces would struggle to provide the necessary care for critically ill patients, even if healthcare demands are suppressed below national capacity. Local triggers, using thresholds which take into account provincial health resource capacities, could help mitigate this to some degree. However, this would rely on sufficiently timely and accurate surveillance, for example of COVID-19 hospital admissions, across the country. Local triggering may also require some provinces to spend even longer under lockdown than a national trigger strategy.

While it may be possible to refer critical patients in provinces surrounding Phnom Penh to better resourced hospitals in the capital, this could present a greater challenge in more remote rural provinces. Strengthening the capacity and resilience of existing healthcare resources, especially the workforce and critical care capacity, is crucial to ensure appropriate care could be provided for COVID-19 inpatients in all scenarios of community transmission, even if suppressed. This might involve consideration of innovative safeguarding, resource mobilisation, and patient referral strategies.

4.1. Study limitations and further considerations

The compartmental transmission model used in this study does not capture individual-level variation in transmission, which recent evidence suggests is high for COVID-19 [18]. This can result in super-spreading or stochastic extinction, which play an important role in disease dynamics and the success of control measures when case numbers are low. On the other hand, the role of superspreader events in triggering explosive epidemics [19] further highlights the need for countries which have yet to observe widespread transmission to continue to prepare for a mitigation/suppression phase, which was the scenario under investigation in our study.

The study focussed on NPIs which aim to reduce contacts in the general population. We do not consider more targeted NPIs such as testing, contact tracing and isolation (TTI). These cannot be robustly addressed using the type of data and compartmental models used for this analysis. Further work is needed to identify optimum TTI strategies in resource limited contexts for controlling SARS-CoV-2 outbreaks, both alone and in combination with other NPIs.

There is increasing evidence that contacts in indoor spaces pose a substantially higher risk of transmission than outdoors [20–22]. Other than households, settings such as worker dormitories, meat packing plants, and religious gatherings have been linked to numerous, sometimes large, COVID-19 clusters [20,23]. In the Cambodian context, the large number of factories (for example associated with garment manufacturing) could be one of the settings to be prioritised, where working environments could generate superspreading events.

Early detection and containment of transmission clusters could enhance prospects of averting the generalised epidemic scenarios modelled here. However, evidence from other studies show that even high performance TTI systems may struggle to contain SARS-CoV-2 outbreaks unless used in combination with other NPIs, such as moderate physical distancing measures [24–26]. The latter can also reduce strain in TTI systems by reducing the number of tests needed, the number of contacts that need to be traced, and the number of people under quarantine [26,27].

The choice of R_0 values in this study were informed by a meta-analysis on of estimates [6], and cover the range of estimates of the time-varying reproduction number (prior to implementation of intensive measures) in other Southeast Asian countries such as Malaysia and the Philippines [28,29]. With such low reported case numbers in Cambodia, model calibration to country data was not possible, nor was a retrospective analysis to assess the relative impacts that previous or ongoing interventions have had. Although uncertainty in R_0 would impact the model projections in terms of the absolute numbers of health resources required, it would have less impact on the relative effectiveness of the different NPIs modelled here.

We used weekly COVID-19 hospital admissions as an adaptive trigger and assumed the completeness of these data would be a week delayed. While COVID-19 admission data was considered to be more feasible to collect, and less prone to under-reporting, than other indicators such as a number of infected individuals, it has its own limitations. The accuracy of this indicator is likely to exhibit spatio-temporal variation in relation to epidemic progression and surveillance and testing capacities.

The above caveats, along with uncertainty around other parameters and assumptions, such the serial interval, hospital/ICU length of stay, and the impact that NPIs would have on reducing social contacts, mean that the absolute values from our model projections should be interpreted with caution. Many parameters were informed by evidence from other countries, and may differ in the Cambodia context. For example, our estimates of the age varying proportion of cases requiring hospitalisation and critical care, and hospital/ICU length of stay, are based largely on data from China and Europe [6,30,31]. It is possible that younger age-groups in Cambodia and LMICs may be at higher risk of complications from COVID-19 than in high income settings, due to a higher prevalence of risk factors [13].

4.2. Conclusion

Should widespread transmission occur in Cambodia, it would present profound challenges for the country's healthcare system. In a mitigation phase, moderate measures aimed at reducing social contacts, particularly in public spaces and with home visitors, along with self-isolation of symptomatic cases and protecting elderly and vulnerable populations, could meaningfully reduce healthcare demands. However, such measures alone are unlikely to prevent healthcare systems becoming overwhelmed. More intensive measures, such as periodic triggering of lockdowns if and when COVID-19 hospital admissions rise, could dramatically suppress the burden and healthcare demands. However, these would likely need to be in place frequently, and over a prolonged period, to keep healthcare demands within available capacity. Such an approach would also rely on sufficiently timely and accurate surveillance indicators to inform when to trigger and relax intensive interventions, and would need to be balanced against the adverse social, economic and health burdens imposed by restrictive lockdowns. Sustaining and augmenting containment measures, which thus far appear to have been successful in Cambodia, are of utmost importance to try to avert, or at least further delay, the challenges of COVID-19 mitigation and suppression highlighted by this study.

Availability of data and material

Simulation codes can be found here. https://github.com/arata-hidano/Covid19_Cambodia/tree/master/Cambodia_model/codes

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Declaration of Interests

The authors declare no competing interests.

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Appendix 1 – Detailed Methods

Disease transmission model

We adapted a deterministic Susceptible-Exposed-Infectious-Removed (SEIR) transmission model developed by Prem et al., [5], introducing a pre-clinical infectious compartment in alignment with recent models evidence on infectiousness prior to symptom onset [32] (**Figure A1**). The model is stratified into 5-year age bands up to 65+, allowing for heterogeneous contact rates between age-groups. Infectious individuals are either pre-clinical, clinical or asymptomatic with recovered individuals becoming immune at the end of the infectious period. SEIR dynamics were implemented at provincial level, while a metapopulation approach was used to implement population mobility between provinces. The latter was based on a radiation model, and reported frequencies of travelling outside one's home provinces in the Cambodia contact survey. Population mobility between provinces was implemented for 17 weeks after seeding, after which the impact of mobility on the disease trajectories was negligible. All simulations were seeded with 10 cases in each age group in Phnom Penh.

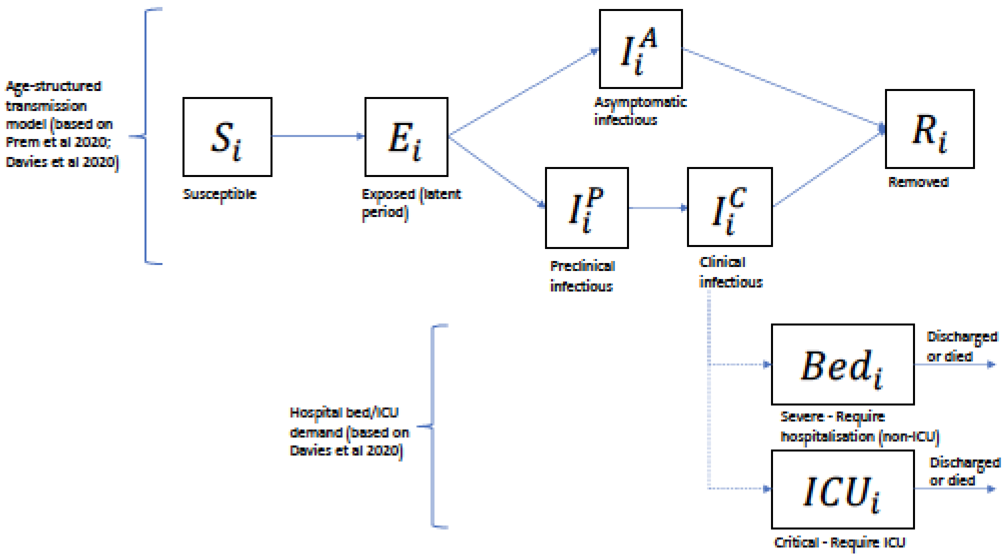

Figure A1. Schematic of the disease transmission and combined health resource model Following infection with SARS-CoV-2, susceptible individuals (S) enter a latent period (E) and then become infectious, either with preclinical (I^P) and then clinical infection (I^c) or subclinical infection (I^A), after which they are no longer infectious (R). The clinical course for individuals with clinical COVID-19 infection was then simulated using a stochastic health resource needs model, in which a proportion of clinical cases become severe (requiring hospitalisation;$\mathrm{Bed_i}$) or critical (requiring intensive care; $\mathrm{ICU_i}$).

The equations for the transmission model are as follows:

$$S_{i,t+1} = S_{i,t} - \sigma_i \beta S_{i,t} \sum_{j=1}^{n} C_{i,j,k} (I_{j,t}^C + I_{j,t}^P)/N_j - \alpha\sigma_i \beta S_{i,t} \sum_{j=1}^{n} C_{i,j,k} I_{j,t}^A / N_j$$

$$E_{i,t+1} = \sigma_i \beta S_{i,t} \sum_{j=1}^{n} C_{i,j}(I_{j,t}^{C} + I_{j,t}^{P})/N_j + \alpha\sigma_i \beta S_{i,t} \sum_{j=1}^{n} C_{i,j} I_{j,t}^{A}/N_j + (1-\mu)E_{i,t}$$

$$I_{i,t+1}^{P} = \rho_i \mu E_{i,t} + (1-\theta)\, I_{i,t}^{P}$$

$$I_{i,t+1}^{A} = (1-\rho_i)\mu E_{i,t} + (1-\gamma_{I^A})\, I_{i,t}^{A}$$

$$I_{i,t+1}^{C} = \theta I_{i,t}^{P} + (1-\gamma_{I^C})\, I_{i,t}^{C}$$

$$R_{i,t+1} = R_{i,t} + \gamma_{I^C} I_{i,t}^{C} + \gamma_{I^A} I_{i,t}^{A}$$

Where β is the baseline transmission parameter, $C_{i,j,k}$ describes the contacts of age group i made by age group j at location k , σ_i is the age-specific susceptibility. Both asymptomatic and symptomatic cases contribute to transmission, ρ_i denotes the probability of an infected case eventually developing clinical signs and α is the relative infectiousness of asymptomatic individuals. $\mu = 1 - exp\,(-1/d_E)$ is the daily probability exposed individuals become infectious, with d_E representing the duration of the latent period. $\theta = 1 - exp\,(-1/d_P)$ is the daily probability at which pre-clinical individuals become clinical with d_P being the duration of the preclinical period before showing clinical signs. $\gamma_{I^A} = 1 - exp\,(-1/d_A)$ and $\gamma_{I^C} = 1 - exp\,(-1/d_C)$ are the daily probabilities that infectious asymptomatic and clinical individuals recover, respectively. We assume that the progression of clinical cases to severe or critical illness, and their subsequent hospitalisation status, does not impact upon transmission dynamics.

Heath resource model

Projections of healthcare resource demands were implemented through a stochastic compartmental model, in which clinical cases have an age-dependent probability of developing severe or critical illness requiring hospitalisation or critical care, respectively. The progression of clinical cases to severe/critical illness, and their subsequent hospitalisation status, is assumed not to impact upon transmission dynamics (following [6]). The number of serious cases requiring hospitalisation during each time-step was drawn from a binomial distribution $Binomial\left(\theta I_{i,t}^{P}, \delta_i\right)$, where $\theta I_{i,t}^{P}$ is the number of individuals in age group i with newly developed clinical symptoms and δ_i is the probability that clinical patients developing severe symptoms requiring hospitalisation in age group i. The amount of time between symptom onset and hospital admission, and the amount of time between hospitalisation and death/discharge for ICU and non-ICU cases were drawn from gamma distributions (Table A1).

Key model parameters

Model parameters are presented in Table A1. Given the few reported cases in Cambodia at the time of this study, most of which are imported, it was not possible to calibrate simulations of generalised epidemic scenarios to case data from the country. We therefore explored the uncertainty in unmitigated transmission scenarios by drawing R_0 values from a normal distribution with mean 2.5 and standard deviation 0.5, representing a 95% confidence interval of 1.5 - 3.5. This was informed by the posterior distribution of R_0 estimates in a recent meta-analysis [6]; thus we assume that unmitigated transmission potential in Cambodia is comparable to that observed across other settings. We assumed that susceptibility to infection with COVID-19 (σ), probability of clinical signs among those infected (ρ) and probability of developing severe clinical signs after symptom onset (δ) were all age-dependent [12,30]. Subclinical cases were assumed to be half as infectious as pre-clinical and clinical cases (with the latter two states considered equally infectious) [6].

Table A1. Model parameters

Parameter	Description	Value/distribution		Notes/Reference
R_0	Basic reproduction number (unmitigated transmission)	$Normal(2.5, 0.5)$		[6]
$C_{i,j,k}$	Contact rate between an individual in age group *i* and individuals in age group *j* at a given location type *k*	(per day)		Estimated (contact survey)
σ_i	Age-specific susceptibility	Age 0-9 10-19 20-29 30-39 40-49 50-59 60-64 65+	Value 0.33 0.37 0.69 0.81 0.74 0.8 0.89 0.82	[12]
α	Relative infectivity of subclinical cases compared to preclinical and clinical cases	0.5		Assumed [6]
d_E	Duration of latent (pre-infectious) period	4 (days)		[13] and references therein
d_P	Duration of preclinical infectious period	1.5 (days)		Assumed to be 30% of average infectious period [13]
d_C	Duration of clinical infectious period	3.5 (days)		Calibrated with d_E and d_P to give mean serial interval of 6.5 days [13] and references therein
d_A	Duration of subclinical infectious period	5 (days)		Assumed to be the same as the infectious period of clinical cases $(d_P + d_C)$

ρ_i	Proportion of clinical cases among infected individuals in age group i	Age 0-9 10-19 20-29 30-39 40-49 50-59 60-64 65+	Value 0.4 0.25 0.37 0.42 0.51 0.59 0.72 0.73	[12]
δ_i	Proportion of clinical cases that require hospitalisation	Age 0-9 10-19 20-29 30-39 40-49 50-59 60-64 65+	Value 0.4 0.25 0.37 0.42 0.51 0.59 0.72 0.73	Derived from: [6,30]
ϵ	Proportion of hospitalised individuals that require ICU	Age 0-29 30-39 40-49 50-59 60-64 65+	Value 0.050 0.052 0.068 0.127 0.224 0.401	[30,33]
d_H	Delay from symptom onset to hospital admission	$Gamma(\mu = 7, k = 7)$		[6]
d_{Bed}	Duration of hospitalisation for severe (non-ICU) patients	$Gamma(\mu = 6.44, k = 1.73)$		Fitted to median and IQRs in [31]
d_{ICU}	Duration of hospitalisation for critical (ICU) patients	$Gamma(\mu = 8.23, k = 2.07)$		Fitted to median and IQRs in [31]
	Duration of supplemental oxygen requirement for severe (non-ICU) patients	5.44 (days)		1 day less than LOS
	Duration of supplemental oxygen requirement for critical (ICU) patients	7.23 (days)		1 day less than LOS
	Proportion of critical (ICU) patients that require invasive mechanical ventilation	0.72		[33]

	Minimum HCW: patient ratios needed in 'surge mode' Nurses per ICU patient day Doctors per ICU patient day Nurses per non-ICU patient day Doctors per non-ICU patient day	 2 0.6 0.5 0.225	[34,35]
	Estimated oxygen requirement per critical patient per day (PSA plant per day; Bulk liquid per day) Estimated oxygen requirement per severe patient per day (PSA plant per day; Bulk liquid per day)	43.2m^3/day; 0.05m^3/day 14.4m^3/day; 0.017m^3/day	[36]

Contact matrices

Province-specific contact matrices describing contact rates between different age groups were generated from a survey of social mixing patterns carried out in urban and rural areas of Cambodia in 2012 (Figure A2). This survey involved 2,016 participants in four provinces (Phnom Penh, Kandal, Kampot, and Kratie), in which contacts were defined as either a two-way conversation in the physical presence of another person, or physical contact. From these data, we included physical contacts, or conversational contacts not shorter than 15 mins, assuming that these were most relevant for disease transmission. Separate matrices were generated for people living in urban and rural locations, and according to the social setting in which the contact took place: at home with household members, at home with non-household members, at work, at school/college, or in other settings, using the same age bands as for the transmission model. Matrices were weighted to account for non-representative sampling in the contact survey. An adjustment was applied to account for oversampling of people reporting contacts made on weekends, and of non-employed participants using age and location specific employment rates reported in the 2012 Cambodian Socio Economic Survey (National Institute of Statistics, 2013). Finally, matrices were adjusted to make them symmetric using the 2013 demographic data. All matrices were generated using the R package 'socialmixr' v.0.1.6 [37].

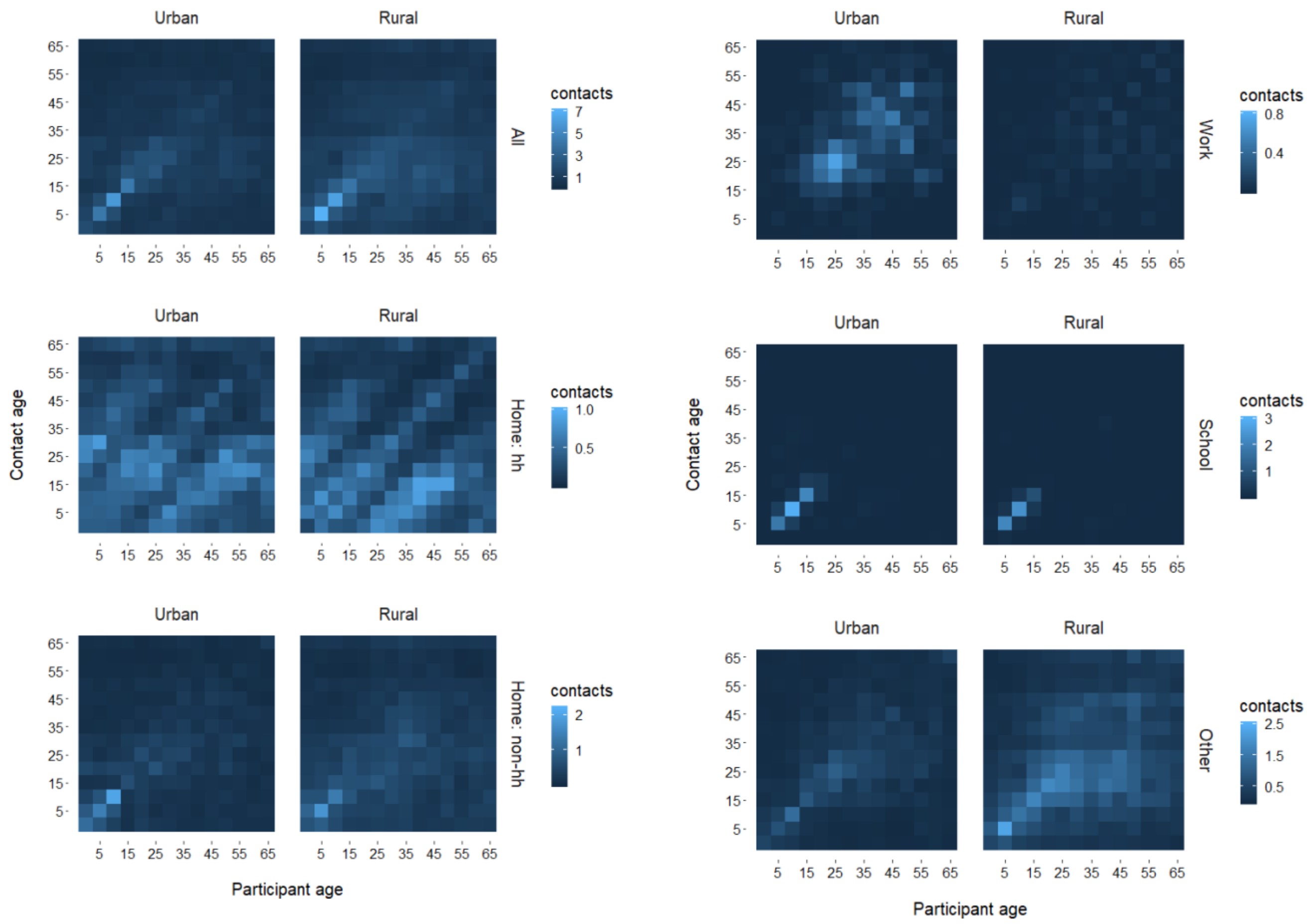

Figure A2. Age-mixing matrices in urban and rural areas of Cambodia at home (with household members), home (with non household members), work, school, and other settings. Matrices show the mean number of daily contacts adjusted for an average day in the week.

Estimation of healthcare resource demands

The daily oxygen need for patients in each severity category was calculated based on WHO recommended flow rates [36], and we assumed that severe and critical patients would require supplemental oxygen for one day less than their average duration of hospitalization. We assumed 72% of ICU patients would require invasive mechanical ventilation [33]. To estimate the numbers of healthcare workers (HCWs) needed, HCW:critical (ICU) patient ratios were based on optimal ICU staffing capacity estimated by Carenzo et al. [34]. For the acute medical unit (non-ICU) staffing needs we adopted the assumptions made in a pandemic influenza modelling study by Rudge et al. [35].

Demographics and health resource data

Provincial population sizes were based on 2019 census data. Since age-stratified data by province were not available from this census, demographic profiles were based on projections made in 2017 (National Institute of Statistics, 2008a, 2019 & 2017). Total health resources including the number of inpatient and ICU beds, nurses and doctors in each province were estimated by extrapolating data collected in 2009 to 2019 population sizes [7,8], assuming that health resources per capita remained constant between the two periods (Supplementary Figure A3).

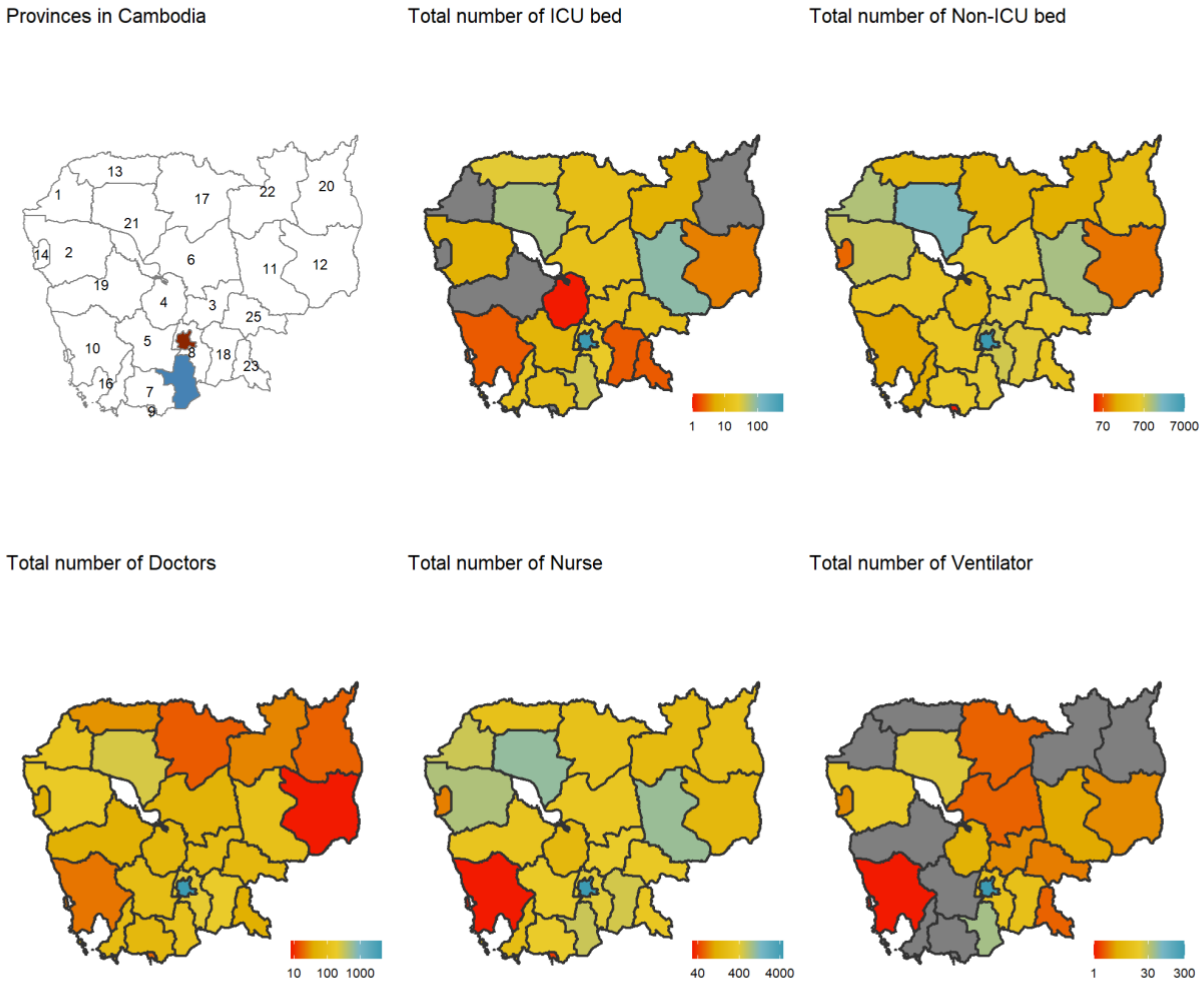

Figure A3: Provinces in Cambodia and health resource capacities in each province [7,8]. (Top left) The capital, Phnom Penh is colored in red and Takeo in blue. Each number represents one province; 1 Banteay Meanchey, 2 Battambang, 3 Kampong Cham, 4 Kampong Chhnang, 5 Kampong Speu, 6 Kampong Thom, 7 Kampot, 8 Kandal, 9 Kep, 10 Koh Kong, 11 Kratie, 12 Mondul Kiri, 13 Oddar Meanchey, 14 Pailin, 16 Preah Sihanouk, 17 Preah Vihear, 18 Prey Veng, 19 Pursat, 20 Ratanak Kiri, 21 Siemreap, 22 Stung Treng, 23 Svay Rieng, 25 Tboung Khmum.

Interventions

We considered a range of intervention strategies, consisting of one or more social distancing NPIs assumed to reduce contact rates between individuals in specific settings or, in the self-isolation strategy, infectiousness of symptomatic individuals (Table 1). Adjusted contact matrices were generated for each intervention strategy, reducing baseline contact rates at school, work, home and 'other' settings. We assumed that school closure and partial public space closures would reduce contacts in school and other settings to 0% and 50% of baseline, respectively. As our contact survey data recorded whether contacts made at home were with household members or non-household members, we also simulated "reduced home visitor" scenarios involving 50% reduction in home contacts with non-household members.

Strategies involving workplace closures and advice to work from home are likely to be less feasible in some sectors, particularly among agricultural workers due to the need to maintain food production and supply chains. Under moderate social distancing strategies involving partial workplace closure/work from home, we assumed that workplace contacts could not be reduced among agricultural workers, but could be reduced by 50% in industry and service sectors. In a more extreme lockdown scenario, we assumed that workplace contacts could be reduced by 20% among agricultural workers, and 80% among industry and service sectors (Table 1). Contact matrices for reduced workplace contacts in each province were then weighted according to province-level employment rates in each of these sectors. The latter were inferred based on national socio-economic survey data for urban and rural populations of Cambodia (National Institute of Statistics, 2018), and urban:rural population ratios for each province.

For simulating an elderly shielding strategy, we assumed that individuals aged 65 and older are advised to stay at home with reduced visitors from other households, thereby reducing their contacts outside of home, and with non-household members at home, to 25% of baseline. In scenarios including self-isolation of symptomatic individuals, we reduced the infectiousness of symptomatic individuals to 65%. (Similarly to Davies et al. [6], contact patterns data from Cambodia indicate that approximately 70% of contacts occur either outside the home, or with non-household members while at home, and we assumed that self-isolation could reduce these contacts by 50%).

To assess the rudimentary impacts of intervention scenarios, each intervention was applied for a period of four months, timed to coincide with the peak incidence in the unmitigated scenarios. We also explored the impact of adaptive interventions, alternating between a stringent lockdown phase, and a 'relaxed' phase (during which reduced visits to other households, elderly shielding, and self-isolation were maintained, but schools, workplaces and public spaces were fully open). We simulated different thresholds for triggering and relaxing lockdowns, both at a national and local (provincial) level. We used the number of new hospital admissions in the previous week (hereafter referred to as new admissions) as the trigger, and assumed a one-week delay in the completeness of hospital admission reporting for any given week. Lockdown was implemented when the number of new admissions reached a certain threshold relative to the total number of beds in the country for the national trigger scenario, or in each province for the local trigger scenario. A relaxed phase replaced lockdown when a reduction in new admissions fell below the same threshold.

Appendix 2 – Additional Results

Uncontrolled disease trajectories in each province

The incidence of infected cases has its peak at different timings in each province because we used a meta-population model in which the initial infected cases were only seeded in Phnom Penh. Figure S3 is a realisation of one simulation using R0 = 2.5.

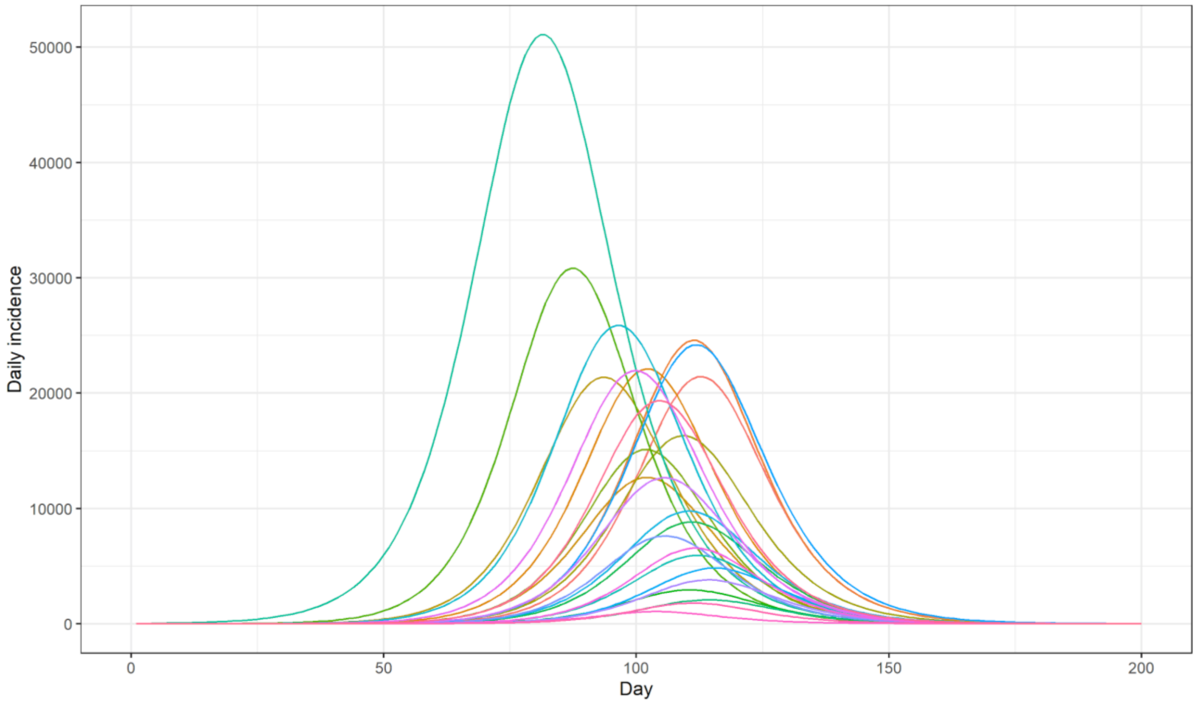

Figure A4. Projected daily incidence of infected cases in each of 25 provinces in an unmitigated scenario for R_0=2.5.

Sensitivity analysis of the impact of key assumptions on model projections

At the time of writing, the relative infectiousness of asymptomatic individuals, and variation in susceptibility by age group, it still unclear. There is also uncertainty around how risk of transmission varies with intensity and duration of contact. A sensitivity analysis was carried out by estimating reductions in R_0 through social distancing measures under the following assumptions (1) asymptomatic individuals are as infectious as symptomatic individuals or 50% a infectious, (2) susceptibility is constant across age groups or age-dependent, and (3) contact matrices based on all reported contacts regardless of duration, or on physical contacts, and non-physical contacts lasting at least 15 mins. As shown in Figure A5, these assumptions had minimal impacts on the estimated reductions in R_0 to reductions in contact rates in each setting.

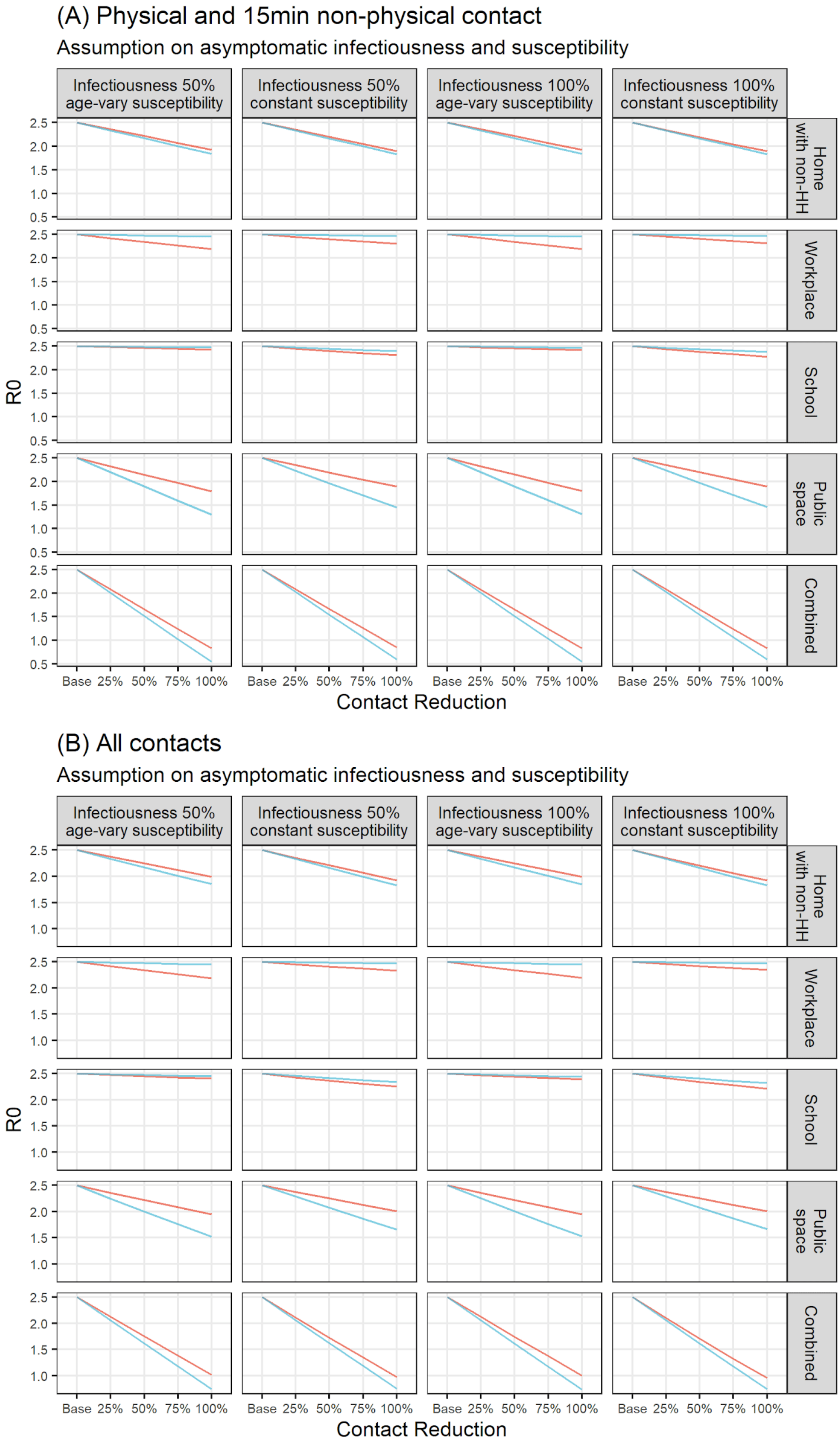

Figure A5. Sensitivity analysis of model assumptions for the projected effectiveness of interventions for reducing transmission. Red and blue lines represent Phnom Penh and Takeo, respectively.

Table A2. Additional model outputs for the projected impact of suppression strategies through adaptive triggering of lockdowns, over an 18 month period. In the national trigger scenarios, nationwide lockdown is implemented when national weekly COVID-19 hospital admissions (that require ICU or non-ICU) reached 0.5%, 1%, 3%, or 5% of the total number of beds in the country, and relaxed after falling below the same threshold. In the local trigger scenario, lockdowns are triggered independently in each province according to provincial COVID-19 admissions and bed capacities. Elderly shielding, reduced home visitors, and self-isolation were maintained throughout.

			Lockdown strategy and threshold							
Transmission scenario	**Variable**	**Unmitigated (Do nothing)**	**National 0.5%**	**Local 0.5%**	**National 1%**	**Local 1%**	**National 3%**	**Local 3%**	**National 5%**	**Local 5%**
	Infection attack rate (%)	86	4	5	9	8	21	19	30	26
	Total clinical cases	5,673,077	297,400	365,218	601,091	570,320	1,419,157	1,244,523	2,016,980	1,700,312
	Total critical cases	70,888	3,734	4,206	7,111	6,636	15,812	14,272	22,076	19,108
	Total severe cases	232,381	16,569	19,310	32,370	30,428	73,578	65,688	103,422	89,007
	Peak of daily incidence	285,020	4,164	3,679	7,833	6,177	19,469	14,908	30,921	21,738
Moderate (R0=2.5)	Peak of daily clinical incidence	122,174	1,700	1,598	3,166	2,667	7,972	6,413	12,647	9,407
	Peak non-ICU beds required	35,330	509	502	849	825	2,190	1,955	3,363	2,881
	Peak ICU beds required	13,010	187	179	309	286	766	674	1,141	991
	Peak HCWs required	59,362	835	809	1,377	1,316	3,521	3,121	5,337	4,620
	Peak nurses required	43,636	614	595	1,014	966	2,584	2,289	3,913	3,388
	Peak doctor required	15,729	221	214	364	350	937	832	1,423	1,232
	Peak ventilators required	9,367	135	129	222	129	552	129	822	129
	Infection attack rate (%)	55	1	1	2	2	4	4	9	5
	Total clinical cases	3,667,257	82,000	67,263	139,457	106,116	271,559	238,964	571,542	348,360
	Total critical cases	44,224	758	464	1,334	888	2,672	2,218	5,404	3,333
	Total severe cases	151,996	3,712	2,431	6,572	4,534	13,207	11,201	27,267	16,828
	Peak of daily incidence	81,173	1,038	581	1,819	1,060	4,438	2,463	6,955	3,662
Low (R0=1.5)	Peak of daily clinical incidence	35,201	448	250	787	458	1,930	1,071	2,998	1,597
	Peak non-ICU beds required	10,670	122	68	225	129	550	323	858	498
	Peak ICU beds required	3,804	42	23	72	44	175	101	267	160
	Peak HCWs required	17,557	185	101	344	198	848	486	1,295	752
	Peak nurses required	12,901	136	74	252	146	621	355	948	551
	Peak doctors required	4,661	49	27	93	53	227	130	348	201
	Peak ventilators required	2,739	30	17	51	17	126	17	192	17
	Infection attack rate (%)	95	32	33	35	36	46	45	51	50
	Total clinical cases	6,210,546	2,154,485	2,239,744	2,363,120	2,429,753	3,033,483	2,985,455	3,390,944	3,341,626
	Total critical cases	78,030	27,354	28,369	29,564	30,422	36,720	36,440	40,700	40,239
	Total severe cases	251,576	119,968	124,424	130,514	134,020	163,428	161,999	181,622	179,586
	Peak of daily incidence	442,674	24,603	33,623	37,627	42,154	74,639	73,307	74,639	95,353
High (R0=3.5)	Peak of daily clinical incidence	188,290	11,002	14,855	16,355	18,642	30,293	31,455	30,293	41,247
	Peak non-ICU beds required	52,259	3,703	4,811	5,421	6,003	8,766	9,549	8,735	12,319
	Peak ICU beds required	19,437	1,405	1,761	2,040	2,219	3,201	3,406	3,201	4,342
	Peak HCWs required	88,275	6,288	8,050	9,210	10,076	14,580	15,772	14,563	20,172
	Peak nurses required	64,905	4,628	5,914	6,774	7,409	10,718	11,584	10,706	14,807
	Peak doctors required	23,377	1,664	2,135	2,440	2,667	3,865	4,187	3,862	5,366
	Peak ventilators required	13,994	1,012	1,268	1,469	1,268	2,305	1,268	2,304	1,268

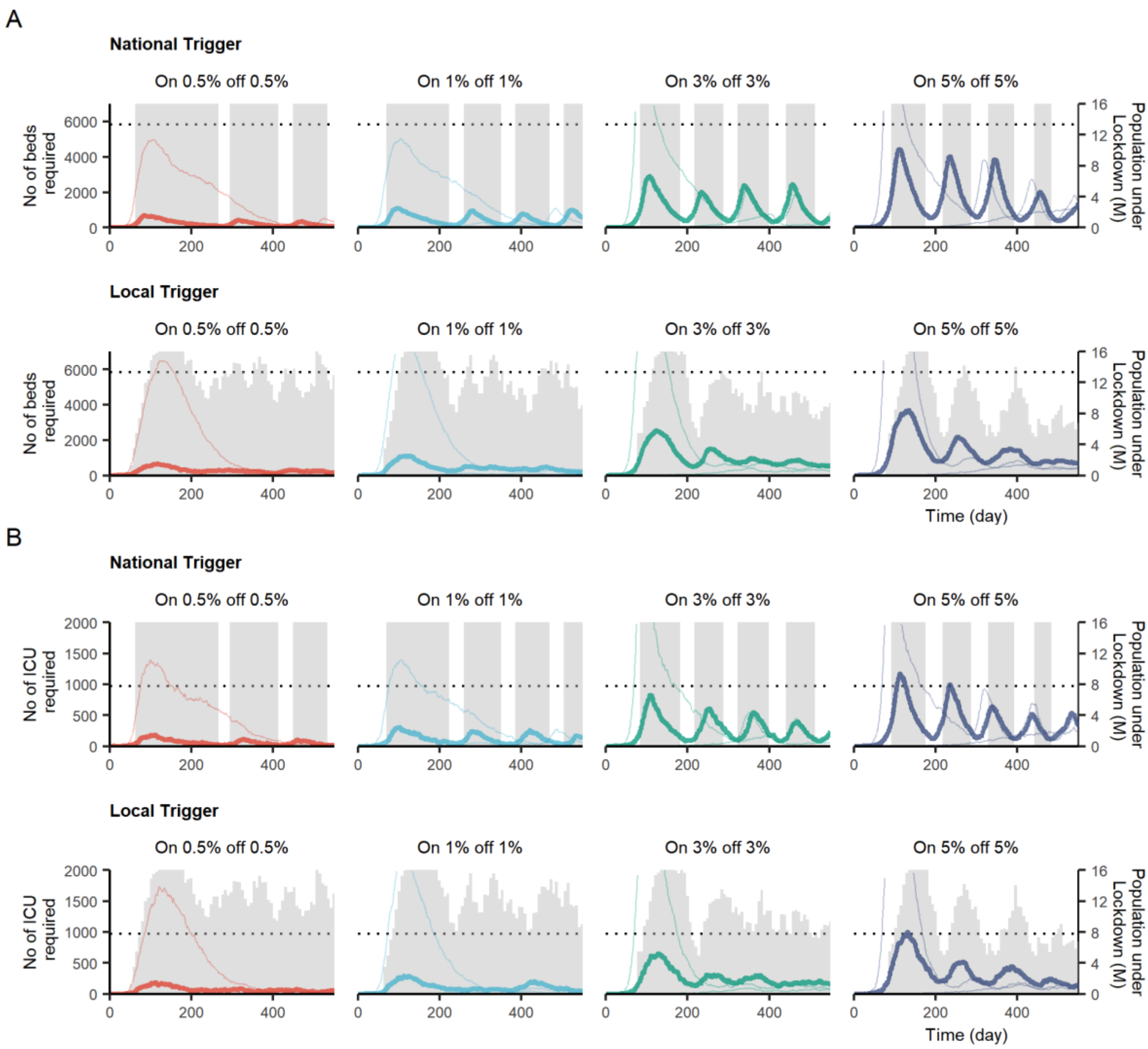

Figure A6. The impact of national and local trigger scenarios on hospital bed demands over time. (A) Hospital bed demands (median and 95% projection interval). The dotted lines indicate the assumed 30% surge capacity. (B) ICU bed demands (median and 95% projection interval). The dotted lines indicate the assumed the maximum ICU capacity in the country. Shaded areas show lockdown periods, with heights representing the population under lockdown.

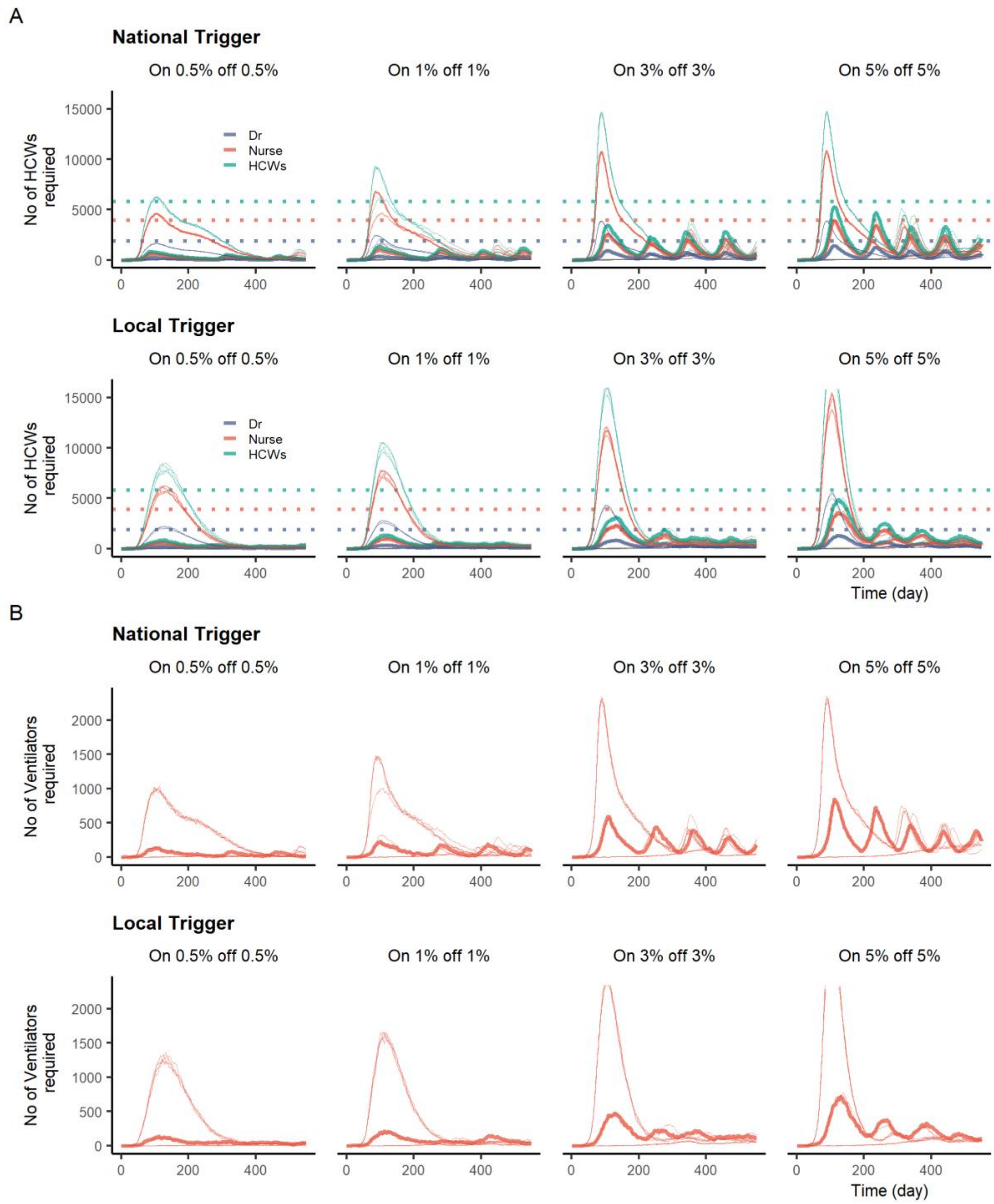

Figure A7. The impact of national and local trigger scenarios on health resources over time. (A) The number of HCWs required over time in each scenario (median and 95% projection interval). The dotted lines indicate the assumed surge capacity for doctors (light blue), nurses (red) and their total (green). (B) The number of ventilators required over time (median and 95% projection interval). The dotted lines indicate the total number of ventilators estimated in the country.

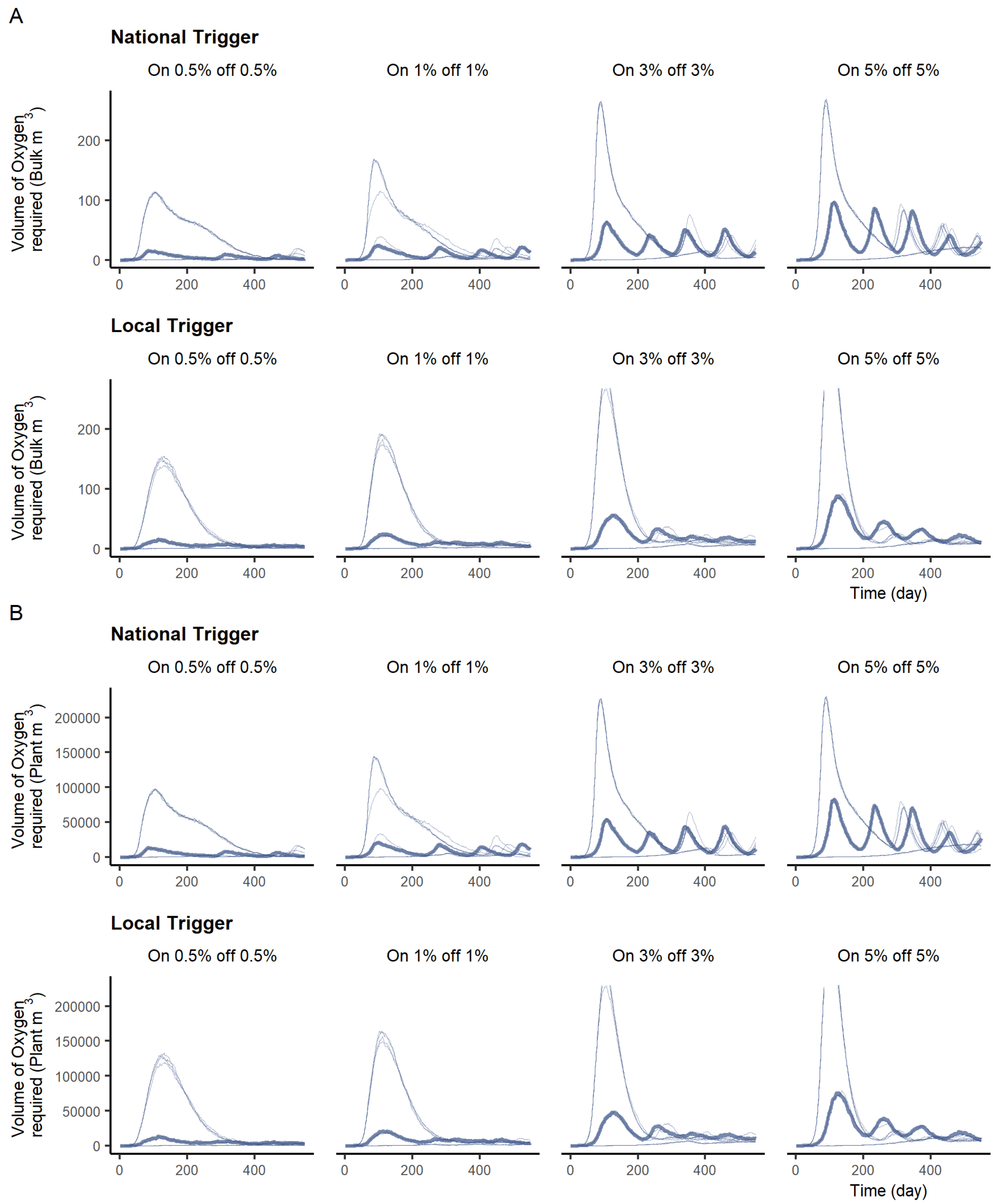

Figure A8. Daily oxygen needs estimated in adaptive trigger interventions. (A) Liquid oxygen, and (B) PSA plant oxygen. Plots show medians and 95% projection intervals.