Why lockdown? Simplified arithmetic tools for modelling COVID-19 transmission, morbidity, mortality and containment for medical and public health practitioners, decision-makers, journalists and the general public

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Summary

For all but the most expert specialists, the silent early phase of an epidemic, when there is still time to contain it, is often imperceptible and difficult to grasp the significance of. This is especially true for pathogens like COVID-19 that largely exhibit mild, non-specific symptoms, if any. Currently, half the world's population is already under lock-down of some kind, meaning vertically enforced and severe restrictions of movement, and the remainder will have to follow if the ongoing COVID-19 virus pandemic is to be contained. Faced with such brutally difficult decisions, it is essential for health professionals, policy-makers and the general public that as many people as possible understand (1) why lock-down interventions represent the only realistic way for individual countries to contain their national-level epidemics before they turn into public health catastrophes, (2) why these need to be implemented so early, so aggressively and for such extended periods, and (3) why international cooperation to conditionally re-open trade and travel between countries that have successfully eliminated local transmission represents the only way to contain the pandemic at global level. Here we present simple models of COVID-19 transmission, control and elimination in user-friendly Shiny and Excel formats that allow non-specialists to explore, query, critique and understand the containment decisions facing their country and the world at large. Based on parameter values representative of the United Republic of Tanzania, which is still early enough in its epidemic cycle and response for a national catastrophe to be averted, the simplified model predicts that national containment and elimination with less than 10 deaths may be achieved by highly rigorous lockdown within 5 weeks of the first confirmed cases and maintained for 15 weeks. However, elimination may only be sustained if case importation from outside the country is comprehensively contained by isolating for at least 21 days all incoming travellers, except those coming from countries certified as free of local transmission by WHO in the future. Any substantive relaxation of these assumptions, specifically shortening the lock-down period, less rigorous lock-down or imperfect importation containment, are predicted to enable re-initiation of the epidemic, resulting in over half a million deaths unless rigorously contained a second time. Removing contact tracing and isolation has minimal impact on successful containment trajectories because high incidence of similar symptoms caused by other common pathogens attenuates detection success of COVID-19 testing. Nevertheless, contact tracing is recommended as an invaluable epidemiological surveillance platform for monitoring and characterizing the epidemic, and for understanding the influence of interventions on transmission dynamics.

Introduction

For all but the most expert specialists, the silent early phase of an epidemic, when there is still time to contain it, is often imperceptible and difficult to grasp the significance of. This is especially true for pathogens like COVID-19 that largely exhibit mild, non-specific symptoms, if any. Currently, half the world's population is already under lock-down of some kind, meaning vertically enforced and severe restrictions of movement, and the remainder will have to follow if the ongoing COVID-19 virus pandemic is to be contained. Faced with such brutally difficult decisions, it is essential for policy-

makers and the general public that as many people as possible understand (1) why lock-down interventions represent the only realistic way for individual countries to contain their national-level epidemics before they turn into public health catastrophes, (2) why these need to be implemented so early, so aggressively and for such extended periods, and (3) why international co-operation to conditionally re-open trade and travel between countries that have successfully eliminated local transmission represents the only way to contain the pandemic at global level.

An educational tool to help non-specialists understand COVID-19 transmission dynamics and containment strategies

Here we introduce a simplified arithmetic modelling tool for predicting COVID-19 transmission dynamics and how it is likely to respond to different containment, delay or mitigation strategies. We coin the term arithmetic modelling, as distinct from the ubiquitously used term mathematical modelling, to convey the fact that it uses only addition, subtraction, multiplication, division, rounding off, a few conditional statements (eg. if, less than/greater than, and/or) and two unavoidable power terms to make the necessary calculations. This tool includes no differential equations, calculus, limits, distributions, stochastic simulations or agent-based approaches that would render it opaque to most non-specialist readers, such as medical and public health practitioners, decision-makers, journalists and the general public. The model is presented in userfriendly Shiny® and Excel® formats that allow non-specialists to explore, query, critique and understand the containment decisions facing their country and the world at large. For those content to accept the underlying arithmetic, the Shiny® format provides a convenient interactive web application that can used on any device. For those who wish to satisfy themselves that the calculations make intuitive sense, the Excel® version provides a complementary spreadsheet format in which the formula for each cell can be critically examined. While a formal mathematical description of this model has been critically reviewed by specialist experts, it is provided only as an online supplement because none of the principles, assumptions or predictions are particularly new, and because in our experience nothing deters non-specialists from reading an article faster than equations do.

We caution readers not to expect too much from any predictive model in terms of exact numerical accuracy. We specifically advise against interpreting the exact numbers this tool generates at face value: Any predictive model is, by definition, a deliberately simplified representation of complex real-world processes and this one is no different. The exact numerical predictions should therefore not be used to confidently define precise operational timelines for introducing and sustaining interventions, or effectiveness thresholds required of specific containment measures. Instead, the purpose of this tool is to help users broadly understand the inevitable consequences of an uncontained epidemic, explore the likely outcomes a wide range of different possible containment strategies, identify those which could plausibly succeed and understand the failures of those which seem unlikely to do so.

Any users finding themselves forced to use numerical predictions from this model to make programmatic intervention decisions, presumably for want of a more reliable alternative in their specific context, should therefore assume sizable imprecisions that will not be possible to quantify prospectively and will be too late to quantify retrospectively. They should therefore factor such unknown levels of uncertainty into their response plans by allowing for wide margins for error when planning the timing, intensity and duration of new interventions, always being more ambitious and cautious whenever in any doubt.

Tanzania as an illustrative example of national containment options and requirements

Assumed input parameters values were chosen to be representative of the United Republic of Tanzania (Table 1), because it is still early enough in its epidemic cycle and response for a national catastrophe to be averted. Tanzania has also had more opportunity to learn from ongoing experiences in Asia, Europe and north America, and prepare by establishing full testing capacity at

the outset of the national epidemic, more consistent with that simplifying assumption of the model than countries affected earlier in the pandemic would be. Tanzania is also a typically vulnerable, low-income African country, which had only 38 ICU beds in all four national referral hospitals combined in 2019, ¹ and is representative of the pandemic that is now imminent all across Africa.²

Table 1. Assumed values for input parameters of the arithmetic model as intended to be representative of COVID-19 transmission and successful epidemic containment in the United Republic of Tanzania (Figure 1). A detailed formal description of how the model calculations are made, the underlying assumptions are provided in the online methodological supplement to this paper.

Input parameter description	Assumed value	References
Basic reproductive number (Average number of new infections arising from a single existing infection over its full duration if allowed to do so in an immunologically naïve population in the absence of any control measures)	4.0	3-9
Duration of infection (Average number of weeks an infection lasts in a human before it is eliminated by the immune system).	3	10,11
Asymptomatic proportion of cases (Proportion of all cases who lack or don't report any overt symptoms associated with the infection)	50%	12-14
Human population size	57 million	15
Baseline incidence of unrelated similar symptoms (Minimum plausible proportion of population per week experiencing similar symptoms to COVID-19 but caused by other common pathogens like the common cold, malaria etc)	1%	16,17
Initial importation rate (Number of new primary cases arriving into the country each week)	5	Assumed
Time to initiation of importation containment intervention (Number of weeks since the first imported cases before inbound travellers to the country are isolated on arrival)	2	Assumed
Time to initiation of lock-down intervention (Number of weeks since the first imported cases before population-wide restrictions are introduced to prevent personal exposure behaviours)	5	Assumed
Duration of lock-down intervention (Number of weeks since initiation of population-wide restrictions to prevent personal exposure behaviours until these restrictions are lifted)	15	Assumed
Proportion of symptomatic cases which are clinically severe (Percentage of all cases exhibiting and reporting with severe symptoms, all of whom are assumed to be tested unless the limits of testing capacity are exceeded)	20	12,18
Proportion of symptomatic cases requiring intensive care (Percentage of all cases exhibiting and reporting with symptoms who need intensive care)	4%	12,18
Intensive care unit (ICU) capacity (Maximum achievable percentage of the population that could be admitted to an ICU at a given time, allowing for maximum emergency expansion of capacity at short notice)	0.0002%	1
Case fatality rate in ICUs (Percentage of cases needing intensive care who access it but die nevertheless)	20%	18
Case fatality rate outside ICUs (Percentage of cases needing intensive care but who cannot access it and die subsequently)	50%	Assumed
Maximum achievable diagnostic testing rate (Percentage of entire population per week)	0.02%	Assumed

Proportional containment of imported cases (Percentage of secondary cases arising from primary imported cases which are prevented by travel restrictions and isolation of inbound travellers from affected countries on arrival)	100%	Assumed
Proportional containment of contact clusters of confirmed cases (Percentage of secondary cases arising from diagnostic-confirmed primary cases which are prevented by contact tracing and isolation)	90%	17,19
Proportional lock down coverage (Percentage of entire population included in and compliant with interventions to reduce exposure behaviours)	90%	12
Proportional lock down effectiveness (Percentage reduction of exposure behaviours among the fraction of the population included in and compliant with the lock down interventions)	90%	12

COVID-19 may be eliminated and excluded by ambitious national containment campaigns

The simplified model predicts that national containment and elimination may be achieved and sustained, without ever exceeding national ICU capacity, by using a full, timely package of interventions. The national epidemic may be contained with only 1486 cases and 6 deaths by highly rigorous 15-week lockdown (90% effective exposure prevention behaviours by 90% of the population) as soon the first cases are confirmed, 5 weeks into the epidemic, complemented by 90% effective tracing and isolation of all contacts for confirmed cases (Figure 1).

Predicted successful national containment and elimination though prompt, rigorous lockdown plus rigorous contact tracing and isolation, and then sustained with complete containment of imported cases

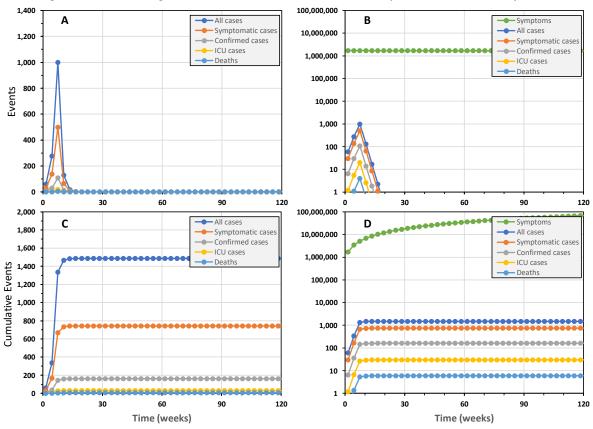


Figure 1. The predicted trajectory of a successfully contained national COVID-19 epidemic in the United Republic of Tanzania. In this simulation, a rigorous 15-week lock down was initiated from week 5 onwards and complemented by complete containment of imported cases, as well as contact tracing and isolation of confirmed cases. Rigorous lock down was assumed to achieve 90% reduction of exposure behaviours by 90% of the population. Complete 100% containment of imported cases assumes that all inbound international visitors are fully isolated for at least three weeks, except perhaps

those coming from countries that may be certified as free of local transmission by WHO in the future. Contact tracing and isolation follow up from confirmed cases was assumed to be 80% effective at preventing onward transmission from entire contact clusters.

As points of reference against which ongoing national containment campaigns may benchmark themselves, the epidemic was predicted to grow 59% bigger each week at the outset and shrink by 48% each week once rigorous lock down had been in place for several weeks. Note, however, that even these alarming projections for the rate of expansion of the epidemic and the rate of contraction required to contain it may under-represent the scale of the challenge in real epidemics. For example, at the outset of the epidemic in China, numbers of confirmed cases doubled every week. 7,20 Furthermore, subsequent analyses allowing for frequent carriage without overt symptoms indicate much higher viral reproduction rates than assumed in table 1, and suggest true doubling time for all cases may be less than 3 days. 4,6

Interesting, almost exactly the same containment trajectory is predicted even if contact tracing and isolation is completely removed from the intervention package (Supplementary figure 1), resulting in only 276 more cases and one more death. The explanation for this becomes apparent when one examines the trajectories of confirmed versus all cases: Even though the number of real cases never approaches an optimistically-assumed full testing capacity of 11,400 patients per week, half of all cases are never tested because they are asymptomatic and most of the remainder are only mildly symptomatic, so they get lost in the mass of other people who appear equally sick for unrelated to COVID-19. As illustrated in figure 1D, the background noise of similar mild symptoms caused by other common pathogens dwarfs the mild COID-19 cases, so almost all of them go untested and undetected. Less than one in every 4000 tests is conducted on a mildly symptomatic case of COVID-19, so even though we assume all severe cases are tested, only 11% of cases predicted to occur were confirmed. With contact tracing and isolation only being possible for this very small fraction of cases, there are obvious limits to how much it can achieve as a containment intervention in its own right.

Even the slightest relaxation of lock down or importation controls cause containment failure

However, successful containment (Figure 1) does requires that the lock down intervention is maintained for the full 15 weeks (Figure 2A and B) to eliminate the virus. Delaying a 15-week lockdown by only 3 weeks, the duration of one generation of viral infection, also allows the virus to persist and the epidemic resumes soon afterwards (Figure 2C and D). A slightly less rigorous lock down of the same duration, which nevertheless achieves 80% coverage with 80% reductions of personal exposure behaviours, also fails to eliminate the epidemic with tragic consequences (Figure 2E and F).

Furthermore, elimination may only be sustained by comprehensively containing case importation from outside the country (Figure 2G and H). Preventing reintroduction requires isolation of <u>all</u> incoming travellers, except perhaps those coming from countries that may be certified as free of local transmission by WHO in the future, to achieve 100% prevention of onward local transmission (Figure 1). Even 90% containment of imported cases seems unlikely to protect the country against reintroduction of the virus and re-initiation of the epidemic (Figure 2G and H). Tanzania therefore did the right thing by isolating all inbound travelers since March 23rd (over 600 so far) for two weeks following their arrival). However, for such importation containment measures to effectively exclude new cases from a COVID-free Tanzania in the future, isolation periods may need to be extended to three weeks. ^{10,21-24} However, it is also notable that all the scenarios in figure two, except for panels G and H, assume 100% effective containment of imported cases. It is therefore clear that local transmission must be eliminated before such rigorous control of inbound travellers can usefully protect the country against reintroduction.

All these delays, truncations or inadequacies of lock down, or imperfections of importation containment, result in failure to eliminate local transmission that then rebounds and rapidly spirals out of control without a second full containment campaign (Figure 2). The implications of such an

uncontained rebound scenario are essentially identical to doing nothing in the first place: In all cases, 99% of the population is expected to become infected over about a year, resulting in approximately 540,000 deaths and ICU demand exceeding capacity about 800 times over.

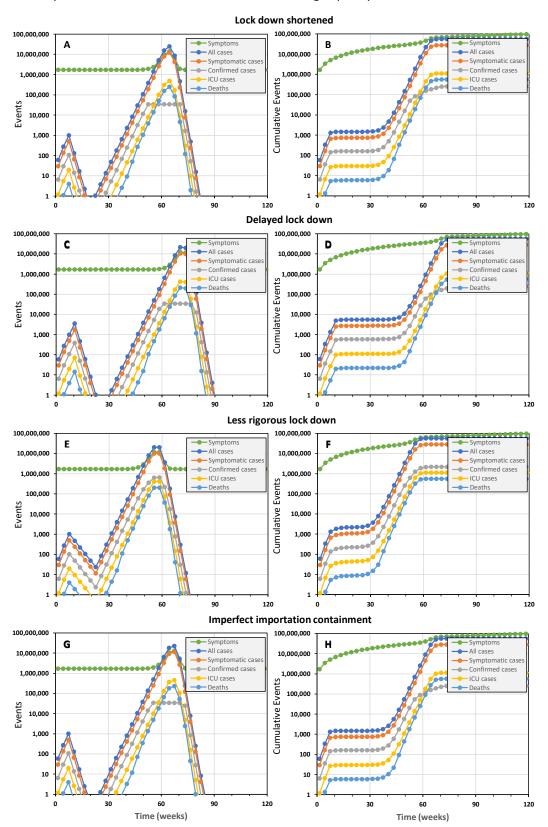


Figure 2. The simulated epidemic trajectories for slightly less robust national COVID-19 epidemic containment responses in the United Republic of Tanzania than that illustrated in figure 1, all of which are predicted to fail and result in a catastrophic rebound of transmission, morbidity and mortality. All these simulations have identical input parameters to

figure 1 except for (1) shortening the lock down period by 3 weeks, from 15 to 12 weeks (Panels A and B), (2) reducing importation containment from 100% to 90%, (3) delaying the lock down by 3 weeks (Panels C and D), starting on week 8 rather than week 5 (Panels E and F), and (4) reducing the coverage and protective effectiveness of exposure behaviour reduction from 90% to 80% (Panels G and H).

It is also worth noting that total national hospital inpatient capacity of approximately 50,000 beds²⁵ would be overwhelmed by cases of severe COID-19 disease peaking at 2.3 million over a three-week period. Under such conditions of a full-blown public health catastrophe, the mitigating effect of stronger health systems in high income countries are largely negated, so our predictions of over half a million deaths in Tanzania compare well with those of others for the United Kingdom,²⁶ which has a similar population size. Considering also the travel distances and household costs of hospital attendance in Tanzania²⁷⁻³⁰, it also raises the question as to whether severe COVID patients should be cared for in hospitals and other health facilities which are already 52% understaffed³¹ or at home with support from a rapidly mobilized cadre of Community Health Workers, for which well-characterized curricula and training platforms already exist.³²⁻³⁴

Even simply expressing ICU capacity as a proportion of overall population size is also useful for pragmatically putting suggestions that countries should aim to slow and mitigate this epidemic into perspective. Even in high income countries like the UK,²⁶ slowing the epidemic to match even rapidly augmented critical case capacity would necessarily extend it for several years, and in Tanzania the equivalent strategy would take decades.

In the event of such a failed containment campaign and catastrophic epidemic resurgence, contact tracing becomes a rather pointless exercise, even for targeting clinical disease management. At the peak of the epidemic, when over 4 million new symptomatic cases may occur per week, even mortality rate may outstrip testing capacity, so case confirmation success rates may plummet to below 0.2%.

The spiralling costs of catching up on lost time to implement a lock down

If a lock down is delayed by three weeks, approximately the duration of one viral infection, the epidemic may still be contained be extending it by the same length of time, from 15 weeks to 18 weeks (Figure 3A and B). Note, however, that the epidemic peaks at an almost four-fold higher incidence of cases, resulting in 5,485 cases and 22 deaths overall. Although ICU capacity is not expected to be overwhelmed, timely access will clearly represent a challenge for many patients in country with a surface area of almost a million square kilometres and only four national referral hospitals. Longer delays of 6, 9 and 12 weeks necessitate prolonged lock downs (21 weeks for the latter) to contain epidemics of rapidly expanding scale: 19925, 77055 and then 260103 cases, exceeding ICU capacity by 151, 994 and 4597 patients, and resulting in 125, 586 and 2420 fatalities, respectively.

The hidden dangers of stealthy epidemics

Note, however, that none of this will be obvious during the silent early phase of the epidemic, during which time the number of undetected cases snowballs: Even if the lock down response is initiated after only 5 weeks post-initiation, immediately after the first 6 cases are confirmed in this simulation, the epidemic has already quietly progressed much further than most members of the public would guess. Indeed, far enough that another 271 people are already actively infected and almost 1000 new cases are predicted to occur in the subsequent 3-week period, out of which only 108 (11%) will be detected.

Infectious carriers who exhibit little or no symptoms ^{10,12-14,21-23,35,36} clearly contribute to the cryptic nature of an early-stage COVID-19 epidemic: In this case we assumed this accounts for 50% of cases lacking symptoms overt enough to consider self-reporting and seeking a test (table 1). However, a much more important factor is the sheer volume of background noise arising from similar symptoms caused by more common pathogens, such as the common cold and malaria. Even though these simulations assume that capacity for conducting 11,400 COVID-19 tests per week would have been

established in Tanzania before the outbreak began, total confirmed cases are only expected to exceed 100 about 3 weeks after the lock down is introduced. Most of these confirmed cases are accounted by the clinically severe fraction we assume will all be tested. Only 4% (8/899) of predicted mild or asymptomatic cases are expected to be confirmed because the relatively small number of COVID-19 cases are so easy to miss in a population of 57 million people, out of whom we assume 1% or 570,000 will experience a fever, cough or stomach pains in any given week for unrelated reasons (Figure 1B and D). Note, however, that that even this is a very conservative assumption about background rates of illness with similar symptoms to COVID-19: In the first contact-tracing study in the USA, over 12% of all carefully-followed contacts became symptomatic within 2 weeks, even though none of them became infected with COVID-19.

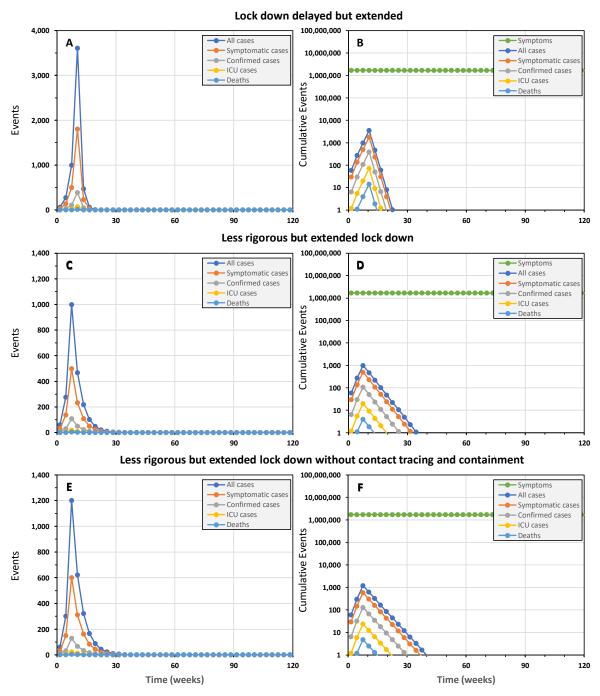


Figure 3. The simulated epidemic trajectories for national COVID-19 epidemic containment responses in the United Republic of Tanzania with slightly delayed or less rigorous lock down than illustrated in figure 1, all of which necessitated extension of the lock down period to achieve successful containment. All these simulations have identical

input parameters to figure 1 except for (1) delaying the lock down by 3 weeks, starting on week 8 rather than week 5 (Panels A and B), (2) reducing the coverage and protective effectiveness of exposure behaviour reduction from 90% to 80% (Panels C, D, E and F), (3) removing the contact tracing and isolation component (Panels E and F), and (4) necessarily extending the lock down period from 15 to 18 weeks (Panels A and B) or from 15 to 40 weeks (Panels C, D, E and F).

These simulations are nevertheless useful in that they illustrate how no perceptible increase in the incidence of such common symptoms may be obvious to the general population unless containment efforts fail and a full-scale, resurgent epidemic sweeps through the country (Figure 2). Tanzania therefore did exactly the right thing by reacting fast during the silent earliest phase of the epidemic, announcing school closures within a day of the first confirmed case report and introducing additional restrictions immediately afterwards.

The vital importance of ambition and rigour to lockdown outcome: Who dares loses least!

As illustrated by figure 3C and D, it is now crucial that Tanzania urgently builds on that early momentum to ramp up lock down efforts to the most rigorous level practically attainable. The implications of even a slightly less rigorous lock down appear less daunting in epidemiological terms but far more severe in practical and economic terms, because it greatly prolongs the lockdown period required: Even reducing coverage and effectiveness of personal protection measures by only 10%, from 90% to 80% requires that the lock down period is extended by more than 150%, from 15 weeks to 40 weeks (Figure 3C and D). The practical social and economic sustainability of such a protracted lock down period is very questionable, but much can be learned from the predicted benefits of getting such an imperfect lock down started in good time: The 1,108 cases and 11 deaths predicted over the course of such a "slow burn" containment campaign are only marginally higher than for the best case scenario illustrated in figure 1. It is therefore important to get some form of reasonably rigorous lock down in place as early as possible, and then intensify it as rapidly as possible. Like any race, it is critical to get an early head-start by any means possible, but then build up speed towards a strong finish.

While compliance and enforcement is of great importance to lock down effectiveness, so is acceptability and socio-economic feasibility. While high income countries move to facilitate population-wide compliance with direct financial support and augmented social services, different tactics will be required in low income countries like Tanzania. Although Tanzania is urbanizing very rapidly, most of the population still resides in rural areas³⁷ where propagation of directly-transmitted diseases like COVID-19 is always less intense. Fortunately, Tanzania is currently in the midst of this year's farming season, during which many rural families are out in the fields where social distancing is relatively easy. While farming season also conveniently brings a lull in trading activity at commercial hubs in rural towns and villages, it also represents a seasonal low point in the domestic food reserves of many rural households, so selective food support may be invaluable for enabling the most vulnerable families to comply effectively with self-quarantine and self-isolation directives. However, the growing urban population represents a much larger challenge, because far fewer people rely on farming for their livelihoods. Many live in crowded informal settlements where lack of shelter, water, sanitation and space, relying on unreliable, informal sources of income to survive on a day-to-day basis. Informal livelihoods and settlements in the busiest urban centres of the country will therefore require particularly urgent attention and creativity, to support daily food, water and hygiene needs. It may also be useful to consider providing safe transport with managed social distancing (to be followed by self-isolation) for those with options to sit out the epidemic with family and friends in rural areas.

As is the case for elimination of other diseases, such as malaria for example³⁸, it may be more useful to think about gaps in coverage and effectiveness to understand how such apparently minor deficiencies can make all the difference between success and failure: While a shift from 90% to 80% lock down coverage and effectiveness might seems small in relative terms, a 20% shortfall relative to perfect containment is twice as big as 10%. And the difference between 100% prevention of onward local transmission from imported cases contrasts starkly with even such high targets as 90%: when

you need to achieve zero new cases in a country, any other number simply isn't good enough. In practical terms, such lock down coverage and effectiveness gaps will be accounted for by the most important exceptions to restrictions and those exceptional individuals most determined to evade them.

Unfortunately, the most obvious exceptions to lock down restrictions who will facilitate continued transmission will be health service personnel, notably those caring for those most vulnerable to the disease. However, all other essential workers in shops, markets, kitchens, food processing facilities, factories, banks, post offices, transport services and law enforcement agencies will also inevitably mediate more transmission than they would if they stayed at home. Indeed, it the crew that enabled self-sustaining levels of COVID-19 transmission to persist aboard the quarantined Diamond Princess cruise ship.³⁹ It is also worth remembering that the anti-hero of infectious disease epidemiology, the infamous Typhoid Mary (real name Mary Mallon) was a cook by profession who infected at least 53 people, three of whom died.⁴⁰ Like many COVID-19 cases, ^{10,12-14,21-23,35,36} Mary was a silent carrier of the disease: She herself lived to a ripe old age and died of a stroke rather than typhoid. This is not to say that such essential services should necessarily be suspended, but rather that the roles and working practices of these personnel should be scrutinized particularly carefully. How essential is essential? What is the minimum level of service needed to facilitate extended lock down while mitigating indirect effects on health, well-being and economic welfare that are even worse than COVID-19? What procedures, behaviours and protective equipment could most effectively minimize persistent workplace transmission?

And with so many people's livelihoods on the lines, we may be asking too much of human nature by expecting everyone to do the right thing voluntarily. Many of the greatest public health campaigns in history have necessitated an authoritarian style, and it may be necessary for people all over the world to temporarily embrace and accept new restriction measures they would otherwise justifiably describe as draconian. Perhaps the single most important take-home message of the widely-accepted 80-20 rule of epidemiology (less than 20% of people cause more than 80% of transmission)⁴¹ is that the extremes of human circumstances and behaviour are more important to the survival of pathogens than the average. It inevitably follows that such exceptions are vitally important to target if one wishes to completely eliminate a disease.⁴¹

Again, it is worth remembering Typhoid Mary⁴⁰, who resisted repeated efforts to get her out of the kitchen and did nothing to disprove stereotypes about the stubborn Irish. She repeatedly returned to working as a cook because it paid better and frequently changed jobs as people fell ill around her, even changing her name to evade more than 30 years of quarantines imposed on her. It took 4 policemen over three hours to apprehend her despite a stealthy approach and forced entry to her home. Eventually Mary was found hiding in an outside closet at the rear of a neighbour's house, and things remained spicy following her arrest:

"She fought and struggled and cursed. I tried to explain to her that I only wanted the specimens and that then she could go back home. She again refused and I told the policemen to pick her up and put her in the ambulance. This we did and the ride down to the hospital was quite a wild one."40

When we read about the ongoing "Coronavirus challenge" game mediated through social media, we are inclined to think the spirit of Mary Mallon is alive and well and needs to be curbed. The experiences of those who knew Mary Mallon seem extreme but are difficult to disregard completely in the context of a pandemic threatening a global population of over 7 billion people with more eccentric characters, miscreants and outright criminals than we would wish in the circumstances:

"Mary was now about forty-eight years of age and a good deal heavier than she was when she slipped through a kitchen full of servants, jumped the back fence and put up a fight with strong young policemen. She was as strong as ever, but she had lost something of that remarkable energy and activity which had characterized her young days and urged her forward to meet undaunted

whatever situation the world presented to her. In these eight years since she was first arrested, she had learned what it was to yield to other wills than her own and to know pain."⁴⁰

Contact tracing as an epidemiological surveillance platform, rather than an in intervention per se

As for the full the full, timely intervention package simulated in figure 1 (Compare with figure S1), removing contact tracing from the less rigorous but extended lock down intervention package has only a modest effect on the overall containment trajectory, with only 797 more cases and 3 additional fatalities. However, that does not in any way imply that contact tracing and isolation should be de-prioritized because this simplified model only accounts for the direct preventative effects of follow up on subsequent transmission. In particular, it does not account for the invaluable functions of contact tracing for monitoring and characterizing the epidemic, and for understanding the influence of interventions on transmission dynamics. For example, the tracing of transmission to a relatively small number of clusters in Korea, and especially the incrimination of venues like the Shincheonji Church provide invaluable insights that guide more rigorous, effective follow on lock down measures.³ In Ireland, early observations that mean size of close contact clusters had shrunk from 20 to 5 were reported to the public as an encouraging early sign that behavioural interventions were impacting risks of onward transmission. Without such essential detailed information about how transmission persists, as well as the strengths and weakness of ongoing intervention efforts, any national containment programme would be flying blind.

It should be noted, however, that testing, contact tracing and isolation of known contacts is only useful as part of a deliberate containment strategy that keeps an epidemic manageably small. While testing is always useful for clinical management of severe cases, once 1% or more of the population has been infected even this important subset of cases alone overwhelms testing capacity (Figure 2B, D, E and F) and the fraction of non-severe cases confirmed plummets to negligible levels. In any case, population-wide testing of mildly symptomatic cases becomes unhelpful as a guide to targeting containment measures: How does one selectively target those at immediate risk when that means everyone? And how would we attempt contract tracing if we allowed the epidemic to grow to tens or hundreds of thousands of new cases each week? Note, however, that the expected failure of contact tracing, and indeed testing generally, is just one more good reason to contain national COVID-19 epidemics before they progress from emergencies (Figures 1 and 3) into outright catastrophes (Figure 2).

Limitations, caveats and comparisons with other models

Like other recent models of COVID-19, our simplified formulation does not attempt to predict complex indirect effects of the pandemic upon morbidity and mortality from other causes that will be exacerbated by the expected pressures on a health system that is already overstretched. Nor does it attempt to anticipate the extent of economic and social damage that will arise from different epidemic containment scenarios, partly because doing so would defeat the purpose of developing a simplified arithmetic formulation.

Despite its limitations as a relatively simple and untested model, the predictions described above are consistent with those of most other models using more sophisticated mathematical formulations and specialist software. 7-9,26,42-45 In fact, perhaps the most useful lessons to be learned from studies that reach substantively different conclusions lie in the differences in underlying assumptions.

Our predictions that contact tracing and isolation will play only a minor role in successful containment contrast with those of other modelling studies⁴⁶ which consider asymptomatic carriage by only 10% of cases or less, and which do not account for the detection dilution effect of similar mild symptoms caused by other common pathogens (Figure 2B, D, F, H).

On the other hand, the predictions presented here appear relatively optimistic when compared with recent reports suggesting viral reproduction rates are higher than generally thought^{4,6} because previous analyses failed to consider the likelihood that large fractions of cases may go undetected¹²⁻¹⁴ because they exhibit only mild, non-specific symptoms, if any^{10,21-23,35,36} As underlined right at the outset of the global response,^{20,47} the most important remaining question that needs to be answered to reduce the uncertainties of model predictions is the extent of asymptomatic carriage and infectiousness. Learning lessons from other diseases like endemic malaria, which is primarily a chronic illness transmitted by semi-immune adult carriers,⁴⁸ the term *asymptomatic* may well be a misnomer not only because some individuals become infectious before exhibiting symptoms,^{10,22,35} but also because it is often applied to those who shrug off mild symptoms to get on with their daily lives.^{12,49,50}

A particularly important caveat arising from current uncertainty about the role of cryptic carriers is that it also has a major influence on estimation of fatality rate for infections rather than clinical cases. The latest analyses allowing for this phenomenon suggest that fatality rates are may be 30 times lower per infection than per confirmed case,⁴ consistent with our conclusion that the vast majority of cases are never confirmed. It also suggests, reassuringly, that the surge of severe cases and fatalities in an uncontained epidemic may level out at a far lower level than those predicted in figure 2. While the worst-case scenario may therefore be less catastrophic than previously considered, it will nevertheless overwhelm critical care capacity several times over and should be avoided if at all possible.

Conclusions

The current global health emergency demands immediate, bold, pre-emptive decisions in the absence of unambiguous evidence, ^{51,52} based on our best understanding of COVID-19 epidemiology as it stands today. ^{44,53} The three key sequential actions every country needs to embrace as early and emphatically as possible are *contain*, *eliminate* and *exclude*. Even when faced with the prospect of lock downs lasting 4 months or more, there is no place for more timid terms like *slow*, *flatten* or *mitigate* when faced with an epidemic capable of overwhelming ICU capacity hundreds of times over or taking several years of restrictions to slowly burn through an entire population at rates that ICUs can cope with.

And tackling this pandemic will rely overwhelmingly upon widespread understanding and mass participation by the entire global public, rather than just the health professionals and high-level decision makers who will lead the response. Currently, half the world's population is already under lock down of some kind, meaning vertically enforced and severe restrictions of movement and physical interaction, and the remainder will have to follow if the ongoing COVID-19 virus pandemic is to be contained. Faced with such brutally difficult decisions, it is essential to policy-makers, health professionals and the general public that as many people as possible understand why lock down interventions represent the only realistic way for individual countries to contain their national-level epidemics before they turn into public health catastrophes. It also vital for as many people as possible to understand why these need to be implemented so early, so aggressively and for such extended periods.

Over the medium-to-long term, it will also be vital for us all to understand why widespread national action and international co-operation will be required to conditionally re-open trade and travel between countries that have successfully eliminated local transmission. As explained by the simulations presented here, this appears to be the only means by which national elimination efforts can be sustained, following which pandemic eradication may be pursued at global level.

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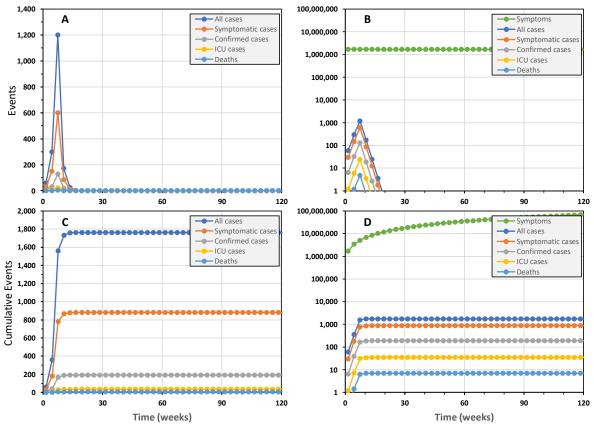
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Predicted successful national containment and elimination though prompt, rigorous lockdown, and then sustained with complete containment of imported cases, despite lack of contact tracing and isolation



Supplementary Figure 1. The predicted trajectory of a successfully contained national COVID-19 epidemic in the United Republic of Tanzania, achieved without any contact tracing and isolation. In this simulation, a rigorous 15-week lock down was initiated from week 5 onwards and complemented by complete containment of imported cases, as well as contact tracing and isolation of confirmed cases. Rigorous lock down was assumed to achieve 90% reduction of exposure behaviours by 90% of the population. Complete 100% containment of imported cases assumes that all inbound international visitors are fully isolated for at least three weeks, except perhaps those coming from countries that may be certified as free of local transmission by WHO in the future. However, these simulations differ from figure 1 in that absolutely no contact tracing and isolation was assumed.