

What is the impact of lockdowns on dengue?

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Abstract:

Purpose of Review

Societal lockdowns in response to the COVID-19 pandemic have led to unprecedented disruption to daily life across the globe. A collateral effect of these lockdowns will be a fundamental, if brief, change to transmission dynamics of a wide range of infectious diseases that are all highly dependent on rates of contact between humans. Such changes will be exacerbated by lockdown imposed impacts on disease surveillance and control programmes. The impact of lockdowns on dengue deserves special attention because it is one of the few infectious diseases that has seen consistent expansion over the past decades with over 4 billion people now at risk. As a major cause of acute hospital admissions in endemic areas, dengue could compete for triage, diagnostic and treatment resources with COVID-19, worsening patient outcomes for both diseases. Understanding the impacts of lockdown are important because some changes are likely to increase dengue virus transmission, while others will benefit control efforts. With timing, duration and intensity of lockdowns varying country-to-country, the wave of lockdowns in 2020 present a unique opportunity to observe how changes in human contact rates, disease control and surveillance affect dengue virus transmission in a global natural experiment.

Recent Findings

In this review we explore the theoretical basis for the impact of lockdowns on dengue transmission, surveillance then summarise the current evidence base from country reports.

We find high considerable variation in the intensity of dengue epidemics reported so far in 2020 with some countries experiencing historic low levels of transmission while others are seeing record outbreaks. Despite many studies warning of the risks of lockdown for dengue transmission, few empirically quantify the impact and issues such as the specific timing of the lockdowns and multi-annual cycles of dengue are not accounted for. In the few studies where such issues have been accounted for the impact of lockdowns on dengue appears to be limited or not detectable.

Summary

The impact of lockdowns on dengue is important both in how we deal with the immediate COVID-19 and dengue crisis, but also over the coming years in the post-pandemic recovery period. It is clear lockdowns have had very different impacts in different and that further studies are needed to understand the diverse dengue outcomes across countries in 2020 and beyond. Such studies might ultimately allow this unique natural experiment to provide insights into how to better control dengue that will ultimately lead to better long-term control.

Key points (4-5 key messages are required for COID)

1. The impact of lockdowns on dengue matters because they threaten to exacerbate long-term growth in dengue worldwide and because co-occurrence of both diseases could lead to worse patient outcomes for both diseases.
2. Lockdowns have the potential to impact dengue transmission, control efforts and surveillance in both positive and negative ways.
3. So far evidence is mixed on impact with some countries experiencing far worse dengue epidemics but some experiencing historically low levels of transmission in 2020, but long term impacts are unknown and will be important to measure.
4. This natural experiment provides a unique opportunity to better understand dengue epidemiology including the balance of home vs away from home transmission, the effectiveness of current vector control tools and the role of international mixing of dengue virus genotypes.
5. If such timely analysis can be done, it presents a unique opportunity to improve dengue control efforts with renewed vigour in a post lockdown world.

Lockdowns and their impact on infectious diseases

In response to the COVID-19 pandemic, many countries around the world had to resort to lockdowns with strict mobility restrictions and social distancing(1). Lockdowns indeed showed great success in containing the COVID-19 outbreak in the initial epicentre in Wuhan, China(2) and flattened the curve in many other countries(3). Each country has taken different approaches to lockdowns with the restrictiveness, adherence, target population and duration of lockdowns varying considerably between countries(4). The unprecedented lockdowns, despite their major repercussions on the economy and mental health(5), also led to the decline of other diseases that are transmitted from human to human. Influenza incidence for example experienced a major decline in China and the Northern Hemisphere in early 2020, in parallel with lockdowns (6, 7). Although measles incidence has been on the rise in recent years(8-10), social distancing during 2020 resulted in a major decline of measles(11)(12). On the other

hand, measles vaccine coverage rates dropped due to the COVID-19 pandemic as lock-downs interrupted routine immunization programmes and a further resurgence of measles is expected in the years to come(13). In addition to the decline of measles, varicella and rubella(14) saw a lower incidence in 2020. In Switzerland, all diseases due to respiratory pathogens, sexually transmitted diseases and gastrointestinal diseases saw a more than 50% reduction(15), and travel-associated importations such as malaria also declined.

The burden of dengue and its impact on the health system

Dengue is an acute arthropod-borne viral (arboviral) infection that places a significant socioeconomic and disease burden on many tropical and subtropical regions of the world(16). With 100 million cases estimated annually, dengue is regarded as the most frequent arboviral disease globally(17), and also increasingly presents a health problem encountered by international travelers(18-22). GeoSentinel, an international network of travel medicine providers(23), has seen a substantial increase in dengue over the past two decades(24). Transmitted by *Aedes* mosquitoes, dengue is a public health problem mainly in the tropics and subtropics where approximately 50% of the world's population reside. Asia accounts for 75% of the dengue disease burden, followed by Latin America and Africa(17). Similar to COVID, urbanization and overcrowding facilitates the spread of dengue(25, 26). Although severe outcomes for COVID-19 appear to be predominantly in older persons(27) while dengue affects more children and young adults in most dengue endemic countries (16), dengue has also emerged to be a major cause of morbidity and mortality in the elderly in places such as Singapore and Taiwan(28, 29). The percentage of febrile episodes due to dengue requiring hospitalization was 19% in the Asia and 11% in Latin America(30). WHO estimates that globally about 500,000 hospitalizations occur every year due to dengue(31). Resurgence of dengue and other arboviral diseases would therefore be a real threat during the COVID-19 pandemic thereby overwhelming already fragile healthcare systems. The impact of combined dengue and COVID-19 epidemics could have potentially devastating consequences in tropical and subtropical cities. Although the first vaccine against dengue has been licensed, but its use is limited due to the fact that pre-screening for serostatus is required(32) and only those identified as seropositive individuals should receive the vaccine(33). Vector control remains the mainstay to reduce the dengue burden.

Why understanding the impact of lockdowns on dengue is important

The impact of lockdowns on dengue has the potential to exacerbate both the continuing global expansion of dengue and the severity of the COVID-19 pandemic. With over 128 countries facing some level of dengue and COVID-19 risk,(34) and with dengue being the only infectious diseases to show sustained growth over the past decades the impact of lockdowns on dengue is a global issue. In many countries dengue is a leading cause of acute morbidity and the immediate and long term impacts of current lockdowns need to be better characterised to shape a long-term recovery plan to get dengue

control back on track. In the short term, because dengue shares many similar clinical manifestations with COVID-19 (35) and because dengue virus infection can result in prolonged hospital stays, it competes for triage, clinical diagnosis, laboratory testing and treatment resources (36). The risk of each of these being overwhelmed in an overlapping dengue and COVID-19 outbreak could substantially exacerbate the fatality rate of both diseases and compromise efforts to control transmission. Finally, with COVID-19, dengue and lockdowns all shown to disproportionately affect poorer populations, understanding their interaction has key importance for understanding equity in global health (37-39). Understanding unequal impact is essential to avoid catastrophic impacts in areas where dengue, COVID-19 and humanitarian crises overlap, such as Venezuela and Yemen.

Theoretical impacts of lockdown on dengue transmission and surveillance

There are a variety of mechanisms by which lockdowns could plausibly affect dengue virus transmission, with both increases and decreases in risk possible. The primary negative effects of lockdown for dengue transmission are likely to come from the disruption to routine vector control programmes. Interruption of activities that kill adult mosquitoes, such as indoor residual spraying and, where effective, space spraying, are likely to have the most immediate and possibly largest impact (40). Over time, lockdown-related disruption is also likely to lead to more abundant mosquito populations as existing breeding habitat treatments degrade and new breeding habitats are not cleaned up. With more people spending more time at home rather than their usual visited locations, lockdowns are likely to influence the contact rate between human and mosquito populations. In areas where mosquito populations usually thrive outside the home e.g. public spaces, places of work or schools, there might be a detectable decrease in transmission. These reductions are likely to be even more pronounced in areas where transmission is sustained by a wide variety of visitors to a small number of key super spreader premises. Conversely in settings where mosquitoes congregate in and around the home, exposure to mosquito bites and dengue virus is likely to substantially increase.

Movement of infected humans has played an important role in the spread of dengue at a variety of spatial scales (41) and we would expect unprecedented decreases in travel volume and distance induced by lockdown to impact dengue transmission. Reducing between household movement could drive a reduction in transmission, particularly in smaller households where within house immunity quickly builds up extinguishing chains of transmission (42, 43). At a city or national scale, movement restrictions could slow or even prevent the spread of a dengue epidemic from high transmission intensity city centres to lower suitability suburbs or more remote provinces (44, 45). The substantial reduction in international movement may also reduce the risk of importation of novel dengue virus genotypes (46, 47). It should be noted, however, that the positive effects of lockdown on dengue transmission are unlikely to be long lasting. Like the effect of lockdowns on COVID-19, without permanent changes to human, vector populations or the way in which they interact, dengue virus infections will be deferred rather than prevented. That isn't to say that delays cannot be beneficial, particularly if they flatten the

curve to avoid overwhelming the health system, or suppress outbreaks until the arrival of the dengue low season, but fundamentally any positive effects of lockdown on dengue transmission are likely to be short-lived.

Lockdowns are also likely to disrupt detection and reporting of dengue cases by routine surveillance systems. Lockdowns could reduce the proportion of dengue infections reported (underreporting), and reduce the timeliness and accuracy of reported dengue data, particularly for non-severe cases. COVID-19 epidemics substantially reduce treatment seeking and it is likely that the majority of minor dengue infections are unlikely to have any contact with formal care providers. Among those dengue infected individuals who do seek treatment, availability of dengue testing could be restricted as many laboratories prioritise COVID-19 testing in the face of overwhelming demand. Finally, lockdowns are likely to lead to disruption to the workforce involved with dengue reporting, from data entry personnel at the hospital to those tasked with collating, cleaning and ensuring the accuracy of national dengue statistics. Particularly for those countries that have yet to make a full transition to electronic web-based reporting systems, lockdowns could lead to substantial delays or reductions in completeness and accuracy of case counts. Compromised dengue surveillance systems could lead to increases in transmission due to reduced efficiency of targeted vector control. Changes in data consistency might also compromise our ability to detect the true impacts of lockdowns on dengue from routine surveillance datasets.

Reported impacts of lockdown on dengue in different countries

Despite COVID-19 spreading throughout the dengue endemic world, the reported impact of COVID-19 lockdowns on dengue transmission remains variable with increases, decreases and no impact reported with no strong regional patterns. A considerable number of papers have been published warning of the potential impact of overlapping dengue and COVID-19 epidemics for different stakeholders, but few collect or analyse dengue data from 2020 to see if such effects can be observed(48-51).

[Table 1: Countries reporting above or below average dengue case numbers in the year 2020. * as reported on the Health Information Platform for the Americas (PLISA) using data reported by Ministries and institutes of health of the countries and territories in the Americas last accessed 11th November 2020]

Worse than average dengue incidence in 2020 has so far been reported from Pakistan(52), Peru(53), Singapore(54), Thailand(55) and Ecuador(56). In addition data from PAHO suggests Paraguay, Bolivia, French Guiana and Suriname are having substantially larger outbreaks of dengue in 2020 than their historical average (Table 1). A number of countries in the Americas have also reported higher than

expected number of cases earlier in the year, but are now back within the historical year average such as Colombia, Mexico, Guatemala, Honduras, Nicaragua and Panama. It should be noted, however, that the dengue season in much of Central America only begins later in the year (August – December), so the impacts of overlapping lockdowns and dengue epidemics may not be seen until data from this time period becomes available. Significant impacts of coinciding dengue and COVID-19 epidemics on excess mortality have also been observed in Guayaquil, Ecuador and Iquitos, Peru (57) while the impact of lockdowns on increasing vector indices has also been directly observed in India(58).

Conversely, a number of countries have reported significantly lower than average dengue case counts in 2020 including Taiwan(59), Bhutan, Sri Lanka and parts of Brazil and Colombia(51, 55, 60-62). As acknowledged, these decreases could reflect underreporting due to the impacts of COVID-19 response measures on dengue surveillance activities, however the age profiles and case fatality rates of reported cases remain stable, suggesting surveillance systems are still capable of detecting milder cases of disease. Some countries, such as Bhutan, have designated vector control as an essential service during lockdown, suggesting the that reduction in dengue may be a genuine epidemiological effect(61).

The issue with crude comparisons of 2020 dengue case counts is main centred on two issues. First, lockdowns are interventions that only act at a specific time for a specific (often difficult to measure) duration and its effects on dengue transmission through the mechanisms identified above would likely be delayed by anywhere between a couple of days to months. Only one analysis, to date, has conducted a more detailed statistical comparison of the trajectory of dengue incidence in response to the exact timing of lockdown, finding an association between lockdowns increased dengue cases in Thailand, but had no significant difference in Malaysia or Singapore(55). Second, a wide variety of factors influence dengue dynamics in different places at different times and estimating associations from observational analyses may be vulnerable to confounding. The year 2019 saw the largest global dengue outbreak ever with over 4.2 million cases reported and the tail of this global outbreak is still being seen in some countries, for example Peru, Bolivia and Paraguay. This may lead us to overestimate the effects of lockdown in countries that are still experiencing this outbreak or conversely underestimate the impact of lockdowns in countries that have higher than average levels of immunity to dengue in 2020. If such confounding data can be assembled and analytical models appropriately specified, the wide range of deviations in dengue case timeseries following lockdowns could be used to test hypotheses about dengue epidemiology or the impact of current vector control practices.

What insights could further analysis of dengue data during lockdown give?

The relative role of within-home vs outside-home transmission

While the *Ae. aegypti* mosquito is classically thought of as within-home dwelling vector species with a limited flight range, there is still considerable debate over exactly where dengue virus transmission

occurs. While in many settings dengue cases appear to occur in local clusters, studies that aim to detect within-household transmission events rarely find high household attack rates. How much dengue virus transmission occurs within household vs household visitors vs other local shared spaces vs more distal shared locations like work or school remains an unknown. With lockdowns restricting household visitors then gradually resuming certain movements (e.g. school or work attendance or limited visitor numbers), lockdowns present a unique opportunity to test hypotheses about the importance of different settings for the local spread of dengue viruses.

How effective are current vector control methods?

Despite the widespread use of vector control for dengue, the evidence-base for different strategies is lacking, leading some to suggest that certain methods have limited effectiveness. If data can be assembled on disruption to vector control activities and entomological surveys can be rapidly resumed post-lockdown it may be possible to generate new estimates of effectiveness for existing vector control tools.

What is the relative contribution of different age groups to dengue virus transmission?

Lockdowns vary in their severity from country-to-country with some permitting school attendance and others emphasising extreme social distancing (shielding) in vulnerable elderly populations. The impact of these changes in human contact patterns can be used to answer important questions about the relative role of younger and older aged individuals in dengue virus transmission, particularly in endemic areas vs areas where dengue has recently arrived.

Would quarantining dengue-infected international travellers prevent the spread of dengue serotypes

International air travellers are frequently blamed for spreading novel dengue serotypes across borders (e.g.). With lockdowns forcing international travel to historically low levels, it will be important to continue sequencing circulating dengue viruses to assess any impact on global dengue virus dispersal. If effects are sizable, it may renew interest in testing arrivals from high risk countries during outbreaks of novel serotypes or new emerging arboviruses.

How feasible would sustaining dengue elimination be?

Finally, if lockdowns do have protective effects through isolation in some areas it is plausible that we may see examples of local elimination of dengue in areas that have previously sustained transmission over multiple years. Observing the rate of re-invasion and resurgence in such communities will provide valuable insight into the sustainability of dengue elimination and suggest what levels of monitoring and reaction would be required to maintain absence of local transmission.

What needs to be done now to avoid adverse effects of lockdowns on dengue

Until the full extent of these impacts are known the most pragmatic advice for now is to maintain and strengthen existing dengue control practices, particularly during lockdown. During stay-at-home orders, community participation in mosquito control activities should be strengthened including intradomicile application or targeted indoor residual spraying, reduction in peridomicillary water containers and appropriate coverage of water storage tanks, and reduction of man-made containers than can collect rain water. During lockdowns when schools are often closed, it is important to maintain vector control measures to prevent dengue outbreaks when children return to school after the lockdown has been lifted(36). Public health messaging and community engagement should include both COVID-19 and dengue.

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