Report 39: Characterising COVID-19 epidemic dynamics and mortality under-ascertainment in Khartoum, Sudan

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Summary

- A mitigated COVID-19 epidemic (slowing but not stopping epidemic spread) occurred in Khartoum between April and September 2020.
- In order to predict the trajectory of the emerging second wave, we estimate the level of mortality detected during the first wave and subsequently infer levels of immunity.
- Between April and September 2020, we estimate that **2% (sensitivity range 2% - 5%) of deaths due to COVID-19 were reported** in official reported mortality numbers.
- We estimate there were **16,090 (95% CI: 14,300 - 17,990) undetected COVID-19 deaths up to 20 November**.
- We estimate high levels of immunity after the end of the first wave of COVID-19 in Khartoum with 38.0% (95% CI: 35.0% - 41.1%) infected by 20 November 2020.
- Reductions in COVID-19 incidence during the first wave were due to both the implemented interventions and increasing immunity in the population.
- Interventions lead to a reduction in R from 3.5 to 1 by 20 April.
- The effective reproduction number continued to fall after 20 April, falling to 0.8 at the beginning of July due to increasing immunity.
- The ending of stringent suppression measures in July resulted in transmission increasing, with continued increases in mobility resulting in R rising above 1 during September.
- In the absence of further increases in transmission, we predict that the second wave will peak before the beginning of 2021.
- We project the second wave to be similar in size to the first wave sustained in the summer if transmission is maintained at current levels.
- If instead mortality under-ascertainment is at the upper end of our range (5%), then we estimate a smaller first wave. This means that fewer people will be immune and hence we would project a larger second wave.
- In the absence of implementing new suppressive measures, continued shielding of high risk individuals is important to help reduce mortality during the second wave.
- Historic mortality investigations are needed to help confirm the level of mortality missed and to inform the trajectory of the second wave and how long shielding should be maintained.

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1. Report

The COVID-19 pandemic has impacted modern life, with restrictions being implemented in the majority of countries to stop the spread of SARS-CoV-2.[1] Despite this, large epidemics have been observed in multiple countries with over a million deaths reported to date. However, whilst the pandemic has strained health systems to near-capacity in many high income countries, the absence of comparable epidemics in many African countries is notably perplexing.[2] Under-reporting of COVID-19 deaths is a likely explanation of these patterns, however, it is difficult to measure given that vital registration systems and excess mortality data are absent in many countries. Understanding the true mortality due to COVID-19 is crucially important with COVID-19 mortality frequently used to provide a more complete understanding of the size of epidemics. However, under-ascertainment of deaths will change the outcome of such approaches as well as altering our understanding of herd-immunity thresholds for COVID-19.

In September, we published a report looking into the COVID-19 epidemic in Damascus, Syria.[3] In this, we estimated that only 1 in 80 deaths due to COVID-19 have likely been reported. This scale of under-reporting of mortality suggests that a largely unmitigated and unobserved COVID-19 epidemic has occurred in Damascus. This was hinted at by media reports and anonymous testimonials from within the country that the health system was at capacity,[4] but would likely have remained unconfirmed without leveraging alternative datastreams. Recently, similar levels of under-ascertainment have been estimated in Aden, Yemen. In this analysis, satellite images were used to reveal a largely unobserved COVID-19 epidemic during the summer.[5] These are just two settings, but there have been numerous media reports of health systems reaching capacity and large numbers of deaths not being detected.[6–8] If these reports are true, it is likely that early predictions of the global spread of COVID-19 have largely been born out.

Reports of increased burial numbers from gravedigger testimonials[9] and documented low testing capacity[10] prompted this investigation to understand whether COVID-19 mortality has been under-ascertained within Khartoum state, Sudan. This is of particular importance with trends in case incidence in Sudan during November suggesting the epidemic is entering a second wave. In order to predict the trajectory of the second wave we need to understand how large the first wave was and the resultant level of immunity in the population. We fit a previously published[11] and recently re-parameterised[12] age-structured COVID-19 transmission model to daily COVID-19 deaths reported in Khartoum state. Using an analogous modelling framework as in our previous study in Damascus,[3] we focus on the assumption that official reported daily mortality due to COVID-19 is informative of the true epidemic shape. Using this assumption, the trajectory of officially reported deaths should mirror the shape of the epidemic after accounting for under-ascertainment. We explore a range of under-ascertainment levels within our transmission modelling framework to relate the deaths predicted by the model to the official reported deaths. We evaluate the likelihood of each under-ascertainment fraction by comparing the inferred epidemic trajectory against two alternative data sources; 1) a social media conducted survey of symptomatic prevalence[13] and 2) a paired serology and molecular diagnostic cross sectional survey.[14] We review the potential biases in the data sets before estimating the proportion of deaths due to COVID-19 that have been reported, which is subsequently used to provide epidemic trajectories of the second wave.

1.1 COVID-19 Epidemiological Situation in Khartoum State

Sudan reported its first COVID-19 death in Khartoum on 12 March, with a total of 315 deaths recorded in the city in the period up to 31 August (Figure 1). Across Khartoum and other Sudanese states, both reported cases and deaths suggest a significant epidemic peaking in early June followed by declines to low levels of transmission by the beginning of September (Supplementary Figure 1). However, early signs of a second wave are being observed with cases increasing significantly since November. In order to understand the likely trajectory of the second wave, we need to understand the true spread of COVID-19 during the first wave. We therefore restrict our initial analyses to this period spanning the first death in March until September, with the aim of this initial analysis to better understand the transmission dynamics and burden of COVID-19 experienced in Khartoum during the first wave.

To explore the epidemic dynamics in Khartoum, we initially sought to use case data (Supplementary Figure 1) to infer changes in transmissibility (R_t, the time-varying reproduction number of the virus). However, limitations in diagnostic capacity make it hard to rely on trends in incidence, with test positivity rates equal to 55% for tests conducted in Sudan up to 3 July 2020.[10] In response, we assume changes in transmission can be explained by mobility patterns,[3] which we infer from the timing and nature of population-level control measures sourced from the Oxford Government Response Tracker (Figure 1).[15] The first lockdown in Khartoum was announced on 18 April, which included restrictions on accessing shops and suspension of religious services. Intriguingly, the observed peak in mortality in June is approximately 45 days after the first lockdown, which is significantly longer than the delay distribution from infection to death from COVID-19 (typically approximately 20 days). Motivated by both the limitations in testing capacity and the delay between lockdown implementation and the peak in mortality we sought to characterise the under-ascertainment of mortality in Khartoum.

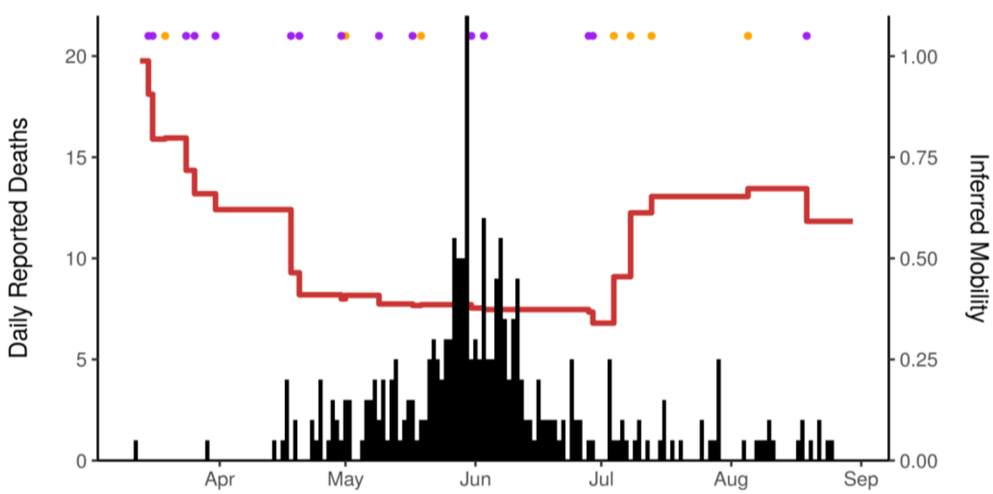

Figure 1. Incidence of confirmed deaths due to COVID-19 in Khartoum before September 2020. Reported deaths in Khartoum are shown in black bars, with the inferred mobility pattern for Sudan shown with the red line. The timing of government interventions and policy changes is indicated with points at the top of the y-axis, with purple points indicating when policies were implemented or extended, whereas orange indicate intervention policies being relaxed. As of 27th August, 315 total deaths had been reported in Khartoum.

1.2 Estimating the under-ascertainment of deaths

Prompted by these results suggesting an inconsistency between intervention timing in Khartoum and subsequent declines in mortality, we investigated whether the under-reporting of deaths might help explain the observed epidemic dynamics. To estimate the under-ascertainment of COVID-19 deaths, we scan across a range of under-ascertainment levels to relate the deaths predicted by the model to the officially reported deaths. To evaluate the likelihood of each level of under-ascertainment we compare outputs from the inferred epidemic curves to two sources of alternative data.

The first source of data is taken from a social media survey conducted in Khartoum. The survey was circulated as a Google form and collected information on whether participants had suffered any symptoms associated with COVID-19.[13] Symptomatic individuals were asked to report the symptoms they had suffered and all individuals were asked both i) if they had received a COVID-19 diagnostic test and ii) the outcome of any test taken. From this survey, the authors created a statistical model to infer the COVID-19 infection status of survey participants who had not received a COVID-19 test based on reported symptoms and through this, infer the symptomatic attack rate in the general population by 2 June. We use three estimates of the symptomatic attack rate in 15+ year olds from the study to reflect the uncertainty in the inferred attack rates: 8.3%, 11% and 13.7%. Using these estimates, we estimate the likelihood of different levels of under-ascertainment of deaths by comparing the model predicted symptomatic attack rate in 15+ year olds on 2 June to the observed attack rate estimated from the social media survey. We are aware of likely biases in the survey collection, with individuals recruited by voluntary sign up, which may select for individuals more likely to have been infected. To account for this bias, we also estimate the level of under-ascertainment under the assumption that people infected with COVID-19 were twice as likely to complete the survey (see Supplementary Table 2).

The second source of data is a joint serological and molecular survey conducted in Khartoum between May 22 and July 5 through the Sudan Field Epidemiology Training Program (FETP). In the FETP survey, participants were tested for both current infection and for antibodies.[14] The survey screened 1135 individuals from 22 neighborhoods and eight health facilities across Khartoum using reverse transcription polymerase chain reaction (RT-PCR, detecting active infections) and rapid antibody immunochromatography (ICT, detecting prior exposure) tests. Recruitment was via voluntary enrollment, with community health workers utilising neighborhood groups known as Resistance Committees to engage with communities. As a result, this survey is likely a biased sample, probably selecting for individuals who have been infected or are currently infected. Indeed, the observed two-by-two table of test outcomes (Table 1) reveals a very high prevalence of active infection, with 35% of participants PCR+. Despite this bias however, joint administration of both RT-PCR ICT tests provides additional information on epidemic dynamics. Having information on both the kinetics of viral loads and of human antibodies (which differ in their timescales) allows us to infer when individuals were infected prior to sample collection. If many individuals are both ICT+ than PCR+, this suggests that most infections have occurred recently and the epidemic is growing. By contrast, if most individuals are ICT+ but PCR -, this suggests that comparatively few infections have occurred recently and the epidemic is likely declining.

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Table 1. Joint Serological (ICT) and Molecular (PCR) FETP survey results, May 22 - July 5[14]

	PCR		
ICT	Positive	Negative	Total
Positive	100	55	155
Negative	191	506	697
Total	291	561	852

To compare the outputs from our transmission model to these data, we construct an observational model for the serological and molecular data. To estimate the number of infected individuals who would be PCR+ on a given day, we use a previously published relationship between time since infection and the probability of being detectable by PCR (Figure 2a). To estimate the number of individuals who are seropositive on a given day, we combine a previously fitted Weibull survival model for seroreversion[16] with a delay to seroconversion described by an exponential distribution with mean 13.3 days[17] to estimate the probability of being seropositive on a given day (Figure 2b). These allow us to describe the probability of a sampled individual being PCR or seropositive. However, relating this and our modelled dynamics to the conducted surveys remains challenging due to the likely extensive enrollment bias in both studies. To circumvent this potential enrollment bias, we compare the model predicted mean ratio of PCR+ to seropositive individuals during the survey period. Whilst this accounts in part for enrollment bias more generally, additional bias could occur if individuals are more likely to enrol if recently infected. We therefore additionally estimate the level of under-ascertainment under the assumption that an increased proportion of individuals PCR+/ICT- (to reflect recent infections) were enrolled, the results of which are contained in Supplementary Table 2.

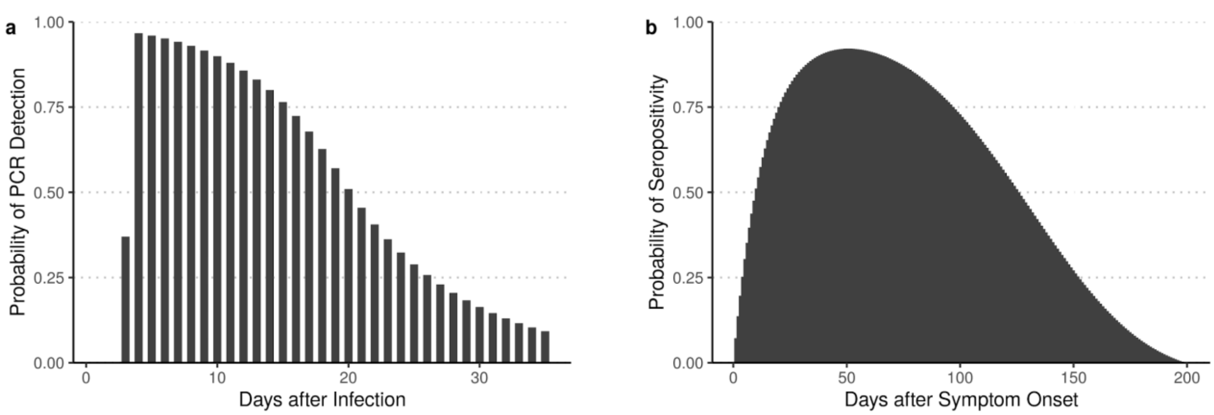

Figure 2. Observational assumptions relating infection history to molecular and serological diagnosis. In a) the assumed probability of being detected by PCR is shown for each day after infection, with PCR detection assumed to fall to 0 after 35 days. In b) the probability of being seropositive and being detected by rapid antibody immunochromatography is shown for 200 days after the onset of symptoms. Both distributions are used to relate the transmission model outputs back to the joint serological and molecular survey.

By the end of August, 315 COVID-19 related deaths were reported in Khartoum state. Using the described alternative data sources, we estimate that this likely comprises 2-5% of total COVID-19 deaths. This was determined by comparing both the model-predicted symptomatic attack rate (calculated using the age-dependent clinical fraction estimated in Davies et al[18]) in individuals aged 15+ (Figure 3a) and the model predicted ratio between PCR+ and ICT+ individuals (Figure 3b) against the related measures in the symptomatic and FETP surveys respectively. The sensitivity range reported reflects the range of uncertainty both in our model parameters and the described biases and uncertainty in the two survey sources (Supplementary Table 2). 2% provided the best fit to the observed data, however, we are aware that these surveys are susceptible to bias that has likely resulted in the attack rate being overestimated. In response, we use a conservative estimate of 3% of deaths reported (i.e. a smaller degree of underascertainment) within our main modelled scenario in which we consider the implications of under-ascertainment on the inferred epidemic dynamics and the trajectory of the second wave.

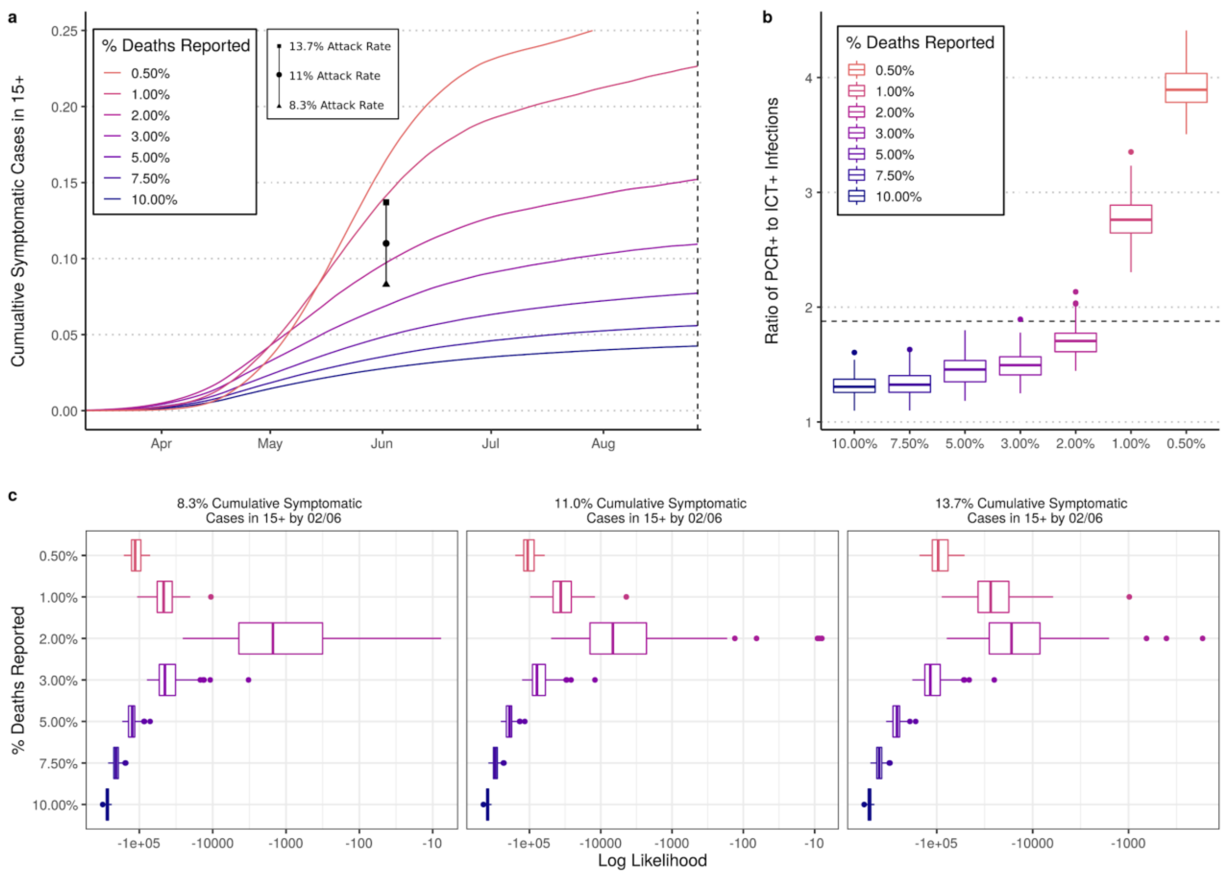

Figure 3. Estimates of under-ascertainment of deaths in Khartoum. In a) the cumulative symptomatic attack rate in individuals older than 15 years is shown for a range of values for the under-ascertainment of COVID-19 deaths. The range of observed attack rate estimates are shown with the vertical black segment and 3 points, showing 13.7%, 11% and 8.3% attack rates. In b) the model predicted ratio between PCR+ individuals and seropositive (ICT+) individuals is shown. Boxplots represent 100 simulation repetitions, with the mean ratio taken across the 23rd May and 2 July. The horizontal dashed line shows the observed ratio of PCR+ to ICT+ from the FETP survey (conducted 23 May - 2 July). In c) the log likelihood for each reporting fraction is shown for each attack rate in the observed data in b). Model log likelihoods presented reflect the mean model log likelihood, suggesting that under-ascertainment, without accounting for upward bias in the survey, is equal to 2% based on the symptomatic survey data in a), which is in agreement with the results in b).

1.3 Implications of under-ascertainment for the Khartoum epidemic

The scale of inferred under-ascertainment yields a significantly more mature epidemic than suggested by reported deaths and has profound implications for our understanding of the epidemic trajectory since September. To reconstruct the course of the epidemic to date we assumed that 3% of COVID-19 deaths have been reported in Khartoum. We choose to model 3% rather than the best fitting 2% inferred in Figure 3 in order to account for the perceived upward bias in the surveys that likely increased the enrollment of infected individuals. As of 20 November 2020, 477 COVID-19 related deaths were reported in Khartoum state, which incorporates periodic revisions of COVID-19 data made by the Sudan FMOH. Based on this level of underascertainment, we estimate that during this time 16,090 COVID-19 deaths have been missed (95% CI: 14,300 - 17,990) (Figure 4c). Consequently, we predict that a cumulative total of 38.0% (95% CI: 35.0% - 41.1%) of the population in Khartoum state had been infected by 20 November 2020 (Figure 4b).

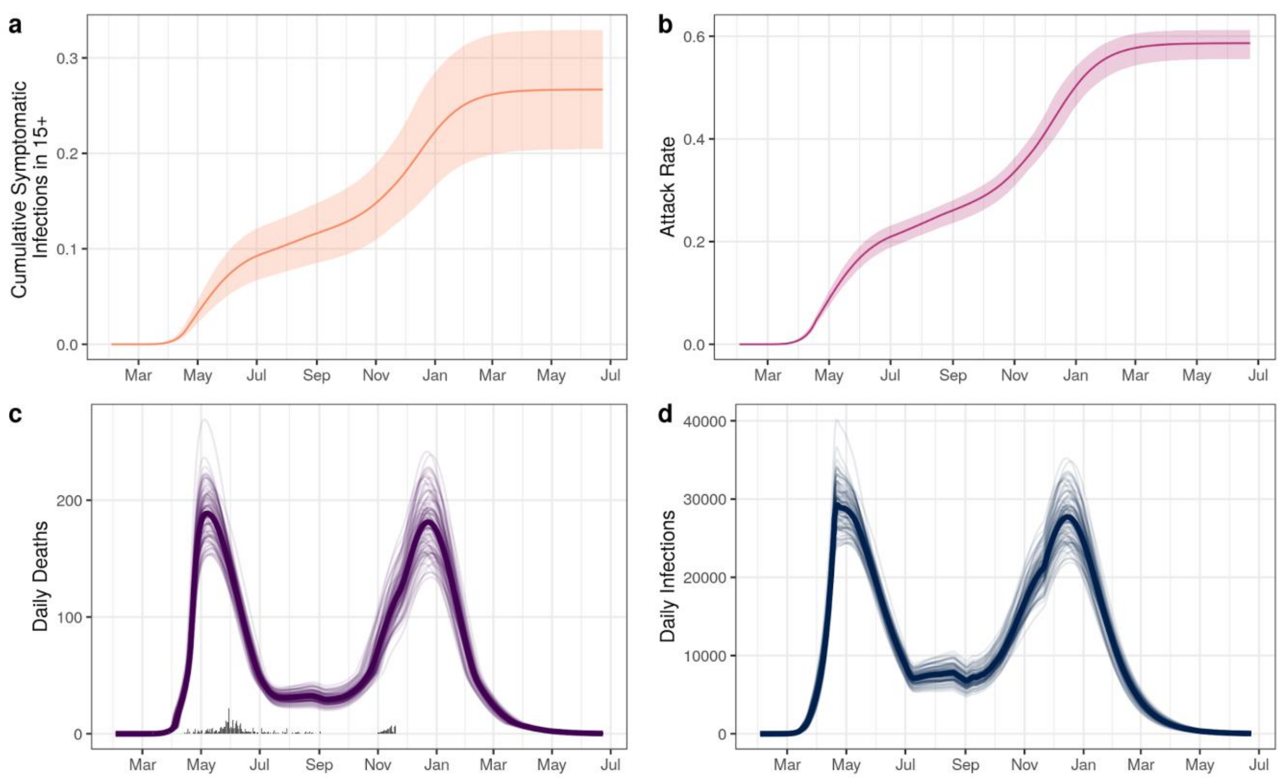

Figure 4. Model-predicted attack rates, deaths, infections and hospital occupancy due to COVID-19 for Khartoum under an assumed 3% mortality ascertainment. In a) the model predicted 15+ symptomatic attack rate is shown, with the range calculated using the assumed clinical fraction estimated in Davies et al,[18] using the 95% quantile range. In b) the overall attack rate is shown, with the confidence interval representing the 95% quantile range of 100 simulations. In c) and d) the reported daily deaths and infections due to COVID-19 respectively are shown, with the individual simulation replicates shown behind the median prediction in bold.

Using the fitted model we project forward until July 2021. During forward projections, we assume transmission will be maintained at the same level as estimated for 20 November based on mobility and government intervention data (see Supplementary Figure 2). In forward projections, we predict that despite estimated high levels of population level immunity in Khartoum currently, there is still a significant risk of a large second wave of COVID-19. If no change in transmission occurs, we predict an additional 27,690 deaths (95% CI: 17,110 - 31,150 deaths) could occur before July 2021 (Figure 4c). The peak in transmission is predicted to occur prior to 2021 (Figure 4d), with the effective reproductive number falling below 1 by January 2021 due to increasing immunity in the population (Figure 5).

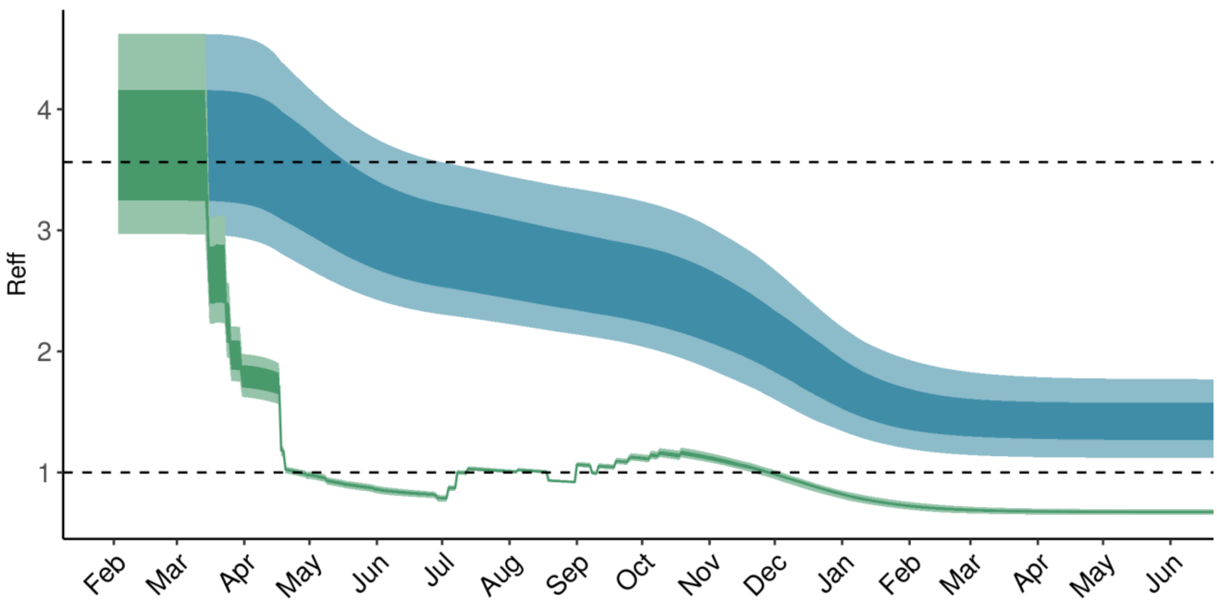

Figure 5. Model fitted reproduction number under the assumption of 3% of deaths being reported. The effective reproductive number (R_{eff}) is shown in green over time, with the reduction in R_0 due to immunity shown in blue. Dark and light shaded regions indicate 50% and 95% CI respectively.

The peak in mortality is predicted to be similar in size to the first peak. However, there is considerable uncertainty in our future projections, with our findings dependent on the assumed level of interventions and our uncertainty in the level of mortality reported during the first wave. If 5% of COVID-19 deaths were reported during the first wave (and by extension, a lower proportion of the population infected compared to scenarios assuming more extensive underascertainment), we predict that the second wave will be larger than the first wave and lead to more deaths due to COVID-19 (Figure 6).

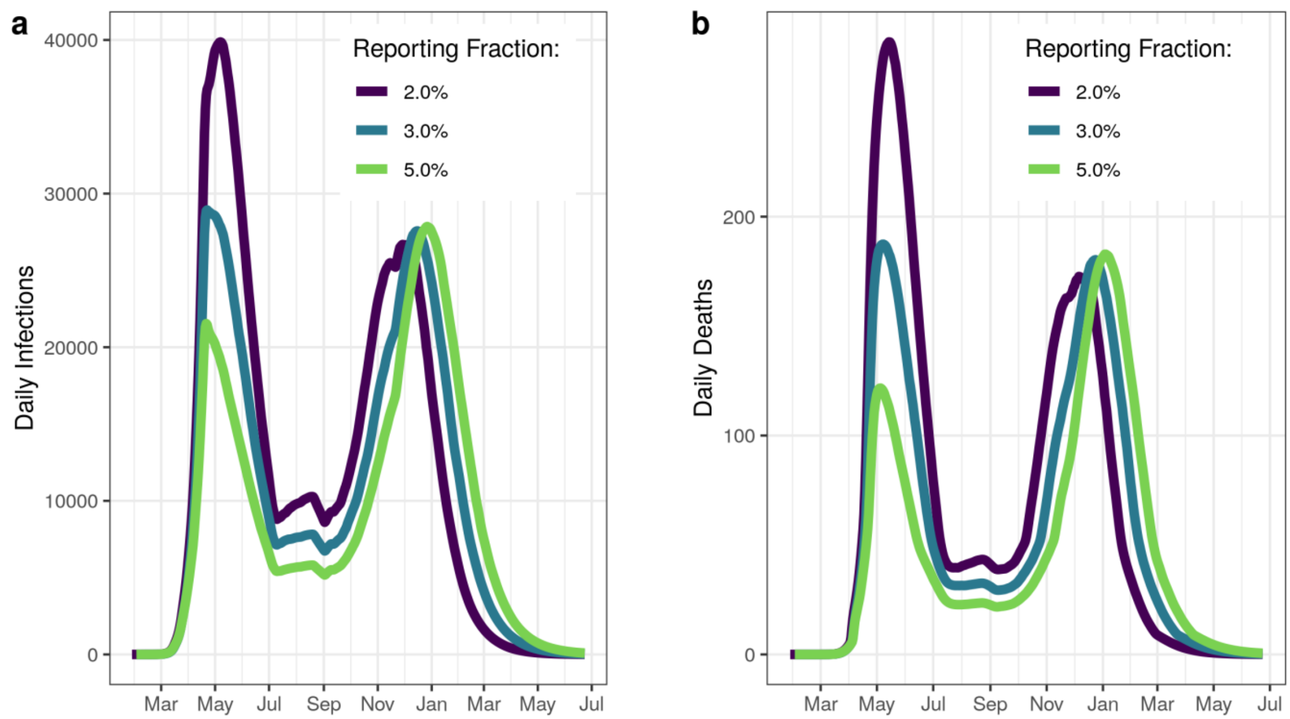

Figure 6. Impact of mortality under-reporting on second wave dynamics. Model predicted a) daily infections and b) daily deaths for three different reporting fractions. For predictions of future epidemic dynamic, transmission is assumed to maintain the same as the estimate for the current day. Under the assumption of high mortality reporting (green = 5% deaths reported) the second wave is predicted to be larger than the first wave due to lower levels of population immunity and will peak later in the year. Each line shows the median of 100 simulations.

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2. Discussion

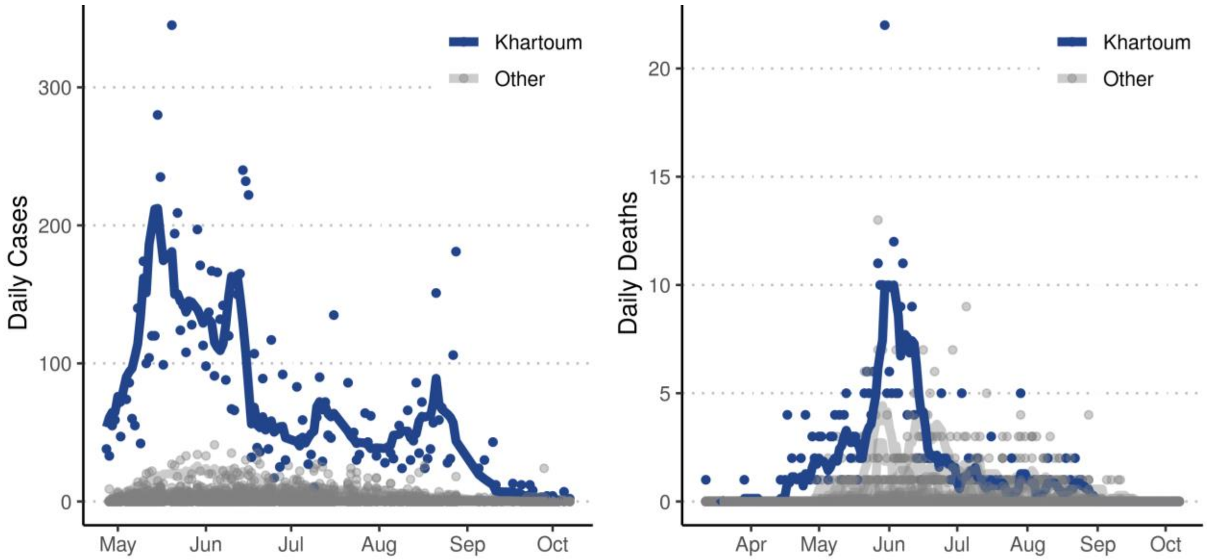
Since the beginning of November an increase in daily case incidence has been reported in Sudan. Questions are now being raised about the potential for a second wave of COVID-19. Fundamental to predicting the burden of any second wave is an understanding of the complete burden in the first wave and the resultant level of population immunity. Without this information it is impossible to make predictions about the size and timing of the second wave. In this analysis, we have collated two sources of alternative data in an effort to characterise the first wave by estimating the under-ascertainment of mortality. We estimate that between 2% - 5% of deaths due to COVID-19 in Khartoum were reported during the first wave. This range incorporates assumed biases in the surveys sourced to infer mortality under-reporting. The levels of under-reporting suggest that the first wave in Khartoum was significantly larger than official reported statistics with profound implications for predictions of the size of the second wave.

The considerable uncertainty in both the mortality ascertained in official statistics and the levels of future transmission result from limitations in relying on two data points to evaluate the likelihood of the inferred epidemic trajectories for each level of under-ascertainment. Despite these limitations, we were encouraged to find both data points suggested the same level of under-ascertainment, which predicts substantial mortality increases due to COVID-19 to occur during the first wave between April and July. During April and May, there were reports of burial numbers increasing in cemeteries in Khartoum.[9] In this report, across six large cemeteries in Khartoum, burials were documented to have roughly tripled from 497 to 1373 between April 2019 to April 2020 and from 704 to 2216 between May 2019 and May 2020. Informally, we can use this increase in burials to evaluate the likelihood of the inferred dynamics in historic mortality as follows. If the same increase in burials was observed across all cemeteries in Khartoum, we would predict mortality to have tripled during the same period. Assuming the annual baseline mortality for Khartoum is similar to World Bank estimates for Sudan in 2019 of 7 deaths per 1,000 people, we estimate that baseline mortality would yield approximately 10,000 deaths during April and May in 2020. The increase in mortality inferred from the cemeteries data yields 20,000 excess deaths during April and May. Our estimate of 2% COVID-19 mortality being reported predicts that 10,800 (95% CI: 8,990 - 13230) COVID-19 deaths occurred during April and May, which would represent roughly half the excess mortality and a third of total mortality estimated. This proportion of mortality attributed to COVID-19 is comparable to reports of a third of mortality increases in North Darfur observed in May due to COVID-19.[19] The increase in mortality we infer in Khartoum is also comparable to undocumented increases in mortality observed in other settings. For example, the COVID-19 attributable proportion of excess mortality we infer is similar to estimates in Kano state, Nigeria. In Kano, baseline mortality was observed to have quadrupled during April, with further investigation suggesting that half of the excess deaths due to COVID-19.[20] Both of these informal calculations lend support to our estimates of the mortality missed in Khartoum during the first wave and the resultant levels of population immunity we infer exist in Khartoum.

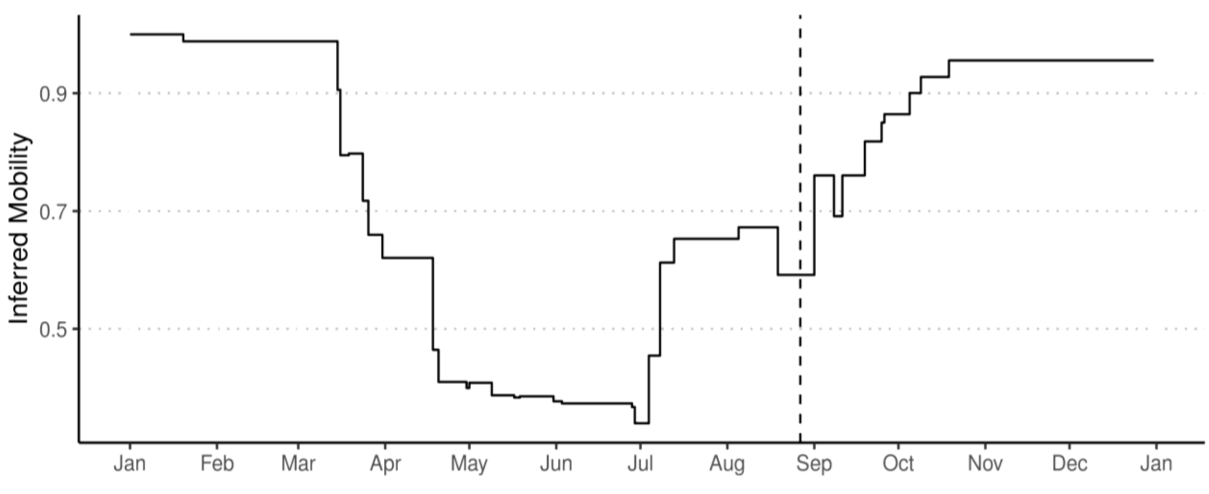
In our analysis, we predict that the high levels of population immunity acquired during the first wave will limit the size of the emerging second wave. It is important, however, to note that this is dependent on the estimated mortality ascertained and infection conferring effective immunity for the duration of the analysis. We have noted that the two surveys used in this analysis are likely upwardly biased, which could mean that up to 5% of COVID-19 deaths have been reported. If true, the level of immunity in the population would be lower and there would be greater potential for the emerging second wave to be larger than the first wave. Crucially, the early signs of a second wave could follow trajectories in mostly high income countries, which due to effective lockdowns have resulted in low levels of immunity. If this is the case, the second wave will continue to increase in the absence of new suppression measures.[21] Alternatively, the early signs of a second wave could lead to a smaller epidemic which is being sustained by infection circulating within specific communities who were able to shield effectively during the first wave. This is a pattern that has been observed in a number of Latin American cities that reached herd immunity after suffering large, unmitigated epidemics.[22] These epidemics were then followed by smaller second waves with transmission circulating in wealthier individuals who were able to shield and work from home effectively during the first wave.[23] Regardless, effective shielding and epidemic profiling within Khartoum will help to both reduce ongoing transmission and help identify the more likely of the two hypothesised epidemic trajectories.

3. Supplementary Material

3.1 Supplementary Figures



Supplementary Figure 1. Incidence of COVID-19 cases and deaths due to COVID-19 in Khartoum and other states. The majority of cases and deaths have been reported in Khartoum (shown in blue), with the epidemic declining after June and fading by September in all states. Each point is a daily recorded number of deaths or cases, with the weekly average shown as a line. Cases data is only presented between May and October.

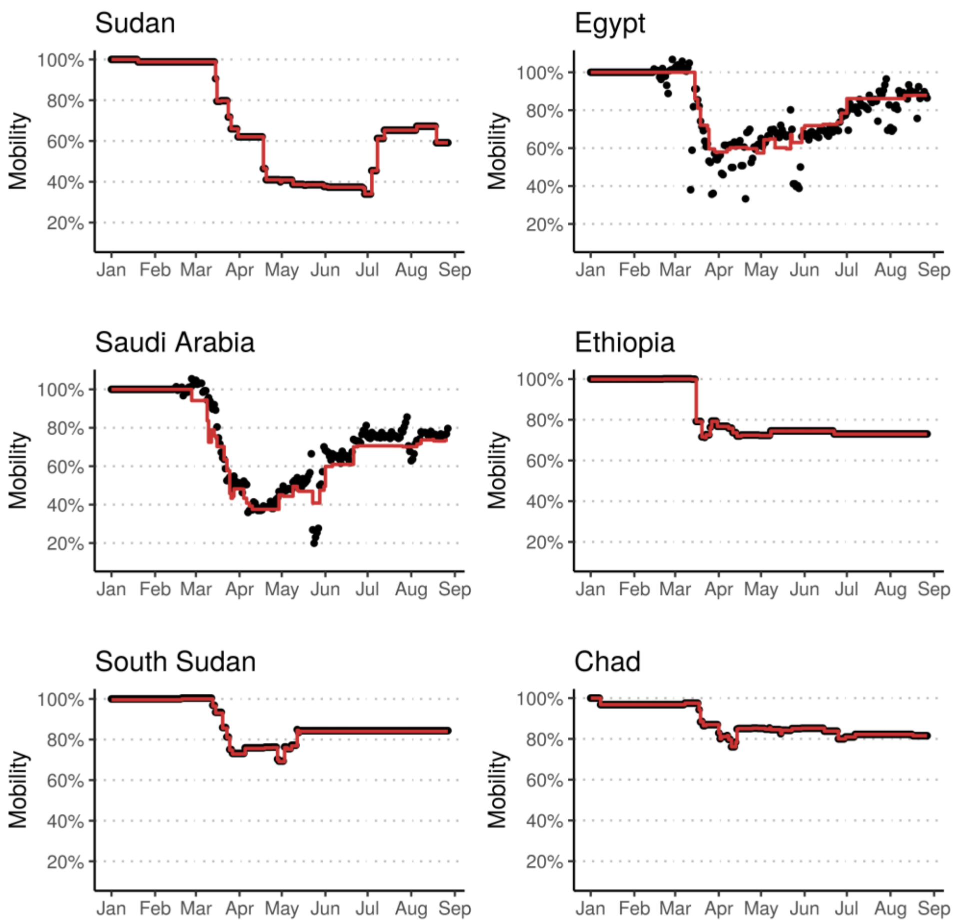


Supplementary Figure 2. Inferred mobility trends for Khartoum in 2020. The vertical dashed line was the final date when conducting model fitting to mortality.

3.2 Supplementary Methods

3.2.1 *Further notes on mobility and parameters assumed for modelling Khartoum*

In our work in Damascus, we believed our approach of inferring mobility based on government intervention was justified due to the strong predictive performance of the model we use for inferring relative mobility in neighbouring countries. We make the same decision, however only two nearby countries to Sudan (Egypt and Saudi Arabia) have Google mobility data (Supplementary Figure 1). Of interest is that of the immediate neighbouring countries, Sudan has a significantly lower mobility inferred, likely due to their continued use of lockdowns, curfews, travel bans and stricter penalties for non-adherence between May and July.



Supplementary Figure 1. Performance of Boosted Regression Tree model for predicting mobility in North East Africa and Saudi Arabia. The points in the Saudi Arabia and Egypt plot show the observed national mobility from the Google Mobility Reports. The red line shows the prediction of the Boosted Regression Tree model that infers mobility based on government interventions reported in the ACAPs database. The true mobility profile is only known for Egypt and Saudi Arabia, with mobility in other countries having to be predicted from intervention data.

3.2.2 Model Parameters

Model parameters and sensitivity analysis conducted is shown in Supplementary Table 1 below. Although not a model parameter, uncertainty in the serological survey and the symptomatic social media survey was explored by altering the observed

Supplementary Table 1: Sensitivity Analysis Details. All combinations of parameters below were explored. The default parameter values are shown in bold, with % of Deaths ascertained not having any value in bold as this was the investigated parameter we were scanning across.

Description	**Values**
% of Deaths Ascertained	0.50%, 1.00%, 2.00%, 3.00%, 5.00%, 7.50%, 10.00%
Number of functional hospital beds	2 000, **4 640,**[24] 6 000
Number of functional ICU beds	50, **75,**[25] 100
% of beds occupied by non-COVID-19 patients	35%, **55%,**[24] 75%
Population Size of Khartoum	8,877,147[26]
Demographic Profile of Damascus Relative to Sudan	**Older,**[26] Same as Sudan
Poorer health outcomes for patients with oxygen indicated due to insufficient oxygen supply	**True** (CFR elevated in individuals with high flow oxygen indicated as in Walker et al[11]), False (Same IFR as in Verity et al.[27])
Bias in surveys used as alternative data source	**No bias**, 50% reduction in estimated symptomatic attack rate and a 25% reduction in individuals enrolled in FTEP survey who are PCR+/ICT- to reflect increased enrollment in individuals currently infected

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