Lockdowns and Vaccines: Did Covid-19 Interventions Help Reduce the Long-Term Health Economic Consequences in Ghana?

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Abstract

COVID-19 has accounted for over 40,000 job losses and US$35 million in direct management costs in Ghana in 2021 with over 1,400 deaths so far. This study simulated the plausible long-term health economic consequences of COVID-19 and the scale of mitigation that lockdowns and vaccines could offer using the CoronAvirus Lifelong Modelling and Simulation (CALMS) algorithm, a published and fully validated agent-based model.

The results showed that a whole population vaccination and periodic lockdown intervention could reduce the long-term COVID-19 infections, mortalities hospitalisations, long COVID and direct healthcare costs by more than 90% in the next ten years in Ghana. Among the simulated interventions, the whole population and periodic lockdown could be the most effective intervention. However, it could be the most expensive intervention (£291 million), followed by lockdowns (£251 million) and vaccinating clinically vulnerable populations (£42,115) at the end of the cohort’s lifetime.

A periodic lockdown and whole-population vaccination could be the most effective intervention to reduce Ghana’s long-term COVID-19-related health economics outcomes. Increasing the whole population vaccination target alone could reduce Ghana’s long-term COVID-19 health economics outcomes. Future studies will need to look at wider outcomes (than just the health outcomes) to establish the full cost-benefit of these interventions.

Introduction

Infectious disease outbreaks are demonstrably imminent. This is evident in the number of infectious disease outbreaks in world history [1]. For centuries, these outbreaks have had catastrophic impacts on humanity, necessitating continuous advancement in science, medicine and public health innovations to ensure effective mitigating intervention [2]. However, given the nature of these outbreaks, most of the mitigating policies are immediate interventions to address the short-term effects of the outbreak, with very little attention on interventions to address any long-term consequences [3]. For example, in the early stages of the COVID-19 pandemic, most globally implemented interventions were aimed at reducing the pandemic’s immediate effects with little consideration of interventions to prevent or alleviate any long-term effects.

While the immediate interventions were necessary to address the instantaneous effects of the COVID-19 outbreak and avoid overwhelming health and economic systems [4], particularly given the uncertainties associated with the outbreak, it was also important to consider interventions that could have a longer-term health economic impact, especially as the long-term effects of the outbreaks could be equally debilitating as their short-term impacts [5]. Arguably, given the benefits of hindsight, some of the described long-term effects of COVID-19, like long COVID and depression, could have been curtailed if considerable emphasis had also been on interventions to address the disease’s long-term effects [4].
Most of the immediate COVID-19 interventions were argued to have longer-term health economics spill-over effects \([6]\); however, current evidence argues the need for a more sustainable longer-term mitigating COVID-19 interventions that could address the long-term effects of the disease and also potentially mop up any undesirable impacts of the immediate interventions \([7]\). This argument has resulted in several mathematical, compartmental and agent-based modelling studies aimed at predicting the long-term health economics burden of COVID-19 to proffer interventions that could mitigate these predicted burdens \([8, 9, 10, 11]\). The findings from some of these studies have informed government interventions to address the long-term health economic consequences of COVID-19 \([8, 11]\), and their effects could serve as a basis for similar approaches to address pathogen x.

Notably, most of the modelled studies were conducted in developed countries \([8, 10, 11]\), highlighting literature scarcity on such studies for developing countries. In Ghana, a few studies have modelled the long-term health economic burden of COVID-19 to inform effective strategies \([12, 13, 14]\). While robust, the studies assume homogeneous populations, which do not account for the real-life scenarios associated with population heterogeneity, thus, limiting the extent of the findings’ applicability. In addition, the studies only modelled the number of COVID-19 infections and mortalities in the long-term in Ghana. However, given that COVID-19 has also had monumental impacts on direct healthcare costs in Ghana, with the cost being consequential due to the economic position of the country \([15]\), COVID-19 modelling studies should include the wider health outcomes to inform comprehensive strategies as done in other jurisdictions \([8]\). Such studies could provide robust evidence to augment current socioeconomic interventions to address potential long-term COVID-19 health economic effects.

We, therefore, adopted the CALMS model \([8]\) to predict the long-term health economic burden of COVID-19 for heterogenous populations in Ghana. CALMS is a validated agent-based model developed to forecast the long-term health economic consequences of COVID-19 to inform potential mitigating policies \([8]\). Accordingly, it uses individual-level data, such as demographic, health and lifestyle data, to predict the longer-term COVID-19 infections, admissions, mortalities, long COVID, and healthcare costs for individuals and populations, thus, addressing the earlier highlighted literature gaps in Ghana. Again, unlike the previous studies in Ghana, CALMS also imbibes hypothetical intervention scenarios throughout the lifetime of the study population, and this allows a comparative assessment of the interventions’ influence on the examined health economic outcomes. In addition to its long-term direct health economic predictions, CALMS also predicts the cost of the hypothetical interventions, and this output, together with its healthcare care costs outputs, could inform future COVID-19 cost-benefit analysis in Ghana.

**Results**

The results show the influence of varied lockdown and vaccination interventions on predicted long-term COVID-19 health economics consequences based on the CALMS algorithm, a published and fully validated agent-based model \([8]\). The model randomly selected a 1,000 cohort from the 4,344 agents for the long-term modelling. It ran 100 replications for each modelled year. Therefore, the health economics burdens presented here represent the average of 100 replications per year, and the presented means
represent the average replication by 1,000 cohorts. The long-term COVID-19 related health economic burden are presented below:

**COVID-19 Infections**

All interventions predicted a reduction in the total number of COVID-19 infections among the cohort in years 5 and 10 compared to the no-intervention scenario, except in year 70, which predicted a 0.92% increase in the total number of COVID-19 infections when the clinically vulnerable populations are vaccinated compared to no intervention (Infections difference: n = 399). Among the interventions, the combined intervention, i.e., the whole population vaccination with periodic lockdowns scenario (scenario 4), was predicted to result in the highest reduction in the total number of COVID-19 infections throughout the lifespan of the cohort. See Fig. 1 and Table 1.

<table>
<thead>
<tr>
<th>Year</th>
<th>Scenario 1 N (Mean ± SD)</th>
<th>Scenario 2 N (Mean ± SD)</th>
<th>Scenario 3 N (Mean ± SD)</th>
<th>Scenario 4 N (Mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>4888 (4.89 ± 0.91)</td>
<td>4160 (4.16 ± 0.92)</td>
<td>1167 (1.17 ± 0.77)</td>
<td>705 (0.70 ± 0.55)</td>
</tr>
<tr>
<td>10</td>
<td>9712 (9.71 ± 1.91)</td>
<td>7947 (7.94 ± 1.56)</td>
<td>2152 (2.15 ± 1.14)</td>
<td>857 (0.9 ± 0.7)</td>
</tr>
<tr>
<td>70</td>
<td>42883 (42.88 ± 22.01)</td>
<td>43282 (43.28 ± 19.49)</td>
<td>26118 (26.12 ± 16.64)</td>
<td>4465 (4.47 ± 3.51)</td>
</tr>
</tbody>
</table>

**Hospital Admissions**

The total number of COVID-19-related hospital admissions is simulated to increase steadily throughout the lifespan of the cohort when no interventions are implemented, with the highest increase seen in year 70. The number is also predicted to increase with increasing years for all the interventions. However, this increase will be lower than the no-intervention scenario. For instance, vaccinating the clinically vulnerable (scenario 2) in the cohort is expected to decrease the total number of COVID-19 hospital admissions by nearly 92% compared to no intervention in year 5. This is similar to the percentage reductions in years 10 (94%) and 70 (89%). No COVID-19 hospital admissions will be recorded in year 5 if the whole population with periodic lockdown intervention (scenario 4) is implemented. The total hospital admission will, however, increase to 1 and 17 in years 10 and 70, respectively. Nonetheless, this number will still be about 99% and 98% lower than the no-intervention scenario in years 10 and 70, respectively. Among the
interventions, the periodic lockdown policy (Scenario 3) will have the lowest reduction in COVID-19-related hospital admissions when compared to the baseline (no intervention). See Fig. 2 and Table 2.

### Table 2
Predicted long-term COVID-19-related hospital admissions.

<table>
<thead>
<tr>
<th>Year</th>
<th>Scenario 1</th>
<th>Scenario 2</th>
<th>Scenario 3</th>
<th>Scenario 4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N (Mean ± SD)</td>
<td>N (Mean ± SD)</td>
<td>N (Mean ± SD)</td>
<td>N (Mean ± SD)</td>
</tr>
<tr>
<td>5</td>
<td>37 (0.04 ± 0.19)</td>
<td>3 (0.00 ± 0.04)</td>
<td>9 (0.01 ± 0.09)</td>
<td>0 (0.00 ± 0.01)</td>
</tr>
<tr>
<td>10</td>
<td>79 (0.07 ± 0.29)</td>
<td>5 (0.01 ± 0.07)</td>
<td>17 (0.02 ± 0.12)</td>
<td>1 (0.00 ± 0.01)</td>
</tr>
<tr>
<td>70</td>
<td>819 (0.82 ± 0.84)</td>
<td>94 (0.09 ± 0.30)</td>
<td>680 (0.67 ± 0.79)</td>
<td>17 (0.02 ± 0.11)</td>
</tr>
</tbody>
</table>

### ICU Admissions

Implementing interventions will reduce the total number of COVID-19-related ICU admissions throughout the lifespan of the cohort compared to no interventions (scenario 1). For example, in year 70, the whole population vaccination with periodic lockdown intervention (scenario 4) and the vaccination of the clinically vulnerable cohorts (scenario 2) will reduce the baseline (no intervention) ICU admissions by 98% and 89%, respectively and the lockdown scenario (scenario 3) will reduce it by 17%. By inference, at the end of the cohorts’ lifespan (year 70), the scenario 4 intervention will reduce the number of baseline ICU admissions more than the other scenarios, with the lockdown scenario having the least reduction. Comparatively, the lockdown scenario will reduce the baseline scenario more in years 5 and 10 (% reduction: 75%) than in year 70 (% reduction: 17%), suggesting that the influence of the lockdown scenario in reducing baseline COVID-19-related ICU admissions will decrease with increasing years. See Fig. 3 and Table 3.
Table 3
Predicted long-term COVID-19-related ICU admissions.

<table>
<thead>
<tr>
<th>Year</th>
<th>Scenario 1 N (Mean ± SD)</th>
<th>Scenario 2 N (Mean ± SD)</th>
<th>Scenario 3 N (Mean ± SD)</th>
<th>Scenario 4 N (Mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>8 (0.01 ± 0.08)</td>
<td>1 (0.00 ± 0.01)</td>
<td>2 (0.00 ± 0.03)</td>
<td>0 (0.00 ± 0.00)</td>
</tr>
<tr>
<td>10</td>
<td>16 (0.02 ± 0.13)</td>
<td>1 (0.00 ± 0.03)</td>
<td>4 (0.00 ± 0.05)</td>
<td>0 (0.00 ± 0.00)</td>
</tr>
<tr>
<td>70</td>
<td>168 (0.17 ± 0.39)</td>
<td>19 (0.02 ± 0.14)</td>
<td>140 (0.14 ± 0.37)</td>
<td>4 (0.00 ± 0.04)</td>
</tr>
</tbody>
</table>

Mortalities

The model predicted an increasing number of COVID-19-related mortalities over the lifespan of the cohort, with no intervention resulting in the highest number of mortalities. Twenty-four (n = 24) COVID-19-related mortalities are estimated in year 5 when no interventions are implemented, and this could reduce by 92% if the clinically vulnerable groups are vaccinated (scenario 2) or 100% if the whole population vaccination with periodic lockdown scenario is implemented. Throughout the cohort’s simulated years, the lockdown intervention will have the lowest reduction in the total number of COVID-19-related mortalities among the intervention scenarios. Scenario 4 will have the highest reduction in the number of mortalities, reducing the lockdown (scenario 3) numbers by 100% in years 5 and 10, and 98% in year 70. See Fig. 4 and Table 4.

Table 4
Predicted long-term COVID-19-related mortalities.

<table>
<thead>
<tr>
<th>Year</th>
<th>Scenario 1 N (Mean ± SD)</th>
<th>Scenario 2 N (Mean ± SD)</th>
<th>Scenario 3 N (Mean ± SD)</th>
<th>Scenario 4 N (Mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>24 (0.02 ± 0.15)</td>
<td>2 (0.00 ± 0.03)</td>
<td>5 (0.01 ± 0.06)</td>
<td>0 (0.00 ± 0.01)</td>
</tr>
<tr>
<td>10</td>
<td>52 (0.05 ± 0.22)</td>
<td>4 (0.00 ± 0.05)</td>
<td>11 (0.01 ± 0.09)</td>
<td>0 (0.00 ± 0.01)</td>
</tr>
<tr>
<td>70</td>
<td>547 (0.55 ± 0.5)</td>
<td>63 (0.06 ± 0.24)</td>
<td>455 (0.46 ± 0.49)</td>
<td>11 (0.01 ± 0.08)</td>
</tr>
</tbody>
</table>
Long COVID

The total number of long COVID cases in scenario 1 (no intervention - baseline) will be more than the predicted numbers in scenarios 2, 3 and 4 in years 5 and 10. Among the interventions, the whole population with periodic lockdown scenario (scenario 4) will reduce the baseline long COVID cases by 86%, 91% and 90% in years 5, 10 and 70, respectively, while the vaccinating the vulnerable cohort scenario (scenario 2) will reduce it by 15%, 18% in years 5 and 10, and increase it by 1% in year 70. The lockdown policy (scenario 3) will reduce the baseline cases by 76%, 78% and 40% in years 5, 10 and 70, respectively. Therefore, compared to the other intervention scenarios, scenario 2 will have the slightest reduction in the baseline long COVID cases in years 5 and 10. In year 70, it will have 1% more cases of long COVID than the baseline cases. Like the other health burden, the scenario 4 intervention will be the most case reduction intervention for long COVID, with its optimal reduction in year 10. See Fig. 5 and Table 5.

<table>
<thead>
<tr>
<th>Year</th>
<th>Scenario 1</th>
<th></th>
<th>Scenario 2</th>
<th></th>
<th>Scenario 3</th>
<th></th>
<th>Scenario 4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N (Mean ± SD)</td>
<td></td>
<td>N (Mean ± SD)</td>
<td></td>
<td>N (Mean ± SD)</td>
<td></td>
<td>N (Mean ± SD)</td>
</tr>
<tr>
<td>5</td>
<td>160 (0.16 ± 0.39)</td>
<td></td>
<td>136 (0.14 ± 0.36)</td>
<td></td>
<td>38 (0.04 ± 0.19)</td>
<td></td>
<td>23 (0.02 ± 0.15)</td>
</tr>
<tr>
<td>10</td>
<td>312 (0.32 ± 0.56)</td>
<td></td>
<td>257 (0.26 ± 0.49)</td>
<td></td>
<td>70 (0.07 ± 0.26)</td>
<td></td>
<td>28 (0.03 ± 0.16)</td>
</tr>
<tr>
<td>70</td>
<td>1402 (1.40 ± 1.37)</td>
<td></td>
<td>1417 (1.41 ± 1.33)</td>
<td></td>
<td>845 (0.85 ± 1.05)</td>
<td></td>
<td>146 (0.15 ± 0.38)</td>
</tr>
</tbody>
</table>

Direct Healthcare Cost

CALMS predicts a higher direct healthcare cost if no COVID-19-related interventions are implemented throughout the lifespan of the cohort. However, the non-intervention healthcare cost could reduce by 92% in year five if the clinically vulnerable agents are vaccinated (scenario 2) and by almost 99% if the whole population is vaccinated and periodic lockdowns are triggered (scenario 4). In years 5, 10 and 70, the most healthcare cost reduction intervention is the whole population vaccination with periodic lockdowns (scenario 4), followed by the vaccinating the clinically vulnerable cohort intervention (scenario 2). Throughout the cohort's lifespan, the lockdown intervention (scenario 3) will produce the least reduction in healthcare costs compared to the other interventions. However, its associated cost will still be lower than no interventions. See Fig. 6 and Table 6.
Table 6
Predicted COVID-19-related direct healthcare cost

<table>
<thead>
<tr>
<th>Year</th>
<th>Scenario 1</th>
<th>Scenario 2</th>
<th>Scenario 3</th>
<th>Scenario 4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N (Mean ± SD)</td>
<td>N (Mean ± SD)</td>
<td>N (Mean ± SD)</td>
<td>N (Mean ± SD)</td>
</tr>
<tr>
<td>5</td>
<td>639,425.9 (639.4 ± 4251.5)</td>
<td>49,995.5 (49.9 ± 906.0)</td>
<td>156,639 (156.64 ± 1998.69)</td>
<td>7,101.9 (7.10 ± 180.1)</td>
</tr>
<tr>
<td>10</td>
<td>13.9·10^5 (13.9·10^2±65.7·10^2)</td>
<td>99,411.14 (99.41 ± 14.65·10^2)</td>
<td>295,595 (295.60 ± 2772.14)</td>
<td>9,851.6 (9.85 ± 210.4)</td>
</tr>
<tr>
<td>70</td>
<td>14.5·10^6 (14.5·10^3±21.9·10^3)</td>
<td>16.7·10^5 (16.71·10^2±69.6·10^2)</td>
<td>12.1·10^6 (12.1·10^3±2.0·10^4)</td>
<td>31.5·10^4 (315.8 ± 23.9·10^2)</td>
</tr>
</tbody>
</table>

**Intervention Cost**

Figure 7 and Table 7 show the intervention costs for scenarios two, three and four. Vaccinating the clinically vulnerable policy (scenario 2) is predicted to be the least expensive intervention, followed by the lockdown policy (scenario 3) and the whole population vaccination and lockdown policy (scenario 4) at the end of the cohort’s lifespan. However, the cost difference between the lockdown (scenario 3) and whole population vaccination and lockdown policy (scenario 4) in years 5 (0.3%) and 10 (0.5%) is relatively negligible.

Table 7
Predicted long-term Cost (£) of the COVID-19 interventions.

<table>
<thead>
<tr>
<th>Year</th>
<th>Scenario 2</th>
<th>Scenario 3</th>
<th>Scenario 4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N (Mean ± SD)</td>
<td>N (Mean ± SD)</td>
<td>N (Mean ± SD)</td>
</tr>
<tr>
<td>5</td>
<td>2,168.51 (2.17 ± 4.9)</td>
<td>30.1·10^6 (30.1·10^3±32.9·10^2)</td>
<td>30.2·10^6 (30.2·10^3±28.96·10^2)</td>
</tr>
<tr>
<td>10</td>
<td>4,625.59 (4.6 ± 10.35)</td>
<td>60.2·10^6 (60.2·10^3±88.9·10^2)</td>
<td>60.5·10^6 (60.5·10^3±81.4·10^2)</td>
</tr>
<tr>
<td>70</td>
<td>42,114.9 (42.12 ± 50.69)</td>
<td>25.1·10^7 (25.1·10^4±10.8·10^4)</td>
<td>29.1·10^7 (29.1·10^4±11.7·10^4)</td>
</tr>
</tbody>
</table>

**Discussion**
This study used the CALMS model to examine the scale of mitigation that vaccination and lockdown policies could have on the long-term health economics consequences of COVID-19 in Ghana. The model predicted the total number of COVID-19 infections, mortalities, admissions and long COVID in the next five, ten and seventy years using a randomly selected 1000 cohort from a population of 4,344 persons aged ≥ 18 years. It also forecasted total COVID-19 healthcare costs throughout the lifespan of the cohort. Finally, it examined whether vaccination and lockdown scenarios would influence the predicted health economic outcomes. The findings showed that Ghana's relatively lower COVID-19 mortality might remain unchanged in the next ten years (%Mortality = 0.54%: estimated from the number of COVID-19 infections and deaths) even without interventions, and this projected mortality will be about 1.4% and 0.1% lower than the 2020 mortality in Ghana [16] (1.93%) and the global mortality as of 27/03/2023 (0.63%) [17]. Ghana's age characteristics may account for this projected mortality, particularly as the seed population for the modelling was comparatively younger (35.07 ± 17.02 years) than the reported 2020's population [16].

Other factors, like the ongoing COVID-19 vaccination, reported to increase an individual's resistance to severe COVID-19 outcomes [18], and the probable decreasing virulence of the SARS-CoV-2 virus, could also account for the observation. Though these two factors could be mutually inclusive, the latter is still being studied while the effectiveness of the former has been confirmed in a recent systematic review [19]. It is also supported by the modelled findings from the UK study [8] and corroborated by this study's hypothetical scenarios modelling which saw a 92% reduction in the baseline number of COVID-19 mortalities in years 5 and 10 when stratified vaccination intervention (scenario 2) was introduced. This reduction was also observed for the number of COVID-19 infections, which saw an almost 15% and 18% decrease in the baseline infections in years 5 and 10. As of 24/03/2023, Ghana had fully vaccinated 32% of its total population [20], and given the simulation findings herein, increasing this number may decrease COVID-19 mortalities in the coming years.

Noticeably, Ghana's 70-year projected baseline number of COVID-19 mortalities is 25% more than the 80-year projected mortality in the UK [8], despite its comparatively younger seed population (Median age: Ghana 31years; UK [8] = 45 years). This suggests that other sociodemographic and economic factors account for Ghana's lifelong COVID-19 mortality or probably mediate the potential influence of Ghana's age characteristics on its COVID-19 mortality probability. Again, Ghana's seed population had a fewer proportion of NCDs (type 2 diabetes = 3.1%; Cardiovascular diseases (CVDs = 4.2%) than the UK's (type 2 diabetes = 5.5%; CVDs = 10.8%), further corroborating the earlier argument that other inherent drivers, such as wealth indices and healthcare accessibility, could account for the high lifelong mortality in Ghana compared to the UK. The median Body Mass Index (BMI) between the two studies were comparable, thus, precluding its influence on the lifelong mortality differences. However, when both settings introduced a whole population vaccination and periodic lockdown intervention, Ghana's 70-year lifelong COVID-19 mortality reduced to 11, 71% lower than the UK's 80-year mortality (n = 39) [8].

Of the three interventions introduced into the model, the whole population vaccination with periodic lockdowns policy was the most effective in reducing the long-term COVID-19 disease outcomes and
direct healthcare costs of COVID-19 in Ghana, and the most expensive policy at the end of the cohort’s lifespan. However, its cost was relatively comparable to the periodic lockdown policy (scenario 3), the least influential intervention in reducing COVID-19 deaths, admissions and direct healthcare costs. Notwithstanding, a robust cost-benefit analysis may be needed to ascertain its (scenario 4) cost-effectiveness, as the evidence herein is not indicative of cost-effectiveness. Such a deterministic study was recently simulated for over 83 million population in Turkey, and it found a whole population vaccination intervention as even a cost-saving intervention [21]. However, albeit its robustness, the evidence is limited to the vaccination intervention only; therefore, still leaving queries on the cost-effectiveness of the combined whole population vaccination and periodic lockdown policy.

No study on the effectiveness of the combined intervention was identified in the literature; however, a study comparing both interventions found population vaccination to be associated with a lower cost of preventing one COVID-19 mortality than national lockdowns [22]. Though they found vaccinations to be nearly 50 to 500-fold more cost-effective than national lockdowns in preventing COVID-19 deaths, it was unconfirmed whether the vaccination was targeted at the whole population, as per the referenced intervention in this study. Nonetheless, while a cost-effectiveness analysis on the combined intervention is still warranted, the evidence from Arbel and Pliskin [22] is consistent with the literature [23–25], demonstrating that when deciding between vaccination and lockdown policies, the former may be more preferred than the other, particularly for resource-constrained populations like Ghana.

Comparing the periodic lockdown (scenario 3) and vaccinating the clinically vulnerable (scenario 2) policies, scenario 2 is predicted to reduce the number of COVID-19 mortality, hospital and ICU admissions, and direct healthcare costs more than scenario 3, while scenario 3 is projected to reduce the number of COVID-19 infections and long COVID more than scenario 2. The comparatively lower influence of scenario 2 on infections and long COVID is because scenario 2 is assumed to address the COVID-19 disease severity and not the infection rate or the duration of COVID-19 symptoms (long COVID) [8]. This explains why the complementary intervention (scenario 4) was more effective in reducing the COVID-health burden than the single interventions (scenarios 2 and 3).

Apart from the model severity assumption, the influence of scenario 3 in reducing COVID-19 infections more than scenario 2 is also logical in the context of the Susceptible, Infectious, Recovered, Death (SIRD) model as it is more likely to reduce COVID-19 transmission probability than scenario 2 [26]. Scenario 3’s influence in a real-life situation could, however, be limited by contextual factors like socio-economic status and housing systems, which were not captured in the model. For example, implementing lockdown interventions in settings with household crowding characteristics, like Ghana, could amplify viral spread and defeat the purpose of the lockdown [27].

The above argument was confirmed in Ghana when it saw an increase in COVID-19 cases per day during and post its partial lockdown intervention [20]. In Ghana’s example, though the number of COVID-19 cases attributable solely to the partial lockdown is unclear, its related outcomes, such as starvation, decreased earnings and extreme poverty, particularly for those in the lower socio-economic echelon, made
the intervention unsustainable [28]. Therefore, despite the study’s finding on the influence of periodic lockdown on COVID-19 infection probability in the longer term, developing countries like Ghana must assess its overall outcome comprehensively with a focus on its potential to trigger poverty before implementing it. Perhaps, given the evidence in the literature [8, 29] and the one presented here, developing countries could consider introducing lockdown interventions at the beginning of outbreaks, for outbreaks with similar characteristics like the COVID-19 outbreak, to avoid overburdened healthcare systems. However, the timing of the introduction must be assessed critically to maximise the healthcare benefits and minimise any adverse spill-over effects.

This study’s findings agree with a similar study that the whole population vaccination with periodic lockdowns intervention would result in the highest reduction in COVID-19 long-term health economics burden [8]. However, while the study identified the lockdown policy to result in the greatest reduction in the number of long COVID [8], this study found its influence in reducing the number of long COVID second to the whole population vaccination with periodic lockdown policy. This heterogeneity is likely to result from the timing of the lockdown in the two studies, which was triggered by the predicted number of severe and critical COVID-19 cases in the cohort. Given the sample characteristics variations in the two studies, the predicted number of severe and critical COVID-19 cases was expected to differ with resultant differences in the lockdown timings.

The projected COVID-19-related total direct healthcare costs at the end of the cohort’s lifespan also differed between the two studies, with this study predicting a higher healthcare cost, except for scenario 4. Again, possible differences in the total number of hospitalised agents between the two studies could have accounted for this variation. Also, using the UK’s cost of hospital management to estimate the total healthcare costs in Ghana could have resulted in the higher healthcare costs reported in this study. However, when the healthcare costs were re-estimated using Ghana’s hospital management cost, the total healthcare costs at the end of the cohort’s lifespan were still comparably higher for Ghana when no interventions were implemented and lower when the vaccination with periodic lockdowns policy was implemented. Apart from the number of hospitalised agents in the two studies, dissimilarities in hospital management costs for COVID-19 patients could justify the variations in the healthcare cost burden between the studies. While these differences could be explored further in the context of healthcare disparity, the settings in the two studies must focus on implementing the most cost-effective COVID-19 interventions to reduce related healthcare costs.

This study provided data to augment ongoing efforts to mitigate the outbreak’s long-term health economics consequences. However, the implications discussed here are for just the health economic consequences and not the wider economy, given that the study is not a comprehensive cost-benefit research. Therefore, the discussions herein must be interpreted as such. The simulation results suggest that Ghana could reduce its direct COVID-19 health economics consequences if it ensures a whole population vaccination with periodic lockdowns. While the cost-benefit of the lockdown is still debatable, the literature suggests that the whole population vaccination target alone could reduce the number of infections and deaths associated with the outbreak. Therefore, Ghana can aim to increase its current
vaccination effort, which stands at 32%, to prevent or reduce severe COVID-19 outcomes. Furthermore, even though the model could not account for cost-effectiveness, it demonstrated that the whole population vaccination could reduce any associated direct healthcare costs than vaccinating only the populations with comorbidities. This output could guide Ghana’s vaccination intervention implementation.

For effective strategies for future outbreaks like COVID-19, Ghana can implement a lockdown at the beginning of the outbreak to avoid potentially overwhelming health systems and introduce vaccinations at the early stage of the outbreak to reduce the population's risk of the disease and its direct outcomes. However, these recommendations will largely be informed by the outbreak’s nature and the availability and affordability of the required vaccines. Given this pandemic’s lessons on vaccine inequity, it is anticipated that global health systems will promote vaccine equity to avoid disproportionate burdens in future outbreaks. Most importantly, given that every outbreak might be unique, the merit of the recommended future interventions, particularly the lockdown policy, should be assessed on a case-by-case basis to determine their suitability.

This study is the first to provide insights into Ghana's long-term COVID-19 infections, deaths, hospital and ICU admissions and healthcare costs using an agent-based model. It is also one of the few to foretell and compare the influence of no intervention, lockdown and vaccination interventions on the long-term health economic consequences of COVID-19 in Ghana. Therefore, it provides policy direction to inform mitigating interventions. However, the findings generated here may not apply to the wider economy of Ghana to inform related policies. In addition, the model was limited in stratifying the COVID-19 health economic consequences by sociodemographic characteristics to allow for targeted intervention. Additionally, it could not access individual-level BMI and physical activity status data to allow precise estimations.

In conclusion, a whole population vaccination with periodic lockdowns could be more effective in reducing Ghana's long-term COVID-19-related health economics burden. A whole population vaccination policy alone could reduce the number of COVID-19 infections, admissions, mortality and associated healthcare costs in Ghana. Ghana could boost its COVID-19 vaccination programme to reduce the current and long-term health economic burden of the COVID-19 pandemic. Future studies should establish the full cost-benefit of these interventions.

**Methods**

The CALMS model was operationalised in three phases as described below:

**Population Initialisation**

At the population initialisation phase, the study generated a 4,344 cohort from the Ga East Municipal Hospital (GEMH). Their ages ranged from 18 to 100 and the majority were women (n = 3,053; 70.3%) and
of black ethnicity (n = 3,759; 86.5%). A few of them had type 2 diabetes (n = 134, 3.1%), hypertension (n = 237, 5.5%), and CVDs (n = 183, 4.2%). Their mean BMI and age were 24.55 ± 1.47kg/m² and 35.07 ± 17.02 years, respectively.

CALMS Algorithm

The CALMS algorithm predicts an agent’s long-term risk of COVID-19 infections, deaths and other health outcomes using their demographic, lifestyle and health profiles. These profiles include the agent’s age, sex, BMI, type 2 diabetes, hypertension, CVDs and physical activity statuses, and these are updated throughout the simulation. For example, the algorithm uses established Q-risk algorithms to calculate and update an agent’s CVDs probability and status every three months in the model [30, 31]. The algorithm then predicts an agent’s risk of COVID-19 infection by determining their daily COVID-19 infection probability based on the transmission probability of the virus and the number of exposures to infected individuals throughout the simulation. It is estimated using the formula in Eq. 1:

\[ I_p = T_p C_n C_i \] (1)

Where Ip refers to the agent’s risk of COVID-19 infection, Tp is the virus’s transmission probability, Cn is the number of persons an agent comes into contact with within a day, and Ci is the proportion of infectious agents in the cohort/population.

The model further predicts the agents’ COVID-19 severity after predicting their probability of COVID-19 infection. Agents with critical and severe COVID-19 infections are forecasted to be admitted into ICUs and hospitals, respectively. Based on predicted hospital and ICU admissions, the algorithm determines the COVID-19-related direct healthcare cost for each agent and the entire cohort. It estimates this cost by multiplying the hospital and ICU admission cost by the length of admissions – calculated using gamma distributions [8].

During this prediction exercise, the algorithm imbibes hypothetical intervention scenarios, like lockdowns and vaccinations [8]. Therefore, this study simulated the influence of four varied hypothetical lockdown and vaccination intervention scenarios on long-term COVID-19 health outcomes (Table 8). These scenarios were informed by the two key policies implemented to lessen the COVID-19 burden in Ghana. The long-term analysis was simulated for year one and up to year seventy (70), when all the agents were assumed to have reached their lifespan. During operations, the algorithm calculates the costs of each intervention and sums the cost of the interventions at the end of the simulation period. This intervention cost output and the healthcare cost output discussed above provide a basis for potential future cost-benefit analyses.
Table 8
Simulated hypothetical scenarios.

<table>
<thead>
<tr>
<th>Scenarios</th>
<th>Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scenario 1</td>
<td>No interventions</td>
</tr>
<tr>
<td>Scenario 2</td>
<td>Vaccinating the clinically vulnerable populations (Defined as those with hypertension, type 2 diabetes, CVDs, ( \text{BMI} \geq 40 \text{kg/m}^2 )). Scenario is triggered 9 months into the simulation</td>
</tr>
<tr>
<td>Scenario 3</td>
<td>Periodic lockdown scenarios (Triggered when the number of hospital admissions reaches a predefined peak/threshold – captured as the average of the percentage of the population in COVID-19 related admissions during the 3 lockdowns in the UK)</td>
</tr>
<tr>
<td>Scenario 4</td>
<td>Periodic lockdown and whole population vaccination</td>
</tr>
</tbody>
</table>

Data for the CALMS Algorithm

The model required data on age, sex, ethnicity, physical activity status, BMI, hypertension, type 2 diabetes, and cardiovascular diseases. All these data were included in the GEMH dataset, except for BMI and physical activity status. Therefore, BMI data was developed using the age subgroups’ average BMIs as reported in a related study \([32]\). For the physical activity status, the model assumed that all the agents were moderately active as no relatable data was found in the literature. This homogenous assumption resulted in a uniform influence of physical activity on the simulated COVID-19 health outcomes.

CALMS Output

CALMS generate COVID-19-related health economics consequences for each agent and the entire population from year one up to a defined year, when many cohorts are dead. The health economics consequences specifically includes annual COVID-19 infections, hospital and ICU admissions, mortalities, long COVID, direct healthcare costs and intervention costs.

Ethics approval

This research was conducted in accordance with all the relevant guidelines and regulations in the Helsinki Declaration. The College of Health, Medicine and Life Sciences (CHMLS) Research Ethics Committee, the committee overseeing all research protocols in Brunel University - the affiliation of all the authors in this study, approved this study to be conducted. The Ethics Reference Number is 25803-NER-Nov/2020- 28436-2. Informed consent was not required for this study because it accessed a secondary data.
Data availability

The dataset generated and analysed during the current study is available in the Figshare repository [https://doi.org/10.6084/m9.figshare.22894337.v1] and the CALMS code used for the modelling is available in the GitLab repository [https://gitlab.com/anabrunel/calms] [https://doi.org/10.1371/journal.pone.0272664.s002] PDF.

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Author contributions

SC and NA conceptualised the study. SC drafted the manuscript. SC and KM accessed and analysed the data. NA, SP and AA revised the manuscript. All authors agreed on the final manuscript.

Additional Information

Competing interests

The authors declare no competing interests.

References


**Figures**

![Figure 1](image-url)
Figure 1
Predicted COVID-19 infections: Influence of no interventions (scenario 1); vaccinating clinically vulnerable individuals (scenario 2); periodic lockdowns (scenario 3); and whole population and periodic lockdowns (scenario 4) on the long-term annual COVID-19 infections in Ghana.

Figure 2
Predicted COVID-19 hospital admissions: Influence of no interventions (scenario 1); vaccinating clinically vulnerable individuals (scenario 2); periodic lockdowns (scenario 3); and whole population and periodic lockdowns (scenario 4) on the long-term annual COVID-19 hospital admissions in Ghana.
Figure 3

Predicted COVID-19 ICU admissions: Influence of no interventions (scenario 1); vaccinating clinically vulnerable individuals (scenario 2); periodic lockdowns (scenario 3); and whole population and periodic lockdowns (scenario 4) on the long-term annual COVID-19 ICU admissions in Ghana.
Figure 4

Predicted COVID-19 mortalities: Influence of no interventions (scenario 1); vaccinating clinically vulnerable individuals (scenario 2); periodic lockdowns (scenario 3); and whole population and periodic lockdowns (scenario 4) on the long-term annual COVID-19 mortalities in Ghana.
Figure 5

Predicted Long COVID-19: Influence of no interventions (scenario 1); vaccinating clinically vulnerable individuals (scenario 2); periodic lockdowns (scenario 3); and whole population and periodic lockdowns (scenario 4) on the long-term annual long COVID in Ghana.
Predicted COVID-19-related direct healthcare cost (£): Influence of no interventions (scenario 1); vaccinating clinically vulnerable individuals (scenario 2); periodic lockdowns (scenario 3); and whole population and periodic lockdowns (scenario 4) on the long-term annual COVID-related direct healthcare costs in Ghana.
Figure 7

Cost (£) of hypothetical interventions: Predicted long-term annual costs of vaccinating clinically vulnerable individuals (scenario 2); periodic lockdowns (scenario 3); and whole population and periodic lockdowns (scenario 4) interventions.