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Indirect impacts of the COVID-19 pandemic at two tertiary neonatal units in Zimbabwe and Malawi: an interrupted time series analysis

Simbarashe Chimhuya,[1] Samuel R Neal ,[2] Gwen Chimhini,[1] Hannah Gannon,[2] Mario Cortina Borja,[2] Caroline Crehan,[2] Deliwe Nkhoma,[3] Tarisai Chiyaka,[4] Emma Wilson ,[2] Tim Hull-Bailey,[2] Felicity Fitzgerald ,[2] Msandeni Chiume,[5] Michelle Heys[2]

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SC and SRN are joint first authors.
MC and MH are joint last authors

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For numbered affiliations see end of article.

Correspondence to
Dr Michelle Heys;
m.heys@ucl.ac.uk

ABSTRACT

Objectives To examine indirect impacts of the COVID-19 pandemic on neonatal care in low-income and middle-income countries.

Design Interrupted time series analysis.

Setting Two tertiary neonatal units in Harare, Zimbabwe and Lilongwe, Malawi.

Participants We included a total of 6800 neonates who were admitted to either neonatal unit from 1 June 2019 to 25 September 2020 (Zimbabwe: 3450; Malawi: 3350). We applied no specific exclusion criteria.

Interventions The first cases of COVID-19 in each country (Zimbabwe: 20 March 2020; Malawi: 3 April 2020).

Primary outcome measures Changes in the number of admissions, gestational age and birth weight, source of admission referrals, prevalence of neonatal encephalopathy, and overall mortality before and after the first cases of COVID-19.

Results Admission numbers in Zimbabwe did not initially change after the first case of COVID-19 but fell by 48% during a nurses' strike (relative risk (RR) 0.52, 95% CI 0.41 to 0.66, p<0.001). In Malawi, admissions dropped by 42% soon after the first case of COVID-19 (RR 0.58, 95% CI 0.48 to 0.70, p<0.001). In Malawi, gestational age and birth weight decreased slightly by around 1 week (beta −1.4, 95% CI −1.62 to −0.65, p<0.001) and 300 g (beta −299.9, 95% CI −412.3 to −187.5, p<0.001) and outside referrals dropped by 28% (RR 0.72, 95% CI 0.61 to 0.85, p<0.001). No changes in these outcomes were found in Zimbabwe and no significant changes in the prevalence of neonatal encephalopathy or mortality were found at either site (p>0.05).

Conclusions The indirect impacts of COVID-19 are context-specific. While our study provides vital evidence to inform health providers and policy-makers, national data are required to ascertain the true impacts of the pandemic on newborn health.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ We address the need for increased research into the indirect impacts of the COVID-19 pandemic on neonatal care in low-income and middle-income countries.
⇒ We collected data digitally and in real time using the Neotree application, which enabled a large sample size of 6800 neonates with minimal missing data.
⇒ It is possible that unobserved events occurred close to the first case of COVID-19 in either country, which could have influenced our results.
⇒ We only collected data on neonates admitted to the neonatal unit and did not capture stillbirths or neonatal deaths that occurred in the community.

INTRODUCTION

The WHO declared COVID-19 a Public Health Emergency of International Concern on 30 January 2020.[1] Almost 2 years later, confirmed cases have exceeded 281 million globally with over 5.4 million deaths to the end of 2021.[2] Zimbabwe recorded its first case on 20 March 2020 and, to date, has reported over 200 000 cases with nearly 5000 deaths.[2] Malawi confirmed its first three cases on 3 April 2020 and has reported more than 72 000 cases and over 2000 deaths in this same period.[2]

Before the COVID-19 pandemic, considerable improvements were made in global child health: the global neonatal mortality rate fell from 31 to 18 deaths per 1000 live births between 2000 and 2018.[3] Yet there were disparities in the rates of decline with the sub-Saharan Africa region facing highest neonatal mortality rates.[3] Now, there is a danger that health outcomes in low-income and middle-income countries (LMICs) will fall further behind high-income countries. While countries worldwide face challenges related to the COVID-19 pandemic, LMICs are particularly struggling with financial constraints, limited testing capacity, lack of personal protective equipment, staff shortages,[4 5] and limited

access to vaccines.[6] As children are at low risk of infection or severe disease from COVID-19,[7–11] any impacts on their health outcomes will likely be attributable to the indirect effects of the pandemic on health systems, as in previous disease outbreaks.[12 13] These include increased rates of parental unemployment, food and housing insecurity, and reduced access to routine care, including antenatal and perinatal care, with potentially damaging downstream impacts on neonatal outcomes.[14 15]

We hypothesised that the COVID-19 pandemic would negatively impact care seeking behaviours, neonatal care provision and, ultimately, neonatal outcomes in LMICs. To test this hypothesis, we aimed to examine trends in markers of neonatal care before and during the initial months of the COVID-19 pandemic at Sally Mugabe Central Hospital (SMCH), Zimbabwe and Kamuzu Central Hospital (KCH), Malawi. Specifically, we compared the:

1. Number of admissions to the neonatal unit (NNU).
2. Gestational age and birth weight of admitted neonates.
3. Source of admission referrals.
4. Prevalence of neonatal encephalopathy (NE).
5. Overall mortality rate before and after the first reported cases of COVID-19.

METHODS

This study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology statement (online supplemental appendix 1).

Setting

Health facilities

SMCH is a public referral hospital in Harare, Zimbabwe. It has the largest of three tertiary NNUs nationwide with 100 cots. KCH, Lilongwe, is one of four regional referral hospitals in Malawi and the NNU has 75 cots. Neonatal care at SMCH is predominantly doctor led while neonatal care at KCH is mostly nurse led. Both units accept local and national referrals for specialist surgical care.

Government response to the pandemic

In response to the COVID-19 pandemic, Zimbabwe and Malawi both implemented response measures in an attempt to control the outbreak. In Zimbabwe, the Government closed borders to non-essential travel within days of the first in-country confirmed case of COVID-19 and imposed a full national lockdown that lasted from 30 March to 11 June 2020, which was followed by phased relaxations of the restrictions.[16] In Malawi, public events were banned and public gatherings restricted to fewer than 100 people on 20 March 2020, with all educational institutions closed several days later.[17] Borders were closed to non-essential travel on 1 April 2020 and a full national lockdown was announced to last for 21 days from 18 April 2020; however, a High Court injunction prevented this. Further restrictions were announced on 9 August 2020, mandating the wearing of face masks in public, closing places of worship, restaurants, and bars, and restricting public gatherings to less than 10 people initially, although these were revised within days to reallow gatherings up to 100 people.[18]

Industrial action by health workers in Zimbabwe

Two periods of national industrial action occurred in Zimbabwe during our study. Doctors went on strike from 3 September 2019 to 22 January 2020 (pre-COVID-19 period) citing insufficient pay and poor working conditions, which put significant pressure on the public health system.[19] Additionally, there was a period of strikes by nurses from 17 June to 9 September 2020 (post-COVID-19 period) over pay and availability of personal protective equipment during the pandemic.[20]

Participants

All neonates admitted to each NNU over a 16-month period from 1 June 2019 to 25 September 2020 (69 complete weeks) were eligible for inclusion. We applied no specific exclusion criteria.

Data collection

Data were collected prospectively using the Neotree application (app), an Android tablet-based quality improvement platform that aims to reduce neonatal mortality in low-resource settings.[21] Developed in collaboration with local stakeholders, it is embedded in routine practice at two NNUs in Zimbabwe and Malawi, providing real-time clinical decision support, neonatal care education and digital data capture.[22 23]

Health workers complete a digital form when a neonate is admitted to the unit (admission form) and when they are discharged or die (outcome form). The app guides assessment of the neonate and collects data on patient demographics, examination findings, diagnoses and interventions. Pseudonymised forms are uploaded monthly to University College London servers (Zimbabwe data) and Amazon Web Services (Malawi data). Admission and outcome forms are linked by a unique identifier generated by the app at admission.

Outcomes

We evaluated five outcomes:

1. Number of admissions: determined from the admission date of each completed admission form.
2. Gestational age at birth (weeks) and birth weight (grams): as entered into the admission form from obstetric records.
3. Source of admission: defined as ‘within’ (labour ward, postnatal ward, antenatal ward, obstetric theatre or fee-paying ward (KCH only)) or ‘outside’ (referral from another health facility or postnatal self-referral from home).
4. Diagnosis of NE: defined as ‘hypoxic ischaemic encephalopathy’ or ‘birth asphyxia’ recorded as a diagnosis, cause of death or contributory cause of death on the outcome form.
5. Mortality: defined as an outcome of “neonatal death” on the outcome form. All other neonates, including

those discharged, transferred to another facility or who left on parental request, were considered alive.

Statistical analysis

Analyses were performed in R V.3.6.3,[24] running on RStudio V.1.2.5033.[25] First, admission forms were matched with their corresponding outcome form based on the unique identifier generated at admission. Lack of completed outcome forms (SMCH: n=325 (9.4% of admission forms completed); KCH: n=245 (7.3%)) or errors in entry of the unique identifier at discharge (SMCH: n=310 (9.9% of outcome forms completed); KCH: n=182 (5.9%)) meant we were unable to match some admission forms with outcome forms (SMCH: n=635 (18.4% of admission forms completed); KCH: n=427 (12.7%)). For outcomes 1–3, we based analyses on data from all admission forms, regardless of match status. For outcomes 4 and 5, we based analyses on matched records only. Matched records implying a negative admission duration (ie, outcome date prior to admission date) were excluded (SMCH: n=57 (2.0% of matched records); KCH: n=24 (0.8%)). See online supplemental appendix 3 for a flow diagram of record inclusion. Missing data were excluded using pairwise deletion for each analysis as frequencies of missing values were minimal (online supplemental appendix 4).

This study used an interrupted time series design with weekly data windows. We considered the first confirmed case of COVID-19 in each country as the intervention (Zimbabwe: 20 March 2020; Malawi: 3 April 2020).[2] For all outcomes, we hypothesised a level change impact model without a lag, and this was tested using interrupted time series regression models.[26] Gestational age and birth weight were modelled with linear regression. Count data were modelled using generalised linear models with Poisson or negative binomial responses and logarithmic link functions. We assessed for dispersion by dividing the residual deviance by the df for the Poisson model. Where this quotient was much greater than one (greater than approximately 1.10) we instead used a negative binomial model to account for overdispersion. Accordingly, source of admission referral, prevalence of NE and overall mortality at SMCH were modelled using Poisson models, while number of admissions and overall mortality at KCH were modelled using negative binomial models.

All models for SMCH were adjusted for the periods of doctors' strikes (3 September 2019 to 22 January 2020) and nurses' strikes (17 June to 9 September 2020). For count data, we adjusted for variation in the number of admissions over time by including the logarithm of the number of admissions in each weekly window as an offset term. Presence of autocorrelation was assessed using autocorrelation function plots and by examining models' residuals. Seasonality was included in the interrupted time series models with cosine functions with variable amplitude and shift. We tested models fitting cosine functions on week of admission with 6-month and 12-month periods, and a model including these two harmonic terms. To achieve this, we transformed each cosine function into a sine term and cosine term, and included these terms in the regression models for each outcome (as described by Stolwijk *et al*).[27] The final models presented were selected by minimising the Bayesian information criterion and by comparing goodness-of-fit with the χ^2 test for nested models. Adjusting for seasonality did not improve the fit of any of the models tested and, thus, all presented models are unadjusted for seasonality. See online supplemental appendix 5 for model selection and estimates.

Patient and public involvement

Although patients and the public were not directly involved in this study, within the broader Neotree co-development project we are carrying out a series of workshops and focus group discussions with healthcare workers and parents of admitted babies to ensure local ownership and relevance of this digital quality involvement tool aimed at improving healthcare outcomes for vulnerable neonates.

RESULTS

Outcome 1: admissions to the NNU

We included 3450 neonates at SMCH and 3350 neonates at KCH. Figure 1 shows the 7-day moving average of admissions to the NNU.

At SMCH, the mean (SD) number of weekly admissions was 54.6 (23.5) before the first case of COVID-19 (pre-COVID-19) and 42.8 (19.9) afterwards (post-COVID-19). The negative binomial regression model showed no evidence of a change in admissions after the first case of COVID-19 (relative risk (RR) 0.87; 95% CI 0.65 to 1.17; p=0.37) (figure 2A). However, this model estimated that admissions fell by 48% during the nurses' strike period (RR 0.52, 95% CI 0.41 to 0.66; p<0.001) and by 51% during the pre-COVID-19 doctors' strikes (RR 0.49, 95% CI 0.41 to 0.60; p<0.001).

At KCH, the mean (SD) number of weekly admissions was 54.5 (10.8) in the pre-COVID-19 period and 38.0 (10.9) in the post-COVID-19 period. The negative binomial regression model yielded a 42% reduction in admissions after the first case of COVID-19 (RR 0.58; 95% CI 0.48 to 0.70; p<0.001) (figure 2B).

Outcome 2: gestational age and birth weight

At SMCH, the mean (SD) gestational age at birth was 36.1 (4.4) weeks in the pre-COVID-19 period and 36.0 (4.2) weeks in the post-COVID-19 period. The mean (SD) birth weight was 2500 (908) g in the pre-COVID-19 period and 2487 (896) g in the post-COVID-19 period. Linear regression analysis indicated no significant change in gestational age at birth nor birth weight after the first case of COVID-19 (gestational age: beta 0.07; 95% CI −0.50 to 0.64; p=0.81, birth weight: beta 3.4; 95% CI −117.0 to 123.8; p=0.96) (online supplemental figure 1A, C).

At KCH, the mean (SD) gestational age was 35.0 (3.9) weeks in the pre-COVID-19 period and 34.8 (3.9) weeks in the post-COVID-19 period. The mean (SD) birth weight

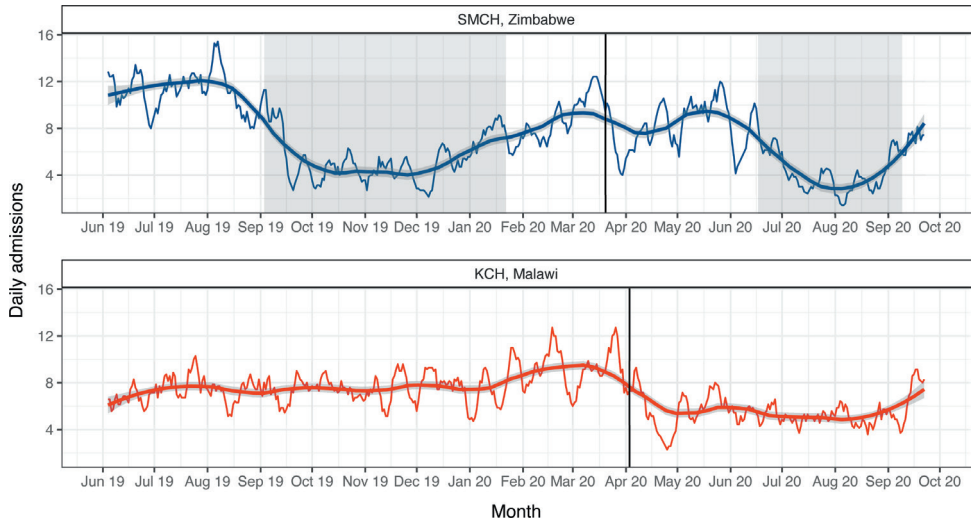

Figure 1 Trend in daily admissions to the neonatal unit. The 7-day moving average of daily admission numbers has been plotted. Smoothed line: local regression (LOESS) model fitted on the 7-day moving average of daily admission numbers; shaded region: 95% CI. Solid vertical line: first confirmed case of COVID-19 in each country. Shaded periods on SMCH, Zimbabwe panel: industrial action by doctors (3 September 2019 to 22 January 2020) and nurses (17 July 2020 to 9 September 2020). Counts based on all admission forms completed, irrespective of match status. KCH, Kamuzu Central Hospital; SMCH, Sally Mugabe Central Hospital.

was 2402 (883) g in the pre-COVID-19 period and 2299 (870) g in the post-COVID-19 period. Gestational age significantly decreased by 1 week in the post-COVID-19 period (beta −1.14; 95% CI −1.62 to −0.65; p<0.001) (online supplemental figure 1B) and birth weight significantly decreased by 300 g (beta −299.9; 95% CI −412.3 to −187.5; p<0.001) (online supplemental figure 1D).

Outcome 3: source of admission referral

At SMCH, the mean (SD) percentage of outside referrals to the NNU was 39 (11)% in the pre-COVID-19 period and 35 (9)% in the post-COVID-19 period. The Poisson regression model showed no evidence of a change in the percentage of outside referrals after the first case of COVID-19 (RR 0.97; 95% CI 0.77 to 1.22; p=0.81) (figure 3A). However, this model did imply a 39% relative increase in the percentage of outside referrals during the doctors' strikes in the pre-COVID-19 period (RR 1.39; 95% CI 1.20 to 1.61; p<0.001).

At KCH, the mean (SD) percentage of outside referrals was 61 (8)% in the pre-COVID-19 period and 51 (10)% in the post-COVID-19 period. Poisson regression analysis resulted in a 28% relative reduction in outside referrals after the first case of COVID-19 (RR 0.72; 95% CI 0.61 to 0.85; p<0.001) (figure 3B).

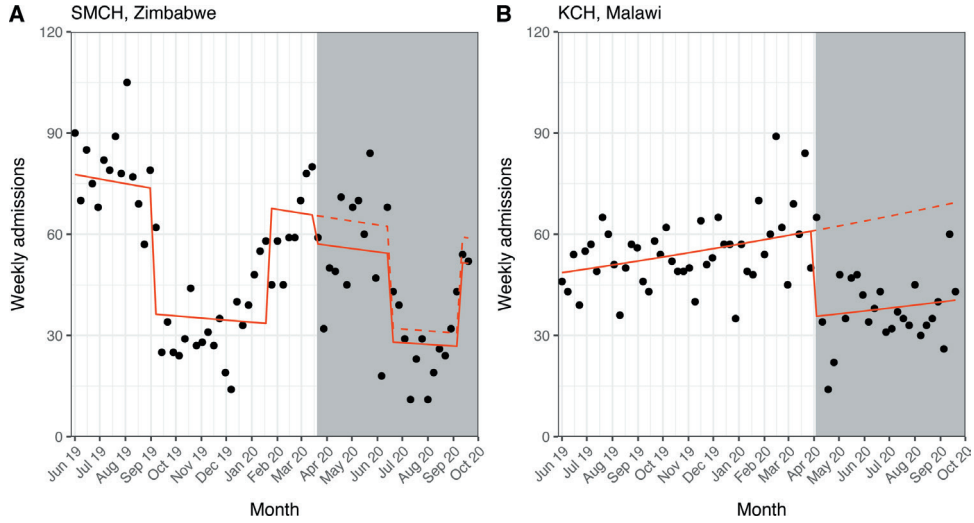

Figure 2 Interrupted time series for weekly admissions to the neonatal unit. White background: pre-COVID-19 period; grey background: post-COVID-19 period. Solid line: predicted trend from negative binomial regression model; dashed line: counterfactual scenario. SMCH model (A) adjusted for doctors' and nurses' strike periods; KCH model (B) unadjusted. Counts based on all admission forms completed, irrespective of match status. KCH, Kamuzu Central Hospital; SMCH, Sally Mugabe Central Hospital.

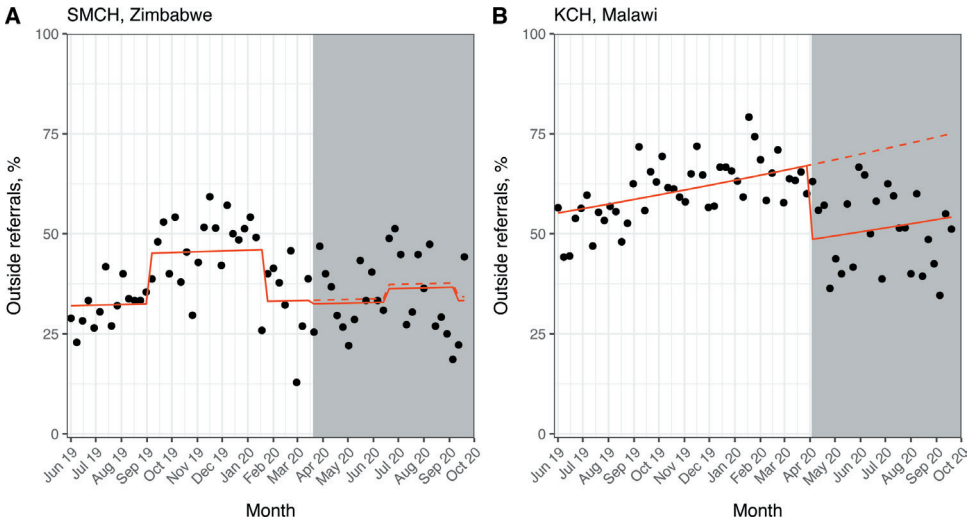

Figure 3 Interrupted time series for outside referrals to the neonatal unit. White background: pre-COVID-19 period; grey background: post-COVID-19 period. Solid line: predicted trend from Poisson regression model; dashed line: counterfactual scenario. SMCH model (A) adjusted for doctors' and nurses' strike periods, KCH model (B) unadjusted. Data from all admission forms completed, irrespective of match status. KCH, Kamuzu Central Hospital; SMCH, Sally Mugabe Central Hospital.

Outcome 4: prevalence of NE

At SMCH, the mean (SD) percentage of admitted neonates diagnosed with NE was 16 (6)% in the pre-COVID-19 period and 21 (12)% in the post-COVID-19 period suggesting a possible increase. Poisson regression analysis showed no statistically significant change in the percentage of neonates diagnosed with NE post-COVID-19 (RR 1.06; 95% CI 0.74 to 1.52; p=0.74) (online supplemental figure 2A).

At KCH, the mean (SD) percentage of admitted neonates diagnosed with NE was 15 (6)% in the pre-COVID-19 period and 13 (5)% in the post-COVID-19 period. The Poisson regression model implied a possible increase in diagnoses of NE after the first case of COVID-19, but this was not statistically significant (RR 1.31; 95% CI 0.91 to 1.88; p=0.15) (online supplemental figure 2B).

Outcome 5: overall mortality

For SMCH, the mean (SD) percentage of deaths per week of admission was 25 (10)% in the pre-COVID-19 period and 26 (16)% in the post-COVID-19 period. The negative binomial regression model pointed towards a possible decrease in mortality after the first case of COVID-19, but this was not statistically significant (RR 0.72; 95% CI 0.52 to 1.00; p=0.05) (figure 4A). However, this model did show an 81% relative increase in mortality during the nurses' strike period (RR 1.81; 95% CI 1.31 to 2.49; p<0.001).

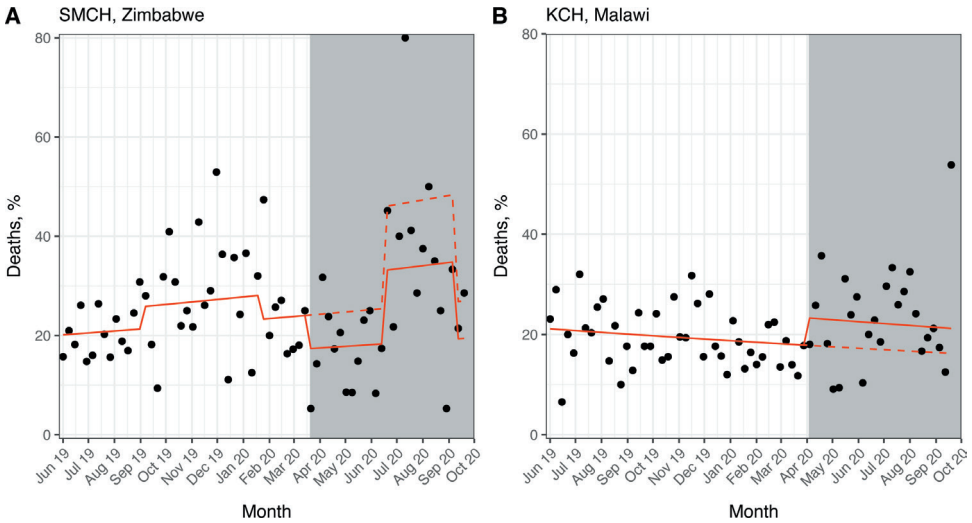

Figure 4 Interrupted time series for overall mortality. White background: pre-COVID-19 period; grey background: post-COVID-19 period. Solid line: predicted trend from negative binomial regression model (SMCH, A) or Poisson regression model (KCH, B); dashed line: counterfactual scenario. SMCH model (A) adjusted for doctors' and nurses' strike periods; KCH model (B) unadjusted. Data from matched admission and outcome forms only. KCH, Kamuzu Central Hospital; SMCH, Sally Mugabe Central Hospital.

For KCH, the mean (SD) percentage of deaths per week of admission was 19 (6)% in the pre-COVID-19 period and 23 (10)% in the post-COVID-19 period. The Poisson regression model implied a possible increase in mortality after the first case of COVID-19, but this was not statistically significant (RR 1.31; 95% CI 0.97 to 1.76; p=0.08) (figure 4B).

DISCUSSION

Summary

We performed an interrupted time series analysis to examine changes in neonatal care provision at two tertiary NNUs in Zimbabwe and Malawi after the first cases of COVID-19 in each country. We found that admissions at SMCH did not change significantly after the first case of COVID-19 when considering this period as a whole, but there was a considerable decrease (around 50%) in the number admissions in June to August 2020, coinciding with a nurses' strike. We did not find significant changes in gestational age or birth weight, source of admission referrals, prevalence of NE or mortality at SMCH. Conversely, we found several changes in markers of neonatal care at KCH after the first case of COVID-19 in Malawi. The number of admissions fell by 42% and we noted a decrease in the gestational age and birth weight of admitted neonates (by around 1 week and 300 g, respectively), and a 28% relative decrease in outside referrals after the first case of COVID-19. Although this study is descriptive, we can speculate about explanations for our results based on existing literature and discussions with local health workers.

Interpretation

The number of admissions at SMCH fell by around 50% between June to August 2020, but we noted no change outside this strike period, suggesting some resilience to the impact of the pandemic. However, nurses went on strike over pay and availability of personal protective equipment,[20] so the strike is itself an indirect consequence of COVID-19. A recently published audit of maternal health service provision at two tertiary hospitals in Harare, Zimbabwe (including SMCH) found a 25% reduction in hospital deliveries and an increased odds of stillbirth (OR 1.8; 95% CI 1.5 to 2.2) in March to August 2020 compared with the same period in 2019,[28] which might partially explain the reduction in admissions to the NNU. A similar reduction in admissions was seen at KCH, but, unlike at SMCH, this 42% decrease was noted within a week of the first case of COVID-19. In figure 5, we propose several interlinked factors that might explain reduced admissions to the NNU. Several of these factors, such as fear of using health services, disrupted transport networks and staff shortages have been directly reported by local sources in low-resource settings and were highlighted in a recent report by Graham *et al*.[29]

We found a slight decrease in gestational age and birth weight of neonates at KCH, but not SMCH. Studies have reported increased rates of preterm birth in pregnant women with COVID-19 compared with those without the disease, mostly from medically induced preterm birth; although none of these studies were conducted in LMICs.[30] Preliminary analysis suggests rates of emergency caesarean section increased at SMCH and KCH, with a more marked increase at KCH (online supplemental appendix 6). This is one potential explanation for our findings. However, we noted that the number of outside referrals decreased by 28% at KCH, and neonates referred from outside KCH are more likely to be from lower-risk pregnancies that delivered in a health centre with higher gestational ages and birth weights. Further

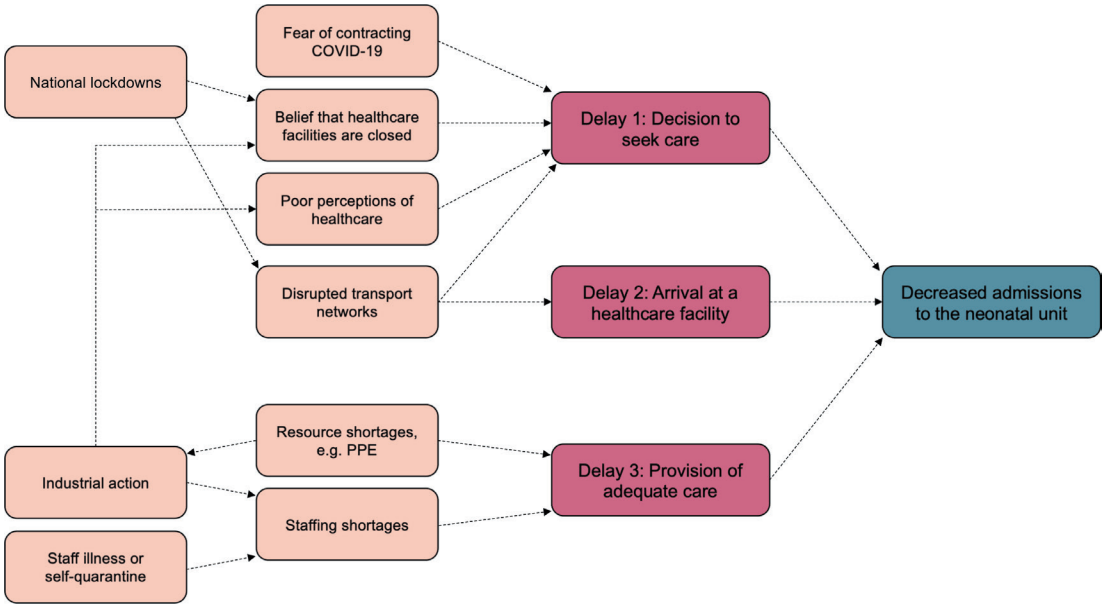

Figure 5 Possible factors influencing the decrease in admissions to the neonatal unit. Delays (red boxes) derived from the 'three delays' model of pregnancy-related mortality.[36] PPE, personal protective equipment.

analysis should stratify by source of admission referral to clarify this finding, but the relative reduction in outside referrals is supported by the fact that referrals were rigorously triaged by the on-call paediatrician during the pandemic, and that referrals from some areas were diverted away from KCH to more appropriate centres for the level of care required.

We hypothesised that rates of NE would increase during the pandemic. NE is the clinical manifestation of disordered brain function and can have multiple aetiologies.[31] The term 'hypoxic-ischaemic encephalopathy' is reserved for cases where there is evidence of intrapartum asphyxia.[31] In LMICs, obstructed labour is a major cause of maternal mortality and can lead to intrapartum asphyxia with subsequent neonatal morbidity and mortality, including NE.[32] Therefore, the prevalence of NE might be expected to increase as a marker of delayed presentation to a health facility. It is reassuring that we did not find increased rates of NE at SMCH or KCH. However, these findings should be interpreted cautiously as some neonates with NE may not have presented to a health facility at all, for example, due to an increased number of home deliveries, as documented in other sub-Saharan countries.[33]

Finally, we did not observe a significant change in overall mortality at KCH nor SMCH, except during the nurses' strikes at SMCH. In fact, there was a suggestion that mortality decreased after the first case of COVID-19 in Zimbabwe when adjusted for the nurses' strike period, but this was not statistically significant. The reasons for this are unclear but could include factors such as increased stillbirth rates or improved care for the smaller number of neonates on the NNU. More complete analysis of facility-based and community-based neonatal mortality is greatly needed.

Limitations and future work

A limitation intrinsic to interrupted time series analysis is the possibility that another event occurred close to the first case of COVID-19 in either country causing spurious observations. Another potential threat to validity is changing data collection practices. For example, overstretched clinicians might not input data into the Neotree app for all admitted neonates. However, this is unlikely as the Neotree app is embedded into routine practice at SMCH and KCH and discussions with local collaborators suggest use of the app has continued without issue. At present, there is limited guidance on power and sample size calculations for interrupted time series analyses.[34] Therefore, we did not perform specific power calculations and relied on the data available at the time of analysis. Also, our results suggest that our study has relatively low power to detect true changes in some outcomes, particularly NE, so these results should be interpreted cautiously in the absence of further data.

The Neotree app only collects data on neonates admitted to the NNU. Therefore, our analysis does not capture stillbirths or neonatal deaths that occur in the community. It is troubling to see a dramatic fall in admissions at both sites, raising the possibility that many unwell neonates did not attend a health facility and died at home. A recent study found that facility births decreased by over 50% during the lockdown in Nepal, and facility stillbirth and neonatal mortality rates increased significantly.[35] The Neotree research team is currently collecting data on stillbirths at SMCH and KCH, but these data will still only represent stillbirths that occurred in a health facility. Given the COVID-19 pandemic is not over, it will be important to repeat our analysis to further examine longer-term trends in neonatal care provision.

CONCLUSION

The indirect impacts of COVID-19 are context-specific, with more significant and evident effects on neonatal care provision seen at KCH (Malawi) than SMCH (Zimbabwe). While this study provides vital evidence to inform health providers and policy makers, national data are required to ascertain the true impacts of the pandemic on newborn health.

Author affiliations
[1]Child and Adolescent Health Unit, University of Zimbabwe, Harare, Zimbabwe
[2]UCL Great Ormond Street Institute of Child Health, University College London, London, UK
[3]Parent and Child Health Initiative, Lilongwe, Malawi
[4]Biomedical Research and Training Institute, Harare, Zimbabwe
[5]Department of Paediatrics, Kamuzu Central Hospital, Lilongwe, Malawi

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Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Ethics approval Research ethics approval was granted by the UCL Research Ethics Committee (17123/001) and ethics committees in Malawi (P.01/20/2909) and Zimbabwe (MRCZ/A/2570) (online supplemental appendix 2). The need to

obtain informed consent was waived as we collected only pseudonymised data routinely documented for clinical care.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request. Data collected for the study cannot yet be made publicly available because primary analysis for the pilot implementation evaluation of the Neotree, as well as secondary analysis are ongoing. A goal of our pilot implementation is to establish an open-source anonymised research database of Neotree data to maximise the reach and utility for researchers aiming to improve outcomes for neonates in low-income settings. This database is under development and subject to negotiation with relevant Ministries of Health.

ORCID iDs
Samuel R Neal http://orcid.org/0000-0001-6832-9839
Emma Wilson http://orcid.org/0000-0001-7091-2417
Felicity Fitzgerald http://orcid.org/0000-0001-9594-3228

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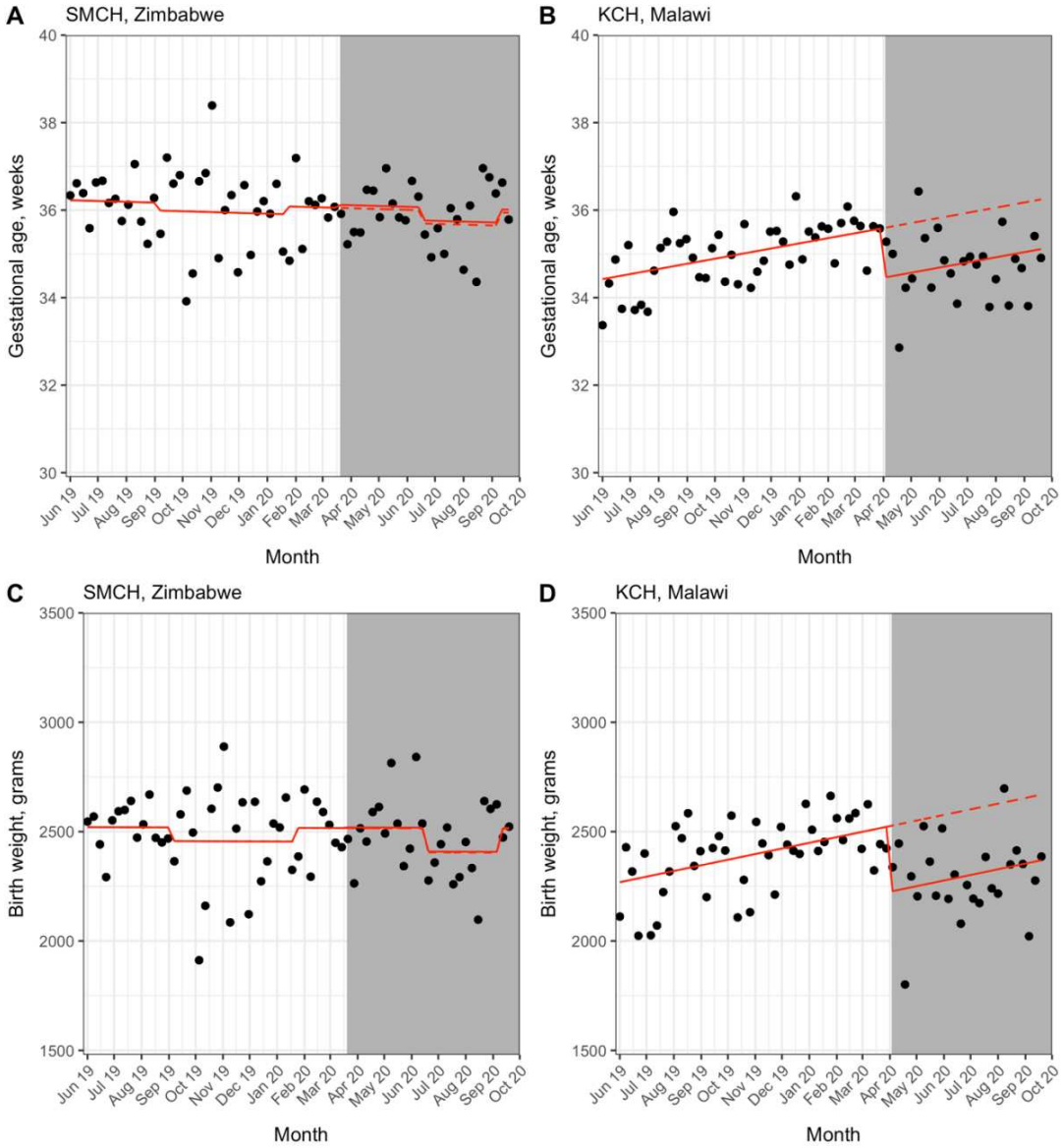
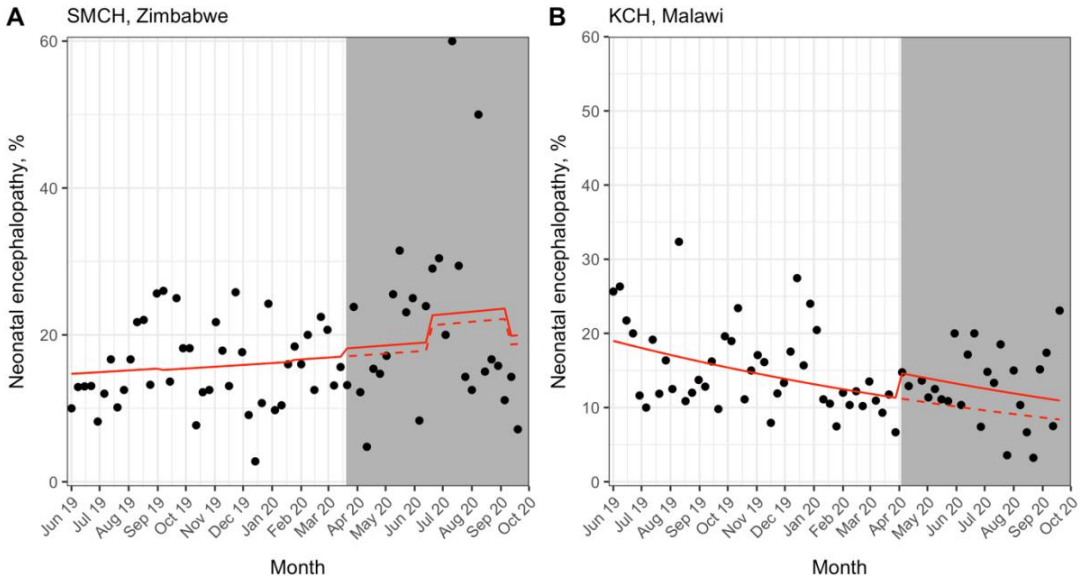
SUPPLEMENTARY FIGURES



Supplementary Figure 1: Interrupted time series for gestational age and birth weight

- Data points represent weekly mean gestational age or birth weight to avoid overplotting.
- White background: pre-COVID-19 period; grey background: post-COVID-19 period.
- Solid line: predicted trend from linear regression model; dashed line: counterfactual scenario.
- SMCH models (panels A & C) adjusted for doctors' and nurses' strike periods, KCH models (panels B & D) unadjusted.
- Data from all admission forms completed, irrespective of match status.
- *SMCH: Sally Mugabe Central Hospital; KCH: Kamuzu Central Hospital*

Chimhuya S, *et al. BMJ Open* 2022; 12:e048955. doi: 10.1136/bmjopen-2021-048955



Supplementary Figure 2: Interrupted time series for prevalence of neonatal encephalopathy

- White background: pre-COVID-19 period; grey background: post-COVID-19 period.
- Solid line: predicted trend from Poisson regression model; dashed line: counterfactual scenario.
- SMCH model (panel A) adjusted for doctors' and nurses' strike periods, KCH model (panel B) unadjusted.
- Data from matched admission and outcome forms only.
- *SMCH: Sally Mugabe Central Hospital; KCH: Kamuzu Central Hospital*

Chimhuya S, *et al. BMJ Open* 2022; 12:e048955. doi: 10.1136/bmjopen-2021-048955

APPENDIX 1: STROBE CHECKLIST

	Item No.	Recommendation	Page No.
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1-2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	9-10
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-8
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	7
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	n/a
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7-8
Bias	9	Describe any efforts to address potential sources of bias	9-10
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9-10

Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	9-10
		(*b*) Describe any methods used to examine subgroups and interactions	9-10, Appendix 5
		(*c*) Explain how missing data were addressed	9-10, Appendix 4
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	9
		(*e*) Describe any sensitivity analyses	9-10, Appendix 5
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	12, Appendix 3
		(b) Give reasons for non-participation at each stage	9, Appendix 3
		(c) Consider use of a flow diagram	Appendix 3
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	12-13, Appendix 5
		(b) Indicate number of participants with missing data for each variable of interest	Appendix 4
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	7
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	12-15
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	n/a
		Cross-sectional study—Report numbers of outcome events or summary measures	n/a
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	12-15
		(*b*) Report category boundaries when continuous variables were categorized	12-15
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	12-15

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Appendix 5, Appendix 6
Discussion			
Key results	18	Summarise key results with reference to study objectives	16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	18-19
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	16-19
Generalisability	21	Discuss the generalisability (external validity) of the study results	16-19
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	26

Adapted from: von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, et al. (2007) The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: Guidelines for Reporting Observational Studies. PLOS Medicine 4(10): e296. https://doi.org/10.1371/journal.pmed.0040296

APPENDIX 2: ETHICAL APPROVAL

Ethical approval for this study was granted by the following ethics committees.

Table A2.1: Ethical approval

Committee	Reference
United Kingdom	
University College London Research Ethics Committee	17123/001
Malawi	
College of Medicine Research and Ethics Committee	P.01/20/2909
Zimbabwe	
Medical Research Council of Zimbabwe	MRCZ/A/2570
Joint Research Ethics Committee for the University of Zimbabwe, College of Health Sciences and Parirenyatwa Group of Hospitals	JREC/327/19
Biomedical Research and Training Institute Institutional Review Board	AP155/2020
Sally Mugabe (Harare) Central Hospital Ethics Committee	071119/64

APPENDIX 3: FLOW DIAGRAMS OF RECORD INCLUSION

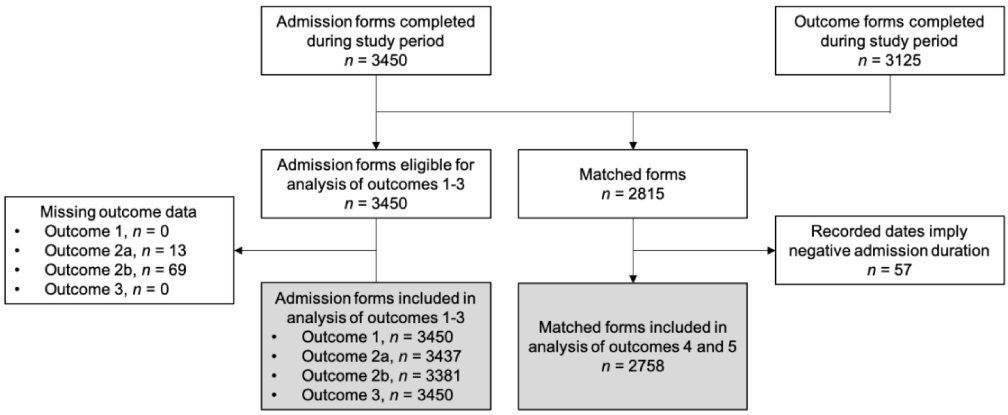


Figure A3.1: Flow diagram of record inclusion for Sally Mugabe Central Hospital, Zimbabwe

- Outcome 1: number of admissions; outcome 2a: gestational age; outcome 2b: birth weight; outcome 3: source of admission; outcome 4: prevalence of neonatal encephalopathy; outcome 5: overall mortality rate

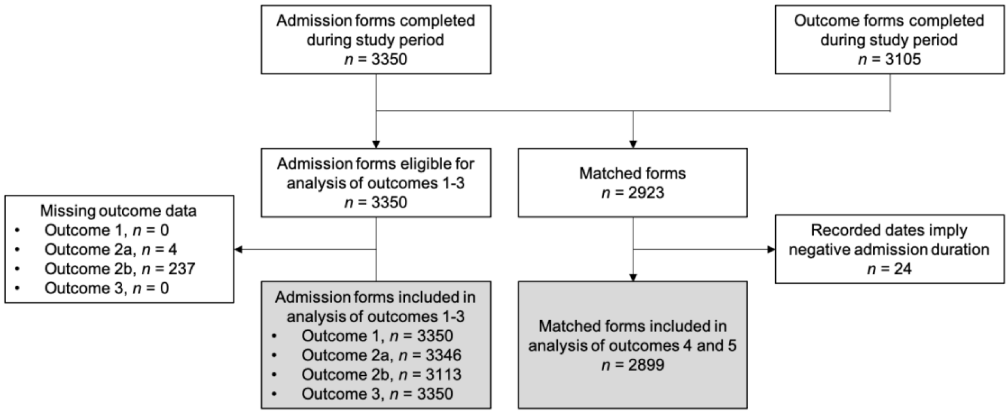


Figure A3.2: Flow diagram of record inclusion for Kamuzu Central Hospital, Malawi

- Outcome 1: number of admissions; outcome 2a: gestational age; outcome 2b: birth weight; outcome 3: source of admission; outcome 4: prevalence of neonatal encephalopathy; outcome 5: overall mortality rate

APPENDIX 4: MISSING DATA

The table below shows the number of participants with missing data for each outcome and the number of participants remaining for each analysis after pairwise deletion of missing values.

Table A4.1: Summary of missing data

Characteristics	*n* missing (%)		*n* remaining*	
	SMCH	KCH	SMCH	KCH
Gestational age	13 (0·4)	4 (0·1)	3437 (99·6)	3346 (99·9)
Birth weight	69 (2·0)	237 (7·1)	3381 (98·0)	3113 (92·9)
Source of admission	0 (0·0)	0 (0·0)	3450 (100·0)	3350 (100·0)
Neonatal encephalopathy	0 (0·0)	0 (0·0)	2758 (100·0)†	2899 (100·0)†
Death	0 (0·0)	0 (0·0)	2758 (100·0)†	2899 (100·0)†

- * Remaining for analysis after pairwise deletion.
- † Only matched admission and outcome forms considered for analysis of neonatal encephalopathy and death.
- *SMCH: Sally Mugabe Central Hospital; KCH: Kamuzu Central Hospital, Malawi*

APPENDIX 5: FURTHER REGRESSION ANALYSIS RESULTS

Outcome 1: Admissions to the neonatal unit

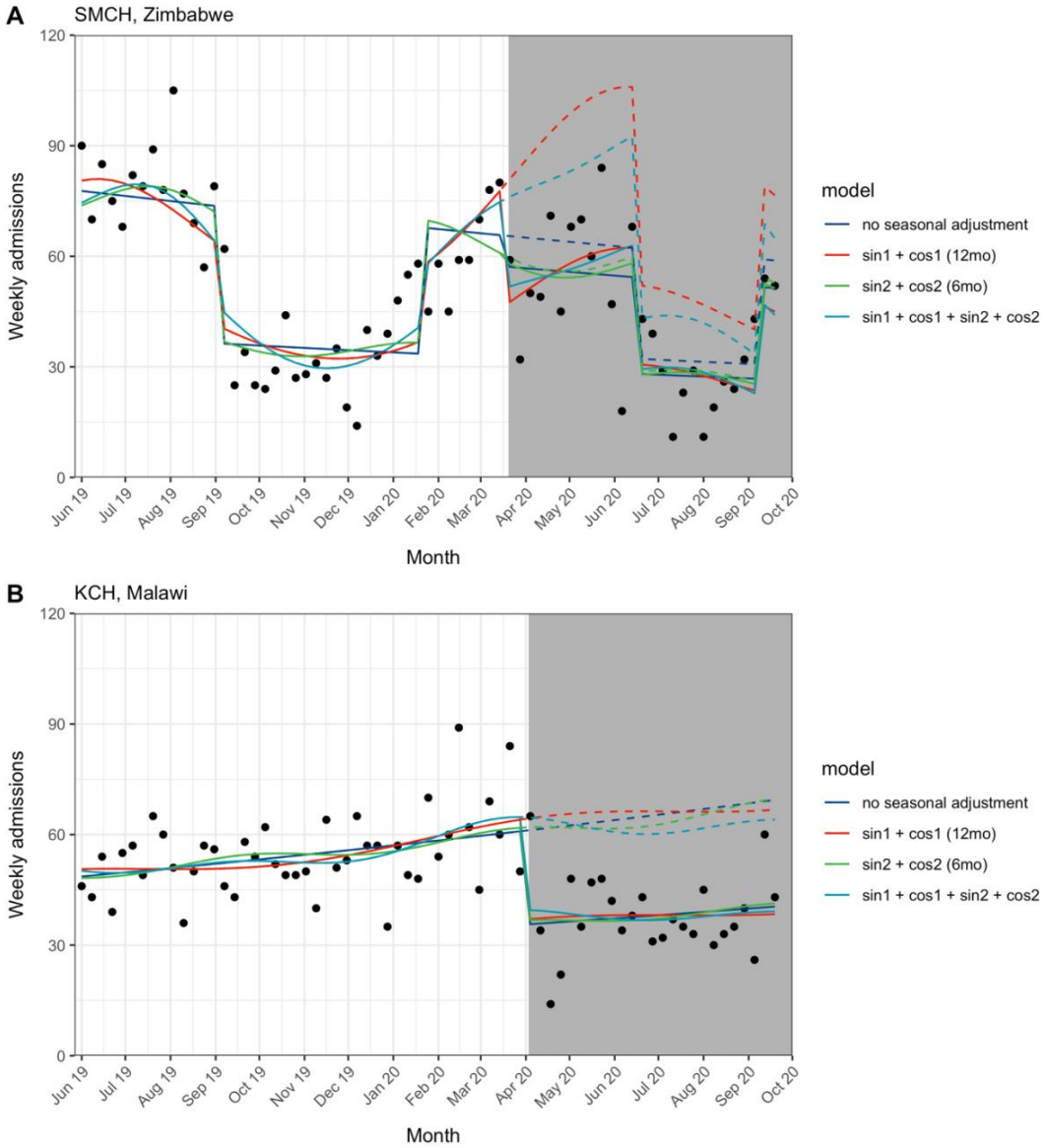


Figure A5.1.1: Interrupted time series for weekly admissions to the neonatal unit, negative binomial regression models with and without seasonal adjustment

Table A5.1.1: SMCH, Zimbabwe; Results of the models with and without adjustment for seasonality

Model*		BIC	LR statistic†	Df	*p*-value
0	Negative binomial, unadjusted for seasonality	585·6	ref		
1	Negative binomial, cosine function with 6-month period	588·9	5·23	2	0·07
2	Negative binomial, cosine function with 12-month period	592·9	1·22	2	0·54
3	Negative binomial, mixture of two cosine functions with 6-month and 12-month periods	595·6	6·96	4	0·13

- * All models adjusted for the doctors' and nurses' strike periods.
- † Likelihood ratio χ^2-test compared to Model 0.

Table A5.1.2: SMCH, Zimbabwe; Negative binomial model, unadjusted for seasonality (Model 0)

	Coef	SE	Exp	95% CI	*p*-value
Intercept	*4·35*	*0·09*			
Post-COVID-19 period, yes	-0·14	0·15	0·87	0·65 – 1·17	0·37
Study time elapsed, weeks	-0·00	0·00	1·00	0·99 – 1·00	0·25
Doctors' strike period, yes	-0·70	0·10	0·49	0·41 – 0·60	< 0·001
Nurses' strike period, yes	-0·66	0·13	0·52	0·41 – 0·66	< 0·001

Table A5.1.3: KCH, Malawi; Results of the models with and without adjustment for seasonality

Model		BIC	LR statistic†	Df	*p*-value
0	Negative binomial, unadjusted for seasonality	534·5	ref		
1	Negative binomial, cosine function with 6-month period	541·5	1·40	2	0·50
2	Negative binomial, cosine function with 12-month period	542·4	0·52	2	0·77
3	Negative binomial, mixture of two cosine functions with 6-month and 12-month periods	549·1	2·36	4	0·67

- † Likelihood ratio χ^2-test compared to Model 0.

Table A5.1.4: KCH, Malawi; Negative binomial model, unadjusted for seasonality (Model 0)

	Coef	SE	Exp	95% CI	*p*-value
Intercept	*3·88*	*0·06*			
Post-COVID-19 period, yes	-0·54	0·10	0·58	0·48 – 0·70	< 0·001
Study time elapsed, weeks	0·01	0·00	1·01	1·00 – 1·01	0·022

Outcome 2: Gestational age at birth and birth weight

a. Gestational age at birth

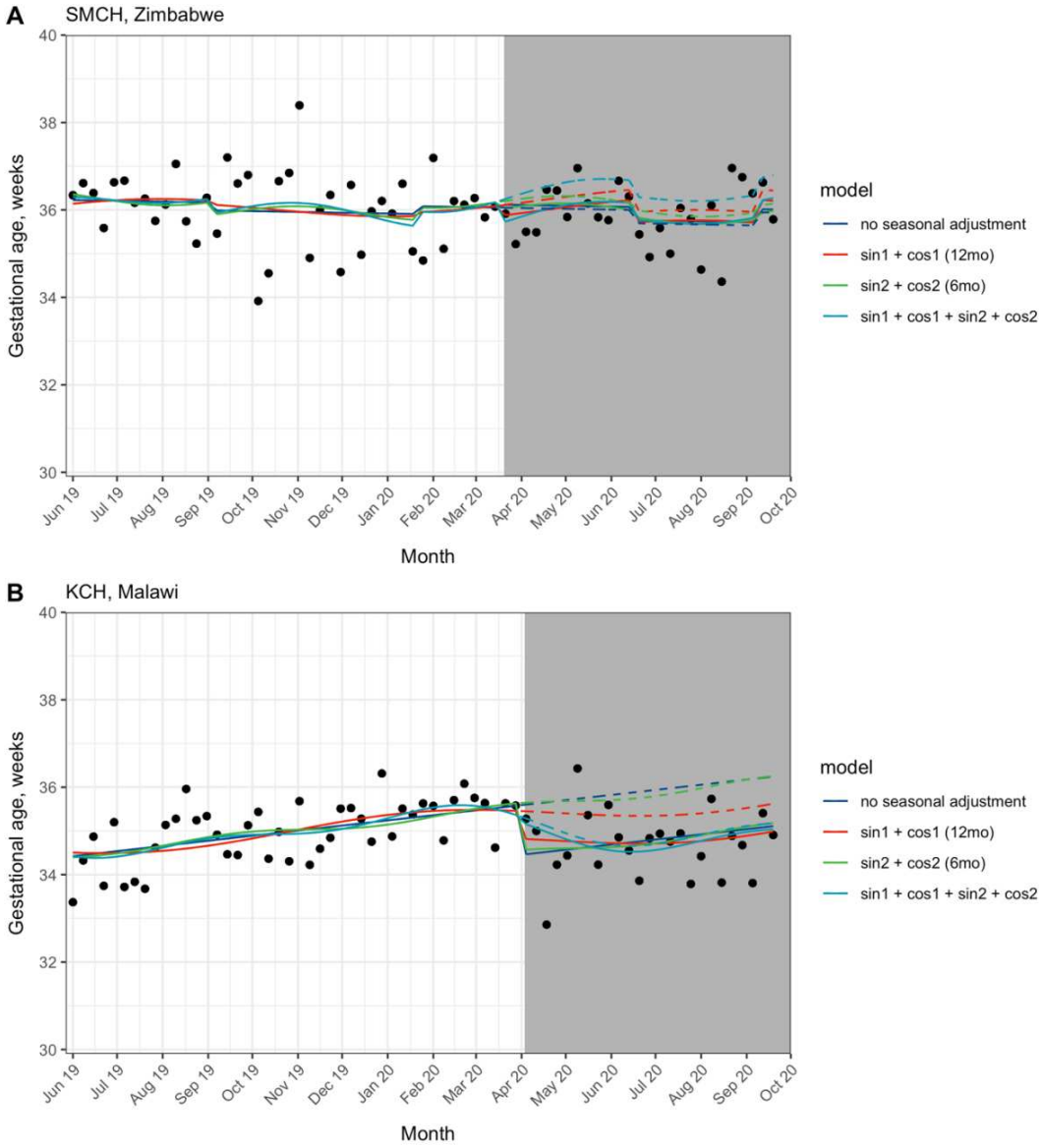


Figure A5.2.1: Interrupted time series for gestational age at birth, linear regression models with and without seasonal adjustment

Table A5.2.1: SMCH, Zimbabwe; Results of the models with and without adjustment for seasonality

Model*		BIC	Deviance†	Df	*p*-value
0	Linear, unadjusted for seasonality	19851·6	ref		
1	Linear, cosine function with 6-month period	19866·6	24·0	2	0·53
2	Linear, cosine function with 12-month period	19867·0	15·8	2	0·65
3	Linear, mixture of two cosine functions with 6-month and 12-month periods	19881·4	50·9	4	0·60

- * All models adjusted for the doctors' and nurses' strike periods.
- † χ^2-test compared to Model 0.

Table A5.2.2: SMCH, Zimbabwe; Linear model, unadjusted for seasonality (Model 0)

	Coef	SE	95% CI	*p*-value
Intercept	*36·23*	*0·15*		
Post-COVID-19 period, yes	0·07	0·29	-0·50 – 0·64	0·81
Study time elapsed, weeks	-0·00	0·01	-0·02 – 0·01	0·52
Doctors' strike period, yes	-0·18	0·20	-0·58 – 0·22	0·38
Nurses' strike period, yes	-0·30	0·29	-0·87 – 0·27	0·30

Table A5.2.3: KCH, Malawi; Results of the models with and without adjustment for seasonality

Model		BIC	Deviance†	Df	*p*-value
0	Linear, unadjusted for seasonality	18631·8	ref		
1	Linear, cosine function with 6-month period	18645·2	43·2	2	0·24
2	Linear, cosine function with 12-month period	18647·2	12·9	2	0·65
3	Linear, mixture of two cosine functions with 6-month and 12-month periods	18658·4	89·0	4	0·21

- † χ^2-test compared to Model 0.

Table A5.2.4: KCH, Malawi; Linear model, unadjusted for seasonality (Model 0)

	Coef	SE	95% CI	*p*-value
Intercept	*34·42*	*0·15*		
Post-COVID-19 period, yes	-1·14	0·25	-1·62 – -0·65	< 0·001
Study time elapsed, weeks	0·03	0·01	0·02 – 0·04	< 0·001

b. Birth weight

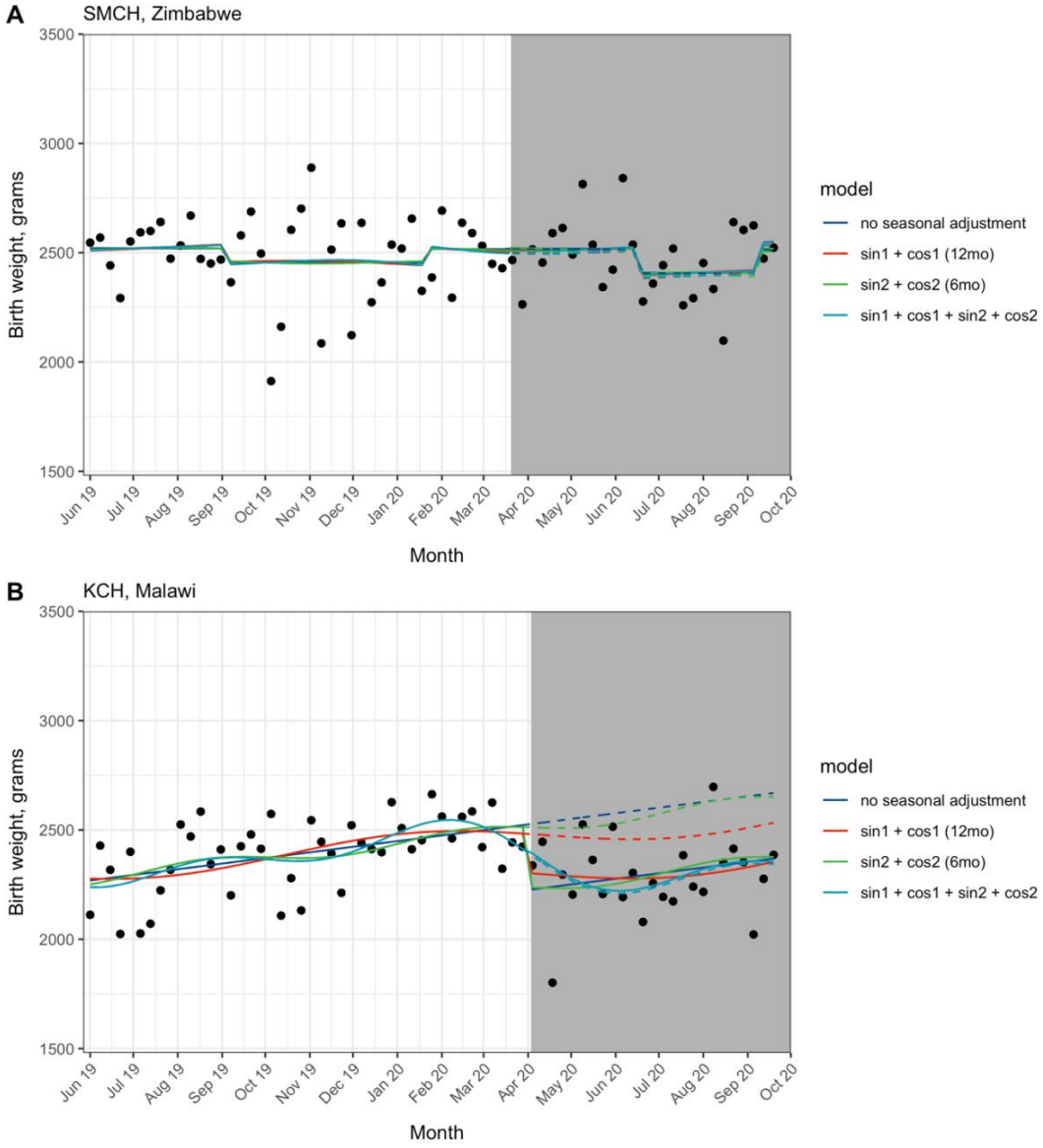


Figure A5.2.2: Interrupted time series for birth weight, linear regression models with and without seasonal adjustment

Table A5.2.5: SMCH, Zimbabwe; Results of the models with and without adjustment for seasonality

Model*		BIC	Deviance†	Df	*p*-value
0	Linear, unadjusted for seasonality	55660·9	ref		
1	Linear, cosine function with 6-month period	55676·8	289194	2	0·84
2	Linear, cosine function with 12-month period	55677·1	28641	2	0·98
3	Linear, mixture of two cosine functions with 6-month and 12-month periods	55693·0	351647	4	0·98

- * All models adjusted for the doctors' and nurses' strike periods.
- † χ^2-test compared to Model 0.

Table A5.2.6: SMCH, Zimbabwe; Linear model, unadjusted for seasonality (Model 0)

	Coef	SE	95% CI	*p*-value
Intercept	*2520·71*	*31·89*		
Post-COVID-19 period, yes	3·38	61·42	-117·0 – 123·8	0·96
Study time elapsed, weeks	-0·11	1·38	-2·8 – 2·6	0·94
Doctors' strike period, yes	-62·52	42·92	-146·6 – 21·6	0·15
Nurses' strike period, yes	-109·4	61·0	-229·0 – 10·2	0·07

Table A5.2.7: KCH, Malawi; Results of the models with and without adjustment for seasonality

Model		BIC	Deviance†	Df	*p*-value
0	Linear, unadjusted for seasonality	51050·5	ref		
1	Linear, cosine function with 6-month period	51064·1	1922568	2	0·29
2	Linear, cosine function with 12-month period	51065·2	1105739	2	0·49
3	Linear, mixture of two cosine functions with 6-month and 12-month periods	51073·9	6744491	4	0·07

- † χ^2-test compared to Model 0.

Table A5.2.8: KCH, Malawi; Linear model, unadjusted for seasonality (Model 0)

	Coef	SE	95% CI	*p*-value
Intercept	*2268·96*	*36·02*		
Post-COVID-19 period, yes	-299·89	57·34	-412·3 – -187·5	< 0·001
Study time elapsed, weeks	5·88	1·37	3·2 – 8·6	< 0·001

Outcome 3: Source of admission referral

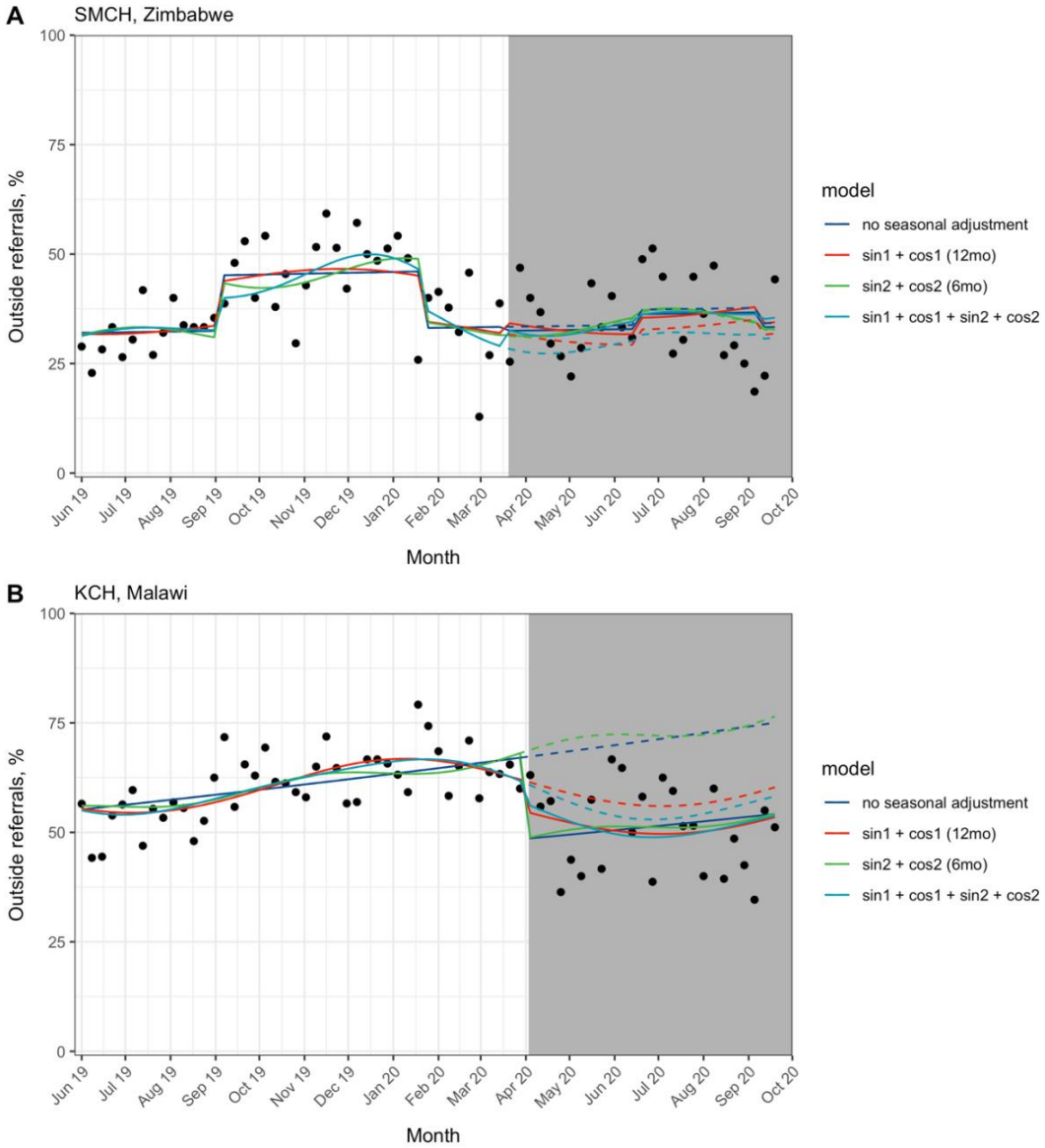


Figure A5.3.1: Interrupted time series for outside referrals to the neonatal unit, Poisson regression models with and without seasonal adjustment

Table A5.3.1: SMCH, Zimbabwe; Results of the models with and without adjustment for seasonality

Model*		BIC	Deviance†	Df	*p*-value
0	Poisson, unadjusted for seasonality	406·3	ref		
1	Poisson, cosine function with 6-month period	414·2	0·56	2	0·76
2	Poisson, cosine function with 12-month period	412·9	1·85	2	0·40
3	Poisson, mixture of two cosine functions with 6-month and 12-month periods	419·8	3·42	4	0·49

- * All models adjusted for the doctors' and nurses' strike periods.
- † χ^2-test compared to Model 0.

Table A5.3.2: SMCH, Zimbabwe; Poisson model, unadjusted for seasonality (Model 0)

	Coef	SE	Exp	95% CI	*p*-value
Intercept	*-1·14*	*0·06*			
Post-COVID-19 period, yes	-0·03	0·12	0·97	0·77 – 1·22	0·81
Study time elapsed, weeks	0·00	0·00	1·00	1·00 – 1·01	0·70
Doctors' strike period, yes	0·33	0·07	1·39	1·20 – 1·61	< 0·001
Nurses' strike period, yes	0·10	0·11	1·10	0·88 – 1·37	0·39

Table A5.3.3: KCH, Malawi; Results of the models with and without adjustment for seasonality

Model		BIC	Deviance†	Df	*p*-value
0	Poisson, unadjusted for seasonality	398·0	ref		
1	Poisson, cosine function with 6-month period	403·3	3·23	2	0·20
2	Poisson, cosine function with 12-month period	405·9	0·58	2	0·75
3	Poisson, mixture of two cosine functions with 6-month and 12-month periods	411·5	3·43	4	0·49

- † χ^2-test compared to Model 0.

Table A5.3.4: KCH, Malawi; Poisson model, unadjusted for seasonality (Model 0)

	Coef	SE	Exp	95% CI	*p*-value
Intercept	*-0·59*	*0·05*			
Post-COVID-19 period, yes	-0·33	0·08	0·72	0·61 – 0·85	< 0·001
Study time elapsed, weeks	0·01	0·00	1·01	1·00 – 1·01	0·020

Outcome 4: Prevalence of neonatal encephalopathy

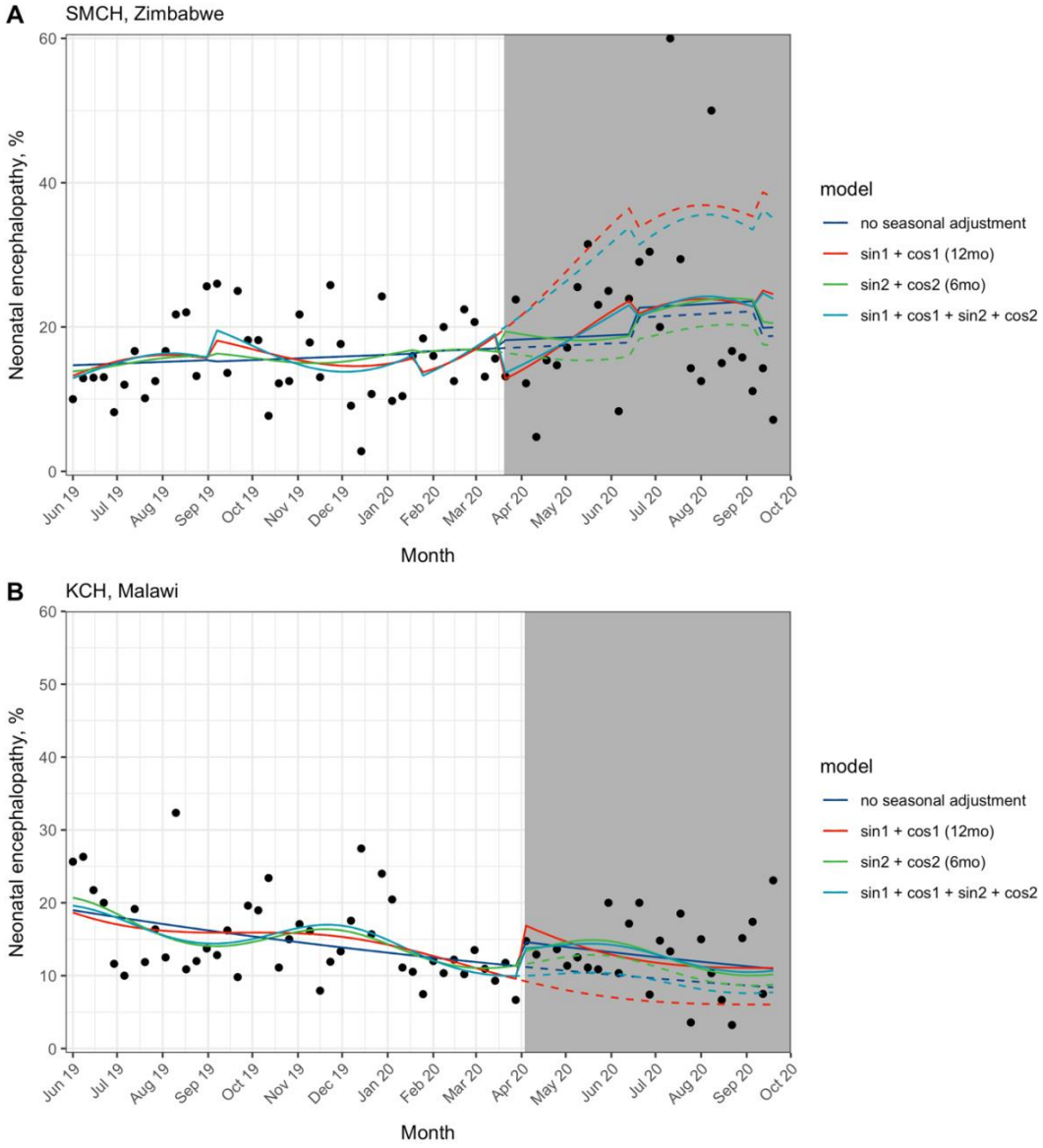


Figure A5.4.1: Interrupted time series for prevalence of neonatal encephalopathy, Poisson regression models with and without seasonal adjustment

Table A5.4.1: SMCH, Zimbabwe; Results of the models with and without adjustment for seasonality

Model*		BIC	Deviance†	Df	*p*-value
0	Poisson, unadjusted for seasonality	333·5	ref		
1	Poisson, cosine function with 6-month period	336·9	5·06	2	0·08
2	Poisson, cosine function with 12-month period	341·5	0·45	2	0·80
3	Poisson, mixture of two cosine functions with 6-month and 12-month periods	345·0	5·39	4	0·25

- * All models adjusted for the doctors' and nurses' strike periods.
- † χ^2-test compared to Model 0.

Table A5.4.2: SMCH, Zimbabwe; Poisson model, unadjusted for seasonality (Model 0)

	Coef	SE	Exp	95% CI	*p*-value
Intercept	*-1·92*	*0·10*			
Post-COVID-19 period, yes	0·06	0·18	1·06	0·74 – 1·52	0·74
Study time elapsed, weeks	0·00	0·00	1·00	1·00 – 1·01	0·39
Doctors' strike period, yes	-0·02	0·13	0·99	0·77 – 1·26	0·91
Nurses' strike period, yes	0·18	0·18	1·19	0·84 – 1·69	0·33

Table A5.4.3: KCH, Malawi; Results of the models with and without adjustment for seasonality

Model		BIC	Deviance†	Df	*p*-value
0	Poisson, unadjusted for seasonality	302·3	ref		
1	Poisson, cosine function with 6-month period	308·9	1·83	2	0·40
2	Poisson, cosine function with 12-month period	307·5	3·29	2	0·19
3	Poisson, mixture of two cosine functions with 6-month and 12-month periods	315·3	3·92	4	0·42

- † χ^2-test compared to Model 0.

Table A5.4.4: KCH, Malawi; Poisson model, unadjusted for seasonality (Model 0)

	Coef	SE	Exp	95% CI	*p*-value
Intercept	*-1·66*	*0·10*			
Post-COVID-19 period, yes	0·27	0·19	1·31	0·91 – 1·88	0·15
Study time elapsed, weeks	-0·01	0·00	0·99	0·99 – 1·00	0·005

Outcome 5: Overall mortality

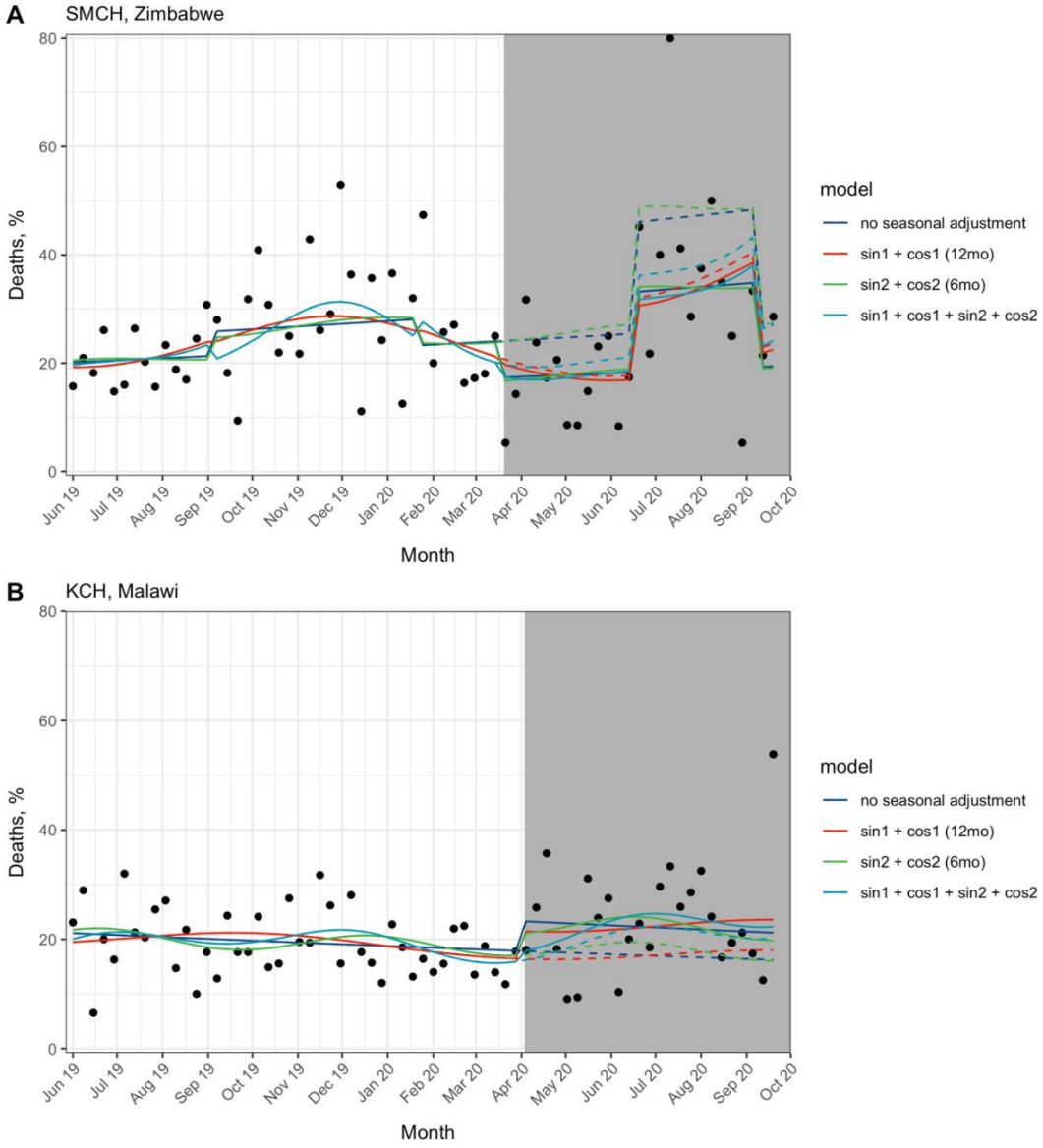


Figure A5.5.1: Interrupted time series for overall mortality, negative binomial regression models (SMCH, Zimbabwe) and Poisson regression models (KCH, Malawi) with and without seasonal adjustment

Table A5.5.1: SMCH, Zimbabwe; Results of the models with and without adjustment for seasonality

Model*		BIC	LR statistic†	Df	*p*-value
0	Negative binomial, unadjusted for seasonality	373·0	ref		
1	Negative binomial, cosine function with 6-month period	379·2	2·32	2	0·31
2	Negative binomial, cosine function with 12-month period	381·2	0·26	2	0·88
3	Negative binomial, mixture of two cosine functions with 6-month and 12-month periods	385·9	4·02	4	0·40

- * All models adjusted for the doctors' and nurses' strike periods.
- † Likelihood ratio χ^2-test compared to Model 0.

Table A5.5.2: SMCH, Zimbabwe; Negative binomial model, unadjusted for seasonality (Model 0)

	Coef	SE	Exp	95% CI	*p*-value
Intercept	*-1·60*	*0·09*			
Post-COVID-19 period, yes	-0·33	0·17	0·72	0·52 – 1·00	0·05
Study time elapsed, weeks	0·00	0·00	1·00	1·00 – 1·01	0·24
Doctors' strike period, yes	0·19	0·10	1·21	0·99 – 1·48	0·07
Nurses' strike period, yes	0·59	0·16	1·81	1·31 – 2·49	< 0·001

Table A5.5.3: KCH, Malawi; Results of the models with and without adjustment for seasonality

Model		BIC	Deviance†	Df	*p*-value
0	Poisson, unadjusted for seasonality	343·1	ref		
1	Poisson, cosine function with 6-month period	349·7	1·86	2	0·39
2	Poisson, cosine function with 12-month period	349·7	1·90	2	0·39
3	Poisson, mixture of two cosine functions with 6-month and 12-month periods	355·4	4·69	4	0·32

- † χ^2-test compared to Model 0.

Table A5.5.4: KCH, Malawi; Poisson model, unadjusted for seasonality (Model 0)

	Coef	SE	Exp	95% CI	*p*-value
Intercept	*-1·56*	*0·09*			
Post-COVID-19 period, yes	0·27	0·15	1·31	0·97 – 1·76	0·08
Study time elapsed, weeks	-0·00	0·00	1·00	0·99 – 1·00	0·29

APPENDIX 6: ADDITIONAL ANALYSES

Mode of delivery of admitted neonates

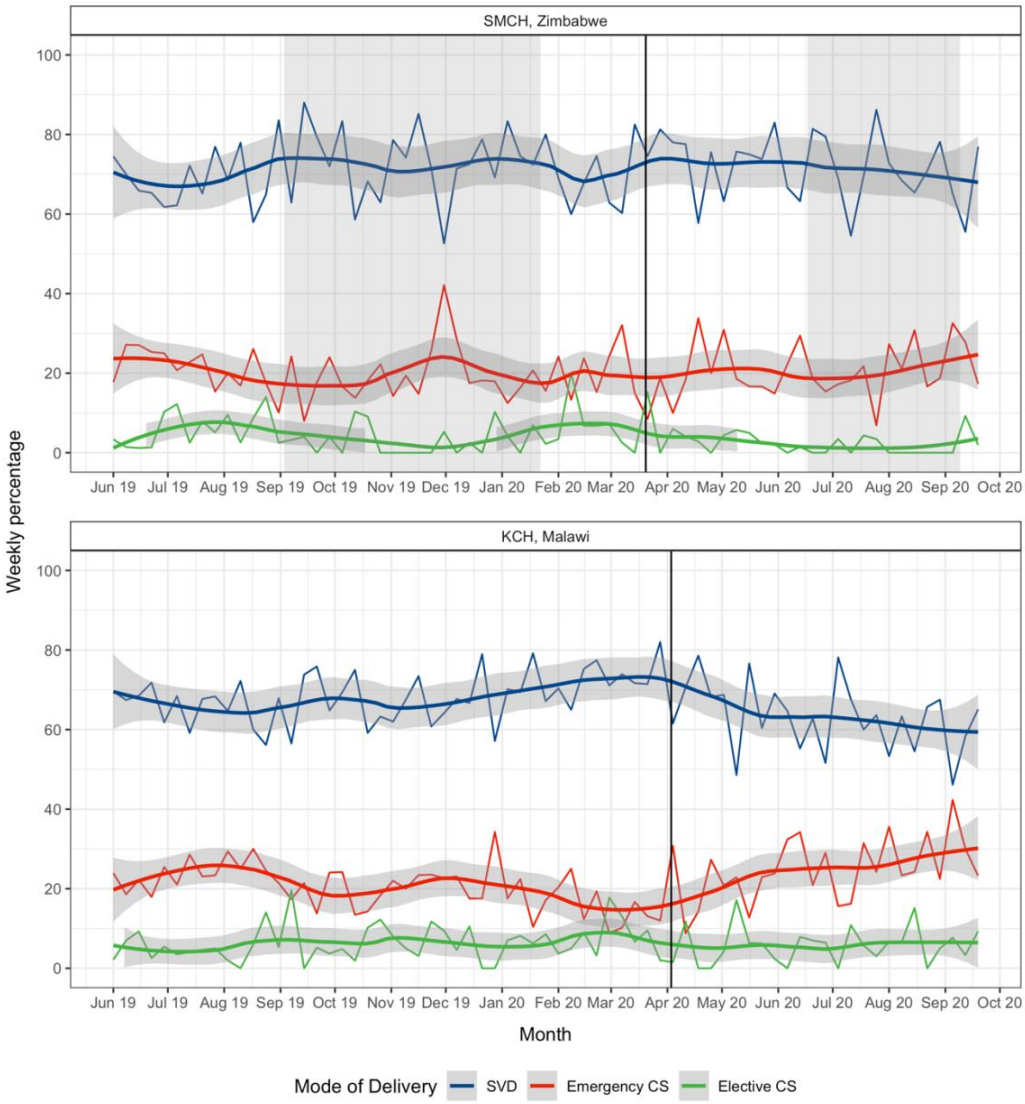


Figure A6.1.1: Trend in mode of delivery of admitted neonates per week

- Only SVD, emergency CS and elective CS displayed here to avoid overplotting.
- Smoothed line: local regression (LOESS) model; shaded region: 95% confidence interval.
- Solid vertical line: first confirmed case of COVID-19 in each country.
- Shaded periods on SMCH, Zimbabwe panel: industrial action by doctors (3 September 2019 to 22 January 2020) and nurses (17 July 2020 to 9 September 2020).
- Counts based on all admission forms completed, irrespective of match status.
- *SMCH: Sally Mugabe Central Hospital; KCH: Kamuzu Central Hospital; SVD: spontaneous vaginal delivery; CS: caesarean section*

Reason for elective caesarean section

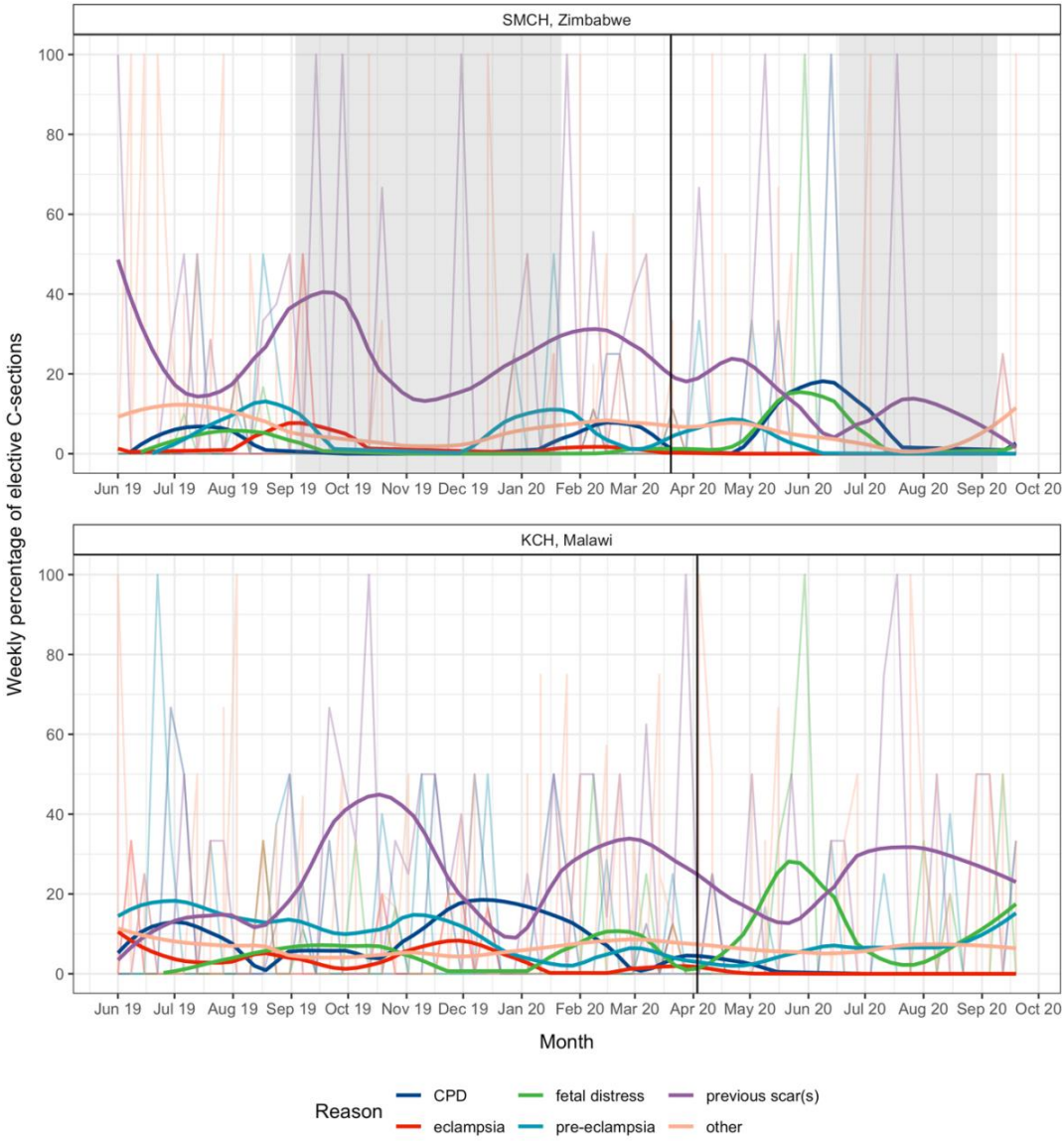


Figure A6.2.1: Trend in reason for elective caesarean section per week

- Smoothed line: local regression (LOESS) model; 95% confidence interval not presented to avoid overplotting.
- Solid vertical line: first confirmed case of COVID-19 in each country.
- Shaded periods on SMCH, Zimbabwe panel: industrial action by doctors (3 September 2019 to 22 January 2020) and nurses (17 July 2020 to 9 September 2020).
- Counts based on all admission forms completed, irrespective of match status.
- *SMCH: Sally Mugabe Central Hospital; KCH: Kamuzu Central Hospital; CPD: cephalopelvic disproportion*

Reason for emergency caesarean section

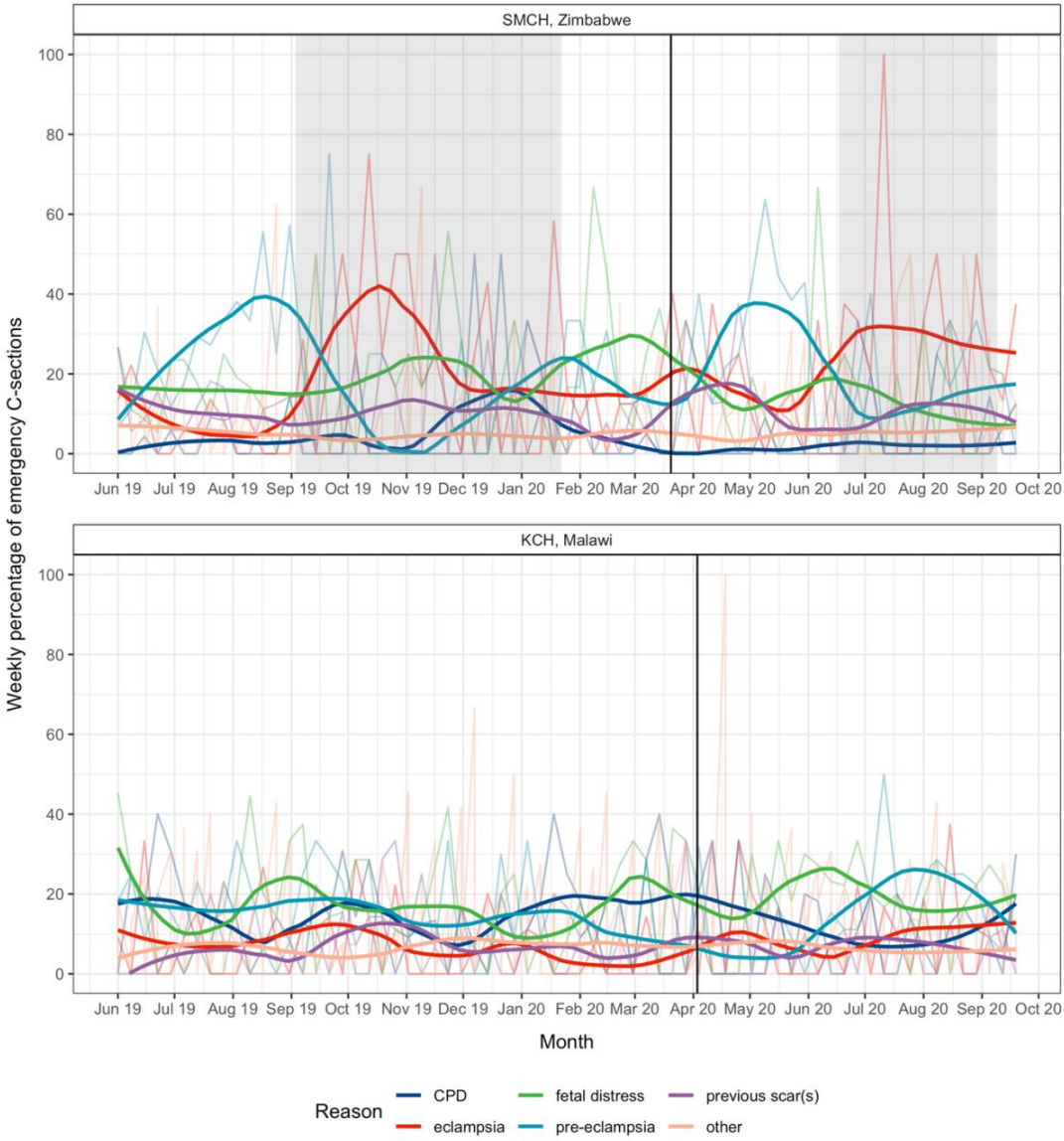


Figure A6.3.1: Trend in reason for emergency caesarean section per week

- Smoothed line: local regression (LOESS) model; 95% confidence interval not presented to avoid overplotting.
- Solid vertical line: first confirmed case of COVID-19 in each country.
- Shaded periods on SMCH, Zimbabwe panel: industrial action by doctors (3 September 2019 to 22 January 2020) and nurses (17 July 2020 to 9 September 2020).
- Counts based on all admission forms completed, irrespective of match status.
- *SMCH: Sally Mugabe Central Hospital; KCH: Kamuzu Central Hospital; CPD: cephalopelvic disproportion*