Access to primary healthcare during lockdown measures for COVID-19 in rural South Africa: an interrupted time series analysis


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Access to primary healthcare during lockdown measures for COVID-19 in rural South Africa: an interrupted time series analysis

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Abstract

Objectives
We evaluated whether implementation of lockdown orders in South Africa affected ambulatory clinic visitation in rural Kwa-Zulu Natal (KZN).

Design
Observational cohort

Setting
Data were analyzed from eleven primary healthcare clinics in northern KwaZulu-Natal.

Participants
A total of 46,523 individuals made 89,476 clinic visits during our observation period.

Exposure of Interest
We conducted an interrupted time series analysis to estimate changes in clinic visitation with a focus on transitions from the pre-lockdown to the level 5, 4, and 3 lockdown periods.

Outcome Measures
Daily clinic visitation at ambulatory clinics. In stratified analyses we assessed visitation for the following sub-categories: child health, perinatal care and family planning, HIV services, non-communicable diseases, and by age and sex strata.

Results
We found no change in total clinic visits/clinic/day at the time of implementation of the level 5 lockdown (change from 90.3 to 84.6 mean visits/clinic/day, 95%CI -16.5, 3.1), or at the transitions to less stringent level 4 and 3 lockdown levels. We did detect a greater than 50% reduction in child healthcare visits at the start of the level 5 lockdown from 11.9 to 4.7 visits/day (-7.1 visits/clinic/day, 95%CI -8.9, -5.3), both for children <1 and children 1-5, with a gradual return to pre-lockdown within three months after the first lockdown measure. In contrast, we found no drop in clinic visitation in adults at the start of the level 5 lockdown, or related to HIV care (from 37.5 to 45.6, 8.0 visits/clinic/day, 95%CI 2.1, 13.8).

Conclusions
In rural KZN, we identified a significant, albeit temporary, reduction in child healthcare visitation but general resilience of adult ambulatory care provision during the first four months of the lockdown. Future work should explore the impacts of the circulating epidemic on primary care provision and longer-term impacts of reduced child visitation on outcomes in the region.
Strengths and Limitations of the Study

- This study is strengthened by a large number of observations per clinic, collection of data using research staff and methods external to the programmatic healthcare system (which can be interrupted during external shocks), and longitudinal observation allowing comparison of the pre- and post-period
- The study was conducted within the public health sector of South Africa, and is generalizable to similarly rural, resource-limited settings, and observation during the lockdown period prior to widespread local COVID-19 transmission
- Our exposure of interest (i.e. the lockdown measures), were not randomly allocated, so there is a risk, however small, that a simultaneous exogenous shock could be responsible for the changes in clinic visitation seen
- The dataset is purely quantitative and focused on clinic visitation events, which prevents deeper exploration of the root causes of trends noted

Keywords
COVID-19, South Africa, Primary Care, Health Systems Resilience, Health and Demographic Surveillance System
Introduction

COVID-19 was declared a global pandemic by the World Health Organization on 11th March 2020, and it has spared no region of the world. Early in the epidemic, the greatest numbers of cases have been reported in Asia, Europe and North America, with more recent dissemination within Latin America and Africa. Although South Africa and a handful of other low-resource settings have reported widespread epidemics, limited testing and surveillance capabilities make it difficult to assess how widely the pandemic has spread in such settings. Such regions are believed to be at particular risk of severe epidemics, due to over-crowding, lower access to clean water and sanitation services, and inherent shortages in health system infrastructure for detection and management of disease.

In response, most nations in sub-Saharan Africa have implemented non-pharmacologic interventions to attempt to prevent large scale epidemics. These measures, which include restrictions on large gatherings, work and school attendance, travel, and in their most stringent forms, shelter-in-place orders, are believed to reduce disease transmission. However, instituting these measures is also associated with deleterious economic and social, impacts, including large projected reductions in manufacturing, access to employment and basic necessities, and educational advancement; and these effects appear to be greatest among those in lower income and vulnerability categories. Across the sub-Saharan African region, the Economic Commission for Africa projects an approximate 1.4% contraction in gross domestic product and that 25 million people are susceptible to entering extreme poverty. Some have hypothesized that non-pharmaceutical interventions might be less effective in settings with large informal economies and limited ability to respond to increases in cases of severe disease, and that their risks might outweigh their benefits.
Of particular concern is how social fear and reduced access to basic public health services might impact morbidity and mortality for non-COVID health conditions. Modeling studies have suggested that even modest reductions in child healthcare access could result in 100,000s of additional deaths in low and middle-income countries. Similar concerns have been raised by the Academy of Science of South Africa and others about provision of chronic disease care among adults. UNAIDS has warned that non-pharmaceutical interventions could challenge manufacturing and supply chains of HIV therapeutics, and modeling estimates suggest that such disruptions could cause as many if not more HIV-related deaths than COVID-19-related deaths. Although empiric data on health outcomes remain sparse, there have been significant reductions in tuberculosis testing in South Africa during the early phases of the lockdown, indicating an interruption in critical services for the most common cause of death in the country. There is also historical precedent from other recent communicable disease outbreaks. Primary healthcare access was significantly impacted during prior infectious disease epidemics, such as Ebola virus disease, resulting in increases in morbidity and mortality. Yet, whether and the extent to which similar effects will be seen during the COVID-19 epidemic is not known.

On 27th March, 2020, South Africa instituted a nationwide shelter-in-place order, termed in South Africa as a Level 5 lockdown. The level 5 order included closure of schools and all non-essential business, restrictions on public transport, and restrictions on movement. Restrictions on movement during the level 5 lockdown specifically required that individuals remain in their place of residence, with the exceptions of “performing an essential service, obtaining an essential good or service, collecting a social grant, pension, or seeking
emergency, life-saving or chronic medical attention.” Over the following months, the
restrictions gradually eased from level 5 down to 4 at the end of April and level 3 at the end
of May, which corresponded with lifting restrictions on intra-province movement,
preinitiation of public transportation, and allowed for reopening of schools and many
business. 32 33 Because the healthcare sector was deemed an essential service throughout the
entire lockdown period, no restrictions were placed on access to or delivery of healthcare
services.

We sought to assess the impact of these lockdown orders in response to the COVID-19
epidemic in South Africa on access to basic healthcare services. We analysed data on clinic
visitation at 11 ambulatory public health clinics in northern KwaZulu-Natal, collected
routinely as part of a demographic health and surveillance system (HDSS) by the Africa Health
Research Institute (AHRI). We hypothesized that there would be immediate and substantial
reductions in clinic visitation after the institution of the lockdown measure, and that this
would pertain to routine clinical care such as immunizations, perinatal care, and chronic
disease management in adults.

Methods

Study Setting

This analysis was conducted using data collected by the AHRI HDSS in the uMkhanyakude
district of the KwaZulu-Natal Province. The HDSS comprises a complete census across a
geographic area of approximately 850 km²; it is a rural region with a single peri-urban centre,
KwaMsane, a town of approximately 30,000 residents. The region ranks among the lowest
nationwide in terms of health indicators and socioeconomic status.34 Approximately 1 in 5
adult men and 2 in 5 adult women are living with HIV. Tuberculosis incidence is among the highest in the world, and above the national average of 577 per 100,000 individuals when last measured in 2015.

Data Collection

Since 2000 AHRI has collected data on births, deaths, migrations through thrice annual data collection encounters across a catchment area of 20,000 households (over 100,000 resident individuals). In 2017, AHRI began placing clinic research assistants at each of the 11 government-run public health clinics in the area. These research staff operate in partnership with the Department of Health, but outside of the standard Health Management Information System (HMIS). For each person who presents to clinic, they collect demographic information and the self-reported reason(s) for the clinical visit. We link data between the HDSS and the clinic medical record system electronically using a unifying identification code for each resident of the catchment area. For this analysis, we included all individuals who presented to ambulatory clinic in the 11 regional clinics in the study catchment area during our observation period. There were no age or sex exclusions. AHRI holds memoranda of understanding with the Provincial and District Department of Health that permit extraction of health record data from primary care and hospital sites for linkage to the household surveillance dataset.

Study Design

We conducted an interrupted time series analysis to estimate changes in clinic visitation in rural KwaZulu-Natal from before to after the national lockdown implementation on 27th March 2020. To do so we fitted linear mixed effects regression models by restricted
maximum likelihood with daily clinic visits as the primary outcome of interest. Our primary exposure of interest was time period, divided into four periods: 1) the pre-lockdown period starting 60-days prior to the initial level 5 lockdown until 27th March 2020; 2) the level 5 lockdown period from 28th March through 30th April 2020; 3) the level 4 lockdown level from 1st of May through 31st of May; and 4) the level 3 lockdown level from 1st of June through our data abstraction date (30th of June). For our primary outcome, we estimated the stepwise change in mean visits per clinic on the date of implementation lockdown level.37 We included a fixed effect for day of the week, a random clinic-specific intercepts, and random clinic-specific slopes on time in our models. We excluded weekends because the study clinics do not provide non-urgent ambulatory care services on weekends. We excluded dates from observation when AHRI staff members who perform data capture for the Clinic-link system were not working, including national holidays and staff trainings.

Our primary outcome of interest was the number of clinic visits for any reason per clinic. In secondary analyses, we stratified models by visit type restricted to: 1) child health visits (immunizations and growth monitoring); 2) antenatal care, postnatal care, and family planning; 3) HIV services (including antiretroviral therapy initiation, antiretroviral therapy continuation, and chronic care medical dispensing program visits); and 4) chronic care of non-communicable diseases (hypertension and diabetes). Clinic visits for more than one reason were treated as visits for both conditions. We also conducted stratified analyses by age category (<1, 1-5, 6-19, 20-45, and >45 years old) and by women and men aged 15 years or older.
We performed a number of secondary and sensitivity analyses to assess model validity and robustness of our findings. In addition to estimating stepwise changes after each lockdown order and change, we estimated trends in weekly visits during each period to determine whether immediate changes were sustained over each period. We graphically depicted the residuals in the model to assess the normality assumption of our linear model structure. To check the robustness of model assumptions about changes from the pre-lockdown to the level 5 lockdown periods, we conducted multiple sensitivity analyses: 1) we specified a Poisson mixed effects regression model in place of a linear model; 2) we fitted linear and Poisson generalized estimating equation (GEE) models clustered by facility; 3) we specified an auto-regressive covariance structure in place of an exchangeable structure in the GEE models; and 4) to assess for the possibility of seasonal changes over multiple years, we constructed LOWESS plots to visually inspect clinical visitation trends over the same observation periods in 2020 versus 2018 and 2019 and fitted a difference-in-differences model that included year (2019 versus 2020) and time (characterized as pre-lockdown versus level 5 lockdown) to assess whether changes before and after the level 5 lockdown differed by calendar year.

Finally, we conducted an additional sensitivity analysis to assess for the possibility of in-migration into the HDSS catchment area during the lockdown period, which would potentially bias clinic visitation frequency upwards. To do so, we calculated annual visitation frequency at the 11 area clinics for each individual in the dataset for the year prior to the lockdown. We then compared the median number of annual visits per individual in the pre- and post-lockdown periods, and the number of individuals with exactly one visit in the past year in the two periods. If significant in-migration did occur during the lockdown period, we
would expect that the median number of annual visits per individual would decrease during
the lockdown, whereas the number of individuals with one visit in the past 12 months would
increase.

Three study investigators designed a statistical plan prior to all analyses (MJS, JDK, MJM). The
initial analysis plan included fitting mixed effects models with random effects by clinic and
inspecting trends in clinic visitation changes from the pre- to level 5 lockdown period for the
overall cohort, and by visit sub-type. We also initially included plans for sensitivity analyses,
including fitting of generalized estimating equations and additions of random slopes to our
models as robustness checks. In response to reviewer requests and with updates to the
lockdown characteristics from levels 5 to 4 to 3 during the review process, we conducted a
number of post-hoc analyses, including construction of LOWESS plots and fitting additional
models to assess for seasonal trends in visitation by year, and fitting mixed effects Poisson
models. All statistical analyses were conducted using Stata and R.

Patient and Public Involvement

This protocol was reviewed and approved by the AHRI Community Advisory Board, who
contributed to the study design and selection of collection measures. Results of studies from
the HDSS project are routinely shared with the community through public communications
and road shows conducted by the AHRI Public Engagement Department. Final, all study
protocols are reviewed and approved by the District and Provincial Department of Health,
and AHRI holds memoranda of understanding with the Provincial and District Departments of
Health that outline methods of extraction of health record data from primary care sites for linkage to the household surveillance dataset.

Ethical Approval

The protocol was reviewed and approved by the University of KwaZulu-Natal Biomedical Research Ethics Committee under reference BE290/16 and the KwaZulu Department of Health Research Committee.

Results

A total of 46,523 individuals made 89,476 clinic visits between 27th January – 30th June 2020 at the 11 area clinics (Table 1). Women and girls accounted for 67% (n=64,125) of visits. Approximately 9% of visits were made by individuals less than 1 year old (n=4,186), 1-5 year old (n=3,944), and 6-19 years old (n=4,460), respectively; whereas those 20-45 years accounted for 48% (n=22,231) and those over 46 the remaining 25% of visits (n=11,702). The most common reason for a clinic visit was ART follow-up care, comprising 43% of all visits (n=38,142), followed by visits for minor ailments (18%, n=16,204), child health (n=9,672, 11%) and hypertension (n=9,273, n=10%).

There was an average of 90.3 (95%CI 67.5, 113.2) clinic visits per day per clinic in the pre-lockdown period. We identified a non-significant drop in visits immediately following the start of the level 5 lockdown (-6.7 visits/clinic/day, 95%CI -16.5, 3.1). The small reduction seen after the level 5 period was reversed by a non-significant stepwise increase between the level 5 and level 4 periods (increase of 11.2 visits/clinic/day, 95%CI -0.5, 23.0), and persistent clinic visitation between the end of level 4 and the start of the level 3 period.
There were no significant changes in trends over time in clinic visits/week in any of the pre- or post-implementation periods (Supplemental Table 1).

In contrast, child health visits suffered a 60% stepwise drop at the initiation of the level 5 lockdown (from 11.9 to 4.6 visits/day/clinic, mean change of -7.1 visits, 95%CI -9.0, -5.3), but remained steady during the transition between the level 5 and level 4 (-0.5 visits/clinic/day, 95%CI -2.7, 1.7), and again between the level 4 and level 3 lockdowns (-0.4 visits/clinic/day, 95%CI -2.5, 1.6) (Table 2, Figure 1). The reduction in child visits at the time of the level 5 lockdown occurred both among children under 1 (mean decrease of -5.4 visits, 95%CI -7.0, -3.7) and those 1-5 years old (mean decrease of -5.5 visits, 95%CI -6.7, -4.4). We did detect fluctuating trends in child visitation during the lockdown periods, with increases of approximately 1 visit/clinic/week in levels 5 and 3, resulting in a similar number of mean visits/clinic/day one month into the level 3 lockdown on 30th June as compared to just prior to the level 5 lockdown (11.2 visits/clinic/day [95%CI 7.4, 14.8] vs 11.9 visits/clinic/day [95%CI 8.6, 15.1], Supplemental Table 1).

In contrast to child health visits, HIV-related clinical visits for adults did not decrease between the pre-lockdown and level 5 lockdown period from 37.6 visits/clinic/day to 45.5 visits/clinic/day (mean change of 7.9 visits/clinic/day, 95%CI 2.1, 13.8), between the level 5 lockdown and level 4 lockdown period (increase of 11.1 clinic/visits/day, 95%CI 4.1, 18.0), or between the transition from the level 4 to level 3 (increase of 4.0 visits/clinic/day, 95%CI 2.5, 10.5) (Table 2, Figure 1). We similarly identified resilience in family planning visits over the observation period, increasing from 7.3 visits/clinic/day in the pre-implementation period to
7.8 visits/clinic/day after transition to level 5 (+0.5 visits/clinic/day, 95%CI -1.0, 2.0) to 8.9 clinic visits/day after transition to level 4 (+1.1 visits/clinic/day, 95%CI -0.7, 3.0) and 11.0 visits/clinic/day after transition to level 3 (+2.0 visits/clinic/day, 95%CI 0.3, 3.7) for a 66% total increase from the pre-period. We did not detect changes in clinic visitation for chronic non-communicable diseases, or more broadly in clinic visitation by men or women 15 years or older.

Graphical depictions of residuals from our linear models demonstrated normally distributed residuals for the total visit, HIV, and child visit models, supporting the specification of a linear model to estimate trends in clinic visitation (Supplemental Figure 1). We found no evidence of changes in clinic visitation during this same period in 2019 to suggest seasonal effects, either graphically in LOWESS plots, or in difference-in-differences in models including both 2019 and 2020 with pre and post-lockdown periods (Table 3, Supplemental Figure 2). Results were robust to modelling assumptions in the sensitivity analyses (Table 3).

Finally, we did not detect evidence of meaningful in-migration during the lockdown period. The median number of visits in the past year per individual attending the clinic slightly increased from the pre-lockdown period to the lockdown period (mean 5.8 [SD 0.02] vs. 5.9 [SD 0.03], P<0.001). This pattern was similar among people attending clinic for HIV-specific visits (mean 6.5 [SD 0.02] vs mean 6.6 [SD 0.04], P=0.01). The number of people with exactly one visit in the past year also did not meaningfully increase during the observation period with 1,960 (February), 2,115 (March), 1,573 (April), 1,893 (May), and 1,986 (June) visits made by individuals with exactly one annual clinic visit over the prior 12 months.
We found evidence of a significant drop in visits for childcare alongside sustained visitation in HIV and adult ambulatory clinic utilization in a rural area of South Africa during the national lockdown for the COVID-19 epidemic. Notably, visits for chronic disease, such as hypertension and diabetes, perinatal care and family planning remained reasonably constant or modestly increased. However, child health visits for immunizations and growth monitoring dropped immediately by over 50% after the start of the lockdown. With gradual increases over time during level 5 and level 3 lockdown, child visits largely returned to pre-lockdown levels in June, approximately 3 months after the lockdown began. We noted an estimated 20% increase in clinic visits for HIV immediately after the lockdown and suspect this might have reflected an urgency to collect medications prior to an anticipated interruption in clinic access or medication availability and/or national programmatic efforts to accelerate transitions to a new first-line regimen. These results demonstrate concerning trends about reductions in preventative child care during the lockdown period. However, they also appeared to disprove our hypothesis about clinic visitation in adults, and potentially demonstrate a resilience in the healthcare sector during a period of concern for access to chronic and essential basic health services.

The key demographic population in our study that experienced significant drops in clinic visitation was children. Child health visits appeared to have modestly rebounded during the lockdown, and eventually return to their pre-lockdown state. Although these data do not suggest the cause of reduced visitation in children, multiple possible factors might be considered. We hypothesize that limited options for childcare for families with multiple children might prevent caregivers from being able to bring individual children to clinic.
Moreover, in contrast to, for example, HIV wellcare visits, well child visits rarely involve medication refills so might be prioritized lower for families. Whatever the cause, our findings are in keeping with data from elsewhere. In Hangzhou, China, pediatric healthcare visits dropped by nearly 75% during the peak of the epidemic and lockdown periods. In the U.S. vaccination rates in children substantially declined after a national emergency was declared in response to the COVID-19 epidemic. Modeling analyses using Lived Saves Tool (LiST) have suggested that a 15% reduction in maternal and child health coverage could result in over 250,000 additional deaths. The World Health Organization has also projected significant increases in deaths due to malaria in children under 5 in endemic regions with disruptions in malaria care and insecticide treated bednet distribution. Although empiric data on healthcare access in South Africa remain scarce, work to date has suggested significant reductions in tuberculosis testing in laboratory databases, and reports of interruptions in care in community-based surveys. Previous disease epidemics in sub-Saharan Africa have also been associated with lapses in primary care access, and drops in facility based births and child healthcare access. Consequently, future work should investigate the impacts of even modest drops in vaccination rates and child health outcomes, to better assess whether the drop we identified resulted in longer term health effects, and whether catch-up vaccination campaigns might help limit the fallout of such interruptions.

Maintaining healthcare access during the epidemic requires a careful balance of primary healthcare provision and protection of vulnerable populations from COVID-19 infection. In other settings, there have been multiple reports of late and severe presentations to care for non-COVID-19 conditions, putatively due to decreased access to care or fear of nosocomial infection at healthcare facilities. At the time of our data abstraction at the end of June
during the level 3 lockdown period, fewer than 200 cases of COVID-19 infection had been reported in uMkhanyakude District.\textsuperscript{49} Thus, our data largely reflect impacts of lockdown measures prior to an epidemic with significant local transmission. Clinics in this district instituted symptom screening at the entryway to clinics, with referral of individuals meeting criteria for persons under investigation to regional COVID-19 testing centres. Future work should revisit the impacts of the epidemic itself on access to primary healthcare.

The COVID-19 epidemic has also led to calls for decentralized care to minimize exposure for high-risk populations,\textsuperscript{50} including those with chronic non-communicable disease, HIV, a history of tuberculosis-related lung disease, and those of older-ages. The lockdown was instituted rapidly in South Africa, before substantial decentralized care systems could be put in place. However, an important unanswered question is how such programs will affect access to care and epidemic transmission in high-risk populations, including the elderly and those with immunosuppressing conditions.

Our study should be interpreted within the context of the relatively short period (3 months) of the lockdown in South Africa. As a result, we are not yet able to assess longer-term repercussions from disruptions to income or from the epidemic itself, or longer-term effects of lapses in primary care and vaccination on health outcomes, and our results should not be generalized over longer time horizons. It is expected that economic barriers to healthcare utilization will increase as the epidemic’s effects persist over time, including secondary effects from non-pharmaceutical interventions. These effects are likely to fall most heavily on those in the informal economy.\textsuperscript{51} South Africa has taken steps to increase social support to counteract economic disruption from the epidemic and control measures.\textsuperscript{52}
longer-term consequences may require governments and development partners to increase access to employment and other social support services during the epidemic.

Our study had multiple strengths. First, our data collection procedures are led by research staff who remained in place during the lockdown period, so these data are not affected by barriers to data collection (e.g., interruptions in staff transportation or workplace access). This is important, since many routine health information systems could be expected to suffer lapses during external shocks to the healthcare system. Second, our study was able to access data collected across 11 clinical centres within a large HDSS, which provided significant power to detect even small interruptions to health care access. A key potential limitation to our study is that it is predicated on the assumption that there were no other external factors that would have caused interruptions to the health care system on or after 27th March 2020 (e.g., power outage, inclement weather). We are unaware of any such shock and believe this to be a minor risk. We saw no evidence of a seasonal effect after comparing our results to similar time periods in 2019. Our analysis should also be interpreted within the context of our study area – one with approximately 200 reported cases of COVID-19 at the time of the analysis, but in a nation with a large epidemic (approximately 200,000 cases as of early July) with established local transmission in other areas.

In summary, we report a reduction in child wellcare visitation but resilience of the adult ambulatory health care system during the early COVID-19 epidemic and lockdown period in rural South Africa. Future work should establish if these trends are maintained, and particularly monitor access to childcare and immunizations as a result of the trends reported in this study. Finally, in rural South Africa and similar areas, efforts to balance ongoing
provision of essential preventative and chronic healthcare services might be needed to ensure healthcare access remains intact while preventing nosocomial spread of COVID-19 among high-risk populations.
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<th>Male n (%)</th>
<th>Female n (%)</th>
<th>&lt;1 year n (%)</th>
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<th>6-19 years n (%)</th>
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<td>(4.9%)</td>
<td>(17.2%)</td>
<td>(14.0%)</td>
<td>(39.6%)</td>
<td>(24.3%)</td>
</tr>
<tr>
<td><strong>All other visits</strong></td>
<td>18,043</td>
<td>6,378</td>
<td>11,658</td>
<td>842</td>
<td>2,222</td>
<td>3,112</td>
<td>8,390</td>
<td>3,477</td>
</tr>
<tr>
<td></td>
<td>(20.2%)</td>
<td>(35.4%)</td>
<td>(64.6%)</td>
<td>(4.7%)</td>
<td>(12.3%)</td>
<td>(17.3%)</td>
<td>(46.5%)</td>
<td>(19.3%)</td>
</tr>
</tbody>
</table>

*Visit types are not mutually exclusive so column totals may exceed 100%

aPNC and FP: Perinatal care and family planning; visits for, antenatal care, prenatal care, and/or family planning

bHIV visits: visits for HIV testing, antiretroviral therapy initiation, antiretroviral therapy continuation, or pharmacy pick-up

C Chronic care: visits for hypertension and/or diabetes
Table 2. Mixed effects regression model results demonstrating changes in mean visits/clinic, by visit type and demographic strata, in the pre-lockdown period, and after each transition to level 5, level 4, and level 3 lockdowns in uMkhanyakude District, KwaZulu-Natal South Africa.

<table>
<thead>
<tr>
<th>Model</th>
<th>Mean daily visits per clinic at time of lockdown period (intercept)</th>
<th>Stepwise change in visits/clinic/day at start of level 5 lockdown</th>
<th>P-value</th>
<th>Stepwise change in visits/clinic/day at start of level 4 lockdown</th>
<th>P-value</th>
<th>Stepwise change in clinic visits/clinic/day at start of level 3 lockdown</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total visits</td>
<td>90.3 (67.1, 113.5)</td>
<td>-6.7 (-16.4, 3.0)</td>
<td>0.18</td>
<td>11.3 (-0.3, 22.9)</td>
<td>0.06</td>
<td>1.2 (-9.6, 12.0)</td>
<td>0.83</td>
</tr>
<tr>
<td>Child health(^a)</td>
<td>11.9 (8.6, 15.1)</td>
<td>-7.1 (-8.9, -5.3)</td>
<td>&lt;0.001</td>
<td>-0.5 (-2.6, 1.6)</td>
<td>0.65</td>
<td>-0.4 (-2.4, 1.6)</td>
<td>0.67</td>
</tr>
<tr>
<td>PNC and FP(^b)</td>
<td>7.3 (4.2, 10.3)</td>
<td>0.5 (-1.0, 2.0)</td>
<td>0.51</td>
<td>1.1 (-0.7, 2.9)</td>
<td>0.22</td>
<td>2.0 (0.3, 3.7)</td>
<td>0.02</td>
</tr>
<tr>
<td>HIV visits(^c)</td>
<td>37.5 (24.4, 50.7)</td>
<td>8.0 (2.3, 13.7)</td>
<td>0.01</td>
<td>11.0 (4.2, 17.8)</td>
<td>0.001</td>
<td>4.0 (-2.3, 10.3)</td>
<td>0.22</td>
</tr>
<tr>
<td>Chronic care(^d)</td>
<td>9.5 (7.1, 11.8)</td>
<td>-0.3 (-1.9, 1.3)</td>
<td>0.70</td>
<td>-0.15 (-2.1, 1.8)</td>
<td>0.88</td>
<td>0.4 (-1.4, 2.2)</td>
<td>0.65</td>
</tr>
<tr>
<td>Men ≥ 15</td>
<td>15.4 (10.8, 19.9)</td>
<td>1.5 (-0.7, 3.6)</td>
<td>0.17</td>
<td>2.3 (-0.2, 4.9)</td>
<td>0.07</td>
<td>0.8 (-1.5, 3.2)</td>
<td>0.50</td>
</tr>
<tr>
<td>Women ≥ 15</td>
<td>52.9 (38.1, 67.7)</td>
<td>3.2 (-3.3, 9.6)</td>
<td>0.33</td>
<td>9.6 (1.9, 17.3)</td>
<td>0.01</td>
<td>2.1 (-5.1, 9.3)</td>
<td>0.57</td>
</tr>
<tr>
<td>Age &lt;1</td>
<td>10.6 (7.6, 13.5)</td>
<td>-5.3 (-6.9, -3.7)</td>
<td>&lt;0.001</td>
<td>0.2 (-1.6, 2.1)</td>
<td>0.83</td>
<td>-0.4 (-2.1, 1.4)</td>
<td>0.67</td>
</tr>
<tr>
<td>Age 1-5</td>
<td>8.9 (7.4, 10.5)</td>
<td>-5.6 (-6.7, -4.4)</td>
<td>&lt;0.001</td>
<td>-0.2 (-1.5, 1.1)</td>
<td>0.80</td>
<td>-0.8 (-2.1, 0.4)</td>
<td>0.18</td>
</tr>
<tr>
<td>Age 6-19</td>
<td>8.0 (6.2, 9.8)</td>
<td>-0.7 (-1.9, 0.6)</td>
<td>0.29</td>
<td>1.5 (0.0, 3.0)</td>
<td>0.05</td>
<td>-0.1 (-1.5, 1.3)</td>
<td>0.91</td>
</tr>
<tr>
<td>Age 20-45</td>
<td>39.3 (26.3, 52.2)</td>
<td>4.4 (-0.7, 9.5)</td>
<td>0.09</td>
<td>7.5 (1.4, 13.6)</td>
<td>0.02</td>
<td>2.2 (-3.5, 7.8)</td>
<td>0.45</td>
</tr>
<tr>
<td>Age &gt;45</td>
<td>25.2 (19.2, 31.3)</td>
<td>0.4 (-3.0, 3.7)</td>
<td>0.83</td>
<td>2.9 (-1.1, 6.9)</td>
<td>0.15</td>
<td>0.5 (-3.2, 4.3)</td>
<td>0.78</td>
</tr>
</tbody>
</table>

\(^a\) Child health: visits for immunizations and growth monitoring  
\(^b\) PNC and FP: perinatal care and family planning; visits for, antenatal care, prenatal care, and/or family planning  
\(^c\) HIV visits: visits for HIV testing, antiretroviral therapy initiation, antiretroviral therapy continuation, or pharmacy pick-up  
\(^d\) Chronic care: clinical visits for hypertension and/or diabetes
**Table 3.** Sensitivity analyses, demonstrating results of the main regression model and alternate models.

<table>
<thead>
<tr>
<th></th>
<th>Mean daily visits per clinic at time of lockdown period</th>
<th>Stepwise change in clinic visits/day at start of level 5 lockdown</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All Visits</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary model</td>
<td>90.3 (67.1, 113.5)</td>
<td>-6.7 (-16.4, 3.0)</td>
<td>0.18</td>
</tr>
<tr>
<td>Poisson(^a) mixed effects model</td>
<td>92.0 (59.3, 124.7)</td>
<td>-6.9 (-11.0, -2.8)</td>
<td>0.001</td>
</tr>
<tr>
<td>Linear GEE (exchangeable correlation matrix)</td>
<td>89.2 (67.0, 111.4)</td>
<td>-6.4 (-16.8, 4.08)</td>
<td>0.23</td>
</tr>
<tr>
<td>Poisson GEE(^a) (exchangeable correlation matrix)</td>
<td>89.2 (84.7, 93.6)</td>
<td>-6.6 (-8.7, -4.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Linear GEE (autoregressive correlation matrix)</td>
<td>90.2 (73.2, 107.2)</td>
<td>-5.4 (-27.4, 16.6)</td>
<td>0.63</td>
</tr>
<tr>
<td>Poisson GEE(^a) (autoregressive correlation matrix)</td>
<td>88.4 (85.0, 91.9)</td>
<td>-5.0 (-9.4, -0.6)</td>
<td>0.03</td>
</tr>
<tr>
<td>Difference-in-Differences(^b)</td>
<td>96.3 (63.6, 129.0)</td>
<td>3.4 (-5.5, 12.4)</td>
<td>0.45</td>
</tr>
<tr>
<td><strong>Childcare Visits</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary model</td>
<td>11.9 (8.6, 15.1)</td>
<td>-7.1 (-8.9, -5.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Poisson(^a) mixed effects model</td>
<td>12.3 (7.1, 17.5)</td>
<td>-7.7 (-11.1, -4.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Linear GEE (exchangeable correlation matrix)</td>
<td>11.8 (8.6, 15.0)</td>
<td>-7.1 (-9.0, -5.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Poisson GEE(^a) (exchangeable correlation matrix)</td>
<td>12.0 (10.5, 13.5)</td>
<td>-7.5 (-8.4, -6.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Linear GEE (autoregressive correlation matrix)</td>
<td>11.9 (9.5, 14.4)</td>
<td>-6.4 (-9.9, -2.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Poisson GEE(^a) (autoregressive correlation matrix)</td>
<td>11.9 (10.7, 13.1)</td>
<td>-6.7 (-8.1, -5.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Difference-in-Differences(^b)</td>
<td>11.8 (8.0, 15.7)</td>
<td>-4.0 (-5.5, -2.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>HIV Visits</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary model</td>
<td>37.5 (24.4, 50.7)</td>
<td>8.0 (2.3, 13.7)</td>
<td>0.01</td>
</tr>
<tr>
<td>Poisson(^a) mixed effects model</td>
<td>39.2 (22.7, 55.8)</td>
<td>9.0 (4.5, 13.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Linear GEE (exchangeable correlation matrix)</td>
<td>37.7 (25.3, 50.1)</td>
<td>8.1 (2.2, 14.0)</td>
<td>0.007</td>
</tr>
<tr>
<td>Poisson GEE(^a) (exchangeable correlation matrix)</td>
<td>37.7 (34.8, 40.6)</td>
<td>8.7 (7.2, 10.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Linear GEE (autoregressive correlation matrix)</td>
<td>38.9 (29.3, 48.5)</td>
<td>6.1 (-6.2, 18.5)</td>
<td>0.33</td>
</tr>
<tr>
<td>Poisson GEE(^a) (autoregressive correlation matrix)</td>
<td>37.9 (35.7, 40.1)</td>
<td>5.7 (2.6, 8.8)</td>
<td>0.002</td>
</tr>
<tr>
<td>Difference-in-Differences(^b)</td>
<td>43.6 (25.1, 62.1)</td>
<td>4.8 (-0.5, 10.1)</td>
<td>0.08</td>
</tr>
</tbody>
</table>

GEE: generalized estimating equations

\(^a\)Poisson GEE results are presented as predictive margins and marginal effects so they represent changes on the same additive scale as the linear models.

\(^b\)Difference-in-differences estimates are estimated as the mean of the level 5 lockdown period minus the mean of the pre-lockdown period, comparing 2020 to 2019. Estimates are based on a period-by-year interaction term fit via linear mixed models.
**Figure Legends**

**Figure 1.** Ambulatory clinic visitation before and after the nationwide lockdown in South Africa at eleven outpatient clinics in rural uMkhanyakude District, KwaZulu-Natal South Africa. Scatterplots represent mean clinic visitation at each clinic on weekdays during the observation period. The black fit line represents the mean visitation across all clinics estimated by post-regression margins from a linear regression model, with a regression discontinuity coefficient at the date of the lockdown (27th March 2020, red line). Gray bars represent 95% confidence intervals. The dotted blue line represents the geometric mean of the number of visits across all clinics on each day.

**Supplemental Figure 1.** Plots of residuals around estimated mean from linear mixed effects regression models of clinic visitation for total visits (A), child health visits (B), and HIV visits (C).

**Supplemental Figure 2.** Scatter and LOWESS plots with smoothed regression functions demonstrating clinic visits per day in the study observation period during 2019 and 2020 for all visits (A), child health visits (B), and HIV adults (C).
# Author contributions

<table>
<thead>
<tr>
<th>Contributor Role</th>
<th>Role Definition</th>
<th>MJS, MJM, JDK, GH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conceptualization</td>
<td>Ideas; formulation or evolution of overarching research goals and aims.</td>
<td>MJS</td>
</tr>
<tr>
<td>Data Curation</td>
<td>Management activities to annotate (produce metadata), scrub data and maintain research data (including software code, where it is necessary for interpreting the data itself) for initial use and later reuse.</td>
<td>DG, KH</td>
</tr>
<tr>
<td>Formal Analysis</td>
<td>Application of statistical, mathematical, computational, or other formal techniques to analyze or synthesize study data.</td>
<td>MJS, MJM, JDK, GH</td>
</tr>
<tr>
<td>Funding Acquisition</td>
<td>Acquisition of the financial support for the project leading to this publication.</td>
<td>KH, WH</td>
</tr>
<tr>
<td>Investigation</td>
<td>Conducting a research and investigation process, specifically performing the experiments, or data/evidence collection.</td>
<td>KH, MJS, CI MS</td>
</tr>
<tr>
<td>Methodology</td>
<td>Development or design of methodology; creation of models.</td>
<td>KH, MJS</td>
</tr>
<tr>
<td>Project Administration</td>
<td>Management and coordination responsibility for the research activity planning and execution.</td>
<td>KH, JS, MS, NN, NM</td>
</tr>
<tr>
<td>Resources</td>
<td>Provision of study materials, reagents, materials, patients, laboratory samples, animals, instrumentation, computing resources, or other analysis tools.</td>
<td>KH</td>
</tr>
<tr>
<td>Software</td>
<td>Programming, software development; designing computer programs; implementation of the computer code and supporting algorithms; testing of existing code components.</td>
<td>KH, DG</td>
</tr>
<tr>
<td>Supervision</td>
<td>Oversight and leadership responsibility for the research activity planning and execution, including mentorship external to the core team.</td>
<td>KH, MS, TM, PG, SD</td>
</tr>
<tr>
<td>Validation</td>
<td>Verification, whether as a part of the activity or separate, of the overall replication/reproducibility of results/experiments and other research outputs.</td>
<td>KH</td>
</tr>
<tr>
<td>Visualization</td>
<td>Preparation, creation and/or presentation of the published work, specifically visualization/data presentation.</td>
<td>KH, MJS</td>
</tr>
<tr>
<td>Writing – Original Draft Preparation</td>
<td>Creation and/or presentation of the published work, specifically writing the initial draft (including substantive translation).</td>
<td>MJS, JDK</td>
</tr>
<tr>
<td>Writing – Review &amp; Editing</td>
<td>Preparation, creation and/or presentation of the published work by those from the original research group, specifically critical review, commentary or revision – including pre- or post-publication stages.</td>
<td>KH, MJS, MJM, JS, DG, GH, EW, JDK, CI, MS, NN, TM, PG, SD, WH, NM</td>
</tr>
</tbody>
</table>

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Transparency declaration
MJS affirms the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as originally planned (and, if relevant, registered) have been explained.

Data sharing
Data from the AHRI HDSS are publicly available upon request to the AHRI research repository which can be made here: https://data.africacentre.ac.za/index.php/auth/login/?destination=

Competing interests and conflicts of interest
All authors have completed the ICMJE uniform disclosure form and declare no financial relationships with any organisations that might have an interest in the submitted work in the previous three years and no other relationships or activities that could appear to have influenced the submitted work.

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References


