# COVID-19 SPECIAL PUBLIC HEALTH SURVEILLANCE BULLETIN

NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES
Division of the National Health Laboratory Service

VOLUME 18. SUPPLEMENTARY ISSUE 4 16 SEPTEMBER 2020


## FOREWORD

The incidence of tuberculosis (TB) in South Africa is especially high. Critical to the control and management of TB is universal testing of all individuals with indicator symptoms. This approach has been severely impacted by the COVID-19 pandemic, primarily because of lockdown restrictions. Data and modelled projections described in this report show how the implementation of Level 5 restrictions resulted in a sudden and dramatic decrease in laboratory investigations for TB across all of South Africa's provinces. These unintended consequences are expected to negatively affect the country's TB control programmes going forward.

This is the fourth special issue of our COVID-19 series. We trust readers will find these publications useful and informative against the backdrop of the ongoing COVID-19 pandemic and easing of restrictions.

**Prof Basil Brooke, Editor**

# IMPACT OF COVID-19 AND PUBLIC HEALTH RESTRICTIONS ON TB TESTING AND CASE DETECTION IN SOUTH AFRICA

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## Summary

The COVID-19 pandemic and associated public health restrictions have disrupted routine health services, including tuberculosis (TB) services, in many countries. The impact of the COVID-19 epidemic and public health restrictions on laboratory investigations and diagnosis of TB in South Africa was therefore investigated. Segmented linear regression models for each level of the COVID-19 lockdown restrictions were fitted to testing rates per 100,000 population at national and provincial levels. Using historical laboratory data from 2018 and 2019 we forecast Xpert TB testing volumes, Xpert positive tests, positivity rate and rifampicin resistant tests that could have been expected in each month of 2020 in the absence of the COVID-19 pandemic and associated restrictions. The implementation of Level 5 restrictions resulted in a sudden and dramatic drop in laboratory investigations for TB across all South Africa's provinces. It is estimated that 308,000 fewer TB Xpert tests were conducted, and 17,700 fewer positive samples detected, between the beginning of April and end of July as a result of COVID-19.

## Background

South Africa (SA) carries a disproportionate burden of tuberculosis (TB) per capita and is therefore listed in all three categories of priority countries by the World Health Organization (TB, TB/HIV and RR-MDR-TB). The estimated number of incident TB cases in SA for 2018 was 301 000 while the estimated number of deaths due to TB in the same year was 63 000.[1] Significant progress has been made in improving the diagnosis of TB in the country with universal testing of all individuals with symptoms suggestive of TB (cough, fever etc.). This is done using the Xpert MTB/RIF Ultra (Xpert) assay with which >2 million individuals are tested annually in South Africa.[2] This assay is highly sensitive in detecting TB and also tests for rifampicin resistant TB. The introduction of new and repurposed drugs to treat drug resistant TB has had a significant impact on improving outcomes and reducing mortality due to drug resistant TB. The overall burden of TB and drug resistant TB has shown positive signs with annual declines in incidence.[3]

The first confirmed case of COVID-19 in South Africa was reported on 5 March 2020. In mid-March social distancing measures, including restrictions on international travel, mass gatherings and school closures, were instituted to slow transmission of SARS-CoV-2 and prepare the health care system. A Level 5 national lockdown, which confined all but essential workers to their dwellings and imposed severe restrictions on all non-essential movement, commenced on 27 March 2020.[4] Restrictions have gradually been relaxed, transitioning to level 4 restrictions on 1 May, Level 3 on 1 June, and Level 2 on 18 August.[5] At time of writing 625,000 cases and 14,000 COVID-19 deaths have been confirmed in South Africa.[6] Weekly mortality reports however indicate that the COVID-19 death toll may be substantially higher, with an estimated 39,087 excess deaths having occurred between 6 May and 18 August 2020.[7]

The COVID-19 pandemic and related public health measures have disrupted routine health services, including screening, diagnosis and treatment of tuberculosis in many countries, including South Africa. [8-12] In early May 2020, the National Institute for Communicable Diseases (NICD) released a preliminary report on the impact of COVID-19 related public health measures on TB diagnosis in South Africa.[12] Using a before-and-after comparison, this preliminary report concluded that the Level 5 restrictions had resulted in a 48% decline in TB testing volumes and a 34% decline in laboratory-confirmed TB cases. A subsequent report, using similar methodology, demonstrated that TB testing volumes had remained suppressed through Level 4 restrictions in May 2020.[11]

Using historical laboratory data, the impact of the COVID-19 pandemic and public health measures on TB testing volumes, laboratory-confirmed TB and rifampicin resistant TB, and proportion of samples testing positive in South Africa at national and provincial levels was estimated.

## Methods

Daily Xpert MTB/RIF (Xpert) and Xpert MTB/RIF Ultra test results for the period 1 January 2018 to 23 August 2020 were extracted from the NICD surveillance data warehouse. Xpert laboratory data were not de-duplicated for this analysis as the primary interest was testing volumes.

Segmental linear regression models of daily Xpert tests per 100,000 population for the period 3 February 2020 to 23 August 2020 were fitted for each COVID-19 lockdown level. Since TB investigations and case detection are seasonally variable, being influenced by the influenza season, data from 2018 and 2019 were used to predict monthly tests, positive tests, rifampicin resistance tests and the proportion of tests showing positive for each month of 2020. Following the example of the SAMRC weekly mortality reports, the excel forecast function, which implements the Holt-Winters triple exponential smoothing allowing for seasonality, was used to predict monthly values and 95% prediction intervals for 2020.[7] The positivity rate was calculated as the number of positive Xpert tests over the total number of Xpert tests conducted. Data on daily COVID-19 cases by province were extracted from the NICD COVID-19 master list. Analysis was conducted using Stata version 15.1 (StataCorp, College Station, TX) and Microsoft Excel.

## Results

During the period 1 January 2018 to 23 August 2020, 5,422,089 Xpert tests were conducted. Of these 504,758 (9.3%) were positive for *Mycobacterium tuberculosis* complex and 25,171 were rifampicin resistant (5% of TB positive tests). Xpert positivity rates were 9.7% (213,741/2,199,307) and 9% (196,606/2,180,422) for 2018 and 2019 respectively.

The daily Xpert tests per 100,000 population, segmental linear regression models for each lockdown level, and the 7-day moving average of laboratory-confirmed COVID-19 cases per 100,000 population for South Africa by province during the period 3 February to 23 August 2020 are shown (Figures 1 and 2). The segmental linear regression shows an initial increase in Xpert testing rates in the pre-intervention period, followed by a sudden decline after the introduction of Level 5 restrictions. Xpert tests remained suppressed at a similar level through the Level 4 and 3 restrictions. A supremum Wald

test for a single structural break in the national Xpert test time series identified a break occurring on 28th March 2020 ($p<0.001$). The declines in TB tests per 100,000 population were similar across all provinces (Figure 2).

Monthly counts of Xpert tests, positive Xpert tests and rifampicin-resistant tests closely tracked the upper confidence bound for the months of January, February and March 2020 (Figures 3a-3c). Xpert tests and positive tests dropped sharply below the lower forecast bound in April, remaining below the lower bound in May, June and July (Figure 3a and 3b). Rifampicin resistant tests remained above forecast in April before dropping below the lower bound in May (Figure 3c). The proportion of Xpert tests positive for TB increased above the upper forecast bound in April, remaining above the upper bound throughout May, June and July (Figure 3d).

Compared to the monthly forecasts for April to July, there were approximately 309,000 fewer Xpert tests, 17,700 fewer positive tests, and 540 fewer rifampicin resistant tests.

## Discussion

Xpert TB testing volumes declined sharply immediately after commencement of the national lockdown on 27 March, continued to decline during Level 5 restrictions, and remained below forecast bounds thereafter. Furthermore, the timing and scale of the decrease in testing volumes was consistent across provinces and preceded the rapid rise in COVID-19 cases. Testing volumes declined more rapidly than the TB positive tests resulting in an increase in the positivity rate. Since both the Xpert test volumes and positive sample tests tracked the upper forecast bounds for the first three months of 2020, our estimate of 309,000 fewer TB tests and 17,700 fewer positive tests as a result of the lockdown restrictions is likely conservative.

The dramatic declines in Xpert tests conducted for TB are not explained by reduced testing capacity as this remained unaffected. Instead, the sustained declines are likely the result of the complex interplay between patients and health systems, with different factors likely predominating at different times. For example, Level 5 restrictions imposed severe restrictions on individual movement. While people were permitted under Level 5 restrictions to leave their dwellings to buy food and access health care, public transport and taxis were not readily available, and were still significantly curtailed during Level 4 restrictions, limiting access to health care services. It is also likely that people avoided using public transport or accessing health care due to fear of contracting COVID-19. The increase in the Xpert positivity rate suggests that people with mild TB symptoms delayed seeking care while those with advanced symptoms were more inclined to seek care.

South Africa's health care system has rapidly repurposed to focus on COVID-19 screening, testing and contact tracing, and this was especially true during Level 5 restrictions. Reports from health care workers suggest that screening for TB declined rapidly during Level 5. Furthermore, as COVID-19 cases increased rapidly during Levels 4 and 3, many health facilities closed for extended periods, usually because of COVID-19 infections amongst staff. Lastly, TB testing generally follows a seasonal pattern, with higher testing rates during the winter influenza season. The public health restrictions to slow the spread of SARS-CoV-2 resulted in a significant reduction in influenza incidence in 2020 in South Africa, and these restrictions likely contributed to the decline in TB testing. However, this

should have been offset by the COVID-19 pandemic, suggesting that health services focused primarily on COVID-19 at the expense of other health conditions.

## Conclusion

Tuberculosis is currently one of the leading causes of death by infectious disease in South Africa.[13] These unintended consequences of reduced TB testing will likely have a negative impact on the country's efforts to control TB. The implications of undiagnosed TB are serious and will compromise past successes in reducing the burden and mortality associated with TB and DR-TB. As both TB and COVID-19 share similar clinical presentation (cough, fever, shortness of breath etc.) and are transmitted through respiratory droplets and aerosols, a combined strategy needs to be applied. This would utilise resources efficiently while providing short- and long-term benefits in terms of controlling both diseases.

## Acknowledgements

The authors would like to thank Trevor Bell for providing the data, and Prof Nazir Ismail for the initial concept and guidance.

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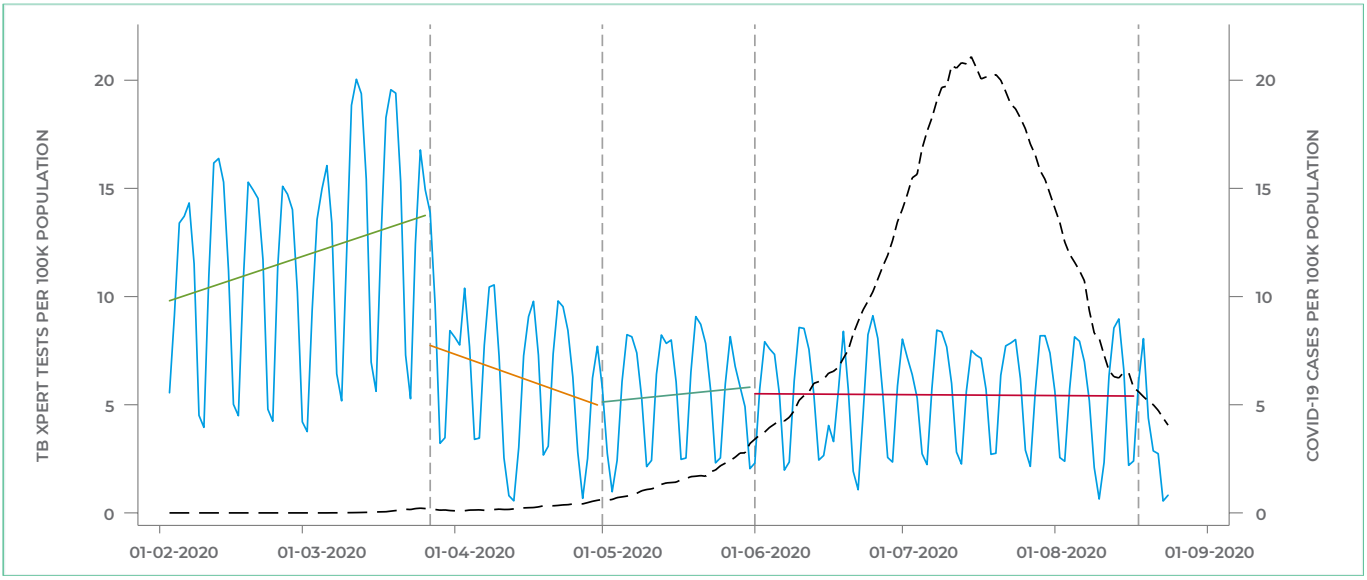
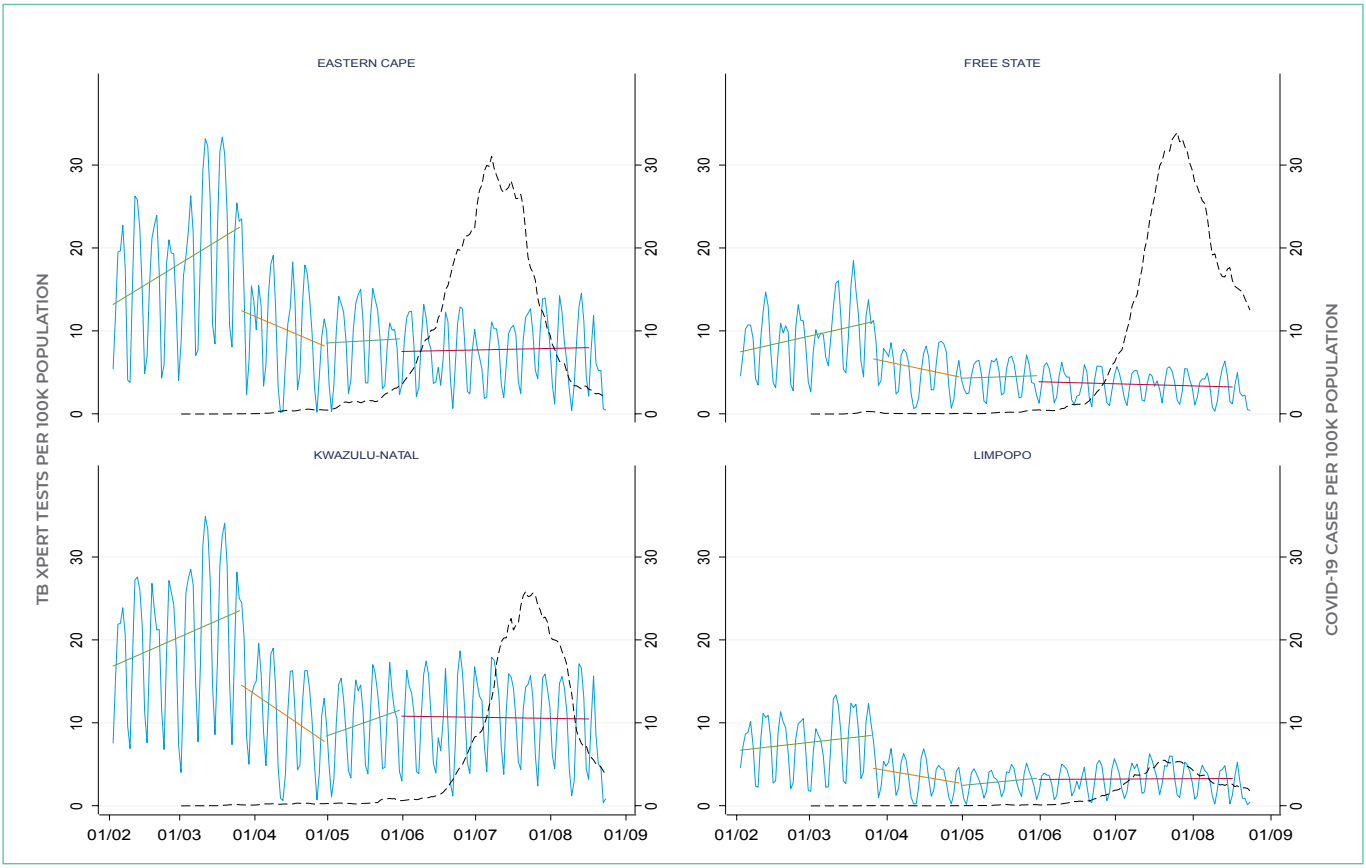



**Figure 1.** Daily Xpert tuberculosis testing rates (navy), segmented linear regression models (green, yellow, teal and red), and 7-day smoothed COVID-19 daily cases per 100,000 population for South Africa (black dash) for the period 3 February to 23 August 2020. Grey dashed vertical lines indicate transitions between restriction levels.



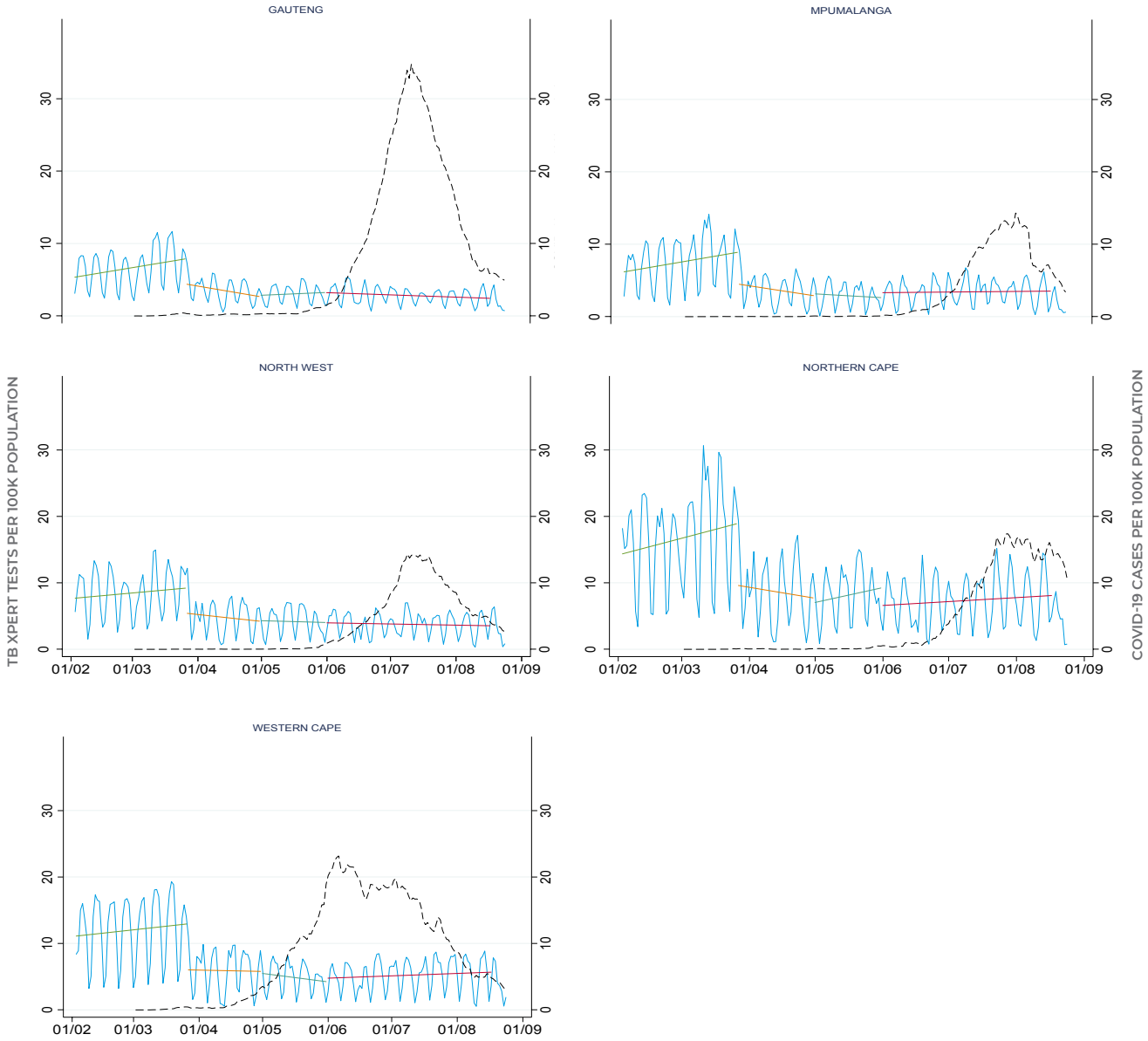



**Figure 2.** Daily Xpert tuberculosis testing rates (navy), segmented linear regression models (green, yellow, teal and red), and 7-day smoothed COVID-19 daily cases per 100,000 population (black dash) by province for the period 3 February to 23 August 2020.

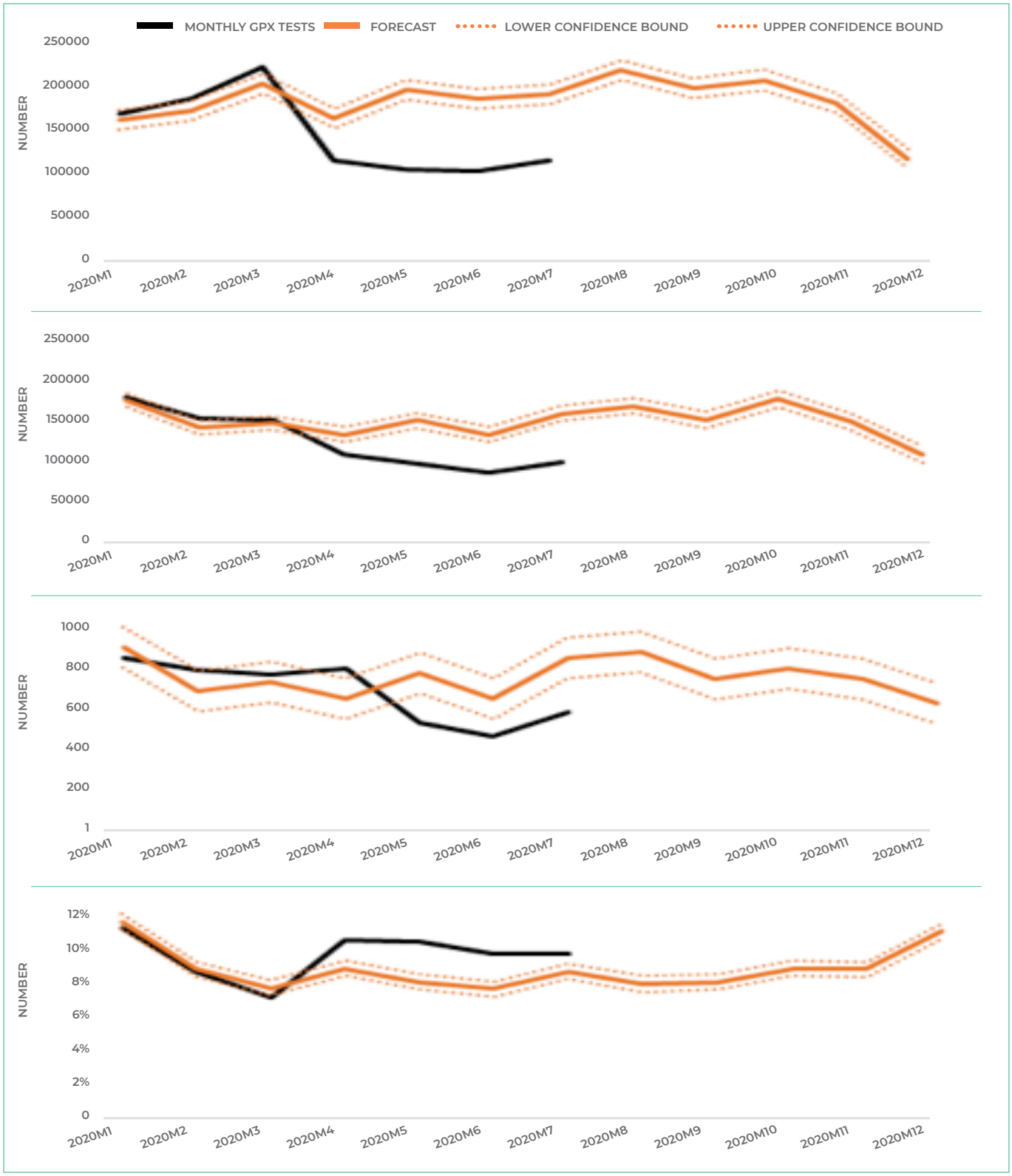



**Figure 3.** Forecast and observed counts of a) Xpert tests b) positive Xpert tests c) rifampicin resistant samples and d) proportion of Xpert samples testing positive for tuberculosis in South Africa, January to July 2020.

**Table 1.** Forecast and observed statistics based on Xpert tests, positive tests and rifampicin resistant tuberculosis samples, South Africa, April to July 2020.

| Month | Xpert Tests | | | Positive Xpert Tests | | | Rif-R samples | | |
|---|---|---|---|---|---|---|---|---|---|
| | Actual | Forecast | Difference | Actual | Forecast | Difference | Actual | Forecast | Difference |
| Apr-20 | 109 383 | 159 857 | 50 474 | 11 041 | 13 472 | 2 431 | 749 | 607 | -142 |
| May-20 | 99 512 | 193 065 | 93 553 | 9 952 | 15 128 | 5 176 | 492 | 733 | 241 |
| Jun-20 | 96 894 | 182 589 | 85 695 | 9 007 | 13 435 | 4 428 | 429 | 611 | 182 |
| Jul-20 | 109 468 | 188 713 | 79 245 | 10 247 | 15 929 | 5 682 | 548 | 802 | 254 |
| **Total** | **415 257** | **724 224** | **308 967** | **40 247** | **57 965** | **17 718** | **2 218** | **2 754** | **536** |

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