The impact of routine pulse oximetry use on outcomes in COVID-19-infected patients at increased risk of severe disease: A retrospective cohort analysis

N Nematswerani,[1] MB ChB, MPharmMed, MSc Clinical Epidemiology; **S Collie,**[1] BSc Hons (Actuarial Science), FASSA; **T Chen,**[1] BSc Hons (Actuarial Science), FASSA, CERA; **M Cohen,**[1] BBusSc Actuarial Science; **J Champion,**[1] MSc Chemical Engineering, PG Diploma Actuarial Science, FASSA; **C Feldman,**[2] MB BCh, DSc, PhD, FRCP, FCP (SA); **G A Richards,**[3] MB BCh, PhD, FCP (SA), FRCP, MASSAf

[1] *Strategic Risk Management and Data Science Unit, Discovery Health, Johannesburg, South Africa*
[2] *Department of Internal Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa*
[3] *Department of Critical Care, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa*

Corresponding author: *S Collie (shirleyc@discovery.co.za)*

Background. The phenomenon of silent hypoxaemia has been described in patients with COVID-19 pneumonia, which is characterised by low oxygen saturation levels of <90% in those who appear clinically well and do not show signs of significant respiratory distress.
Objectives. To assess the impact on clinical outcomes for high-risk COVID-19 patients using a pulse oximeter to monitor oxygen saturation levels in a home setting.
Methods. We performed a retrospective cohort analysis using data from a large South African insurance administrator. Patients were categorised as high risk, based on age and specific underlying clinical conditions, or from predictive models derived from medical scheme administrative claims data. The impact of pulse oximetry home monitoring on COVID-19 clinical outcomes was investigated by the use of Cox proportional hazard models.
Results. Between 2 March 2020 and 31 October 2020, of 38 660 patients analysed, 8 115 were in the intervention group. The 60-day mortality rate for the evaluated high-risk population was 1.35%. After adjusting for age and comorbidity differences, the intervention group was found to have an adjusted hazard ratio of 0.52 (p<0.0001). No statistical significance was found between the intervened and control groups for admission to hospital, admission to intensive care unit (ICU) and use of mechanical ventilation. The intervention group had a lower median C-reactive protein (CRP) level on admission (p=0.03). After adjustment for admission CRP levels, elevated CRP was associated with an increased mortality (p<0.0001), while the statistical significance in mortality between the intervention and the control group was lost.
Conclusions. High-risk COVID-19 patients who used a pulse oximeter to monitor oxygen saturation levels had significantly lower mortality rates compared with other high-risk patients. The mortality benefit may be explained by earlier presentation to hospital, as suggested by lower initial CRP levels.

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The global COVID-19 pandemic was first reported on 31 December 2019 by the World Health Organization (WHO) following a cluster of cases of pneumonia in Wuhan City, Hubei Province, China.[1,2] SARS-CoV-2 was confirmed to be the causative virus of the disease, which was named COVID-19 and declared a global pandemic on 11 March 2020.[1]

The phenomenon of silent hypoxaemia has been described in patients with COVID-19 pneumonia, which is characterised by low oxygen saturation levels of <90% in patients who appear clinically well and do not show signs of significant respiratory distress.[2,3] Early in the disease process, lung mechanics may be preserved and, although the mechanism is uncertain, it may be related to pulmonary microvascular thrombosis and intrapulmonary shunting analogous to the hepatopulmonary syndrome.[2,4] In this initial phase, respiratory effort is not significantly increased, as the lung compliance remains normal, although the tidal volume may increase markedly in response to the hypoxaemia. Thereafter, extensive alveolar and interstitial inflammation occurs with a marked decrease in pulmonary compliance, which resembles the classic acute respiratory distress syndrome (ARDS). Rapid respiratory decompensation occurs as the compliance decreases, and tachypnoea may be the most important clinical warning sign of impending respiratory failure.[2-6]

Monitoring oxygen saturation with pulse oximeters at home can potentially determine the need and appropriate timing for hospital admission more accurately, allowing for early intervention, such as the administration of supplemental oxygen and proning before oxygen saturation drops to <90%, a level which has been associated with higher in-hospital mortality.[3,7,8] NHS England purchased ~200 000 of these devices with the intention that they be given to patients at high risk of developing severe COVID-19 for use at home to detect deterioration early and facilitate timeous transfer to hospital, where indicated.[9] Discovery Health, a large South African (SA) healthcare administrator, similarly provided pulse oximeters to clients with documented comorbidities that had been associated with a high risk of severe COVID-19 illness to evaluate the benefit, if any, of this intervention.

Methods

This was a retrospective analysis using Discovery Health, an SA managed care organisation's anonymised data, including information

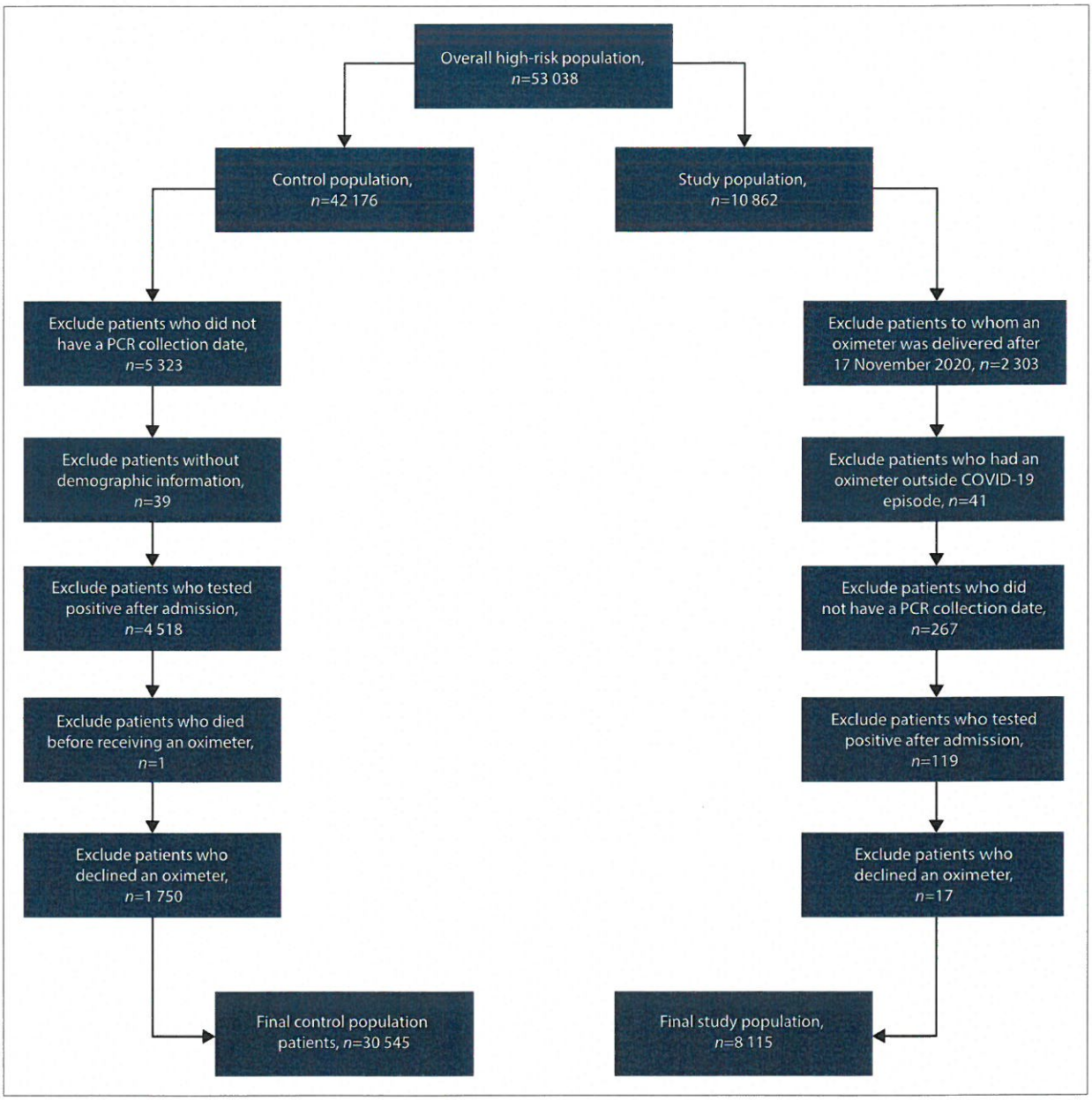

Fig. 1. Study profile. (PCR = polymerase chain reaction.)

Table 2. Baseline characteristics

	Study population (*N*=8 115; 21%)	Control population (*N*=30 545; 79%)	*p*-value
Age (years), mean (SD)	46.4 (15.2)	43.7 (16.6)	<0.0001
Sex, *n* (%)			
Male	3 341 (41)	11 704 (38)	<0.0001
Female	4 774 (59)	18 841 (62)	
Most common conditions, *n* (%)			
Hypertension	2 753 (34)	7 882 (26)	<0.0001
Hypercholesterolaemia	16 789 (21)	4 250 (14)	<0.0001
Diabetes mellitus	1 177 (15)	3 199 (10)	<0.0001
HIV	615 (8)	2 504 (8)	0.03
Asthma	990 (12)	2 070 (7)	<0.0001

SD = standard deviation.

Table 3. Kaplan-Meier estimates for 7-day, 14-day, 30-day and 60-day mortality rates for COVID-19-positive patients since PCR collection

	Mortality rate (%), 95% CI	Deaths, *n*	Mortality rate (%), 95% CI	Deaths, *n*	Mortality rate (%), 95% CI	Deaths, *n*	Mortality rate (%), 95% CI	Deaths, *n*
	7 days		14 days		30 days		60 days	
Overview	0.35 (0.29 - 0.40)	140	0.77 (0.69 - 0.86)	313	1.21 (1.11 - 1.32)	490	1.35 (1.24 - 1.46)	544
Age band 0 - 39 years	0.01 (0.00 - 0.02)	1	0.04 (0.01 - 0.07)	7	0.08 (0.04 - 0.13)	14	0.10 (0.05 - 0.15)	17
Age band 40 - 49 years	0.14 (0.06 - 0.22)	13	0.39 (0.26 - 0.52)	36	0.58 (0.43 - 0.74)	54	0.67 (0.50 - 0.84)	62
Age band 50 - 59 years	0.38 (0.24 - 0.52)	27	0.70 (0.51 - 0.89)	50	1.06 (0.83 - 1.30)	76	1.19 (0.94 - 1.44)	85
Age band 60 - 69 years	0.54 (0.32 - 0.76)	24	1.42 (1.07 - 1.76)	63	2.46 (2.00 - 2.91)	109	2.82 (2.33 - 3.30)	125
Age band 70 - 79 years	1.41 (0.87 - 1.95)	26	2.98 (2.20 - 3.75)	55	5.64 (4.58 - 6.69)	104	6.19 (5.08 - 7.28)	114
Age ≥80 years	5.05 (3.66 - 6.42)	49	10.53 (8.57 - 12.44)	102	13.74 (11.55 - 15.89)	133	14.59 (12.33 - 16.78)	141
No asthma	0.35 (0.29 - 0.41)	129	0.75 (0.66 - 0.84)	279	1.17 (1.06 - 1.27)	433	1.30 (1.18 - 1.41)	482
Asthma	0.34 (0.14 - 0.54)	11	1.06 (0.70 - 1.41)	34	1.77 (1.32 - 2.23)	57	1.93 (1.45 - 2.41)	62
No diabetes	0.27 (0.22 - 0.33)	98	0.58 (0.50 - 0.66)	209	0.85 (0.75 - 0.94)	303	0.94 (0.84 - 1.04)	336
Diabetes	0.93 (0.65 - 1.21)	42	2.30 (1.86 - 2.73)	104	4.14 (3.56 - 4.72)	187	4.61 (4.00 - 5.22)	208
Female	0.21 (0.16 - 0.27)	53	0.51 (0.42 - 0.60)	126	0.80 (0.68 - 0.91)	196	0.87 (0.75 - 0.98)	213
Male	0.55 (0.44 - 0.67)	87	1.19 (1.02 - 1.36)	187	1.87 (1.66 - 2.08)	294	2.11 (1.88 - 2.33)	331
HIV-negative	0.37 (0.30 - 0.43)	136	0.82 (0.73 - 0.91)	304	1.28 (1.16 - 1.39)	474	1.41 (1.29 - 1.54)	525
HIV-positive	0.12 (0.00 - 0.24)	4	0.28 (0.10 - 0.46)	9	0.50 (0.25 - 0.74)	16	0.59 (0.32 - 0.85)	19
No hypercholesterolaemia	0.25 (0.20 - 0.31)	87	0.54 (0.46 - 0.61)	183	0.78 (0.69 - 0.88)	268	0.86 (0.76 - 0.96)	293
Hypercholesterolaemia	0.85 (0.62 - 1.08)	53	2.09 (1.73 - 2.44)	130	3.57 (3.11 - 4.03)	222	4.04 (3.55 - 4.53)	251
No hypertension	0.17 (0.13 - 0.22)	51	0.39 (0.32 - 0.46)	114	0.55 (0.47 - 0.64)	161	0.61 (0.52 - 0.70)	178
Hypertension	0.80 (0.63 - 0.96)	89	1.78 (1.54 - 2.03)	199	2.95 (2.64 - 3.27)	329	3.29 (2.96 - 3.62)	366
No oximeter	0.36 (0.30 - 0.42)	138	0.82 (0.73 - 0.91)	294	1.30 (1.18 - 1.42)	450	1.44 (1.32 - 1.57)	495
Oximeter	0.06 (0.00 - 0.13)	2	0.30 (0.16 - 0.45)	19	0.57 (0.39 - 0.75)	40	0.68 (0.49 - 0.88)	49
Chronic condition, *n*=0	0.15 (0.09 - 0.20)	27	0.28 (0.20 - 0.36)	52	0.40 (0.31 - 0.49)	74	0.43 (0.34 - 0.53)	80
Chronic condition, *n*=1	0.19 (0.11 - 0.27)	21	0.40 (0.28 - 0.52)	44	0.61 (0.46 - 0.75)	67	0.69 (0.53 - 0.84)	76
Chronic conditions, *n*=2	0.66 (0.43 - 0.89)	32	1.24 (0.93 - 1.55)	60	1.86 (1.48 - 2.24)	90	2.04 (1.65 - 2.44)	99
Chronic conditions, *n*≥3	1.00 (0.75 - 1.25)	60	2.61 (2.21 - 3.01)	157	4.31 (3.80 - 4.82)	259	4.81 (4.27 - 5.35)	289

PCR = polymerase chain reaction; CI = confidence interval.

oxygenation (ECMO) between the intervention and control groups.

CRP pathology results on admission to hospital were available for 238 (74%) of the 321 patients and 2 115 (58%) of the 3 642 admitted in the study and control populations, respectively (Table 6). The median CRP result, 56 mg/L in the study group, was lower than that in the control group (70 mg/L; p=0.03).

Using this result as a covariate in the Cox mortality model (Table 4), the study population had no statistically significant difference in mortality (p=0.18), whereas the CRP test result did have a significant impact on mortality (p<0.0001) (Suppl. Table 1; http://samj.org.za/public/sup/15880.pdf). Each additional unit increase in the CRP had a 0.53% increase in mortality risk (p<0.0001). Therefore, a patient admitted with the population median CRP result of 68.3, would have a 43.6% (1.01 × 68.3) higher mortality risk.

Discussion

The aim of providing patients at high risk of severe COVID-19 infection with pulse oximeters was to improve clinical outcomes by earlier identification of silent hypoxaemia or a deterioration in oxygen saturation, thus decreasing the acuity of admissions, the requirement for intensive care and mechanical ventilation, and the number of deaths. The data adjusted for risk showed a statistically significant improvement in 60-day mortality (hazard ratio 0.52; p<0.0001) for the intervention group, despite this group consisting of older patients, with a higher prevalence of the top five comorbid conditions, who should have been at higher risk for worse outcomes.

While there was a trend toward a higher likelihood for admission for the intervention group, this was not statistically significant (hazard ratio 1.03; p=0.59). For those in the intervention group who were admitted, a longer mean length of stay was observed (mean difference 0.58 days; p<0.0001).

In a single-centre retrospective cohort study that included patients

Table 4. Cox regression results for deaths

	Estimate	Hazard ratio	Lower 95% CI	Upper 95% CI	*p*-value
Intervened	-0.66	0.52	0.38	0.70	<0.0001
Age band 40 - 49 years	1.57	4.79	2.78	8.24	<0.0001
Age band 50 - 59 years	1.95	7.03	4.12	12.00	<0.0001
Age band 60 - 69 years	2.78	16.06	9.50	27.15	<0.0001
Age band 70 - 79 years	3.48	32.38	18.96	55.29	<0.0001
Age band ≥80 years	4.48	87.85	51.64	149.47	<0.0001
Male	0.67	1.96	1.64	2.34	<0.0001
Hypertension	0.24	1.27	0.99	1.62	0.06
Hypercholesterolaemia	-0.28	0.75	0.60	0.95	0.02
Diabetes	0.82	2.27	1.85	2.79	<0.0001
HIV	0.12	1.13	0.70	1.84	0.62
Asthma	0.12	1.13	0.85	1.49	0.402
Chronic condition, *n*=1	-0.09	0.92	0.65	1.30	0.63
Chronic conditions, *n*=2	0.35	1.42	0.98	2.06	0.06
Chronic conditions, *n*≥3	0.57	1.76	1.16	2.67	0.01

CI = confidence interval.

Table 5. Summary of impact of pulse oximeter intervention on clinical outcomes

	Rate per patient	HR for impact of the intervention on the study population	Lower 95% CI	Upper 95% CI	*p*-value
Admission*	10.098%	1.03	0.92	1.17	0.59†
Length of stay*	7.50 days	1.078	1.05	1.093	<0.0001‡
ICU§	1.650%	1.02	0.80	1.31	0.86†
Mechanical ventilation¶	0.904%	0.97	0.69	1.36	0.86†
ECMO¶	1.419%	0.52	0.38	0.70	<0.0001†
Mortality	1.49%	0.52	0.38	0.70	<0.0001†

HR = hazard ratio; CI = confidence interval; ICU = intensive care unit; ECMO = extracorporeal membrane oxygenation.
*Excludes 330 patients in the study group who were admitted before receiving a pulse oximeter, resulting in 7 783 remaining patients in the group.
†*p*-value obtained from intervention hazard ratio from Cox multivariable models for each of the analysed outcomes.
‡*t*-test based on mean difference in average length of stay between the study and control populations.
§Excludes 30 patients in the study group who were admitted to an ICU before receiving a pulse oximeter, resulting in 8 083 remaining patients in the study group.
¶Excludes 23 patients in the study group who had mechanical ventilation or ECMO before receiving a pulse oximeter, resulting in 8 090 remaining patients in the study group.

Table 6. Total number of patients admitted, with a CRP test on admission date

	Study population	Control population	Total, *n*	*p*-value
Admissions, *n* (%)	321 (8)	3 642 (92)	3 963	
CRP test results available on day of admission, *n* (%)	238 (10)	2 115 (90)	2 353	
Median CRP test result (interquartile range), mg/L	56 (21.2 - 111.1)	70 (20.5 - 141.7)	68.3 (20.5 - 138.1)	0.03*

CRP = C-reactive protein.
*Test of significance performed using a one-sided Wilcoxon rank-sum test.

with moderate to critical COVID-19 pneumonia hospitalised in Wuhan, 25.7% died during hospitalisation after a median 14-day follow-up. In this study, higher oxygen saturation levels after oxygen supplementation were associated with reduced mortality, independently of age and sex.[7] Access to a pulse oximeter for monitoring oxygen saturation allows patients to detect deterioration timeously and seek healthcare.

Patients who accepted a pulse oximeter may have been more conscientious and aware of symptoms and may potentially have been more likely to seek care timeously, regardless of having a pulse oximeter. The effect, however, is expected to be small, as most members who were contacted accepted the device (83% telephonic acceptance rate).

In a systematic review, Figliozzi *et al.*[11] identified clinical history and laboratory profile as vital to identification of patients with a higher risk of in-hospital mortality. Various severity scores have also been evaluated in COVID-19 for the prediction of in-hospital clinical outcomes, including death.[12] Using these scores at the time of admission could help to identify patients at higher risk of worse clinical outcomes at the time of admission.

Elevated inflammatory markers are associated with severe COVID-19 disease. In a systematic review and meta-analysis by Yamada *et al.*[13] and a study by Luo *et al.*,[14] elevated CRP levels on admission were associated with severe illness and poor clinical outcomes. In our study, of the patients with a CRP test result available on the day of admission, the median CRP in the oximeter group was significantly lower (56 mg/L) than that of controls (70 mg/L; $p=0.03$), and could therefore explain the lower mortality in the group that received a pulse oximeter. This shows that these patients had less severe disease at the time of admission than the control group (median difference 14 mg/L; $p=0.03$).

Study limitations

This was a retrospective analysis of medical aid records and was therefore not structured as a clinical trial at the outset. There may have been patients among the control group who had already used a pulse oximeter, resulting in them being incorrectly allocated to one of the study groups. However, as the use of a pulse oximeter was associated with a favourable mortality outcome, patients with pulse oximeters incorrectly allocated to the control group would have lowered the overall mortality risk for that group, whereas, despite this possibility, the mortality was significantly lower in the intervention group.

Corticosteroids, and in particular dexamethasone, are the only therapies conclusively shown to lower mortality in hospitalised patients with COVID-19 who receive invasive mechanical ventilation or oxygen alone. These therapies are, therefore, not indicated for use in the outpatient setting, unless there is evidence of hypoxaemia.[15,16] The timing of the initiation of corticosteroids and other treatments in hospitalised patients could not be determined from the available data and therefore the differences between the groups could not be established.

It is possible that those who received a pulse oximeter could have had higher admission oxygen saturation levels than the control group and received oxygen sooner, which could explain the mortality benefit. These data were, however, not available for evaluation.

Another factor that might have been relevant was body mass index (BMI), which is an independent risk factor for COVID-19-related deaths, with a 48% higher risk of mortality.[17-19] BMI data were, however, not available for comparison between the two groups. Access to hospital health records would have provided more detail regarding poor prognosticatory factors that may have contributed to the mortality difference observed between the two groups, including BMI data.

Future prospective studies should be undertaken to further evaluate the benefits of pulse oximeter intervention in improving mortality outcomes. Patients included in this study are members of a private medical insurance in SA and have access to better healthcare resources than the majority of patients, who mainly rely on resource-constrained government facilities for care. Because of these disparities in access to healthcare, the study results may not be completely generalisable to the public health setting in SA.

Conclusions

Home monitoring using a pulse oximeter in patients at high risk of developing severe COVID-19 infection resulted in a 48% lower likelihood of death relative to the control group ($p<0.0001$). Higher CRP test results were associated with an elevated mortality risk of 0.53% ($p<0.0001$) per unit increase. Of the individuals with a CRP test result available on the day of admission, the median CRP in the oximeter group (56 mg/L) was significantly lower than that of the controls (70 mg/L; $p=0.03$). The mortality difference of the study population could only be explained by these relatively lower CRP levels, which were a surrogate for disease severity compared with the control population (median difference 14 mg/L; $p=0.03$).

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Author contributions. TC, MC, JC and SC identified patients and collected relevant data. MC, TC and SC ensured that the data were quality checked and complete. SC and NN were responsible for the implementation of analysis. TC, JC, NN, SC, CF and GAR interpreted the results. MC, TC and SC performed the statistical analysis. SC and NN created the initial drafts of the manuscript. SC, NN, CF and GAR were responsible for essential revisions of the manuscript and for incorporation of important intellectual content. All authors reviewed the manuscript and gave final approval for submission.

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Conflicts of interest. None.

Data sharing. De-identified patient data will be made available for any purpose, beginning 6 months and ending a minimum of 36 months after publication of this article, to researchers who provide a methodologically sound proposal, whose proposed use of the data has been approved by an independent review committee identified for this purpose. Proposals may be submitted beginning 6 months and up to 36 months after publication of this article. Proposals should be directed to shirleyc@discovery.co.za; to gain access, data requestors will need to sign a data access agreement.

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