Development of a Clinical Prediction Model for In-hospital Mortality from the South African Cohort of the African Surgical Outcomes Study

Hyla-Louise Kluyts[1,*], Wilhelmina Conradie[2], Estie Cloete[3], Sandra Spijkerman[4], Oliver Smith[5], Ahmed Alli[5], Modise Z. Koto[1], Odisang D. Montwedi[6], Komalan Govender[7], Larissa Cronje[8], Mariette Grobbelaar[9], Jones A. Omoshoro-Jones[10], Nicolette F. Rorke[11], Philip Anderson[12], Alexandra Torborg[13], Christella Alphonsus[13], Panagiotis Alexandris[14], Aunel Mallier Peter[15], Usha Singh[16], Johan Diedericks[17], Busisiwe Mrara[18], Anthony Reed[19], Gareth L. Davies[20], Jody G. Davids[21], Hendrik A. Van Zyl[22], Vishendran Govindasamy[23], Reitze Rodseth[24], Roel Matos-Puig[25], Kajake A.P. Bhat[26], Noel Naidoo[27], John Roos[28], Magdalena Jaworska[29], Annemarie Steyn[30], Johannes M. Dippenaar[31], R. M. Pearse[32], Thandinkosi Madiba[33], Bruce M. Biccard[34]

1. Department of Anaesthesiology, Dr George Mukhari Academic Hospital, Sefako Makgatho Health Sciences University, Pretoria, Gauteng, South Africa
2. Department of Surgery, Tygerberg Hospital, University of Stellenbosch, Cape Town, Western Cape Province, South Africa
3. Department of Anaesthesia and Perioperative Medicine, Groote Schuur Hospital, University of Cape Town, Cape Town, Western Cape Province, South Africa
4. Department of Anaesthesiology, Steve Biko Academic Hospital, University of Pretoria, Pretoria, Gauteng, South Africa
5. Department of Anaesthesia and Critical Care, Charlotte Maxeke Johannesburg Academic Hospital, University of the Witwatersrand, Johannesburg, Gauteng, South Africa
6. Department of Surgery, Kalafong Hospital, University of Pretoria, Pretoria, Gauteng, South Africa
7. Prince Mshiyeni Memorial Hospital, Umlazi, KwaZulu-Natal, South Africa
8. King Edward VIII Hospital, University of KwaZulu-Natal, Durban, KwaZulu-Natal, South Africa
9. Edendale Hospital, University of KwaZulu-Natal, Pietermaritzburg, KwaZulu-Natal, South Africa
10. Department of Surgery, Chris Hani-Baragwanath Academic Hospital, University of the Witwatersrand, Johannesburg, South Africa
11. Department of Anaesthesiology, RK Khan Hospital, University of KwaZulu-Natal, eThekwini, KwaZulu-Natal, South Africa
12. Kimberley Hospital Complex, University of the Free State, Kimberley, Northern Cape Province, South Africa
13. Department of Anaesthesiology, Inkosi Albert Luthuli Central Hospital, University of KwaZulu-Natal, Durban, South Africa
14. Port Elizabeth Hospital Complex, Port Elizabeth, Eastern Cape Province, South Africa
15. Klerksdorp/Tshepong Hospital, University of the Witwatersrand, Klerksdorp, North West Province, South Africa
16. Department of Anaesthesiology, Addington Hospital, University of KwaZulu-Natal, Durban, KwaZulu-Natal, South Africa
17. Department of Anaesthesiology, Universitas Hospital, University of the Free State, Bloemfontein, Free State, South Africa
18. Department of Anaesthesiology, Nelson Mandela Academic Hospital, Walter Sisulu University, Mthatha, Eastern Cape Province, South Africa
19. New Somerset Hospital, University of Cape Town, Cape Town, Western Cape Province, South Africa
20. Paarl Provincial Hospital, Paarl, Western Cape Province, South Africa
21. George Regional Hospital, University of Cape Town, George, Western Cape Province, South Africa
22. Department of Anaesthesiology, Worcester Hospital, Worcester, Western Cape Province, South Africa
23. Department of Surgery, Grey's Hospital, Pietermaritzburg, KwaZulu-Natal, South Africa
24. Department of Anaesthetics, Grey's Hospital, University of KwaZulu-Natal, Pietermaritzburg, KwaZulu-Natal, South Africa
25. General Justice Gizenga Mpanza Regional Hospital, Stanger, KwaZulu-Natal, South Africa
26. Department of Anaesthesiology, Cecilia Makiwane Hospital, Walter Sisulu University, East London Hospital Complex, Eastern Cape Province, South Africa

27. Department of Surgery, Port Shepstone Regional Hospital, University of KwaZulu-Natal, Port Shepstone, KwaZulu-Natal, South Africa
28. Department of Anaesthesia, Mitchells Plain Hospital, Cape Town, South Africa
29. Helderberg and Karl Bremer Hospitals, University of Stellenbosch, Cape Town, Western Cape Province, South Africa
30. Department Anaesthesiology, Potchefstroom Hospital, Potchefstroom, North West Province, South Africa
31. Oral and Dental Hospital, University of Pretoria, Pretoria, Gauteng, South Africa
32. Royal London Hospital, Queen Mary University of London, London, UK
33. University of KwaZulu-Natal, Durban, South Africa
34. Groote Schuur Hospital, University of Cape Town, Cape Town, South Africa

*Correspondence to Hyla-Louise Kluyts. Email: hyla.kluyts@smu.ac.za

Abstract

Background: Data on the factors that influence mortality after surgery in South Africa are scarce, and neither these data nor data on risk-adjusted in-hospital mortality after surgery are routinely collected. Predictors related to the context or setting of surgical care delivery may also provide insight into variation in practice. Variation must be addressed when planning for improvement of risk-adjusted outcomes. Our objective was to identify the factors predicting in-hospital mortality after surgery in South Africa from available data.

Methods: A multivariable logistic regression model was developed to identify predictors of 30-day in-hospital mortality in surgical patients in South Africa. Data from the South African contribution to the African Surgical Outcomes Study were used and included 3800 cases from 51 hospitals. A forward stepwise regression technique was then employed to select for possible predictors prior to model specification. Model performance was evaluated by assessing calibration and discrimination. The South African Surgical Outcomes Study cohort was used to validate the model.

Results: Variables found to predict 30-day in-hospital mortality were age, American Society of Anesthesiologists Physical Status category, urgent or emergent surgery, major surgery, and gastrointestinal-, head and neck-, thoracic- and neurosurgery. The area under the receiver operating curve or c-statistic was 0.859 (95% confidence interval: 0.827–0.892) for the full model. Calibration, as assessed using a calibration plot, was acceptable. Performance was similar in the validation cohort as compared to the derivation cohort.

Conclusion: The prediction model did not include factors that can explain how the context of care influences post-operative mortality in South Africa. It does, however, provide a basis for reporting risk-adjusted perioperative mortality rate in the future, and identifies the types of surgery to be prioritised in quality improvement projects at a local or national level.

Introduction

Inequality in the South African healthcare system must be addressed to enable universal health coverage. Information on risk-adjusted perioperative mortality is important to identify gaps and opportunities in the delivery of surgical care [1]. The information can be obtained by defining an appropriate perioperative dataset that includes predictors for in-

hospital mortality, and encouraging the capturing of data in a clinical registry or surgical database [2] [2]. A registry of routinely or intermittently collected data can be a valuable resource to clinicians, researchers and administrators for understanding the factors impacting on clinical care. Appropriate use of such data has the potential to greatly impact on efforts to improve access to, and the quality of, perioperative care in South Africa [4].

Clinical prediction models are useful to present factors that predict a specific endpoint and the relationships of these factors in influencing the endpoint [5]. When used in the perioperative care pathway, prediction models can assist in identifying high-risk patients. It is also of value in clinical audit to identify areas amenable to quality improvement. This is particularly relevant in the South African setting when considering the impact that context has on outcome [6].

The Surgical Outcome Risk Tool (SORT) [7] is an example of a clinical prediction model developed as a risk stratification tool, incorporating predictors similar to variables captured during the South African Surgical Outcomes Study (SASOS) [8] and the African Surgical Outcomes Study (ASOS) [9]. SORT was developed in the UK from data gathered in the National Confidential Enquiry into Patient Outcome and Death (NCEPOD) Knowing the Risk study. Despite the limitations inherent to such tools, the SORT can be used to predict an individual patient's risk for adverse post-operative outcome. The SORT was validated in the South African ASOS cohort, but did not perform well (unpublished).

The ASOS Surgical Risk Calculator was developed to predict a composite of severe complications and death in order to preoperatively identify patients at risk of severe complications in which 'failure to rescue' (i.e. death following a complication) may contribute to mortality [10]. The Lancet Commission for Global Surgery has suggested that in-hospital mortality can be used as an indicator to estimate perioperative mortality [11]. Furthermore, since the ASOS Risk Calculator included only preoperative predictors, it may be useful to evaluate all variables in the ASOS dataset with regard to their possible contribution to post-operative mortality,

Outcomes after surgery in South Africa were well described in the publication of the SASOS results, where comparisons with data from the European Surgical Outcomes Study were discussed [8].

The aim of this study was to evaluate the contribution of all mortality predictors that could potentially identify variation in the quality of clinical care delivery. This report was prepared according to the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis Or Diagnosis (TRIPOD) Statement recommendations [12].

Methods

Source of data

The source of the data used for model development (the derivation cohort) is the South African contribution to the African Surgical Outcomes Study (ASOS) [9]. This was a 7-day, international, multicentre, prospective observational cohort study of patients ≥ 18 years

undergoing any form of in-patient surgery in hospitals in African countries. Recruitment of South African patients to the study took place during a week in March and April 2016. This study was registered on the South African National Health Research Database (KZ_2015RP7_22), and on ClinicalTrials.gov (NCT03044899). The primary ethics approval was received from the Biomedical Research Ethics Committee of the University of KwaZulu-Natal, South Africa (BE306/15).

The source of data used for model validation is the South African Surgical Outcomes Study (SASOS) [8]. Recruitment for SASOS took place during 2014 in South African hospitals, most of which subsequently participated in ASOS. The validation cohort data are therefore taken during a different time period than the derivation cohort data; however, the sample populations for the two studies were similar (collected at the same hospitals) and the variables in the two datasets were the same.

Participants

All patients undergoing elective and non-elective surgery with a planned overnight hospital stay following surgery during the recruitment week were eligible for inclusion in ASOS. Exclusion criteria included planned day surgery and radiological procedures not requiring anaesthesia. For the purposes of this study, obstetric patients were excluded from the model derivation cohort. Four obstetric patients in the South African ASOS cohort died, and on exclusion, the mortality in the derivation cohort increased from 2.54–3.37%.

The representative sample for the derivation cohort in South Africa in ASOS included case data for 51 public sector hospitals, where data were collected on at least 90% of eligible patients. The majority of hospitals were affiliated with universities (37/51 or 72%) and were regional or central hospitals (39/51 or 76%).

Outcome

The outcome was in-hospital mortality rate for patients undergoing surgery censored at 30-days.

Predictors

Predictor data captured in the derivation cohort included patient data (age, sex, smoking status, ASA-PS classification, comorbid disease, available laboratory values), data associated with the surgery (type of surgery, surgery timing, surgery severity, indication for surgery, surgical duration, anaesthetic technique, intra-operative blood loss, intra-operative events, World Health Organisation (WHO) safe surgery checklist completion), and seniority of the attending anaesthetists and surgeons. Variables were selected for the model by initially analysing the univariate association of all variables including sex, smoking status, comorbidities (coronary artery disease, congestive heart failure, diabetes mellitus, cirrhosis, metastatic cancer, hypertension, stroke or transient ischaemic attack, chronic obstructive pulmonary disease/asthma, human immunodeficiency virus/acquired immunodeficiency syndrome, and chronic renal disease), and procedure-related variables during logistic regression with the primary outcome. The definitions for urgency of surgery, severity of

surgery and specialist/non-specialist physicians were provided to investigators during recruitment for ASOS and SASOS. The definitions are included in the supplement.

Sample size and missing data

There was no pre-specified sample size in ASOS, from which the cohort for model development was drawn. The aim was to recruit as many participating sites as possible using convenience sampling. To minimise bias and collect generalisable data, sites were required as per the ASOS protocol to submit the total number of eligible cases during the recruitment week. In keeping with the ASOS definition of a site with representative data, we excluded sites where data were available on less than 90% of eligible patients. No imputation for missing data was performed as the data were complete for the predictors considered in the model. An 'available case analysis' was performed.

Statistical analysis

Categorical variables were described as proportions and compared using Fisher's exact test. Continuous variables were assessed for normality and described as mean and standard deviation and compared using *t* tests.

A multivariable logistic regression model was developed with 30-day in-hospital mortality as the dependent variable. Preoperative risk variables were considered as predictors when they were significantly associated (p value ≤ 0.05) with the outcome in univariate logistic regression analyses. Forward stepwise regression was employed to select for possible significant predictors prior to model specification. When considering an event per variable rate of 10, the observed mortality rate of 3.37% in the derivation cohort allows for entering up to 12 binary variables or categories from nominal variables [13].

Model performance was evaluated by assessing the calibration (plotting observed against expected outcome) and discrimination (calculation of area under the receiver operator characteristic or c-statistic) of the model. Model performance regarding clinical usefulness [14] was not evaluated.

The SASOS cohort was used to validate the model. In-hospital post-operative mortality was a primary outcome in SASOS and a secondary outcome in ASOS. No further external validation of the model was done due to the lack of available data from a different setting in South Africa. All data were analysed using Stata®/IC 15.1 for Windows, StataCorp LLC, Texas, USA.

Results

Participants

Figure 1 describes the flow of patients through the study.

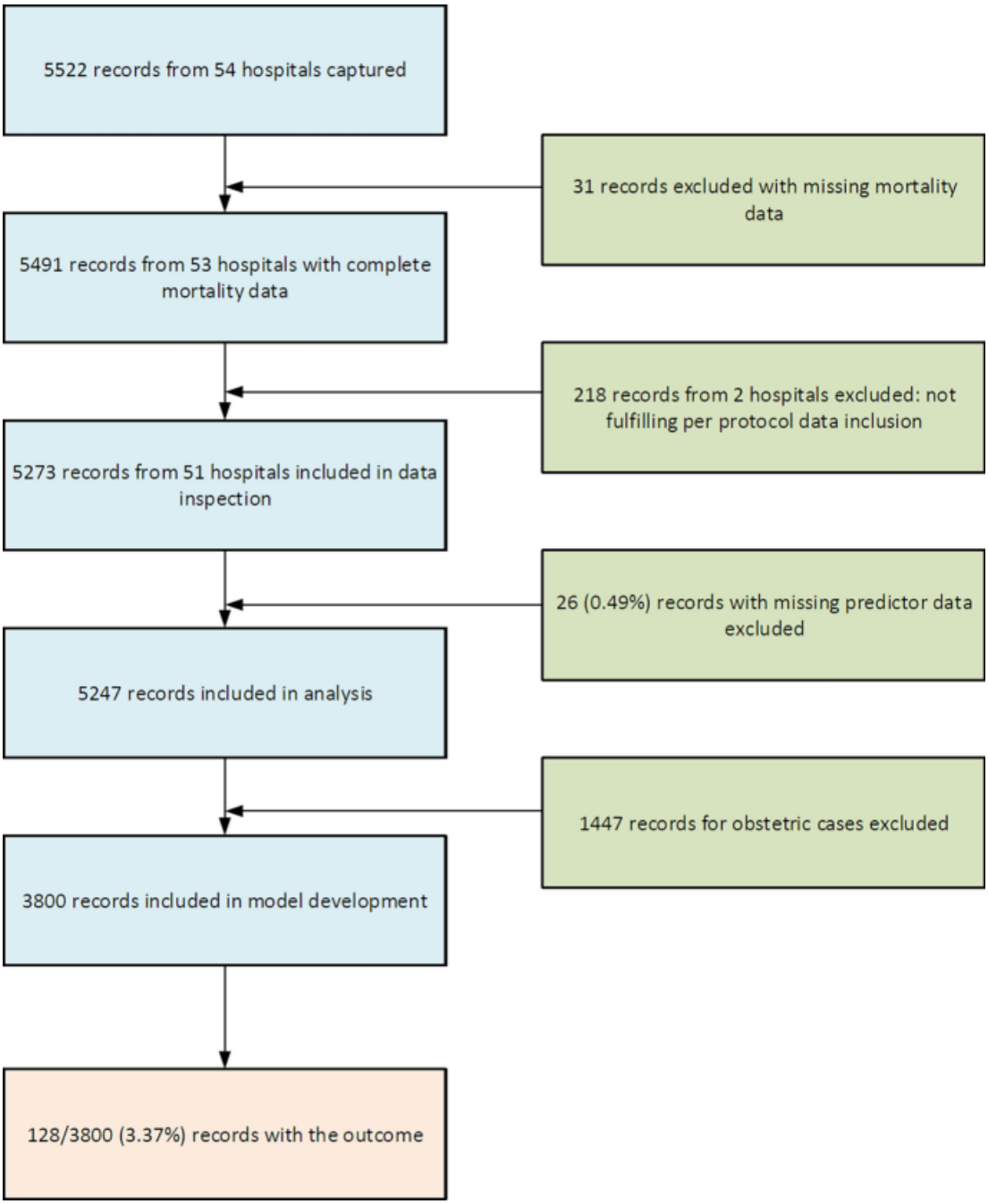

Fig. 1. Diagram illustrating flow of patients through the study

Data were collected on 5522 patients across 54 hospitals and captured in REDCap [15] by the hospital lead investigators. Each hospital lead investigator was responsible for verifying the data for their site. Thirty-one records (0.56%) had missing mortality data. Exclusion of the data resulted in the exclusion of a hospital from the study. Records from two hospitals did not fulfil the criteria for per-protocol inclusion, which required that more than 90% of eligible patients during the recruitment week were recruited to the study and that data were captured on these patients. Most of the cases that were excluded were as a result of

Table 1 Patient characteristics in the derivation and validation cohorts

	SA ASOS Cohort (Derivation Cohort)					SASOS cohort (Validation cohort)			
	All patients (n = 3800)	Patients died (n = 128)	Patients Alive (n = 3672)	Odds Ratio (95% CI)	p value	All patients (n = 3927)	Mortality (n = 123)	Relative risk (95% CI)	p value
Age (yrs)									
< 30	955/3800 (25.2)	18/128 (14.1)	937/3672 (25.5)	Reference	<0.001	1062/3927 (27.0)	13/123 (10.6)	0.7 (0.3–1.3)	0.240
30–49	1452/3800 (38.4)	36/128 (28.1)	1416/3672 (38.56)	1.323 (0.747–2.344)		1448/3927 (36.9)	43/123 (35.0)	1.2 (0.9–1.8)	0.246
50–59	582/3800 (15.1)	21/128 (16.4)	561/3672 (15.28)	1.949 (1.029–3.689)		584/3927 (14.9)	22/123 (18.0)	1.1 (0.6–2.0)	0.632
> =60	811/3800 (21.4)	53/128 (41.4)	758/3672 (20.64)	3.640 (2.114–6.266)		833/3927 (21.2)	45/123 (36.6)	0.9 (0.7–1.3)	0.686
Male	1919/3800 (50.5)	72/128 (56.2)	1847/3672 (50.30)	Reference	–	1994/3925 (50.8)	71/123 (57.7)	1.0 (0.8–1.3)	0.814
Female	1881/3800 (49.5)	56/128 (43.7)	1825/3672 (49.70)	0.787 (0.552–1.123)	0.187	1931/3925 (49.2)	52/123 (42.3)	1.0 (0.7–1.3)	0.814
Current smoker	1122/3794 (29.6)	27/125 (21.6)	1095/3672 (29.84)	0.647 (0.420–0.997)	0.049	1083/3837 (28.2)	26/113 (23.0)	1.1 (0.7–1.7)	0.794
ASA physical status									
I	1514/3800 (39.8)	20/128 (15.6)	1494/3672 (40.69)	Reference	<0.001	1743/3898 (44.7)	12/122 (9.8)	0.6 (0.3–1.2)	0.177
II	1512/3800 (39.8)	31/128 (24.2)	1481/3672(40.33)	1.563 (0.887–2.756)		1347/3898 (34.6)	29/122 (23.8)	1.0 (0.6–1.5)	0.934
III	633/3800 (16.7)	42/128 (32.8)	591/3672 (16.09)	5.309 (3.091–9.118)		663/3898 (17.0)	40/122 (32.8)	1.0 (0.7–1.4)	0.997
IV	137/3800 (3.6)	31/128 (24.2)	106/3672 (2.89)	24.665 (13.760–44.214)		131/3898 (3.4)	37/122 (30.3)	1.2 (0.8–1.9)	0.280
V	4/3800 (0.1)	4/128 (3.1)	0	–		14/3898 (0.4)	4/122 (3.3)	1.0 (0.3–4.1)	0.945
Preoperative co-morbidity									
Coronary artery disease	114/3800 (3.0)	8/128 (6.2)	106/3672 (2.89)	2.243 (1.069–4.707)	0.033	160/3869 (4.1)	8/119 (6.7)	1.1 (0.4–2.8)	0.880
Congestive heart failure	58/3800 (1.5)	6/128 (4.7)	52/3672 (1.42)	3.424 (1.443–8.124)	0.005	55/3869 (1.4)	3/119 (2.5)	0.5 (0.1–2.1)	0.372
Diabetes mellitus	421/3800 (11.1)	31/128 (24.2)	390/3672 (10.62)	2.689 (1.771–4.084)	< 0.001	394/3927 (10.0)	19/123 (15.4)	0.6 (0.4–1.1)	0.087
Cirrhosis	2/3800 (0.05)	0	2/3672 (0.05)	–	–	7/3869 (0.2)	1/119 (0.8)	–	–
Metastatic cancer	64/3800 (1.7)	4/128 (3.1)	60/3672 (1.63)	1.942 (0.695–5.428)	0.206	101/3869 (2.6)	12/119 (10.1)	3.2 (1.1–9.7)	0.037
Hypertension	1006/3800 (26.5)	46/128 (35.9)	960/3672 (26.14)	1.585 (1.096–2.291)	0.014	–	–	–	–
Stroke or Transient ischaemic attack	58/3800 (1.5)	4/128 (3.1)	54/3672 (1.47)	2.161 (0.771–6.062)	0.143	55/3869 (1.4)	8/119 (6.7)	2.1 (0.7–6.9)	0.201

Table 1 continued

	SA ASOS Cohort (Derivation Cohort)					SASOS cohort (Validation cohort)			
	All patients (n = 3800)	Patients died (n = 128)	Patients Alive (n = 3672)	Odds Ratio (95% CI)	p value	All patients (n = 3927)	Mortality (n = 123)	Relative risk (95% CI)	p value
COPD/asthma	219/3800 (5.7)	10/128 (7.8)	209/3672 (5.69)	1.404 (0.725–2.718)	0.314	240/3869 (6.2)	10/119 (8.4)	1.1 (0.5–2.5)	0.865
HIV positive/AIDS	558/3800 (14.7)	14/128 (10.9)	544/3672 (14.81)	0.706 (0.402–1.239)	0.225	509/3869 (13.2)	11/119 (9.2)	0.8 (0.4–1.8)	0.660
Chronic renal disease	108/3800 (2.8)	10/128 (7.8)	98/3672 (2.67)	3.090 (1.572–6.076)	0.001	–	–	–	–
Severity of surgery									
Minor	1328/3800 (34.9)	18/128 (14.1)	1310/3672 (35.68)	Reference	<0.001	1403/3885 (36.1)	16/121 (13.2)	0.9 (0.5–1.7)	0.847
Intermediate	1793/3800 (47.2)	55/128 (43.0)	1738/3672 (47.33)	2.303 (1.346–3.940)		1672/3885 (43.0)	45/121 (37.2)	0.9 (0.6–1.2)	0.354
Major	679/3800 (17.9)	55/128 (43.0)	624/3672 (16.99)	6.414 (3.735–11.015)		810/3885 (20.8)	60/121 (49.6)	1.1 (0.9–1.5)	0.296
Urgency of surgery									
Elective	1878/3800 (49.4)	22/128 (17.2)	1856/3672 (50.54)	Reference	<0.001	1795/3915 (45.8)	25/123 (20.3)	1.2 (0.7–2.0)	0.525
Urgent	1083/3800 (28.5)	41/128 (32.0)	1042/3672 (28.38)	3.319 (1.966–5.603)		1290/3915 (32.9)	42/123 (34.1)	1.1 (0.7–1.5)	0.722
Emergent	839/3800 (22.1)	65/128 (50.8)	774/3672 (21.08)	7.085 (4.337–11.572)		830/3915 (21.2)	56/123 (45.5)	0.9 (0.7–1.20	0.406
Indication for surgery									
Non-communicable disease	1903/3800 (50.1)	47/128 (36.7)	1856/3672 (50.61)	Reference	0.048	1881/3914 (48.1)	49/123 (39.8)	1.0 (0.7–1.3)	0.907
Infection	766/3800 (20.2)	41/128 (32.0)	725/3672 (19.77)	2.233 (1.456–3.424)		736/3914 (18.8)	30/123 (24.4)	0.8 (0.5–1.1)	0.182
Trauma	1126/3800 (29.7)	40/128 (31.2)	1086/3672 (29.62)	1.454 (0.948–2.232)		1297/3914 (33.1)	44/123 (35.8)	1.1 (0.8–1.6)	0.448
Type of surgery									

Table 1 continued

	SA ASOS Cohort (Derivation Cohort)					SASOS cohort (Validation cohort)			
	All patients (n = 3800)	Patients died (n = 128)	Patients Alive (n = 3672)	Odds Ratio (95% CI)	p value	All patients (n = 3927)	Mortality (n = 123)	Relative risk (95% CI)	p value
Orthopaedic	1019/3800 (26.8)	18/128 (14.1)	1001/3672 (27.26)	Reference	<0.001	1112/3922 (28.3)	12/123 (9.8)	0.7 (0.3–1.4)	0.297
Gynaecology	565/3800 (14.9)	3/128 (2.3)	562/3672 (15.31)	0.297 (0.087–1.012)		525/3922 (13.4)	2/123 (1.6)	0.7 (0.1–4.1)	0.686
Upper gastrointestinal	135/3800 (3.5)	11/128 (8.6)	124/3672 (3.38)	4.933 (2.277–10.686)		154/3922 (3.9)	18/123 (14.6)	1.7 (0.8–3.4)	0.141
Lower gastrointestinal	397/3800 (10.4)	26/128 (20.3)	371/3672 (10.10)	3.897 (2.112–7.192)		400/3922 (10.2)	24/123 (19.5)	1.0 (0.6–1.6)	0.874
Hepatobiliary	85/3800 (2.2)	1/128 (0.8)	84/3672 (2.29)	0.662 (0.087–5.020)		88/3922 (2.2)	4/123 (3.2)	4.2 (0.5–36.7)	0.199
Urology and kidney	237/3800 (6.2)	5/128 (3.9)	232/3672 (6.32)	1.198 (0.440–3.261)		225/3922 (5.7)	4/123 (3.2)	0.8 (0.2–3.0)	0.781
Vascular	162/3800 (4.3)	14/128 (10.9)	148/3672 (4.03)	5.260 (2.562–10.801)		134/3922 (3.4)	9/123 (7.3)	0.7 (0.3–1.5)	0.325
Head and neck	204/3800 (5.4)	11/128 (8.6)	193/3672 (5.26)	3.169 (1.474–6.816)		222/3922 (5.7)	6/123 (4.9)	0.6 (0.2–1.5)	0.249
Plastics/cutaneous/breast	423/3800 (11.1)	8/128 (6.2)	415/3672 (11.30)	1.072 (0.462–2.484)		351/3922 (8.9)	8/123 (6.5)	1.0 (0.4–2.7)	0.934
Cardiac	354/3800 (9.3)	11/128 (8.6)	343/3672 (9.34)	1.783 (0.834–3.814)		–	–	–	–
Thoracic	97/3800 (2.5)	6/128 (4.7)	91/3672 (2.48)	3.667 (1.420–9.467)		65/3922 (1.7)	1/123 (0.8)	0.2 (0.0–1.4)	0.102
Neurosurgery	122/3800 (3.2)	14/128 (10.9)	108/3672 (2.94)	7.209 (3.488–14.901)		133/3922 (3.4)	11/123 (8.9)	0.9 (0.4–1.9)	0.742
Other	–	–	–	–		513/3922 (13.1)	24/123 (19.5)	–	–

The association of predictors with mortality in the derivation cohort is illustrated with odds ratios (unadjusted) derived using univariate binary logistic regression analysis. The validation cohort comparison with the derivation cohort is illustrated using relative risk. Data are mean (standard deviation) or n/N (%). *CI* confidence interval, *COPD* chronic obstructive pulmonary disease, *HIV* human immunodeficiency virus

investigators being unable to trace records of patients to complete outcome variables during the post-operative follow-up.

Twenty-six (0.49%) records were incomplete and excluded from analysis. This was considered sufficiently low enough not to influence the ability of the model to validly predict the outcome. Obstetric cases (1447) were excluded from the derivation cohort. The number of cases with the outcome of in-hospital mortality was 129/3800 (3.37%).

The patient characteristics for the derivation (ASOS) and validation (SASOS) cohorts are described in Table 1. Mortality for each characteristic variable is summarised as number of patients with the characteristic per total number of cases where data are available, in percentage. Missing data are reflected per variable in the total number for that variable.

The day-of-surgery death ratio for the study period was 10/3800 cases: 0.3%. The mean age of the patients that died on the day of surgery was 47.3 years (Standard Deviation: 11.0). Duration of the procedure and blood loss were associated with mortality and were considered in the definition of the variable for severity of surgery.

About two-thirds of all cases in the derivation cohort were attended to by non-specialist physicians (anaesthetists and surgeons). In 30.5% (39/128) of deaths, the most senior anaesthetist in the operating room was a specialist, and in 36.0% (46/128) of deaths, the most senior surgeon was a specialist. Intra-operative procedures/events and workforce characteristics for the derivation cohort are summarised in Table 2. The univariate association for these variables with mortality is also shown. Intra-operative event and workforce characteristics in the validation cohort are not available.

Model development

Participants and outcome events

Twenty-six patients had missing data and were not included during model development. Of the 5192 patients included during ASOS, 132 (2.5%) had the outcome of in-hospital death. Of the 3800 patients included in the derivation cohort, 128 (3.4%) had the outcome of in-hospital death. The association of predictors with the outcome during univariate analysis is shown in Table 1.

Model specification

When applying forward stepwise regression, all variables significant in univariate analysis (*p* value ≤ 0.05) were included. Only variables selected during forward stepwise regression were included in the full prediction model. The full prediction model is presented in Table 3, with all regression coefficients and the model intercept.

Table 2 Intra-operative events and workforce characteristics of the derivation cohort

Variable (n = 5247)	Missing n	Frequency n/N (%)	Mortality (n = 128)		
			n (%)	Odds ratio (95% CI)	p value
Most Senior anaesthetist					
Specialist	2	1223/3798 (32.2)	39 (30.47)	Reference	–
Non-specialist physician		2486/3798 (65.46)	89 (69.53)	1.127 (0.769–1.653)	0.438
Non-physician anaesthetist		22/3798 (0.58)	0	–	–
No anaesthetist		67/3798 (1.83)	0	–	–
Most senior surgeon					
Specialist	2	1562/3798 (42.56)	46 (35.94)	Reference	–
Non-specialist physician		2101/3798 (57.25)	82 (64.06)	1.325 (0.918–1.913)	0.133
Non-physician surgeon		7/3798 (0.19)	0	–	–
Anaesthetic technique					
General	2	2670/3800 (73.18)	111 (72.71)	2.450 (1.463–4.103)	<0.001
Spinal		758/3800 (19.95)	18 (14.06)	0.648 (0.391–1.074)	0.092
Epidural		45/3800 (1.18)	0	–	–
Sedation		130/3800 (3.42)	2 (1.56)	0.439 (0.107–1.796)	0.178
Local		227/3800 (5.97)	4 (3.13)	0.499 (0.183–1.362)	0.175
Other regional		198/3800 (5.21)	3 (2.34)	0.427 (0.134–1.357)	0.149
Anaesthetic complications					
Failed intubation	5	5/3800 (0.13)	0	–	–
Aspiration		3/3800 (0.08)	0	–	–
Cardiac arrest		9/3800 (0.24)	7 (5.47)	106.157 (21.825–516.350)	<0.001
Hypoxia		19/3800 (0.50)	5 (3.91)	10.621 (3.766–29.954)	<0.001
Surgical checklist used					
Yes	2	3097/3798 (81.54)	101 (78.91)	0.841 (0.546–1.297)	0.435
No		701/3798 (18.46)	27 (21.09)	Reference	–

Table 3 Final clinical prediction model for in-hospital mortality

Risk predictor	Coefficient	95% Confidence interval	Standard error	z	*p* value
Intercept	− 6.4795	- 7.4438–5.5151	0.4920	− 13.17	<0.001
Age category					
Younger than 30 years	–	–	–	–	–
30–49 years	0.4142	- 0.1943–1.0228	0.3105	1.33	0.182
50–59 years	0.6305	- 0.0728–1.3338	0.3588	1.76	0.079
60 years and older	1.2457	0.6124–1.8789	0.3231	3.86	<0.001
ASA physical status category					
ASA I	–	–	–	–	–
ASA II	0.3702	- 0.2297–0.9702	0.3060	1.21	0.226
ASA III	0.9989	0.3843–1.6135	0.3135	3.19	0.001
ASA IV and more	2.1539	1.4953–2.8124	0.3360	6.41	<0.001
Urgency of surgery					
Elective	–	–	–	–	–
Urgent	1.2671	0.7060–1.8282	0.2863	4.43	<0.001
Emergency	1.7665	1.1972–2.3359	0.2905	6.08	<0.001
Severity of surgery					
Minor	–	–	–	–	–
Intermediate	0.4052	− 0.1660–0.9765	0.2915	1.39	0.164
Major	0.9528	0.3366–1.5691	0.3144	3.03	0.002
Type of surgery					
Orthopaedic	–	–	–	–	–
Gynaecological	− 0.9636	− 2.2214–0.2942	0.6417	− 1.50	0.133
Gastrointestinal	0.8373	0.2032–1.4715	0.3235	2.59	0.010
Hepatobiliary	− 0.5977	− 2.7044–1.5089	1.0748	− 0.56	0.578
Urology and kidney	0.4429	− 0.6134–1.4992	0.5389	0.82	0.411
Vascular	0.3610	− 0.4267–1.1486	0.4019	0.90	0.369
Head and neck	1.2401	0.4148–2.0654	0.4211	2.94	0.003
Plastics/cutaneous/breast	0.1132	− 0.7712–0.9977	0.4513	0.25	0.802
Thoracic	1.1031	0.0989–2.1073	0.5124	2.15	0.031
Neuro	1.2348	0.4231–2.0465	0.4141	2.98	0.003
Cardiac	0.2104	− 0.5961–1.0168	0.4114	0.51	0.609

Model performance

The area under the receiver operating curve (AUROC) or c-statistic was 0.859 (95% confidence interval: 0.827–0.892) for the full model. The Hosmer–Lemeshow statistic indicated goodness of fit ($p = 0.2679$).

The calibration plot of observed against expected outcomes using Lowess smoothing is shown in Fig. 2. The agreement between the expected predictions and observed mortality is not perfect at higher predictions, as indicated by the blue line. The observed outcomes in groups with similar risk (indicated by green circles) all fall below this point, and are close to the ideal dashed line indicating perfect calibration. The distribution of the subjects is indicated as red bars at the bottom of the plot: patients with the outcome above the x-axis, and those without the outcome below the x-axis. The spread of predictions is better in the subjects with the observed outcome than in those without.

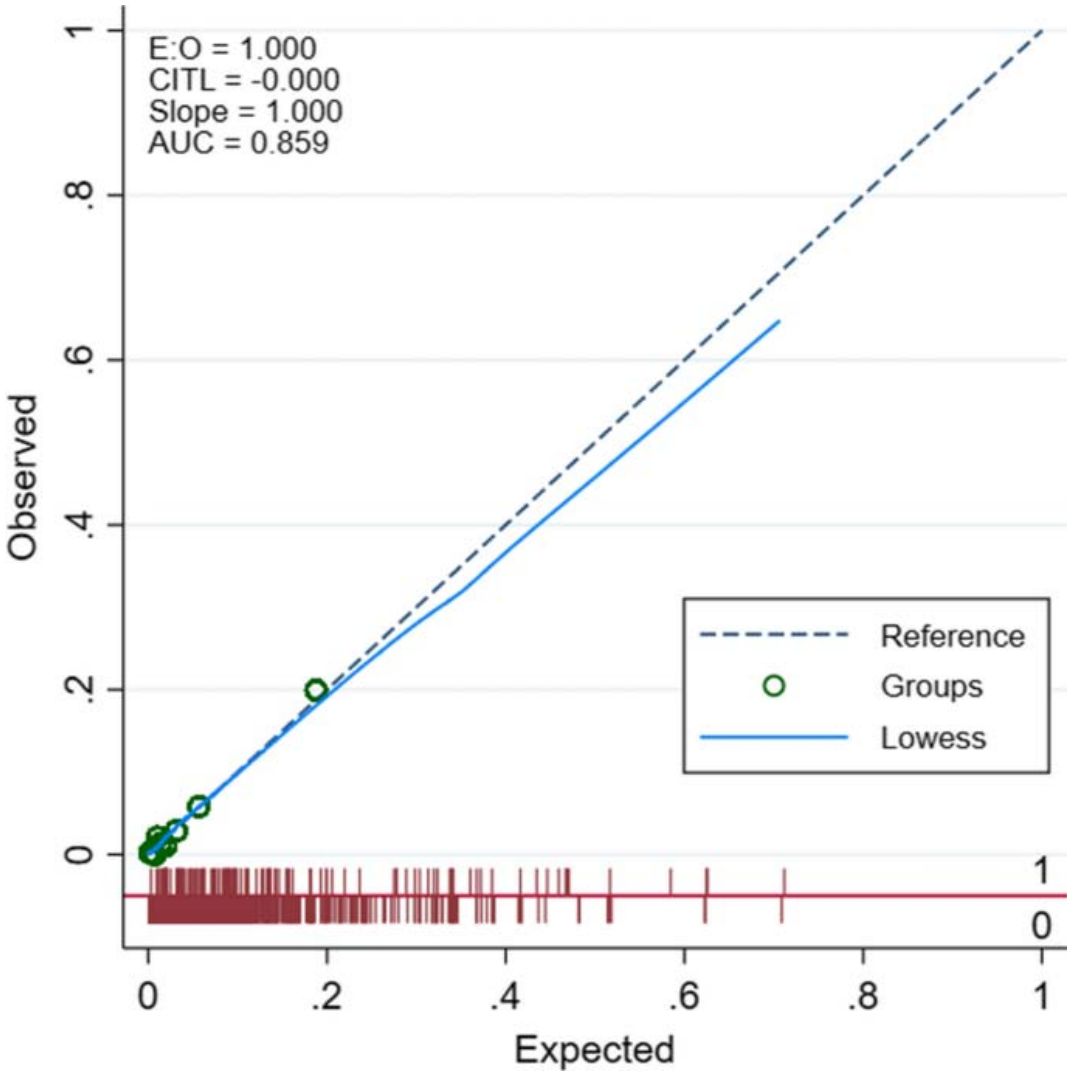

Fig. 2. Calibration plot for the prediction model. *E:O* expected: observed, *CITL* calibration-in-the-large, *AUC* area under curve

The prediction model was internally validated using a bootstrapping technique, before validation using the SASOS cohort. The resulting AUROC was found to be 0.851 (95% CI 0.817–0.886). During external validation of the prediction model, the c-statistic (AUROC) was found to be 0.862 (95% CI 0.826–0.897) in 3850 observations. The Hosmer–Lemeshow statistic indicated adequate goodness of fit (p = 0.397). The calibration plot is shown in Fig. 3. The prediction model performance was similar in the validation cohort when compared to the derivation cohort. The relative risk contribution for individual predictors in the validation cohort compared to the derivation cohort is indicated in Table 1. Table 4 describes the adjusted odds ratios for predictors in the derivation and validation cohorts. The confidence intervals of the odds ratios for all variables overlapped between the derivation and validation cohorts.

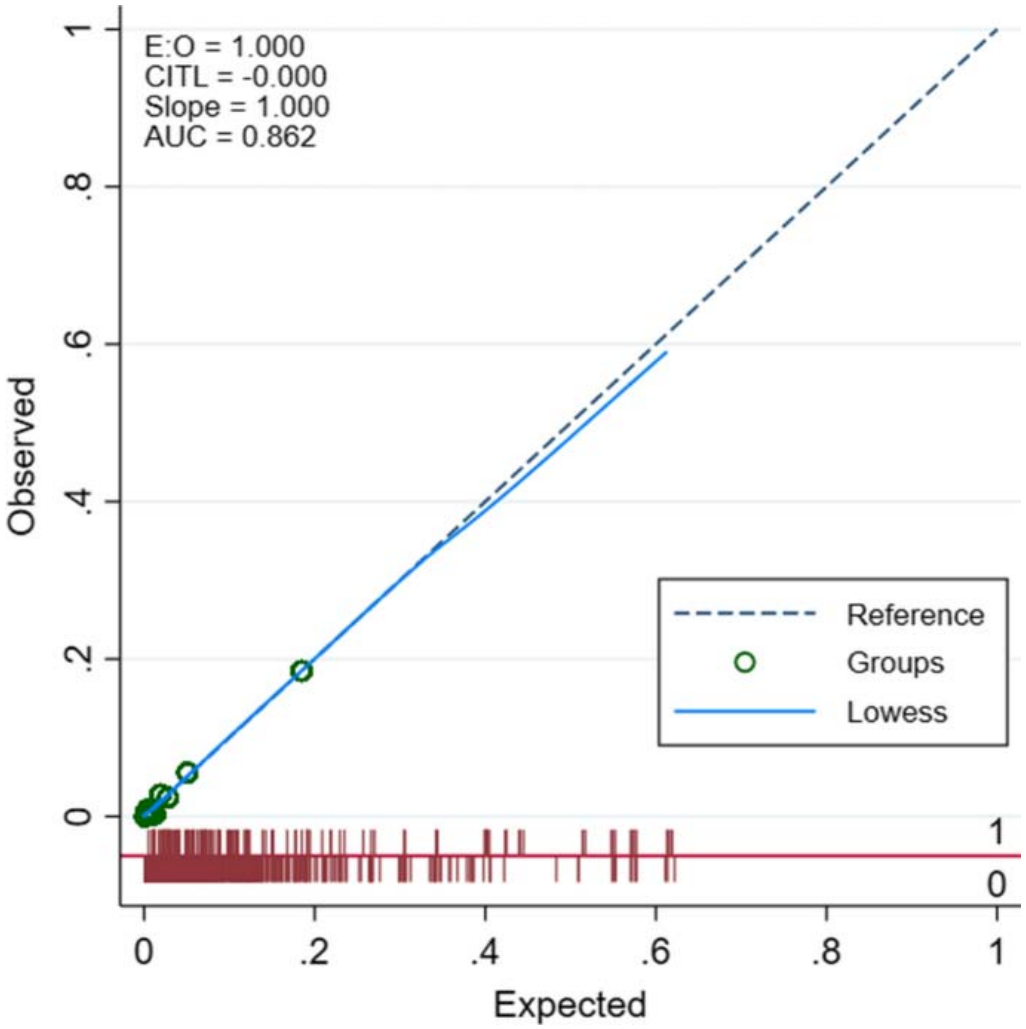

Fig. 3. Calibration plot of the prediction model using SASOS cohort data. *E:O* expected: observed, *CITL* calibration-in-the-large, *AUC* area under curve

Table 4 Odds ratios for predictors in the derivation and validation cohorts

Risk predictor	Odds ratio	Derivation cohort 95% Confidence interval	n = 3800 p value	Odds ratio	Validation cohort 95% Confidence interval	n = 3927 p value
Intercept	0.0015	0.0006–0.0040	0.001	0.0011	0.0004–0.0029	<0.001
Age younger than 30 years	Reference	–	–	–	–	–
Age 30–49 years	1.5132	0.8234–2.7810	0.182	2.5711	1.2864–5.1387	0.008
Age 50–59 years	1.8785	0.9297–3.7956	0.079	2.3477	1.0746–5.1292	0.032
Age 60 years and older	3.4752	1.8448–6.5466	< 0.001	3.0612	1.4835–6.3169	0.002
ASA I	Reference		–	–	–	–
ASA II	1.4480	0.7948–2.6384	0.226	2.5729	1.2710–5.2085	0.009
ASA III	2.7153	1.4687–5.0203	0.001	5.6147	2.7919–11.2919	<0.001
ASA IV and more	8.6181	4.4607–16.6504	< 0.001	25.3075	12.1186–52.8499	<0.001
Elective surgery	Reference	–	–	–	–	–
Urgent surgery	3.5507	2.0259–6.2230	< 0.001	2.4278	1.4105–4.1770	0.001
Emergency surgery	5.8509	3.3111–10.3389	< 0.001	3.1119	1.7790–5.4433	<0.001
Minor surgery	Reference	–	–	–	–	–
Intermediate surgery	1.4996	0.8470–2.6552	0.164	1.6359	0.8913–3.0027	0.112
Major surgery	2.5931	1.4002–4.8025	0.002	3.0228	1.6216–5.6345	<0.001
Orthopaedic surgery	Reference	–	–	–	–	–
Gynaecological surgery	0.3815	0.1084–1.3420	0.133	0.2195	0.0507–0.9504	0.043
Gastrointestinal surgery	2.3102	1.2253–4.3558	0.010	2.0292	1.1952–3.4451	0.009
Hepatobiliary surgery	0.5501	0.0669–4.5218	0.578	2.0121	0.6229–6.4997	0.243
Urology and Kidney surgery	1.5572	0.5415–4.4780	0.411	0.8875	0.3022–2.6061	0.828
Vascular surgery	1.4347	0.6526–3.1539	0.369	0.8354	0.3554–1.9635	0.680
Head and Neck surgery	3.4560	1.5140–7.8887	0.003	1.5695	0.6170–3.9922	0.344
Plastics/cutaneous/breast surgery	1.1199	0.4624–2.7120	0.802	1.3438	0.5933–3.0435	0.479
Thoracic surgery	3.0135	1.1039–8.2262	0.031	0.2564	0.0323–2.0350	0.198
Neurosurgery	3.4376	1.5266–7.7406	0.003	1.5109	0.6908–3.4371	0.291
Cardiac surgery	1.2341	0.5510–2.7643	0.609	–	–	–

Discussion

Principal findings

The predictors included in the prediction model were age category, ASA Physical Status category and predictors related to the surgical procedure: urgency, severity and type of surgery.

Limitations

The prediction model is not an appropriate tool for individual patient risk stratification.

Temporal validation is considered external validation in time, but evaluates model performance in patients from the same centres [16]. It does not truly reflect the generalisability of a prediction model.

The derivation and validation cohort data were collected at public sector hospitals that are mostly university affiliated. The population represented by the sample may differ from other South African populations regarding burden of disease, access to surgery and anaesthesia care and resource (particularly workforce) allocation. It is also possible that the findings may underestimate poor patient outcomes in smaller, more remote hospitals.

Some of the predictors related to procedure-specific risk were not classified according to established systems commonly used in the South African healthcare system. Definitions of predictors are important to consider during further validation and dynamic updating of prediction models.

The type of surgeries that are considered high risk may differ between patient populations. For example, high-risk surgery in SORT is gastrointestinal-, thoracic- and vascular surgery [7], while in the South African model, the type of surgery with significantly increased odds ratios for mortality was gastrointestinal surgery, head- and neck surgery, thoracic surgery and neurosurgery. In the validation cohort, only gastrointestinal surgery had a significantly ($p < 0.05$) higher odds ratio compared to orthopaedic surgery, the reference category (Table 4).

Indication for surgery (categories: non-communicable disease, trauma or infection) is a predictor incorporated in the ASOS Risk Calculator. It was not included in the prediction model, which may be explained by the use of a forward stepwise regression technique to assist in selecting predictors. It may be considered as a clinically significant predictor and would possibly contribute in identifying an additional cohort of patients amenable to quality improvement intervention.

Interpretation

The decision to exclude obstetric cases from the derivation cohort was made based on the fact that the mortality in this cohort was low, and care delivery is guided by reports and recommendations issued by the National Committee on the Confidential Enquiry on Maternal Death [17].

The predictors identified in this analysis are similar to those recommended for use in the risk adjustment of perioperative mortality rate (POMR): age, ASA Physical status category, urgency of surgery and procedure group [18].

The prediction model provides a useful indication of priority areas in which quality improvement initiatives are likely to have the largest impact, such as emergency- and urgent surgery, and specific types of surgery such as gastrointestinal procedures. The dataset does not allow for the capturing of sufficient information (e.g. structure and process indicators) to as yet identify specific areas of intervention for quality improvement.

It may, however, not be feasible to include a large number of additional variables in a core dataset due to the burden of collection. A significant number of quality indicators are used without sufficient evidence to support its use [19]. It is, however, crucial that accurate and reliable data on facilities be captured in parallel with patient data, to further the understanding on how factors such as surgical volume and surgical workforce affect outcome.

Validating a clinical prediction model with all-cause post-operative in-hospital mortality as an endpoint in geographically different populations, and in alternate levels of surgical care to where it was developed, can provide an understanding of the structure and processes

that may improve patient outcomes. Updating the risk-adjusted model in such diverse populations can be informative—resource allocation to areas of need is important during development of universal health coverage. Furthermore, outcomes for specific procedures, e.g. the Bellwether procedures, can be benchmarked nationally with relatively small sample cohorts [20]. Benchmarking will imply standardisation of clinical care pathways for patients with similar risk, undergoing procedures carrying similar risk.

The global surgery movement has gained enormous traction in Africa since the publication of the results of the ASOS in the Lancet. South Africa is leading the way in pragmatic trials developed subsequent to ASOS [21]. Yet, in our own country there is still much to learn about the improvement of perioperative care. Expanding the local investigator network, gathering data to identify variation in practice, and interpreting and using that data to drive change and strengthen the healthcare system should be prioritised for South African clinicians.

Acknowledgements

Dawid EA van Straaten, Bioinformatician, Safe Surgery South Africa NPC.

Funding

None.

Ethics declarations

Conflict of interest

The authors have no conflict of interest to declare.

Ethical approval

Data for the model derivation cohort were obtained from the African Surgical Outcomes Study, registered on the South African National Health Research Database (KZ_2015RP7_22), and on ClinicalTrials.gov (NCT03044899). The primary ethics approval was received from the Biomedical Research Ethics Committee of the University of KwaZulu-Natal, South Africa (BE306/15).

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