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Pediatric Index of Mortality 3—An Evaluation of Function Among ICUs In South Africa*

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OBJECTIVES: To evaluate the performance of the Pediatric Index of Mortality 3 as mortality risk assessment model.

DESIGN: This prospective study included all admissions 30 days to 18 years old for 12 months during 2016 and 2017. Data gathered included the following: age and gender, diagnosis and reason for PICU admission, data specific for the Pediatric Index of Mortality 3 calculation, PICU outcomes (death or survival), and length of PICU stay.

SETTING: Nine units that care for children within tertiary or quaternary academic hospitals in South Africa.

PATIENTS: All admissions 30 days to 18 years old, excluding premature infants, children who died within 2 hours of admission, or children transferred to other PICUs, and those older than 18 years old.

INTERVENTIONS: None.

MEASUREMENTS AND MAIN RESULTS: There were 3,681 admissions of which 2,253 (61.3%) were male. The median age was 18 months (interquartile range, 6–59.5 mo). There were 354 deaths (9.6%). The Pediatric Index of Mortality 3 predicted 277.47 deaths (7.5%). The overall standardized mortality ratio was 1.28. The area under the receiver operating characteristic curve was 0.81 (95% CI 0.79–0.83). The Hosmer-Lemeshow goodness-of-fit test statistic was 174.4 ($p < 0.001$). Standardized mortality ratio for all age groups was greater than 1. Standardized mortality ratio for diagnostic subgroups was mostly greater than 1 except for those whose reason for PICU admission was classified as accident, toxin and envenomation, and metabolic which had an standardized mortality ratio less than 1. There were similar proportions of respiratory patients, but significantly greater proportions of neurologic and cardiac (including postoperative) patients in the Pediatric Index of Mortality 3 derivation cohort than the South African cohort. In contrast, the South African cohort contained a significantly greater proportion of miscellaneous (including injury/accident victims) and postoperative noncardiac patients.

CONCLUSIONS: The Pediatric Index of Mortality 3 discrimination between death and survival among South African units was good. Case-mix differences between these units and the Pediatric Index of Mortality 3 derivation cohort may partly explain the poor calibration. We need to recalibrate Pediatric Index of Mortality 3 to the local setting.

KEY WORDS: case-mix; intensive care units; mortality; Pediatric Risk of Mortality; quality of care; risk adjustment

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A fundamental measure of the quality of care in any PICU is its success at saving the lives of critically ill or injured children. Therefore, a validated measure of the risk of dying to facilitate benchmarking of performance

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is crucial. This benchmarking seems particularly relevant in a resource-constrained country like South Africa, where optimal use of critical care resources is paramount (1). Compared with Australia, the United Kingdom, and New Zealand, where the Pediatric Index of Mortality (PIM) scores were derived, South Africa in 2017 had a lower gross domestic product per capita (7,480 vs 37,700 to 561,000 U.S. dollar) and higher under-five mortality rate (35.3 vs 3.7 to 5.8 deaths per 1,000 live births) (2).

The most commonly used mortality risk assessment scores are the Pediatric Risk of Mortality (PRISM) (3), the PIM (4, 5) scores, and their derivatives (3, 4). These scores, derived in specific populations over specific periods, need to demonstrate acceptable performance across a range of mortality risk categories and case-mix scenarios before applying them in different environments.

The PIM 3 (6) is the latest iteration of the PIM, derived by logistic regression using the PIM 2 variables among nearly 53,000 admissions to PICUs in the United Kingdom (UK), Ireland, Australia, and New Zealand during 2010 and 2011. It demonstrated good discrimination with an average area under the receiver operating characteristic curve (AUC-ROC) of 0.88. PIM 3 performed better in Australia and New Zealand (AUC-ROC, 0.91) than in the United Kingdom and Ireland (AUC-ROC, 0.85).

A few studies have since sought to validate the discriminatory ability and calibration of the PIM 3 outside of the original derivation environments. These have included studies from both high-income countries (South Korea [7], Singapore [8], and Italy [9]) and middle-income countries (India [10], Indonesia [11], and Argentina [12]). In these studies, discrimination was assessed by determining the AUC-ROC for the outcome of PICU mortality, and calibration was evaluated by the Hosmer-Lemeshow test looking at the statistical significance of the difference between actual and predicted mortality, within deciles of increasing mortality risk.

The single-center studies from South Korea (n = 1710) (7) and Singapore (n = 570) (8) both found good calibration of the PIM 3, but discrimination varied with AUC-ROCs of 0.76 (acceptable) and 0.88 (good) respectively. The multicenter Italian study, which included 17 PICUs (n = 11,109), reported an AUC-ROC of 0.88 and good calibration (p = 0.21).

The single-center studies from India (n = 202) (10) and Indonesia (n = 69) (11) both found acceptable discrimination (AUC-ROCs, 0.75 and 0.77, respectively). Calibration was poor in India (p = 0.001), and although not formally assessed in Indonesia, the authors reported a standardized mortality ratio (SMR) of 2.24. The Argentinian (12) study included 49 PICUs (n = 6602) and found good discrimination (AUC-ROC, 0.83) but poor calibration ($p < 0.001$).

Most recently, a secondary analysis of the Paediatric Early versus Late Parenteral Nutrition in Critical Illness (PEPaNIC) study included one PICU each from Belgium, Canada, and the Netherlands (n = 1428) and found good discrimination (AUC-ROC, 0.89) and good calibration (p = 0.58) (13).

Some of the studies noted above also simultaneously compared the performance of the PIM 3 with other established pediatric mortality prediction scores. The PIM 3 outperformed the PIM 2 concerning discrimination in India (AUC-ROC, 0.69; p = 0.001) (10), and although the AUC-ROCs were the same in Italy, the PIM 2 showed poor calibration ($p < 0.001$) (9). The Pediatric Logistic Organ Dysfunction-2 score displayed both similar discrimination (AUC-ROC, 0.86) and calibration (p = 0.24) in Singapore and had a favorable SMR of 1.08 compared with that of the PIM 3 (1.54) (8). Last, although the PRISM-3 had a significantly higher AUC-ROC (0.92, p = 0.04) than the PIM 3, it demonstrated poor calibration (p = 0.04) among the PEPaNIC patients (13).

There are several PICUs in South Africa in both public and private healthcare with a variety of case-mixes (14). Few routinely gather data to assess risk-adjusted mortality by the PIM 3 score. To date, only two single-center studies have superficially investigated the local performance of the PIM 3, reporting SMRs of 3.3 (n = 96) (15) and 1.0 (n = 530) (16), respectively. This study aimed to evaluate, formally, the utility of the PIM 3 as a model of PICU mortality risk assessment in regionally representative PICUs in South Africa.

MATERIALS AND METHODS

Setting

We included nine units caring for children associated with tertiary academic hospitals in South Africa. These units differ in terms of size, human and infrastructure

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resources available, and case-mix. Six are dedicated PICUs, two are mixed adult-pediatric units with dedicated beds and medical staff for children, and one is a dedicated cardiothoracic unit caring for both adults and children.

Methods

This study was a prospective study of all admissions one month to 18 years old to participating PICUs in South Africa over 12 months during 2016 and 2017. Deaths in the PICU and PICU length of stay (LOS) were the primary outcome measures.

Data Collection

A standard data record form, or Microsoft Excel spreadsheet (Microsoft Corporation, Redmond, WA) based on the form, was used. The following data were collected: gender, age, diagnosis and the main reason for PICU admission, outcome data in terms of LOS and death or survival in PICU, and data necessary for the calculation of the PIM 3 score. Collaborating investigators gathered data at each center for the duration of the study.

There was no formal training on how to gather PIM 3 specific data. However, each data gatherer had access to published guidelines for PIM 3 data collection, or some routinely calculated the PIM 3 score by automated databases and the data exported to the protocol-specific spreadsheet.

Analysis

We determined descriptive statistics for the whole cohort and diagnostic and age categories. We reported medians (together with interquartile ranges [IQRs]) for all variables related to age and duration of stay. We reported proportions (percentages) for all other categorical variables. We determined the PIM 3 performance in terms of discrimination and calibration for the whole cohort.

We determined the performance of the PIM 3 regression equation to discriminate between the outcomes of ICU death or survival by the AUC-ROC. This graph plots truly predicted nonsurvivors against falsely predicted nonsurvivors for each value of the score. We determined the AUC-ROC for the whole cohort and each participating unit. A perfect score should yield an AUC-ROC of 1.0, whereas a chance finding would yield an AUC-ROC equals to 0.5. Shann (17) classified the discrimination ability of the PIM 3 score as acceptable if AUC-ROC is between 0.70 and 0.79, good if between 0.80 and 0.89, and excellent if AUC-ROC was greater than 0.9.

Score calibration was assessed across 10 mortality risk strata by the Hosmer-Lemeshow goodness-of-fit test, which yields a chi-square type of statistic and a *p* value. A *p* value of greater than or equal to 0.05 indicates a good fit, whereas *p* value of less than 0.05 indicates lack of fit. We calculated SMR with 95% CI for each risk category and generated a calibration curve for these data (18).

We determined the SMR (with 95% CIs) for the whole cohort, and diagnostic and age categories.

We determined 95% CIs according to the method by Vandenbroucke (19), which assumes a Poisson distribution of the sample. We implemented this determination in Microsoft Excel using the method described by statistician Paikousis, on the website "Stack Exchange":

95% CI lower = ([sqrt(observed) – 1.96 × 0.5]^2)/ predicted and 95% CI upper = ([sqrt(observed) + 1.96 × 0.5]^2)/ predicted

We determined the statistical significance of the difference in proportions of case-mix categories between the PIM 3 derivation and the South African cohorts by two-proportion Z test (two-tailed) for each diagnostic category. A *p* value of less than 0.05 was considered statistically significant.

Interventions

None.

Ethics

We obtained full approval from the Human Research Ethics Committee of the Faculties of Health Sciences of each of the Universities to which the participating PICUs are affiliated and from the Provincial research ethics committees where applicable. Patient confidentiality was maintained by anonymizing all data. This research project adhered to the requirements of the Declaration of Helsinki (2013) (20). Institutional ethics approval references are Ethics Reference No.: 245/2015 UP, ECUFS NR 112/2015, Ethics Reference number: N15/05/036, Reference: 298/15 KZ_2015RP50_564, Reference: HRKM156/15 NHRD Ref.: KZ_2015RP48_815, and HREC REF: 700/2015.

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TABLE 1.
Observed and Expected Outcomes for Diagnostic Categories

Diagnostic Category	*n* (%)	Observed Deaths, *n*	Mortality Rate, %	Expected Deaths, *n*	SMR	95% CI for SMR
Respiratory	1,044 (23.4)	114	10.9	79.8	1.43	1.17–1.7
Cardiac	307 (6.9)	59	19.2	31.1	1.9	1.44–2.41
Postoperative cardiac bypass	315 (7.1)	8	2.5	7.1	1.13	0.48–2.04
Postoperative cardiac nonbypass	89 (2)	10	11.2	8.6	1.16	0.55–1.99
Postoperative noncardiac	999 (22.4)	37	3.7	23.1	1.6	1.12–2.15
Accident	285 (6.4)	26	9.1	29.3	0.89	0.57–1.26
Neurologic	288 (6.5)	61	21.2	34.5	1.77	1.35–2.23
Gastrointestinal tract	321 (7.2)	33	10.3	27.6	1.19	0.82–1.63
Renal/urologic	91 (2.04)	17	18.7	10.2	1.67	0.96–2.55
Hematologic/oncologic	81 (1.8)	25	30.9	9.8	2.55	1.64–3.64
Sepsis	204 (4.6)	49	24	33.6	1.46	1.07–1.89
Toxin/envenomation	89 (2)	7	7.9	9.6	0.73	0.29–1.37
Metabolic	84 (1.9)	6	7.1	7.4	0.81	0.29–1.59
Other	256 (5.7)	6	2.3	5.5	1.1	0.39–2.14

SMR = standardized mortality ratio.

RESULTS

Patient Characteristics

There were 3,681 admissions reported from nine University-affiliated PICUs. Of these, 2,253 (61.3%) were male, and 1,424 (38.7%) female. The median age was 18 months (IQR, 6–59.5 mo).

Outcome

There were 354 deaths (9.6%) among participating PICUs with 277.5 deaths (7.5%) predicted by PIM 3 resulting in an overall SMR of 1.28 (95% CI, 1.15–1.41). PICU median LOS was 3 days (IQR, 1–7 d).

Observed and expected outcomes and SMR (95% CI) for diagnostic categories and age are presented in **Tables 1** and **2**, respectively.

Figure 1 shows ROC analyses for the whole dataset. The AUC-ROC was 0.81 (95% CI, 0.79–0.83) (**Fig. 2**). The AUC-ROC among the participating units ranged from 0.72 to 0.88.

Table 3 shows the Hosmer-Lemeshow goodness-of-fit test ($p < 0.001$). Figure 2 shows the associated calibration curve. This calibration curve shows a significant lack of fit when arranging the data in categories of ascending risk with nearly equal numbers of cases per group. Forty percent of the deaths occurred among those with PIM 3 predicted mortality risks up to 8.3% (143/354 deaths).

Comparison With Derivation Units

Table 4 shows a comparison of the proportions of admissions assigned to diagnostic categories between the South African PICUs and the PIM 3 derivation population. According to the two proportions *z* score (two-tailed) test, there are similar proportions of respiratory patients between the two cohorts. There are significantly larger proportions of neurologic and cardiac (including postoperative) patients in the derivation cohort than the South African PICUs and a significantly greater proportion of miscellaneous including injury/accident victims and postoperative noncardiac

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TABLE 2.
Observed and Expected Outcomes for Age

Age Range (mo)	*n* (%)	Deaths	Mortality Rate, %	Expected Deaths, *n*	SMR	95% CI for SMR
1–4	813 (22.1)	92	11.3	79.1	1.16	0.94–1.41
5–11	612 (16.6)	60	9.8	41.0	1.47	1.12–1.86
12–23	695 (18.9)	70	10.1	53.7	1.3	1.02–1.63
24–59	645 (17.5)	55	8.5	45.9	1.2	0.9–1.54
60–119	555 (15.1)	43	7.7	34.5	1.25	0.9–1.65
≥ 120	361 (9.8)	34	9.4	23.3	1.46	1.01–1.99
Total	3,681	354	9.6			

SMR = standardized mortality ratio.

patients among the South African PICUs than in the derivation units.

DISCUSSION

The PIM 3 was derived from data collected in PICUs in the United Kingdom, Ireland, Australia, and New Zealand. Disease profiles in those populations are likely different from the ones managed in the South African ICUs included in this study. Furthermore, South African units are more constrained in terms of human and capital resources. This constraint accentuates the need for optimized outcomes from PICU utilization, and it is within this context that we have evaluated PIM 3.

We have demonstrated, among diverse units with significant case-mix differences from the derivation cohort, acceptable to good discrimination, despite the considerable difference in available resources. The poor calibration is demonstrated by SMRs exceeding one among most of the deciles of risk, diagnostic and age categories, and a Hosmer-Lemeshow *p* value of less than 0.05. Of note, the highest SMR occurred within the lowest risk decile of the Hosmer-Lemeshow table. This observation means that both the systems and processes of care in our setting are different to the PIM 3 derivation units, or there are risk factors that affect our outcomes that are not incorporated into the PIM 3 model development.

Calibration of the PIM 3 has differed among studies with good calibration reported from Italy, Korea, Belgium, The Netherlands, and Canada, but poor calibration reported from India and Argentina. Difference in resources, skills, and access to healthcare have been proposed as possible factors contributing to the elevated SMR in a Singapore PICU (8), whereas the effect of case-mix on the calibration of the PIM 3 was highlighted by the poor performance among hematology-oncology patients in Korea (AUC-ROC, 0.66) (7). Further reasons postulated for poor calibration have included poor performance of the units in which the PIM 3 was evaluated relative to the derivation units and specific diagnostic groups not considered in the PIM 3 risk variables.

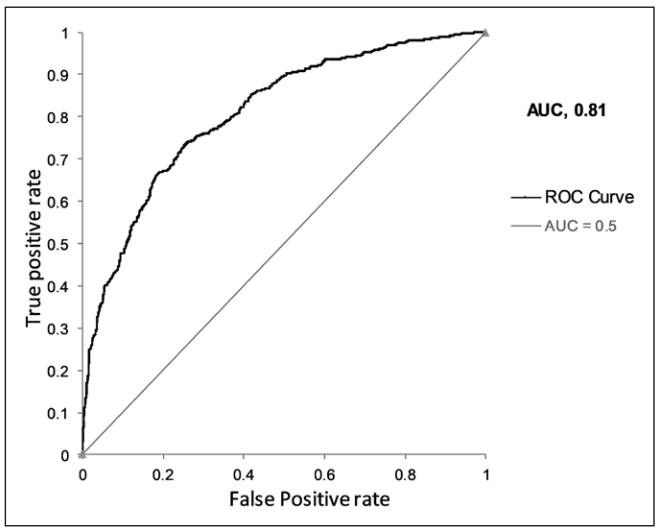


Figure 1. The area under the receiver operating characteristic curve (AUC ROC) for the whole dataset. *x*-axis = the false-positive rate. *y*-axis = the true-positive rate.

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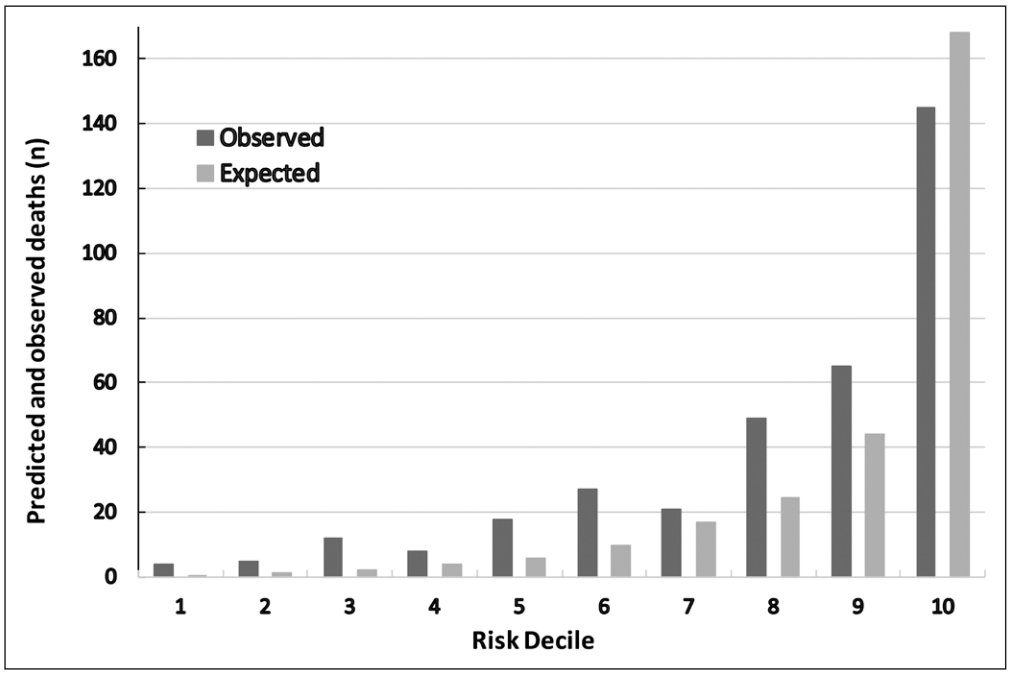


Figure 2. Calibration curve for observed versus expected deaths per decile of risk.

This present study has also demonstrated acceptable discrimination but poor calibration ability of the PIM 3 among South African units, comparable with most of the postderivation PIM 3 evaluation studies. Indeed, only one recent South African study from a mixed pediatric-neonatal ICU has demonstrated good calibration of the PIM 3 with an SMR of 1.00, perhaps due to the high number of patients admitted after cardiac arrest (16). In such a setting where a substantial number of deaths are associated with high predicted-risk, a better model fit is perhaps not unexpected.

The reasons for the increased SMRs reported by studies cited above are not fully understood but likely reflects differences in case-mix and the potential impact of malnutrition and communicable diseases such as HIV and TB, which are much more prevalent in lower middle-income countries. Thus in our study, SMRs above 1 may not only reflect differences in the respective standards of care but also the presence of risk factors, disease patterns, and pathogens

TABLE 3.
Hosmer-Lemeshow Table for Observed Versus Pediatric Index of Mortality 3 Expected Deaths and Survivors

	Hosmer- Lemeshow Table							
Decile Groups	Pediatric Index of Mortality 3 Derived Average Risk	*n*	Observed Deaths, *n*	Expected Deaths	Observed Survivors, *n*	Expected Survivors	Standardized Mortality Ratio	95% CI
1	0.0016	366	4	0.6	362	365.4	6.67	1.73–14.8
2	0.0035	368	5	1.3	363	366.7	3.85	1.21–7.96
3	0.0065	368	12	2.4	356	365.6	5.00	2.57–8.23
4	0.0106	368	8	3.9	360	364.1	2.05	0.88– 3.72
5	0.0155	368	18	5.7	350	362.3	3.16	1.87–4.79
6	0.0269	368	27	9.9	341	358.1	2.73	1.8–3.85
7	0.0455	368	21	16.8	347	351.2	1.25	0.77–1.84
8	0.0668	368	49	24.6	319	343.4	1.99	1.47–2.59
9	0.1197	368	65	44.1	303	324.0	1.47	1.14–1.85
10	0.4574	368	145	168.3	223	199.7	0.86	0.73–1.01

Hosmer-Lemeshow statistic = 174.4; degrees of freedom = 8; $p < 0.001$.

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TABLE 4.
Case-Mix Comparison Between South African PICUs and Pediatric Index of Mortality 3 Derivation PICUs

Diagnostic Category	Pediatric Index of Mortality 3 Derivation Cohort *n* (%)	South African Cohort *n* (%)	*p*[a]
Miscellaneous including injury/accident	8,222 (16.0)	1,196 (28.2)	< 0.001
Cardiac including postoperative	13,838 (27.0)	711 (16.8)	< 0.001
Neurologic	4,760 (9.3)	288 (6.8)	< 0.001
Respiratory	13,317 (26.0)	1,044 (24.6)	0.06
Postoperative (noncardiac)	11,178 (21.8)	999 (23.6)	0.007
Total	51,315	4,238	

[a]*p* values determined by two-proportion Z test (two tailed) for each diagnostic category significance at $p < 0.05$.

prevalent within populations served by South African PICUs which are different from those of the derivation studies.

We have demonstrated that the case-mix between South African and the PIM 3 derivation populations is significantly different concerning neurologic, cardiac, and miscellaneous (including injury/accident) diagnostic classifications. This difference may imply that there are conditions prevalent in our setting associated with worse outcomes than in the derivation populations. This study, however, did not address the effect of malnutrition, HIV, and other factors, which could affect mortality risk outside of the PIM 3 variables. We recommend this for future studies.

A limitation of this study is that there was no formal testing of interrater bias (21), which may, in part account for the variability in the AUC-ROCs among the different units included in the study. Despite this, the AUC-ROC values range from "acceptable" to "good" (17) among all the South African ICUs involved with this study. Another consideration is that assignment of cases to the PIM 3 categories of risk might not have been consistent throughout the dataset, which could lead to erroneous PIM 3 derived mortality risk.

CONCLUSIONS

In this first multicenter study from South Africa, we have demonstrated that the PIM 3 can discriminate reasonably well among a mixed PICU population. Although calibration is poor, case-mix differences and factors not captured by the PIM 3 pertinent to our populations may play a role.

Heterogenous systems of care between, in addition to case-mix differences among PICUs, ICUs participating in this study possibly contribute to the poor calibration of PIM 3 in our context.

Future research should analyze these data and determine how different contexts of care affect SMR as determined by PIM 3. A well-calibrated score would allow benchmarking of quality of care between PICUs in South Africa. Shann (17) outlines how to decide about the appropriate use of a mortality risk assessment score in any setting. Although our study has demonstrated good discrimination, according to Shann (17), we have shown poor calibration with inconsistent ratios of observed versus expected deaths across all deciles of risk and a greater proportion of deaths with higher SMRs within the lower categories of risk. Therefore, we suggest that the PIM 3 needs to be calibrated to our local setting. However, the trade-off is that the recalibrated score will no longer be useful for benchmarking against the derivation populations and systems of care, at the time that PIM 3 was developed.

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