Educational Outcomes of Childhood Survivors of Critical Illness—A Population-Based Linkage Study*

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OBJECTIVES: Major postintensive care sequelae affect up to one in three adult survivors of critical illness. Large cohorts on educational outcomes after pediatric intensive care are lacking. We assessed primary school educational outcomes in a statewide cohort of children who survived PICU during childhood.

DESIGN: Multicenter population-based study on children less than 5 years admitted to PICU. Using the National Assessment Program–Literacy and Numeracy database, the primary outcome was educational achievement below the National Minimum Standard (NMS) in year 3 of primary school. Cases were compared with controls matched for calendar year, grade, birth cohort, sex, socioeconomic status, Aboriginal and Torres Strait Islander status, and school. Multivariable logistic regression models to predict educational outcomes were derived.

SETTING: Tertiary PICUs and mixed ICUs in Queensland, Australia.

PATIENTS: Children less than 5 years admitted to PICU between 1998 and 2016.

INTERVENTIONS: Not applicable.

MEASUREMENTS AND MAIN RESULTS: Year 3 primary school data were available for 5,017 PICU survivors (median age, 8.0 mo at first PICU admission; interquartile range, 1.9–25.2). PICU survivors scored significantly lower than controls across each domain ($p < 0.001$); 14.03% of PICU survivors did not meet the NMS compared with 8.96% of matched controls ($p < 0.001$). In multivariate analyses, socioeconomic status (odds ratio, 2.14; 95% CI, 1.67–2.74), weight (0.94; 0.90–0.97), logit of Pediatric Index of Mortality-2 score (1.11; 1.03–1.19), presence of a syndrome (11.58; 8.87–15.11), prematurity (1.54; 1.09–2.19), chronic neurologic conditions (4.38; 3.27–5.87), chronic respiratory conditions (1.65; 1.24–2.19), and continuous renal replacement therapy (4.20; 1.40–12.55) were independently associated with a higher risk of not meeting the NMS.

CONCLUSIONS: In this population-based study of childhood PICU survivors, 14.03% did not meet NMSs in the standardized primary school assessment. Socioeconomic status, underlying diseases, and severity on presentation allow risk-stratification to identify children most likely to benefit from individual follow-up and support.

KEY WORDS: child; critical care; education; mortality; neurodevelopment; school achievement

In high-income countries, each year between 1.43 and 2.12 per 1,000 children requires PICU admission for treatment or monitoring due to life-threatening illness or surgery (1, 2). Mortality remains the primary measure to assess PICU outcomes, and standardized mortality rates represent the most widely used benchmarks for evaluating the performance of PICUs (3).

***See also p. 1010.**

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Over the past decades, survival for critically ill children has continuously improved with current mortality rates as low as 2.18% (1, 4–6).

An emerging body of literature in critically ill adults has brought the extensive psychologic and cognitive impact of critical illness on patients and their families to attention (7, 8). Sequelae ranging from posttraumatic stress disorder or mental health problems, physical disabilities, to long-term cognitive impairment as a result of brain injury affect up to one in three adult survivors of critical illness. In critically ill children, 28–31% of patients with severe sepsis (9, 10) and up to 38% of infants undergoing surgery for congenital heart disease (11) suffer from substantial disability following PICU discharge (12). Long-term morbidity after critical illness directly affects quality of life in survivors and represents a patient-centered outcome of great relevance to families (13, 14).

To date, pediatric long-term outcome literature has been primarily based on cohort studies with a follow-up duration of less than 24-month post-PICU stay using tests of gross function or quality of life (15, 16). Although persisting functional and cognitive impairments can be more reliably assessed once school age is reached, such follow-up, where available, has been largely restricted to highly selected subgroups such as children with congenital heart disease or extremely low birth weight infants (17, 18). Access to robust long-term outcome data will position us to better understand the long-term cost of disease, provide parents with more accurate prognostic estimates, and allow measuring the long-term impact of different interventions (19).

The aim of this study was to assess educational outcomes at school age in children who had required ICU admission before 5 years old. We analyzed performance during primary school using a standardized national school assessment in a population-based cohort of critically ill children and identified predictors of poor educational outcomes.

PATIENTS AND METHODS

This is a multicenter statewide data linkage study based on the Australian and New Zealand Paediatric Intensive Care (ANZPIC) Registry. The study was approved by the Human Research and Ethics Committee (Children's Health Queensland, Brisbane, Australia; number HREC/16/QRCH/255), including waiver of consent. Children less than 5 years requiring ICU admission in Queensland, Australia, between January 1, 1998, and December 31, 2016, were eligible. During this time, the population of Queensland increased from 3,401,232 to 4,883,739 (Australian Bureau of Statistics). We linked the ANZPIC Registry data with the Registrar General deaths registry and with educational data provided by the Queensland Curriculum and Assessment Authority (QCAA). A combination of deterministic and probabilistic matching was performed by the Statistical Services Branch, Queensland Health, depending on the available identifying information in each data source: using sex, date of birth, post code, facility, date of admission, and name.

The ANZPIC Registry (3, 20) prospectively records data fields among children less than 16 years admitted to ICU, including patient characteristics, diagnoses, severity markers, and physiologic variables, with regular data validation and auditing. The QCAA data cover the National Assessment Program—Literacy and Numeracy (NAPLAN, https://www.nap.edu.au/), a nationwide standardized assessment for all students in school years 3, 5, 7, and 9, and have been administered annually since 2008 across Australian public and private schools (**Supplemental Methods**, http://links.lww.com/CCM/G987). NAPLAN test domains include: 1) reading, 2) writing, 3) spelling, 4) grammar and punctuation, and 5) numeracy.

Control Groups

Averaged NAPLAN test results for all Queensland students participating in a Year 3 NAPLAN test during 2008 to 2017 were used as overall controls. In addition, 1:1 matched controls were extracted from QCAA (Supplementary Methods, http://links.lww.com/CCM/G987) based on the following criteria by order of priority: 1) calendar year of the NAPLAN test, 2) year level (grade), 3) year of birth, 4) sex, 5) socioeconomic status (SES), 6) Aboriginal and Torres Strait Islander status, and 7) school.

Definitions and Outcomes

We extracted critical care variables based on the principal, underlying, and associated diagnoses captured in ANZPIC Registry (4, 20), admission characteristics, and treatment and severity factors such as Pediatric Index of Mortality-2 (21, 22) (PIM-2). SES was

constructed using information on maternal and paternal highest education and profession in the QCAA dataset and was classified into low, middle, and high SES (23, 24). The data captured through the standardized NAPLAN testing performed at year 3 of primary school (children are usually 8 ± 1 years of biological age when sitting this test) were used to construct the outcomes. For each of the five NAPLAN measurement domains, we considered their score and whether a student had been exempt. As per the NAPLAN standards, exempt students are those with significant disability or coexisting conditions that severely limit their capacity to participate in the tests. Exemptions are recorded along with other reasons for missing tests, including being absent on the test day, or having been withdrawn from testing by their parents. A threshold defined as the National Minimum Standard (NMS) exists for each domain, capturing the minimum acceptable standard of knowledge and skills without which a student will have difficulty making sufficient progress at school. Band 2 (lower threshold score of 270) is the minimum standard for Year 3 NAPLAN testing. Children who are exempt are automatically classified as below NMS. Of the five NAPLAN domains, reading and numeracy are considered most important due to their impact on long-term academic achievement (25). Numeracy and reading correlate highly with the other NAPLAN domains, and previous studies demonstrated their utility and stability over time (26). We therefore defined the primary outcome as children classified below the NMS on both NAPLAN numeracy and reading domains in year 3. Secondary outcomes included children classified below the NMS on Numeracy or Reading domains, classified below the NMS on all five NAPLAN domains, and classified below the NMS on at least one of the five NAPLAN domains.

Statistical Analyses

Data are presented as percentages and numbers or medians with interquartile range (IQR). *T* tests were used to compare normally distributed data, and proportion tests were used to compare subgroups. Outcome prediction models were developed using a stepwise logistic regression approach considering patient characteristics, physiologic and severity values at admission, diagnostic codes characterizing main disease and comorbidities, treatment interventions, number of ICU admissions, and SES. We used a backward stepwise elimination procedure to eliminate nonsignificant predictors based on $p > 0.05$, keeping test year in the model. The main multivariable model was based on data available during the first PICU admission before a child's fifth birthday. Sensitivity analyses were conducted including information from all PICU admissions occurring before the fifth birthday in the model. All analyses were conducted using Stata (Version 14.0, Stata Corp, College Station, TX). *p* values of less than 0.05 were considered statistically significant.

RESULTS

Cohort Overview

A total of 6,948 patients were admitted to ICU in Queensland before their fifth birthday between 1998 and 2016 and were eligible for NAPLAN testing based on their age and birth cohort (**Supplementary Fig. 1**, http://links.lww.com/CCM/G987). $n = 414$ (6.0%) had died before the NAPLAN test date including deaths in ICU and deaths postdischarge. A total of 5,017 out of 6,534 eligible children (76.8%) with a median age at first admission to ICU of 8.0 months (IQR, 1.9–25.2) had ICU data successfully linked to Year 3 NAPLAN outcome data and comprised the final study cohort (**Table 1**). Children who were not successfully linked were significantly younger, had a higher proportion of syndromes, had higher predicted mortality, and required more intensive care support in comparison with the children included in the study ($p < 0.05$; **Supplementary Table 1**, http://links.lww.com/CCM/G987).

Description of Educational Outcomes in ICU Survivors

We compared the rates of participation and average scores in the NAPLAN tests between the ICU sample, the average Queensland student population, and matched controls (**Supplementary Tables 2–6**, http://links.lww.com/CCM/G987). ICU cases had lower rates of participation in NAPLAN and significantly higher rates of being exempt from NAPLAN testing, compared with the Queensland student population ($p < 0.001$), and to matched controls (both $p < 0.001$) in each of the five domains. On average, 79.0% ($n = 3,964$) of the ICU survivors were able to participate in

TABLE 1.
Descriptive Statistics of 5,017 Children Surviving PICU Admission Based on First and All PICU Admissions Before the Fifth Birthday

Variables	First Admission (*n* = 5,017)	All Admissions (*n* = 5,017)	All Readmissions (*n* = 5,017)
Demographics			
Sex (male)		2,954 (58.9%)	
Aboriginal and Torres Strait Islander		552 (11.0%)	
Socioeconomic status			
No information		699 (13.9%)	
Low SES		1,377 (27.4%)	
Medium SES		1,513 (30.2%)	
High SES		1,428 (28.5%)	
Age, d, median (IQR)	239 (56–757)	319.50 (80–825)	445 (151–957)
Weight, kg, median (IQR)	7.94 (4.00–12.00)	8.66 (4.60–12.50)	4.50 (3.30–7.90)
No. of PICU admissions before the fifth birthday			
1		3,885 (77.4%)	
2		651 (13.0%)	
≥ 3		481 (9.6%)	
Main disease groups			
Asthma	174 (3.5%)	185 (3.7%)	19 (0.8%)
Bronchiolitis	510 (10.2%)	559 (11.1%)	176 (7.5%)
Invasive infections	312 (6.2%)	379 (7.6%)	96 (4.1%)
Congenital heart disease	1,036 (20.6%)	1,086 (21.6%)	908 (38.8%)
Oncologic conditions	114 (2.3%)	123 (2.5%)	
Chronic respiratory conditions	506 (10.1%)	612 (12.2%)	320 (13.7%)
Chronic neurologic conditions	277 (5.5%)	349 (7.0%)	242 (10.3%)
Prematurity	294 (5.9%)	294 (5.9%)	219 (9.4%)
Trauma	440 (8.8%)	462 (9.2%)	42 (1.8%)
Congenital syndrome	314 (6.3%)	371 (7.4%)	346 (14.8%)
Admission characteristics			
PIM-2 risk of death, mean (SD)	2.29% (5.1%)	2.65% (5.6%)	3.1% (5.9%)
PIM-2 risk of death, median (IQR)	0.90% (0.2–2.5%)	1.02% (0.2–3.0%)	1.3% (0.4–3.2%)
Interhospital transfer	1,191 (23.7%)	1,280 (25.5%)	479 (20.5%)
Elective admission	2,337 (46.6%)	2,625 (52.3%)	1,279 (54.6%)
Recovery from surgery	2,405 (47.9%)	2,754 (54.9%)	1,124 (48.0%)
Severity and treatment			
Intubation, d, median (IQR)	0 (0.00–0.93)	0 (0.00–1.59)	1.0 (0.06–3.63)
PICU length of stay, d, median (IQR)	1.04 (0.72–2.67)	1.43 (0.78–3.85)	1.61 (0.76–4.32)
Hospital length of stay, d, median (IQR)	6.95 (3.31–12.04)	4.36 (0.00–11.16)	13.15 (6.65–29.75)
Respiratory support, d, median (IQR)	0.54 (0.17–1.42)	0.00 (0.00–0.00)	0.74 (0.52–2.50)
Extracorporeal membrane oxygenation	2 (< 0.1%)	5 (0.1%)	10 (0.4%)
Inhaled nitric oxide	34 (0.7%)	70 (1.4%)	43 (1.8%)
Continuous renal replacement	16 (0.3%)	24 (0.5%)	40 (1.7%)
High-frequency oscillatory ventilation	36 (0.7%)	59 (1.2%)	27 (1.2%)

IQR = interquartile range, PIM-2 = Pediatric Index of Mortality-2, SES = socioeconomic status.

Year 3 NAPLAN across the five domains, compared with 93.2% in the Queensland student population, and 87.0% (mean $n = 4,357$) in the matched control sample ($p < 0.001$). On average, 11.7% (mean $n = 588$) of the PICU group were exempt from the five NAPLAN domains, compared with 1.6% in the Queensland student population ($p < 0.001$) and 7.3% (mean $n = 363$) in the matched controls group ($p < 0.001$). In addition, rates of withdrawal due to parental decisions were significantly higher in ICU survivors compared with both control groups across NAPLAN domains ($p < 0.001$). When comparing the average Year 3 NAPLAN scores for those who were able to participate in the tests, ICU survivors consistently scored lower compared with the average Queensland student population and compared with the matched control sample across all NAPLAN domains (**Supplementary Table 7**, http://links.lww.com/CCM/G987; and **Fig. 1*A***). On average, the ICU sample scored 20 points lower than the Queensland population (ICU = 379; Queensland population = 399; $p < 0.001$) and 13 points (ICU = 379; Controls = 392; $p < 0.001$) lower than the matched control sample.

Across all the NAPLAN domains, the proportion of students who were below the NMS in PICU

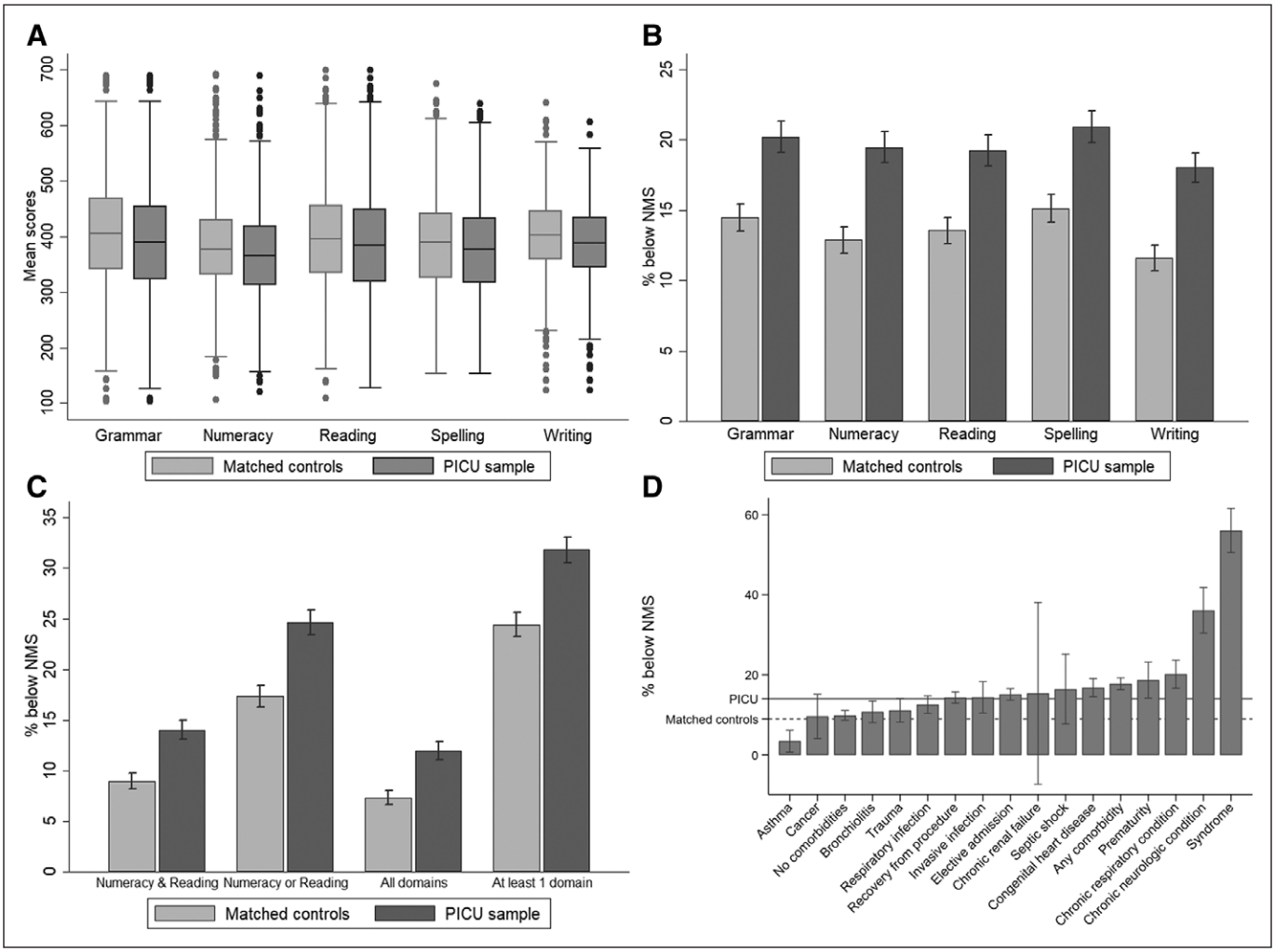

Figure 1. Educational outcomes assessed through the Year 3 National Assessment Program—Literacy and Numeracy (NAPLAN) in 5,017 children who survived PICU admission before their fifth birthday are shown comparing PICU survivors and matched controls. **A**, Box-whisker plots comparing Year 3 NAPLAN scores between PICU survivors and controls for each of the five NAPLAN domains. **B**, Proportion of students failing to meet the National Minimal Standard (NMS) during Year 3 NAPLAN testing between cases and controls for each of the five NAPLAN domains. **C**, Proportion of students failing to meet the NMS during Year 3 NAPLAN testing between cases and controls for both reading and numeracy, either reading and numeracy, all NAPLAN domains, or at least one NAPLAN domain. **D**, Proportion of students failing to meet the NMS during Year 3 NAPLAN is shown in ascending order for different diagnostic groups in comparing with the average outcomes of PICU survivors (*straight horizontal line*) and in relation to matched controls (*dashed horizontal line*). *Error bars* represent 95% CIs.

survivors was higher than the matched control group ($p < 0.001$) (**Table 2** and **Fig. 1**, ***B*** and ***C***). The proportion of PICU survivors who did not meet the NMS for numeracy and reading varied severalfold between different patient diagnostic groups (**Fig. 1*D***). Overall, 14.0% of PICU survivors did not meet the NMS for numeracy and reading, in comparison with 9.0% of matched controls (absolute difference 5.1%, $p < 0.001$). Similar differences were found for the secondary outcomes.

Prediction of Poor Educational Outcomes Using Variables Available at Time of PICU Discharge

We built logistic regression models using data available at the time of PICU discharge to predict poor educational outcomes (**Table 3**), adjusted for SES, age, sex, weight, and Aboriginal and/or Torres Strait Islander status. Low SES was significantly associated with the primary outcome with an odds ratio (OR) of 2.14 (95% CI, 1.67–2.74; $p < 0.001$) compared with high SES. In addition, there was weak evidence for Aboriginal and Torres Strait Islander patients to be at increased risk of not meeting NMS ($p = 0.051$). Higher weight at PICU admission was associated with lower odds of not meeting the NMS (OR, 0.94; 95% CI, 0.90–0.97; $p = 0.001$). In the adjusted models, several clinical variables were independently associated with a higher risk of not meeting the NMS: severity at admission as measured by the probability of death (logit of PIM-2 1.11; 1.03–1.19; $p = 0.006$), presence of a syndrome (11.58; 8.87–15.11; $p < 0.001$), prematurity (1.54; 1.09–2.19; $p = 0.015$), chronic neurologic conditions (4.38; 3.27–5.87; $p < 0.001$), chronic respiratory conditions (1.65; 1.24–2.19; $p = 0.001$), and need for continuous renal replacement therapy (4.20; 1.40–12.55; $p = 0.010$). A diagnosis of asthma was protective (0.39; 0.17–0.92; $p = 0.032$). Additional multivariable analysis showed that the absence of comorbidities was not significantly associated with failure to meet NMS (1.08; 0.82–1.41; $p = 0.590$).

Sensitivity analyses adding variables on cumulative exposure in children who had greater than one PICU admission before their fifth birthday (Table 3) confirmed the main analyses, except that asthma and renal replacement were no longer significantly associated with the outcome. Multivariable logistic regression on the secondary outcomes (**Supplementary Table 8**, http://links.lww.com/CCM/G987) identified the same independent predictors as the main model. In addition, length of ICU stay emerged as a significant predictor ($p < 0.05$). Sensitivity analyses restricted to children after nonelective admission (**Supplementary Table 9**, http://links.lww.com/CCM/G987) did not confirm the association of weight, prematurity, and chronic respiratory conditions with outcomes, whereas length of intubation and length of ICU stay were significant predictors.

TABLE 2.

Incidence of Main and Secondary Outcomes in 5,017 Children Who Survived PICU Admission Before Their Fifth Birthday

Outcome	PICU Sample	Matched Controls	Difference
Main outcome			
% below NMS on both numeracy and reading	14.03	8.96	5.07% *(z = 7.96)*[a]
Secondary outcomes			
% below NMS on numeracy or reading	24.64	17.38	7.25% *(z = 8.92)*[a]
% below NMS on all NAPLAN domains	11.94	7.32	4.62% *(z = 7.83)*[a]
% below NMS on at least one NAPLAN domain	31.81	24.41	7.40% *(z = 8.25)*[a]

NAPLAN = National Assessment Program—Literacy and Numeracy, NMS = National Minimal Standard.

[a]$p < 0.001$,

The proportions of students failing to meet NMS (defined as a score below 270 or being exempt from testing) during the NAPLAN are compared between PICU survivors and matched controls. Data are based on pooled results of NAPLAN testing between 2008 and 2017. *Z*-statistics from proportions test are shown.

Italics indicate significance ($p < 0.001$).

TABLE 3.

Uni- and Multivariate Regression Analyses of Risk Factors for Not Reaching the National Minimum Standard on Year 3 National Assessment Program—Literacy and Numeracy Reading and Numeracy in 5,017 Children Who Survived PICU Admission Before Their Fifth Birthday

	Bivariate Regressions		Multivariate Regressions (First Admission)		Multivariate Regressions (All Admissions)	
Variables	**OR (95% CI)**	***p***	**OR (95% CI)**	***p***	**OR (95% CI)**	***P***
Demographics						
Female	1.02 (0.87–1.20)	0.835	0.96 (0.80–1.15)	0.644	0.92 (0.77–1.11)	0.396
Aboriginal and Torres Strait Islander	1.41 (1.18–1.69)	< 0.001	1.29 (1.00–1.67)	0.051	1.33 (1.03–1.73)	0.032
Socioeconomic status (reference: high SES)						
No information	2.27 (1.87–2.75)	< 0.001	2.28 (1.71–3.03)	< 0.001	2.19 (1.63–2.93)	< 0.001
Low SES	1.85 (1.56–2.19)	< 0.001	2.14 (1.67–2.74)	< 0.001	2.22 (1.73–2.86)	< 0.001
Medium SES	1.19 (0.99–1.42)	0.061	1.28 (1.00–1.65)	0.054	1.27 (0.98–1.64)	0.069
Age, d	1.00 (1.00–1.00)	0.563	1.00 (1.00–1.00)	0.007	1.00 (1.00–1.00)	0.022
Weight, kg	0.98 (0.96–0.99)	0.007	0.94 (0.90–0.97)	0.001	0.96 (0.93–0.99)	0.025
No. of PICU admissions	–	–	–	–	1.06 (0.99–1.13)	0.082
Main disease groups and comorbidities						
Asthma	0.21 (0.09–0.48)	< 0.001	0.39 (0.17–0.92)	0.032	0.66 (0.33–1.34)	0.251
Bronchiolitis	0.72 (0.54–0.96)	0.026	0.79 (0.56–1.12)	0.183	NA	–
Invasive infections	1.03 (0.75–1.43)	0.837	NA	–	NA	–
Oncologic conditions	0.65 (0.35–1.21)	0.176	NA	–	NA	–
Trauma	0.75 (0.55–1.02)	0.068	NA	–	NA	–
Chronic neurologic condition	3.87 (2.98–5.02)	< 0.001	4.38 (3.27–5.87)	< 0.001	5.08 (3.88–6.64)	< 0.001
Prematurity	1.44 (1.07–1.96)	0.018	1.54 (1.09–2.19)	0.015	1.55 (1.09–2.19)	0.014
Congenital syndrome	10.08 (7.93–12.83)	< 0.001	11.58 (8.87–15.11)	< 0.001	10.27 (7.98 –13.21)	< 0.001
Chronic respiratory condition	1.64 (1.30–2.07)	< 0.001	1.65 (1.24–2.19)	0.001	1.90 (1.46–2.47)	< 0.001
Congenital heart disease	1.31 (1.09–1.58)	0.004	1.21 (0.93–1.57)	0.155	NA	–
Chronic renal failure	1.11 (0.25–5.04)	0.888	NA	–	NA	–
Admission characteristics						
Pediatric Index of Mortality-2 risk of death (logit)	1.10 (1.04–1.16)	< 0.001	1.11 (1.03–1.19)	0.006	1.20 (1.13–1.28)	< 0.001
Interhospital transfer	1.08 (0.90–1.30)	0.397	NA	–	NA	–
Elective admission	1.19 (1.01–1.39)	0.034	0.84 (0.66–1.07)	0.150	NA	–

(*Continued*)

TABLE 3. (*Continued*).

Uni- and Multivariate Regression Analyses of Risk Factors for Not Reaching the National Minimum Standard on Year 3 National Assessment Program—Literacy and Numeracy Reading and Numeracy in 5,017 Children Who Survived PICU Admission Before Their Fifth Birthday

	Bivariate Regressions		Multivariate Regressions (First Admission)		Multivariate Regressions (All Admissions)	
Variables	OR (95% CI)	*p*	OR (95% CI)	*p*	OR (95% CI)	*P*
Severity and treatment						
Intubation, d	1.01 (1.00–1.03)	0.022	0.98 (0.96–1.01)	0.269	NA	–
PICU length of stay, d	1.02 (1.01–1.03)	0.003	1.02 (1.00–1.05)	0.102	NA	–
Hospital length of stay, d	1.01 (1.00–1.01)	0.005	NA	–	NA	–
Respiratory support, d	1.07 (0.98–1.16)	0.125	NA	–	NA	–
Invasive ventilation, d	1.06 (0.98–1.15)	0.167	NA	–	NA	–
Extracorporeal membrane oxygenation	6.13 (0.38–98.18)	0.200	NA	–	NA	–
Inhaled nitric oxide	1.32 (0.54–3.19)	0.544	NA	–	NA	–
Continuous renal replacement	4.80 (1.78–12.94)	0.002	4.20 (1.40–12.55)	0.010	2.31 (0.88–6.04)	0.088
High-frequency oscillatory ventilation	1.23 (0.51–2.96)	0.648	NA	–	NA	–

NA = not applicable, OR = odds ratio, SES = socioeconomic status.

Multivariate regression models were built using information from the first PICU admission (main analyses) and using information from all PICU admissions that occurred before the fifth birthday (sensitivity analyses). All analyses are adjusted for year of test (not shown).

DISCUSSION

In this statewide population-based study assessing educational outcomes in the third year of primary school in 5,017 children who had been admitted to PICU before their fifth birthday, 14% failed to achieve the national minimum standard requirements without which a student will have difficulty making sufficient progress at school. The findings were consistent when comparing PICU survivors with statewide controls and matched controls, with comparable effect sizes observed across each of the five domains of educational assessment. SES emerged as a strong nondisease-related predictor of long-term outcomes, highlighting the importance of supporting children from socially disadvantaged families. Disease severity as assessed by PIM-2 and major chronic conditions were identified as key risk factors. Although some of the effects may be caused by underlying, that is, preexisting conditions rather than reflecting solely the sequelae of critical illness, the findings from this large cohort serve to inform parents, clinicians, and policy makers about the long-term outcomes of childhood PICU survivors.

Over the past decade, research on postintensive care syndrome has highlighted the consequences many survivors experience after critical care, affecting emotional, mental, psychomotor, and cognitive functions of well-being (19). Many studies have applied standardized tests such as the Pediatric Quality of Life Inventory or the Functional Status Scale to children around 12-month post-PICU discharge (15, 16). Studies in extremely preterm infants revealed that early testing both over- and underpredicted a substantial proportion of children who manifested long-lasting impairments evident during assessment at school age (18). Hence, reliable assessment of neurodevelopmental outcomes requires comprehensive assessment at school age, as demonstrated in our study where the median follow-up duration was over 7-year post-ICU stay. Using a standardized national program

that has been annually assessing student performance across five domains in all Australian private and public schools since 2008, we were able to analyze long-term educational outcomes of a large cohort of PICU survivors. In contrast to previous studies restricted to specific high-risk groups (27, 28), our findings cover the entire range of causes leading to PICU admission. Major comorbidities known to affect brain development, such as syndromes and chronic neurologic conditions, were associated adverse long-term outcomes. In addition, prematurity and chronic respiratory conditions showed independent associations with educational outcomes. Interestingly, PIM-2 was observed to be the most important severity variable contributing independently to poor educational outcomes. We hypothesize that higher PIM-2 values characterize children exposed to both increased disease-related (such as shock with cerebral hypoperfusion) and treatment-related risks (such as sedation-related neurotoxicity) who, despite a high risk of mortality, survive thanks to modern intensive care.

Importantly, low SES conferred a greater risk of poor educational outcomes than disease features such as prematurity or chronic respiratory conditions. Social disadvantage may expose children to inequities resulting in poor prevention, higher prevalence of infections, delayed recognition of deterioration, restricted access to healthcare, and less support for their well-being and development post-PICU (29, 30). Of note, the matched controls systematically performed worse than the average statewide controls in our cohort, illustrating the importance of thorough matching to avoid bias due to gender, age, geography, school type, and SES. In this context, recent reports of deteriorating indicators of child and adolescent health in high-income countries are of great concern (31, 32) and indicate an urgent need to design post-PICU support measures for vulnerable populations.

The majority of children admitted to PICU are below 5 years old and, in principle, have a life expectancy of 80 years ahead if not limited by congenital conditions or the disease process. Consequently, adverse outcomes related to critical illness will exert an impact on the surviving child, its parents, siblings, and future offspring for many decades to come and translate into professional achievement, economic productivity, and dependency on others, including social welfare. At present, although guidelines recommend structured follow-up for specific patient groups such as high-risk congenital heart disease or extreme prematurity, most countries have no follow-up systems to assess long-term outcomes in critically ill children (19, 33, 34). Considering the resourcing implications to establish structured PICU follow-up programs (14), our study provides a framework to stratify children according to their risk of poor long-term educational outcomes. Children more likely to suffer from adverse long-term outcomes should be prioritized for targeted follow-up such as questionnaires by proxy and face-to-face assessments. Importantly, such strategies may enable research on early developmental interventions by general practitioners, hospital specialists, and early school support (35).

Several limitations of the study design need to be considered that affect the generalizability of results. First, although the outcome assessment was based on a standardized national school assessment that has been performed annually since 2008 in Australian schools, NAPLAN testing has not been internationally normalized. Second, a large proportion of the difference in the primary outcome between PICU survivors and controls was caused by a higher proportion of PICU survivors being exempt from NAPLAN testing. Although the Australian Curriculum Assessment and Reporting Authority rules state that teachers can only issue an exemption if students are affected by factors that severely limit their capacity to participate in the tests, including suffering from substantial disabilities, the exact disability was not documented in the dataset. Third, causality related to PICU exposure cannot be claimed, given the dataset did not contain neurocognitive assessment pre- and post-PICU admissions—which is an inherent limitation of PICU long-term outcome studies given that the majority of children require PICU preschool age, often for congenital conditions. The multivariable analyses show that both preexisting patient factors such as syndromes as well as severity on presentation and treatments affect long-term outcomes. Fourth, linked school outcome data were not available for 23% of the eligible cohort, representing interstate mobility, families moving overseas, home schooling, and true linkage failures. As the PICU admission characteristics of children not included in the linkage revealed slightly higher severity, complexity, and younger age, it is possible that our measures of long-term outcomes underestimate the true burden. Finally, the majority of

students included in this follow-up experienced ICU care over a decade ago in Australia, and the practices and patient population may not be representative of contemporary PICU populations and their care.

In conclusion, we demonstrate and quantify for the first time the long-term educational impacts of pediatric critical illness. In this population-based study of children requiring PICU during early childhood, one in seven survivors did not meet NMSs in the school assessment performed during year 3 of primary school. Failing to meet minimal academic requirement carries a high likelihood of derailing educational and occupational trajectories well into adulthood, affecting both survivors and the society. Our findings indicate a substantial long-term cognitive burden related to critical illness, warranting research on rehabilitation and school support for survivors of critical illness.

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Dr. Schlapbach designed the study and supervised all aspects of study conduct and analyses, and wrote the first draft of the article. Drs. Tomaszewski and Straney contributed to study design, reviewed analyses, and contributed to article drafting. Dr. Ablaza performed the main analyses and contributed to article drafting. Ms. Taylor contributed to study design, performed the data linkage, and contributed to article drafting. Dr. Millar contributed to study design and article drafting. All authors have reviewed and approved the final article.

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