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EDITORIAL

Focus on paediatrics

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The United Nations (UN) sustainable development goal 3.2 is to end preventable deaths in neonates and children under the age of 5 years by 2030. In this focus paper, we present an overview of studies related to critically ill children from 2019, which may help us to achieve this important UN goal.

1. **Clinical trials update**
   We selected five high-quality clinical trials published from acute neonatal and paediatric settings, two from low- and middle-income countries (LMIC) and three from high-income countries, focussed on transfusion and respiratory support.

   (a) *Resource poor settings*. An international study mapped 123 million child deaths, demonstrating that 93% occur in LMIC [1]. Although mortality under the age of 5 years fell (as we shown in Fig. 1), '58% of deaths could have been averted in the absence of geographical inequalities' [1]. While many of these deaths might be from vaccine preventable infectious diseases, a significant proportion might also be prevented by better acute care, hence the focus of this editorial.
   The TRACT group undertook an open-label randomised controlled trial (RCT) comparing high-volume (30 ml kg^{-1}) with low-volume (20 ml kg^{-1}) transfusion, as currently recommended by WHO, in 3196 children admitted to hospitals in Uganda and Malawi with severe anaemia (haemoglobin < 6 g/dl) [2]. The 28-day mortality was not statistically different between groups (3.4% vs. 4.5%). However, high-volume transfusion decreased mortality in afebrile children, whereas low-volume transfusion showed mortality benefit amongst febrile children.
   Bubble continuous positive airway pressure (bCPAP) has been presented as a safe intervention, which might improve survival in childhood pneumonia. McCollum et al. [3] reported an open-label RCT comparing bCPAP with low-flow nasal oxygen in 644 children admitted to hospital in Malawi with pneumonia. Notably, participants did not receive daily physician supervision. A significantly increased mortality rate (17% vs. 11%) in the bCPAP group led to early trial closure. This surprising finding was attributed to post-randomisation harm, related to aspiration and pneumothorax in a minimally monitored environment.

   (b) *High-income settings*. A 10-year epidemiology study from Australia and New Zealand noted a fall in PICU mortality to 2.6%, alongside a rise in PICU admissions by 40.3%. This data suggest there was greater access to PICU care over the decade. The annual national childhood death rate decreased, but the proportion of deaths occurring in PICU increased by 46% over 10 years [4]. The low number of deaths explains why PICU trials in high-resource countries are now rarely powered on mortality [5].
   In a blinded RCT, involving 1538 critically ill children across 50 international centres and comparing fresh (stored < 7 days) with standard issue red-cell transfusion [6], there were no differences between groups for new or progressive organ dysfunction or any other endpoint.
   An open-label RCT in neonatal intensive care units in the UK, Ireland and the Netherlands compared thresholds of platelet transfusion for thrombocytopenia affecting 660 critically ill premature babies with median gestational age of

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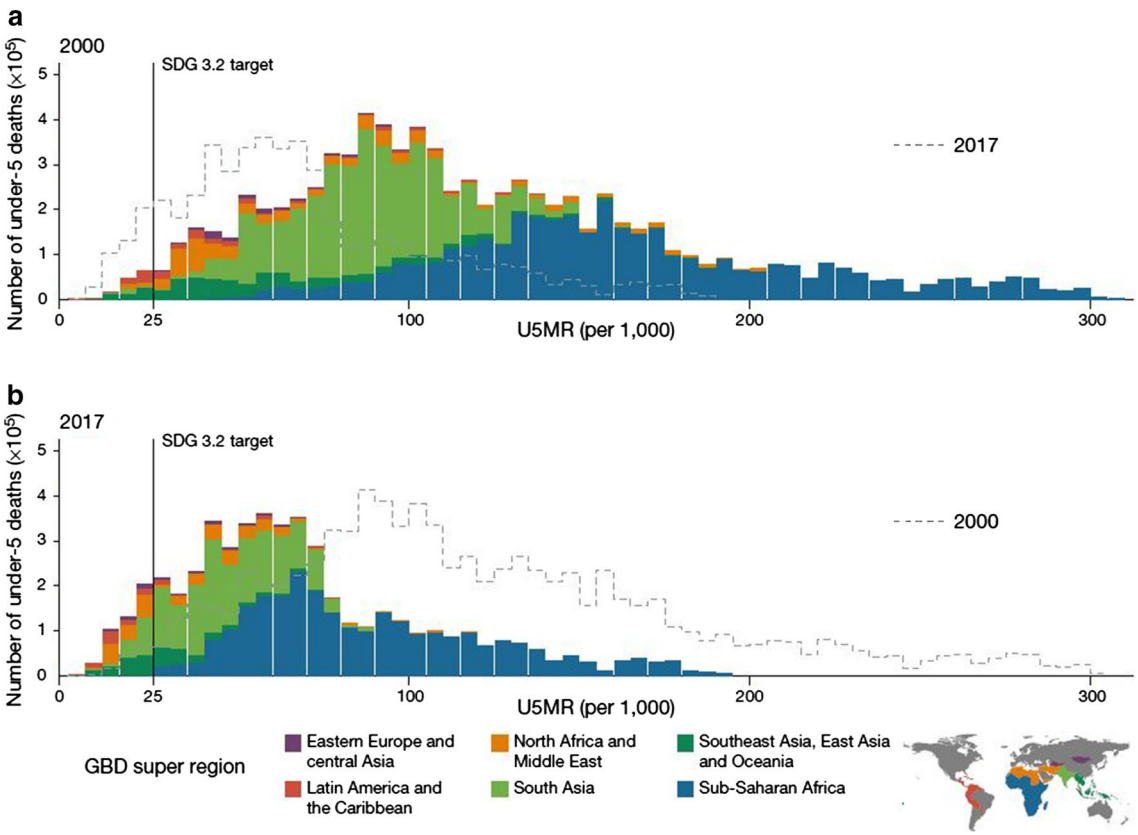

Fig. 1 Number of deaths in children under 5, distributed across level of under 5 mortality rate (U5MR), in 2000 and in 2017 across 99 LMIC

26.6 weeks. The risk of major bleeding or death by day 28 was greater in the high-threshold group (< 50,000 per cubic millimetre) than the low-threshold group (< 25,000 per cubic millimetre). [7].

An Australian RCT in non-tertiary special care nurseries compared CPAP with high-flow nasal oxygen for respiratory distress, in 754 neonates over 31-week gestational age. There were significantly higher rates of treatment failure in the high-flow oxygen group (20.5% vs. 10.2%) [8].

2. **Respiratory failure update**

We highlight the following useful studies of respiratory failure. The paediatric acute respiratory distress syndrome incidence and epidemiology (PARDIE) study captured data from 145 PICUs in 45 countries [9]. It showed that 3.4% of 23,280 children had pediatric acute respiratory distress syndrome (PARDS), the most common cause was infection, and mortality was 17%. There was a greater risk of death in children with comorbidities, severer forms of PARDS and with factors associated with health care delivery (income of country). Interestingly, the pediatric acute lung injury consensus conference (PALICC) definition for PARDS identified 40% more children with PARDS and diagnosed PARDS earlier than the Berlin definition. Then, using over 100,000 blood gas samples from 3582 PICU patients to reconstruct oxygen dissociation curves, Eytan et al. showed that the relationship between the peripheral oxygen saturation (pO2) and the arterial oxygen saturation (SaO2) shows a wide distribution, is right-shifted and confounded in a non-classical way by pCO2, pH and age. In addition, SpO2 appeared to overestimate SaO2 by 4–5%. These finding may be clinically important when oxygen delivery is critical [10]. Two short communications addressed ventilation in PARDS. Saffaran et al. [11] used prospectively collected ventilation data from a cohort with PARDS, to develop and test simulations of lung protective ventilator strategies, noting that children were routinely over ventilated. They found that a strategy simultaneously reducing tidal volume and mechanical power, without compromising gas exchange, appears the best way to achieve protective ventilation. Lia et al. investi-

gated the effect of increasing positive end-expiratory pressure (PEEP) between 4 and 10 cm H_2O in a small cohort of PARDS and non-PARDS children. The PEEP-induced increase in end-expiratory lung volume, and compliance appears lower in PARDS, whereas the PEEP-induced increase in global strain and static stress is more pronounced but occurs later in the disease process [12]. PARDS is one of the conditions in which lung ultrasound has been shown to allow point-of-care diagnostic and therapeutic interventions in children. The point-of-care ultrasonography (POCUS) approach, particularly in the smallest children, can offer similar diagnostic accuracy to chest xray (CXRs) and support safer placement of intercostal drains for pleural effusion and pneumothorax, and therefore this is becoming a central tenet of respiratory care in PICU [13].

3. **Evolution in pathways related to end of life care**
Moynihan et al. [4] demonstrated the increasing prominence of withdrawing and withholding life sustaining therapies within the PICU population of Australia and New Zealand, and over a decade this became the most prevalent mode of death. This study emphasises the importance of studying practice in this area: Butler et al. [14] interviewed 26 bereaved parents, and thematically analysed their experiences of death in PICU, in order to make parent-focussed recommendations for care. Bereaved parents stated the importance of honesty and clarity about their child's prognosis, discussed a range of practical steps that can be put in place for support and strongly recommended the practice of follow-up discussions with professionals from PICU. Weiss et al. [15] undertook a review of special issues in paediatric organ donation, noting that all children for whom a decision has been made to withdraw life sustaining treatments should be referred to the team responsible for coordinating organ donation, so that the case may be considered. The clinician and parental views on this important step can then be explored, with potential to increase donation rates. French et al. [16] undertook whole genome sequence analysis (WGSA) in a prospective cohort of 195 NICU and PICU admissions with congenital anomalies, neurological problems, metabolic abnormalities of unknown causation and unexplained critical illness. WGSA results were available within 21–35 days, and 21% patients received a new genetic diagnosis. Diagnoses were frequently unexpected, and informed management decisions, including enhancing the timeliness and appropriateness of referral to palliative care teams.

Our focus on paediatrics this year led us to report on clinical trials across settings with different resource levels, an update on respiratory care and evolution in PICU end of life pathways. Figure 1 is from Burstein et al. [1] displaying the number of deaths in children under 5, distributed by level of under 5 mortality rate (U5MR), in 2000 and in 2017 across 99 LMIC. The UN sustainable development goal 3.2 target is shown by a vertical line. The figure underlines the importance of continuing research to improve the acute care of children in these countries.

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Compliance with ethical standards

Conflicts of interest
Katherine Brown is the associate editor paediatrics for Intensive Care Medicine, and Daniele De Luca is the President Elect of the European Society for Pediatric and Neonatal Intensive Care (ESPNIC).

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