

Title: Reducing Variations in Neonatal Outcomes: Look at Practices, Systems, and the Patient

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Abbreviations: NICU, neonatal intensive care unit; VLBW, very low birthweight

Word Count (limit 800):

Funding Source: none

Financial Disclosure: none

Conflict(s) of Interest: none

Observation of variation in clinical outcomes has led investigators to examine variations in practice as potential causes, for example the association between supplemental oxygen use and retrolental fibroplasia (retinopathy of prematurity).(1) The move to benchmark care against other units has become widespread, and several benchmark organizations, of which perhaps the best example is the Vermont Oxford Network (VON), are generating wide-ranging comparative data. However, teasing out the complex relationships between practices and outcomes has not proven easy, and eliciting practice change can be even harder.

In addition to cotside clinical practice, higher level organizational factors may contribute psotove and negative effects on outcomes. In large, multi-center studies, centralization of care, access, NICU volume, and nurse staffing have all been implicated in the variation in neonatal mortality rates seen across centers. (2-5) Aggregating data across large populations can obscure the relationship between cotside practice and outcomes, but it increases the power of comparisons and allows the influence of organizational factors to be explored.

In this issue of *Pediatrics*, Adams and colleagues use data from VON to provide a robustly-designed comparison of two near-complete populations to overcome some of the challenges in previous studies. The two cohorts comprised 84% of the US and 95% of

the Swiss very-low birthweight (VLBW) populations.(6) The investigators used uniform definitions and adjusted outcomes for both patient and unit level characteristics. The primary outcome was a composite of mortality and morbidity. Propensity scoring adjusted for differences in cohort sizes and multivariate analysis adjusted both the composite primary and component outcomes. The adjusted risk ratio for the primary outcome was 44% lower in the Swiss Neonatal Network compared to the USA contributors to VON. Adjusted risk ratios for component morbidities also were lower in the Swiss data compared to the US, but mortality rates were similar. Notably, adjustment for hospital ownership, activity, size, and staffing reduced differences in morbidities. The investigators also observed differences in the use of antenatal steroids, delivery room practice and NICU management between the two populations.

That VLBW outcomes in Switzerland are better than in the USA should come as no surprise. Despite spending a higher proportion of Gross Domestic Product on healthcare than any other industrialized nation, the US consistently ranks well below other developed countries in most measures of healthcare quality. In 2014, the Commonwealth Fund noted that, of 11 industrialized countries, the USA health care system ranked last and Switzerland ranked second. (7) In terms of VLBW outcomes, among 10 national and regional networks – not including the US – Switzerland had the lowest rate of composite adverse outcomes. (8) Neonatal morbidities have shown little

temporal variation in a network of US hospitals (9) and vary equally widely across European regions.(10)

The study by Adams and colleagues has its limitations. Even with sophisticated adjustment and propensity scoring, the possibility of residual confounding remains high. There were few measures of antenatal care and the contribution of each morbidity to the composite is disproportionate. Combinations of morbidities may be better predictors of 2-year outcomes than individual conditions,(11) and may be better markers of important longer-term outcomes and economic costs. However, where possible non-modifiable variables have been controlled for, leaving the unexplained variations in outcomes those at which we should direct interventions. This means not simply targeting clinical practice, but also organizational structures (e.g., the Commonwealth Fund report noted that the USA also ranked lowest in access and equity). Working together in networks to reduce practice variation, planning optimally sized services with adequate staffing, and effective postnatal transfer systems where maternal transport cannot be achieved antenatally, are issues that must be addressed.

The traditional reliance of clinical practice on randomized clinical trials has led to a large number of underpowered trials which make much less impact in population outcomes than might be expected. Development of new trial strategies, such as comparative effectiveness trials using large routinely collected datasets, may help to clarify the importance of the small detailed steps we necessarily target in conventional clinical

trials more effectively. (12) Learning from our differences and ensuring we gather all the potentially better practices into our individualized clinical strategies in well planned services are important goals.

Finally, we must recognize that as we increase our understanding of the individual biologic and genetic underpinnings of disease, risk for complications, and responses to treatment, it is likely that a uniform approach to a given population may not represent “best” practice for a given individual. As we embark on our journey towards precision medicine, we must understand that population-based studies can take us only so far; while they may help us achieve the greatest good for the greatest number, there will always be a place for an individualized patient approach within well organized and managed services.

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