Improved National Outcomes Achieved in a Cardiac Learning Health Collaborative Based on Early Performance Level

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Objective Within the National Pediatric Cardiology Quality Improvement Collaborative (NPC-QIC), a learning health network developed to improve outcomes for patients with hypoplastic left heart syndrome and variants, we assessed which centers contributed to reductions in mortality and growth failure.

Study design Centers within the NPC-QIC were divided into tertiles based on early performance for mortality and separately for growth failure. These groups were evaluated for improvement from the early to late time period and compared with the other groups in the late time period.

Results Mortality was 3.8% for the high-performing, 7.6% for the medium-performing, and 14.4% for the low-performing groups in the early time period. Only the low-performing group had a significant change ($P < .001$) from the early to late period. In the late period, there was no difference in mortality between the high- (5.7%), medium- (7%), and low- (4.6%) performing centers ($P = .5$). Growth failure occurred in 13.9% for the high-performing, 21.9% for the medium-performing, and 32.8% for the low-performing groups in the early time period. Only the low-performing group had a significant change ($P < .001$) over time. In the late period, there was no significant difference in growth failure between the high- (19.8%), medium- (21.5%), and low- (13.5%) performing groups ($P = .054$).

Conclusions Improvements in the NPC-QIC mortality and growth measures are primarily driven by improvement in those performing the worst in these areas initially without compromising the success of high-performing centers. Focus for improvement may vary by center based on performance. *(J Pediatr 2020;222:186-92)*.

Patients with hypoplastic left heart syndrome require a series of 3 complex palliative surgeries or interventions to utilize the single ventricle for systemic perfusion while redirecting blood to the pulmonary arteries without passing through the heart. The first procedure is typically performed in the first 1-2 weeks of life and includes the surgical Norwood procedure or a hybrid alternative performed as a combined surgical and cardiac catheterization procedure (stage 1 palliation). Stage 2 palliation consists of anastomosis of the superior vena cava to the pulmonary arteries (ie, the Glenn procedure) and is typically performed at 4-6 months of age. The final planned surgery is performed at 2-5 years of age and consists of anastomosis of the inferior vena cava to the pulmonary arteries (ie, the Fontan procedure). Since the first description of the Norwood operation in 1980,[1] remarkable progress has been made in the care of patients with hypoplastic left heart syndrome, from an inoperable diagnosis to one with a current survival of >75% at 10 years.[2]

Because of the high mortality and morbidity associated with the diagnosis, the National Pediatric Cardiology Quality Improvement Collaborative (NPC-QIC) began enrolling patients in its registry in 2008. The initial goal of the NPC-QIC was to reduce mortality and improve the quality of life for those in the interstage, defined as the time between discharge from stage 1 palliation and admission for stage 2 palliation.[3] This learning health network (LHN) brings together care providers, researchers, and families who share knowledge and experience and employ quality improvement science in an effort to reduce institutional and individual practice process variability. It now consists of 60 North American cardiac programs with each center performing improvement work and reporting successes on monthly action period calls and at twice yearly learning sessions.

Through the work of this LHN, there has been a significant decrease in interstage mortality[4] and a reduction in interstage growth failure,[5] which are 2 of the primary network outcome measures. However, the NPC-QIC includes 60 centers with a wide range of experiences as single ventricle programs and varied outcomes following stage 1 palliation. It remains unclear whether all centers contribute equally to NPC-QIC's success or whether there is disproportionate benefit based on initial performance level. We sought to evaluate improvements in both mortal-

LHN	Learning health network
NPC-QIC	National Pediatric Cardiology Quality Improvement Collaborative
RV-PA	Right ventricular to pulmonary artery

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ity and growth measures seen in NPC-QIC centers based on initial performance level (during June 2008-June 2013).

Methods

Institutional review board approval and parental consent or waiver of consent is obtained by individual centers for participation in the NPC-QIC database. Additional Cincinnati Children's Hospital Medical Center institutional review board approval and waiver of consent was obtained prior to querying the database for this study. The NPC-QIC database represents an extensive database including demographic data, procedural data following stage 1 palliation, interstage readmission and clinic visit data, and data through discharge from stage 2 palliation. These data are collected on patients discharged home after stage 1 palliation by the participating center and entered in to secured Research Electronic Data Capture (REDCap, Nashville, Tennessee).[6] There is a standard dataset with data definitions and data quality checks. Data is housed at the James M. Anderson Center for Health System Excellence at the Cincinnati Children's Hospital Medical Center and distributed to investigators in de-identified format after project approval by the NPC-QIC research committee. For the purposes of this study, all patients lost to follow-up, deemed not to be candidates for stage 2 palliation, undergoing biventricular repair, or listed for transplant instead of stage 2 palliation were excluded. Only patients completing the interstage by undergoing stage 2 palliation and having a weight at both discharge from stage 1 palliation and the time of stage 2 palliation were included in the interstage growth failure outcome.

Participating centers in the NPC-QIC with ≥10 patients in the database during the early period were eligible for inclusion. The date used to divide the early and late performance was June 2013, as this was identified in a previous analysis as the date of the special cause in overall collaborative mortality that initiated the shift to a lower mortality rate.[4] This resulted in the early period being from initiation of the database in June 2008 until June 2013 and the late period being from June 2013 through August 2016. Centers were then divided into tertiles based on early performance with separate tertile groups for mortality and growth failure. Growth failure was defined per the NPC-QIC based on average daily weight gain at the time of stage 2 palliation (**Table I**; available at www.jpeds.com). The tertile groups were evaluated for improvement from the early to late time period and compared with the other groups in the late time period by the χ^2 test. The change in categories for mortality and growth was evaluated from the early to late period using Sankey diagrams. For these diagrams, the percentage mortality (or growth failure rate) that divided 2 tertiles was kept the same in the late time period to demonstrate changes over time graphically with the size of the bars representing the number of patients. In addition, the distribution of mortality category compared with growth category was evaluated for those that had data on both measures to identify patterns of performance. We summarized and compared variables related to potentially modifiable center management practices (median age at stage 1 palliation, median age at stage 2 palliation, median weight at stage 2 palliation, and shunt type distribution) that could have contributed to the improvement in mortality for the low-performing group over time using the χ^2 test for categorical variables and Wilcoxon rank-sum test for continuous variables. Statistical analysis was performed using Stata IC15 (Stata Corp, College Station, Texas) with a P value of <.05 considered significant.

Results

Changes in Mortality Rates

A total of 1835 patients were available with 98 (5.3%) excluded because of undergoing a biventricular repair (n = 9), loss to follow-up (n = 16), heart transplant (n = 37), or not being a candidate for stage 2 palliation (n = 36) with no difference between performance groups in excluded patients ($P = .7$). There were 33 centers eligible for the mortality evaluation in the early time period with a total of 872 patients in the early period and 865 in the late period. In the early time period, mortality was 13 out of 346 (3.8%) for the 11 high-performing centers, 22 out of 290 (7.6%) for the 11 medium-performing centers, and 34 out of 236 (14.4%) for the 11 low-performing centers. The average number of patients entered into NPC-QIC database per year since joining the NPC-QIC varied between the low-, medium-, and high-performing mortality groups (n = 7.6 ± 2.9, n = 8.1 ± 4.5, and n = 12.2 ± 5.4, respectively) but did not reach statistical significance ($P = .06$). The high- and medium-performing groups showed no significant change in mortality between periods ($P = .22$ and $P = .79$, respectively), whereas the low-performing group had a significant decrease in mortality ($P < .001$) from the early to late time period (**Figure 1**, A). In the late period, there was no significant difference in mortality between the high- (21 of 366, 5.7%), medium- (18 of 257, 7%), and low- (11 of 231, 4.6%) performing centers ($P = .5$). Changes in distribution of centers from early to late time period for mortality performance groups can be seen in **Figure 2**, A.

Variables related to potentially modifiable center management practices were evaluated within the low-performing centers to determine if there was a shift from the early to late time period that was associated with the improvement in mortality. These results can be seen in **Table II**. The only significant change was a reduction in the percentage of Norwood procedures with Blalock-Taussig shunts (53.5% vs 41.2%) and a corresponding rise in the percentage with a right ventricular to pulmonary artery (RV-PA) conduit (41.3% vs 54.1%). There was no significant change in frequency of Blalock-Taussig shunt from the early to late time period (31.6% vs 26.6%, $P = .06$) in the other groups.

Changes in Growth Failure Rates

After excluding centers with <10 patients enrolled in the early time period and infants without complete weight information, there were 31 centers included in the growth

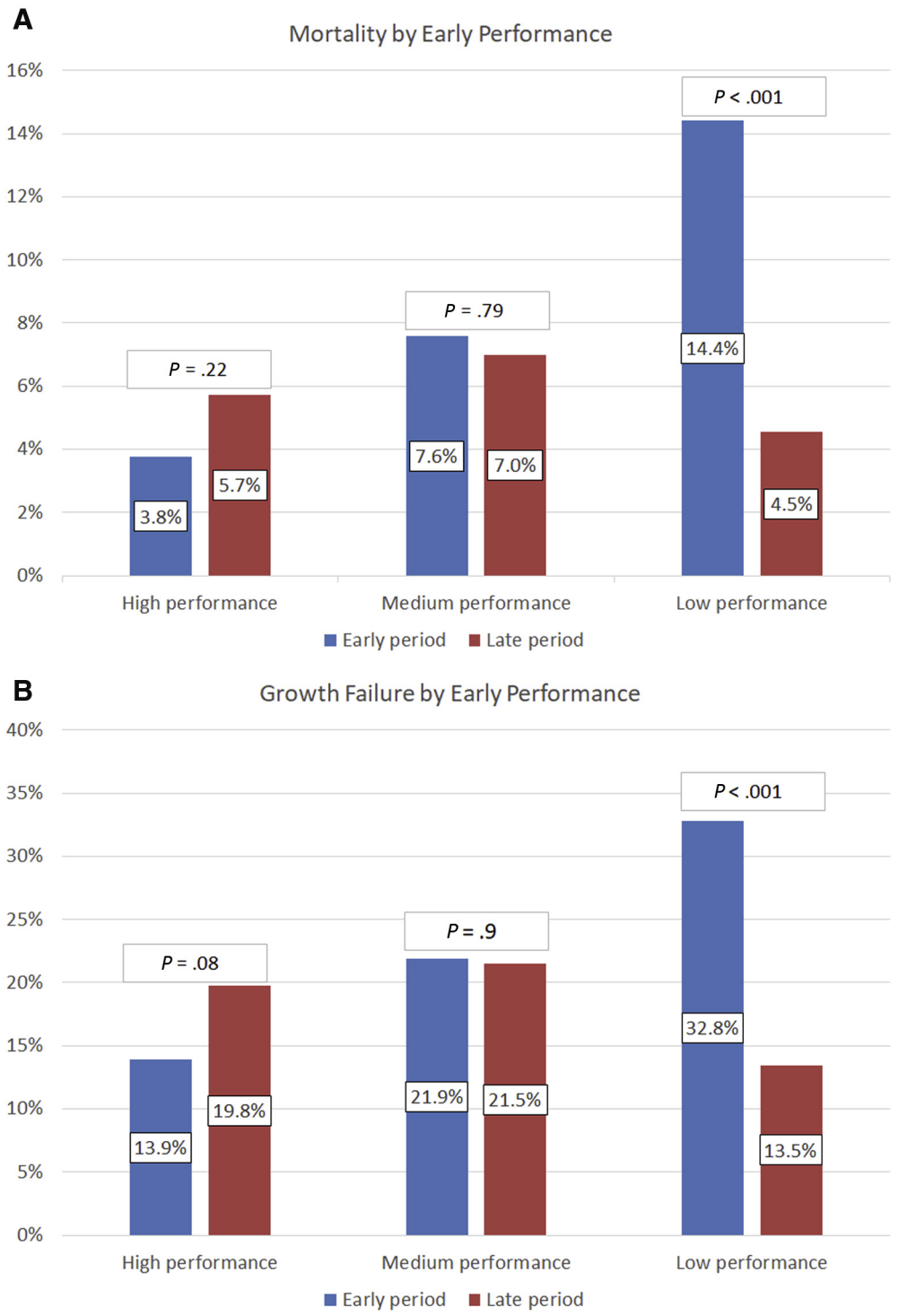

Figure 1. **A,** Mortality in the early and late time periods for the high- (n = 11 centers), medium- (n = 11 centers), and low- (n = 11 centers) performing groups. **B,** Growth failure in the early and late time periods for the high- (n = 10 centers), medium- (n = 11 centers), and low- (n = 10 centers) performing groups based on early performance.

comparison with a total of 782 patients in the early period and 766 patients in the late period. Growth failure occurred in 37 out of 266 (13.9%) for the 10 high-performing centers, 69 out of 315 (21.9%) for the 11 medium-performing centers, and 66 out of 201 (32.8%) for the 10 low-performing centers in the early time period. There was no difference in the average number of patients entered into the database per year between the low-, medium-, and high-performing growth groups (n = 8.2 ± 3.5, n = 9.1 ± 3.6, and n = 7.7 ± 6.1, respectively; $P = .3$). There was no significant change for the high and medium-performing groups ($P = .08$ and $P = .9$, respectively) but a significant improvement for

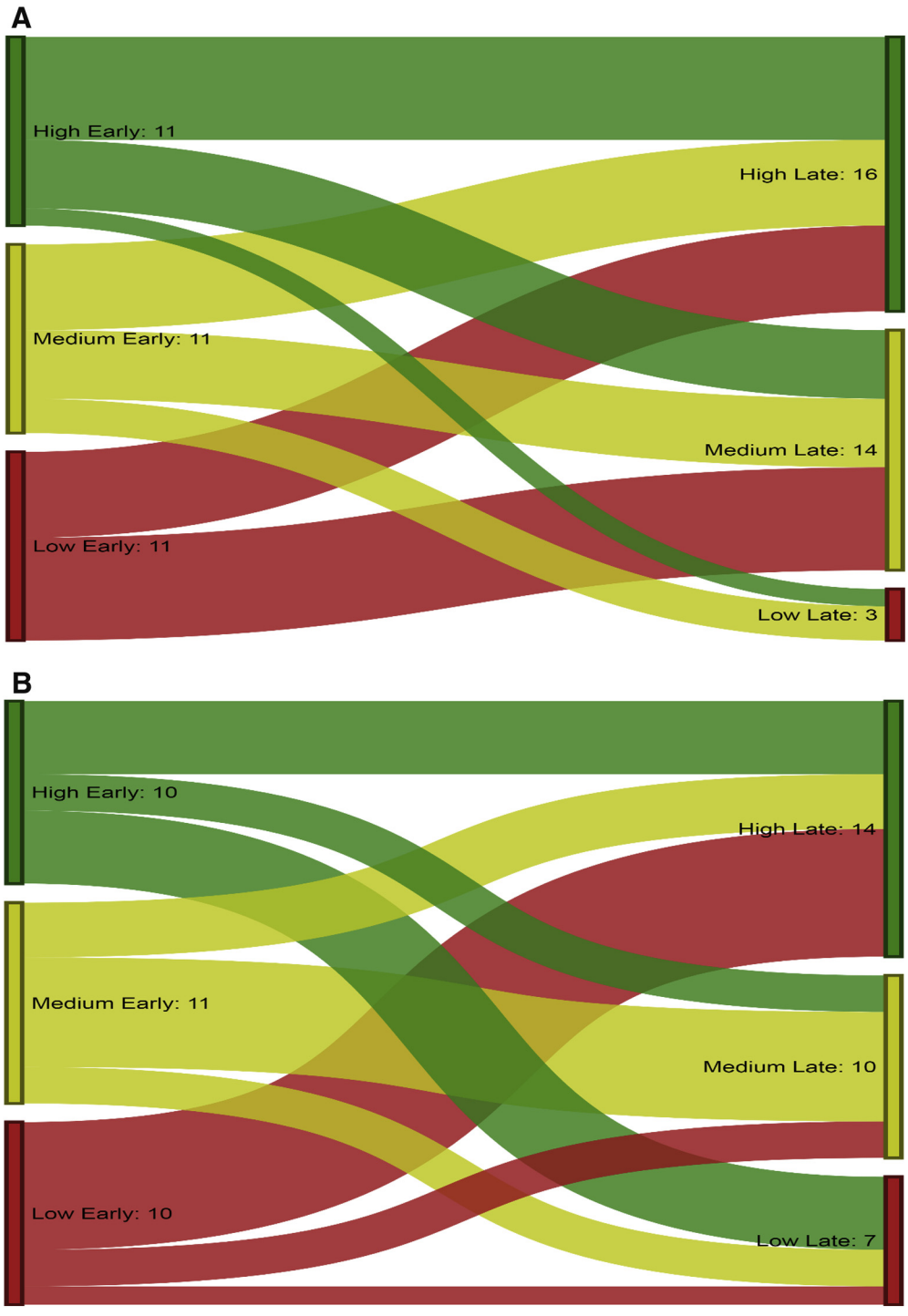

Figure 2. Sankey diagram demonstrating change in **A,** mortality and **B,** growth failure performance groups for centers from the early to late time period. The width of the nodes represents the number of centers in the early (*left-sided bars*) and late (*right hand bars*) time period in each category. The width of the connections represents the number of centers following that pathway as they move from the early to late time period. The determination of groups in the early time period was based on tertiles with the same mortality and growth failure rate kept to define groups in the late time period.

the low-performing group ($P < .001$) from the early to late time period (Figure 1, B). In the late time period, the difference in growth failure rates between groups did not reach significance between the high- (48 of 243, 19.8%), medium- (63 of 293, 21.5%), and low- (31 of 230, 13.5%) performing groups ($P = .054$). Changes in tertiles of centers growth performance from the early to late time periods can be seen in Figure 2, B.

Table II. Comparison of potential programmatic factors from the early to late time period in the low-performing group that may have contributed to improvements in outcomes

Variables	Early time period	Late time period	*P* value
Median age at stage 1 discharge, d (IQR)	42 (28-62)	40 (29-56)	.76
Median age at stage 2 palliation, d (IQR)	164 (135-197)	154 (128-191)	.12
Median weight at stage 2 palliation, kg (IQR)	6.28 (5.6-7.04)	6.08 (5.57-6.9)	.16
Stage 1 type, n (%)			.006
Blalock-Taussig shunt	124 (53.5%)	93 (41.2%)	
RV-PA shunt	105 (41.3%)	138 (54.1%)	
Hybrid	13 (5.1%)	8 (3.1%)	

Comparison of Center Performance in Mortality and Growth Failure

Distribution of early mortality and growth performance can be seen in Table III for the 31 centers with data available on both measures. There was no appreciable pattern to distribution.

Discussion

We found that the overall improvements in interstage mortality and growth outcomes for the NPC-QIC were driven by improvements in the lowest performing group without a significant decline in performance from the other groups. In both mortality and growth measures, the lowest performing group during the early period showed significant improvement, ultimately matching the performance of the other groups. Although it may not be surprising that those at the lowest entry point have the most room for improvement, the degree of improvement seen in the low-performing centers was unanticipated. We demonstrated that for the lowest performing group participation in the learning health network resulted in a reduction in their mortality rate from 14.4% to 4.5%, a 69% reduction in mortality; similarly, the lowest performing group reduced their growth failure rate from 32.8% to 13.5%, a 59% reduction. After this relatively short time period, there was no difference between the groups that performed at a high, medium, or low level in the early period. This suggests that the NPC-QIC model of knowledge sharing to improve a particular outcome is very effective for centers with low performance on that outcome.

Table III. Distribution of centers (N = 31) by mortality and growth performance during the early time period

	Mortality		
Growth	High performer	Medium performer	Low performer
High performer	n = 5	n = 4	n = 1
Medium performer	n = 4	n = 5	n = 2
Low performer	n = 3	n = 4	n = 3

It is important to note, the methods used for defining performance in our study are different from those used in the NPC-QIC to detect special cause variation and identify high or low performers. Within the collaborative special cause variation and exceptional performers are identified using quality improvement methodology. These include methods such as control charts, with special cause being any point outside the control limits or 8 or more consecutive points above or below the centerline, or funnel charts, with exceptional performers being above or below the control limits represented by the 3 times the SE.

We can speculate many reasons that there was no significant improvement for the medium- and high-performing centers from the early to late time period. It is certainly possible that the collaborative is a 1-sided relationship that has functioned to bring lower performers up to level of the other centers without benefit to those other centers. The lowest performing centers in mortality had fewer patients, though not reaching statistical significance, in the NPC-QIC registry and, therefore, may have less experience. The inverse relationship between mortality and program volume has long been described in congenital heart surgery.[7] However, LHNs may provide the ability to learn from the mistakes of more experienced programs and adopt successful strategies more rapidly. However, it is surprising there was no pattern to high performance for mortality outcomes and growth outcomes together as this would be expected if more experienced centers had already learned the lessons necessary for success in both outcomes.

There are other explanations for why significant improvement was only seen in the low-performing group. These groups were divided based on early results but these divisions were made on relatively small numbers of patients meaning that one poor outcome (mortality or growth failure) can have a significant impact on the relative placement. There may be some regression to the mean for both low- and high-performing centers in the later time period. Perhaps most intriguing, although difficult to prove, would be a shift in patient population. Participation in the collaborative may have resulted in a greater appreciation for which patients are particularly high risk and resulted in those patients being referred to higher performing centers. This may have been facilitated by the simultaneous push for increasing transparency and public reporting, further augmented by mainstream news coverage focused on congenital heart surgery outcomes.[8-11] As parents have gained access to programmatic information such as volume and outcomes, this may have led to parent-driven relocation of care to a higher performing center. It is also possible that with greater transparency, this relocation of high-risk patients may have been center driven. Although this "risk-aversion" has been feared as an unintended consequence of transparency and public reporting,[8,9] if done correctly, it could be a practice that is beneficial to patients. A center that knows its own limitations and has a partner that is able to take on cases deemed too high risk would be a compromise toward regionalized medicine, which has been theorized to reduce mortality.[12]

The finding that use of the RV-PA conduit increased in centers with low early performance on mortality is interesting as the results of the Single Ventricle Reconstruction trial were published in 2010, during the early period of this study. This was a randomized trial comparing the 2 shunt types used in the surgical Norwood procedure, the Blalock-Taussig shunt from the innominate artery to the pulmonary arteries and the RV-PA conduit from the right ventricle to the pulmonary arteries. The initial trial demonstrated improved transplant-free survival in those randomized to an RV-PA conduit at 12 months although higher patient volume at a given center negated the advantage of the RV-PA conduit.[13] Subsequent analyses with longer term follow-up demonstrated this early benefit did not persist at either 3 or 6 years.[14,15] It is possible that those centers with worse outcomes may have evolved to use the RV-PA conduit more frequently given the improved early outcomes. It is also notable that the frequency of Blalock-Taussig shunt use in the medium- and high-performing centers was lower compared with the lower performing centers in the early time period.

We believe the most likely explanation for the lack of improvement in early high performers for the mortality measure is that because they were performing well in this area, these centers may have chosen one of many additional outcomes, where they were not performing as well, as a focus of their initial improvement efforts. This theory is reinforced by the lack of overlap between high performers in mortality and growth measures. For those not performing well in growth, we noted the same improvement of the lowest performing centers. This observation suggest that the LHN model has potential benefit for all centers, however, each center may derive benefits differently based on its individual needs and identified outcomes for improvement. Other outcome measures of focus could include a decrease in length of intubation, hospital stay, improvement in neurodevelopmental outcomes, or hospital mortality prior to stage 1 or after stage 2 discharge. These are measures that can be assessed with the current iteration of the NPC-QIC, which includes all patients with a diagnosis that requires a stage 1 Norwood or hybrid alternative regardless of whether they were discharged for the interstage period. Future research is planned to evaluate changes in these additional outcomes.

The benefit of the NPC-QIC to patients has been undeniable. As previously reported, there was a shift in collaborative wide interstage mortality in June 2013 from 9.5% to 5.3%.[4] Work through the collaborative has also identified the association of digoxin with reduced interstage mortality,[16] findings that were confirmed within the Single Ventricle Reconstruction cohort.[17] In addition, the collaborative identified best practices for feeding and growth common to centers with the best interstage growth.[18] After dissemination of this growth bundle through the NPC-QIC, there was decreased variation in practice and improved interstage growth for the collaborative as a whole.[5] Interestingly, Anderson et al reported that the greatest improvement in outcomes was appreciated in those with "poor baseline outcomes."[5] Similarly, in an intensive care unit improvement network, the interventions were noted to have the greatest impact on those with the lowest initial adherence to specific practice guidelines.[19]

The exclusion of patients who remained hospitalized until stage 2 palliation is a limitation of this study, as the population of patients discharged may have changed during the study period and could explain some of the results. The NPC-QIC also had rolling membership with new members joining during the period covered by this study. Although we only included those with at least 10 early patients, a large center that joined the collaborative late may have still been eligible, making the time frame for improvement variable. Finally, there may be shifts in medical personnel and/or patient populations that may drive some of the change in outcomes over time but this would not be collected or accounted for in the NPC-QIC database.

The improvement seen in the NPC-QIC mortality and growth measures is primarily driven by those centers performing the worst in these areas in the early time period. This study also demonstrates that the methods of knowledge sharing used by the NPC-QIC are very effective in improving outcomes of the lowest performing centers. No significant change in the primary measures were seen in the medium- or high-performing centers from the early to late time period but further study may delineate longer term benefits and improvement in alternative outcome measures. ■

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50 Years Ago in *THE JOURNAL OF PEDIATRICS*

Aspirin and Reye Syndrome

Strauss RG, McAdams AJ. Arthritis, aspirin, and coma. J Pediatr 1970;77:156-63.

Strauss and McAdams reported a 22-month-old girl who presented with fever, encephalopathy, hepatomegaly, and metabolic acidosis after the initiation of high-dose aspirin for juvenile arthritis. She ultimately developed intracranial hypertension and died. Her autopsy revealed noninflammatory brain edema and fatty infiltration of the liver. The moderators of this clinical-pathological conference proposed salicylate toxicity as the most likely diagnosis. Reye syndrome was considered and dismissed, given the authors' skepticism that this relatively recently described illness represented a distinct clinical entity.

Despite the authors' doubts, Reye syndrome was diagnosed in children with increasing frequency in the decade following publication of this article. The syndrome was characterized by vomiting, followed by encephalopathy, coagulopathy, and, at its most severe, cerebral edema and liver failure with microvesicular fatty infiltration. These manifestations typically appeared shortly after recovery from a viral illness, especially influenza or varicella. Aspirin, widely used at the time for community-onset childhood illnesses, was suspected as a possible inciter owing to the clinical overlap between Reye syndrome and salicylate toxicity. Indeed, several US-based retrospective case-control studies published in the early 1980s repeatedly demonstrated an association between aspirin use during the antecedent illness and the development of Reye syndrome.

These findings prompted public health officials and the Food and Drug Administration to issue a still-extant warning against the routine use of aspirin in children. Nevertheless, these studies came under intense criticism by some based on their small sample sizes and their suspected design flaws, particularly those surrounding ascertainment and recall bias. A multicenter prospective study initiated in the mid-1980s was designed to address these criticisms, but by then both aspirin use and Reye syndrome had decreased dramatically, and hence this study, although again demonstrating the aspirin–Reye connection, suffered low enrollment.

Critics have further noted that with improved genetic testing, some children with a Reye-like syndrome have a defined inborn error of metabolism, raising doubts, like those expressed by Strauss and McAdams, that the illness was ever a single entity. Notably, Reye himself speculated that the syndrome that bears his name may have encompassed a range of etiologies. Nonetheless, it is difficult to ignore the fact that as aspirin use in children declined precipitously in the 1980s, so did the diagnosis of Reye syndrome, which has virtually disappeared today.

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Table I. NPC-QIC definition of minimum daily weight gain below which was defined as growth failure

Age at stage 2 palliation (d)	Minimum weight gain (g/d)
0-90	20
91-120	19
121-150	18
151-180	17.5
181-210	16.5
211-240	15.5
241-270	15
271-300	14.5
301-360	14
>360	13.5