

Trajectories in Neurodevelopmental, Health-Related Quality of Life, and Functional Status Outcomes by Socioeconomic Status and Maternal Education in Children with Single Ventricle Heart Disease

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Trajectories of neurodevelopment and quality of life were analyzed in children with hypoplastic left heart syndrome according to socioeconomic status (SES) and maternal education. Lower SES and less maternal education were associated with greater early delays in communication and problem-solving and progressive delays in problem-solving and fine motor skills over time. (*J Pediatr 2021;229:289-93*).

eurodevelopmental outcomes in children with hypoplastic left heart syndrome (HLHS) and single right ventricle (RV) anomalies remain poor.¹⁻⁵ Several studies have examined predictors of neurodevelopmental outcomes in children with these anomalies in an effort to reduce the burden of these disabilities. In general, patientspecific factors have eclipsed perioperative factors in their predictive value.^{2,4,6} Among these, low socioeconomic status (SES) and maternal education have been associated with lower performance in the following domains: functional status and fine motor, problem-solving, adaptive behavior, and communication skills.^{6,7}

Several mechanisms have been proposed to explain the relationship between low SES and worse neurocognitive outcomes starting in utero and extending into childhood; nevertheless, little is known about when the differences in behavior and cognition by SES begin to emerge during development or how they change over time. Understanding the evolution of socioeconomic disparities in neurodevelopment and other patient-reported outcomes, such as health-related quality of life (HRQOL) and functional status, may offer insight into factors contributing to this disparity and help target optimal points of intervention. Accordingly, we examined trajectories in neurodevelopmental, HRQOL, and functional status outcomes by neighborhood SES and maternal education in children with single ventricle anomalies.

Methods

We used data from the Pediatric Heart Network Single Ventricle Reconstruction (SVR) trial and extension studies.⁸ In brief, neonates at 15 centers across the US and Canada were assigned to receive either a modified Blalock–Taussig shunt or an RV-to-pulmonary artery shunt during the initial Norwood procedure. The SVR trial and extension study (SVR II) followed children for a minimum of 6 years.

Of the 555 neonates randomized in the SVR trial, 373 were alive and transplantation-free at 14 months. A total of 325 patients were enrolled in SVR II, of whom 293 completed any of the neurodevelopmental, HRQOL, or functional status assessments at years 3 through 6. Of these, data on neighborhood SES were available for 285 patients, and data on maternal education were available for 274 (**Table I**; available at www.jpeds.com).

Standardized forms were used to collect data on patient demographics, birth characteristics, anatomy, perioperative details, and complications. Maternal education was assessed when the child was 14 months of age and was categorized into less than high school, high school or some college, and college graduate or more. Neighborhood SES was assessed at the time of the Norwood procedure using a US censusbased score developed by Diez Roux et al that includes measures related to wealth and income, education, and

| ASQ | Ages and Stages Questionnaire |
|----------|---|
| BASC-2 | Behavior Assessment System for Children, Second Edition |
| FS-II(R) | Functional Status II Revised |
| HLHS | Hypoplastic left heart syndrome |
| HRQOL | Health-related quality of life |
| Peds-QL | Pediatric Quality of Life Inventory |
| RV | Right ventricle |
| SES | Socioeconomic status |
| SVR | Single Ventricle Reconstruction (trial) |

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0022-3476/\$ - see front matter. © 2020 Elsevier Inc. All rights reserved. https://doi.org/10.1016/j.jpeds.2020.09.066 occupation.⁹ Data from the 2000 American Community Survey were used to ascribe neighborhood SES. For the purposes of this analyses, we divided neighborhood SES into tertiles.

Neurodevelopment was evaluated using the Ages and Stages Questionnaire (ASQ) and the Behavior Assessment System for Children, Second Edition (BASC-2).¹⁰⁻¹² The ASQ is a parent-completed questionnaire that evaluates children's communication, gross and fine motor, problem-solving, and personal-social skills. The BASC-2 is a parent-reported measure of behavioral symptoms divided into externalizing problems, internalizing probbehavioral symptoms, and adaptive skills lems, (mean \pm SD score, 50 \pm 10). For the adaptive skills component, lower scores indicate problems, whereas for the components, higher scores indicate problems. HRQOL was measured using the Pediatric Quality of Life Inventory (Peds-QL), which assesses domains of physical, psychosocial, social, and school function (scale of 0-100).¹³⁻¹⁵ Functional status was measured using the Functional Status II revised [FS-II(R)], which assess children's ability to perform daily, age-appropriate functions (scale of 0-100).¹⁶ Higher scores on the PedsQL and FS-II(R) indicate better HRQOL and functional status. Baseline assessments were collected at age 3 years for all questionnaires. The ASQ was completed by parents at years 3-5 during followup telephone visits; all other questionnaires were completed at years 3-6 (Table II; available at www.jpeds.com).

Patient characteristics and baseline neurodevelopmental HRQOL and functional status outcomes at age 3 years were compared across neighborhood SES tertiles at birth and maternal education categories collected at age 14 months using the χ^2 test for categorical variables and analysis of variance or Kruskal-Wallis test for continuous variables. Scores from the BASC-2, Peds-QL, and FS-II(R) questionnaires were modeled as continuous variables because the content of these scales is fixed across age groups. In contrast, the content of ASQ varies by the age of the child with different cutoff scores for identification of developmental concerns and "atrisk" zones. Therefore, we modeled the ASQ as a dichotomous outcome using the "at-risk" cutoff to obtain sufficient outcomes for modeling purposes.

Trajectories of scores on the neurodevelopmental and HRQOL questionnaires were compared across neighborhood SES tertiles and maternal education categories using generalized linear mixed-effects models including time and an interaction term between SES and time. These models incorporate both fixed and random effects to compare score trajectories within patients over time and as a function of multiple covariates. For continuous outcomes [ie, BASC-2, Peds-QL, and FS-II(R)], we used an identity link function; for binary outcomes (ie, ASQ), we used a logistic link function. Analyses were then repeated adjusting for patient characteristics (Hispanic ethnicity, nonwhite race, birthweight, prenatal diagnosis, genetic condition, treatment assignment, and baseline year 3 score). All analyses were performed using SAS version 9.4 (SAS Institute, Cary, North Carolina). Patient sociodemographic and clinical characteristics by neighborhood SES tertile and maternal education are presented in **Tables III** and **IV** (both available at www.jpeds. com). Lower SES and maternal education were associated with Hispanic ethnicity, smaller head circumference at birth, and older age at Fontan surgeries. Response rates varied by year and assessment method and ranged from 75% to 86%.

A greater percentage of patients in the lowest neighborhood SES tertile and patients whose mothers had a high school education or less scored below the "at-risk" cutoff for assessments of communication and problem-solving on the ASQ at 3 years of age compared with patients in higher SES and maternal education categories (**Table V**). There were no differences in performance on the BASC-2 or Peds-QL scales by SES or maternal education. Lower SES was associated with slightly poorer functional status on the FS-II(R).

From 3 to 5 years of age, children in the lowest and middle SES tertiles were at slightly increased odds of developing communication concerns though neither reach statistical significance (lowest tertile: OR, 1.71; 95% CI, 0.99-2.95; *P* = .06; middle tertile: OR, 1.83; 95% CI, 1.00-3.37; P = .05) whereas the odds of developing communication concerns remained stable for children in the highest tertile (P = .32) (Table VI). Similarly, children in the lowest SES tertile were at increased odds of developing fine motor concerns over time (OR, 2.29; 95% CI, 1.46-3.59; P < .001), whereas the odds of having fine motor concerns remained stable for children of higher SES (Figure; available at www.jpeds.com). The odds of having problem-solving concerns decreased over time for patients in the highest and middle SES tertiles (middle tertile: OR, 0.50; 95% CI, 0.30-0.85; *P* = .010; highest tertile: OR, 0.27; 95% CI, 0.16-0.48; *P* < .001) but remained stable for those in the lowest tertile (P = .38). After adjustment, the differences in fine motor and problem-solving trajectories by SES persisted (P = .003 and .047, respectively); however, the differences in communication trajectories by SES were no longer present (P = .17).

Patients in all SES tertiles reported worsening behavioral symptoms (ie, increasing scores) and adaptive skills (ie, decreasing scores), but the trajectory was similar across SES tertiles. Patients in the highest SES tertile reported more externalizing problems but fewer internalizing problems over time. Similar magnitudes of decline in HRQOL, particularly in the physical, psychosocial, and social domains, were observed across the SES tertiles. There was no significant change in functional status over time in any of the SES tertiles. Adjustment for other clinical characteristics did not change these trajectories.

Nearly identical changes in neurodevelopment, HRQOL, and functional status were observed according to maternal education level. Lower maternal education was associated with increased odds of developing communication and fine motor concerns over time, whereas higher maternal

| Sample size | Estimate | Sample size | Estimate | Sample size | Estimate | P value* |
|--------------------|--|--|---|---|---|---|
| Lowest SES Tertile | | Middle SES Tertile | | Highest SES Tertile | | P value" |
| | | | | | | |
| | | | | | 12 (15.4) | .006 |
| 64 | 30 (46.9) | | 32 (15.0) | | 42 (53.9) | .49 |
| 63 | 23 (36.5) | | 25 (35.2) | 78 | 22 (28.2) | .52 |
| 64 | 29 (45.3) | 71 | 20 (28.2) | 77 | 21 (27.3) | .043 |
| 64 | 23 (35.9) | 72 | 21 (29.2) | 78 | 16 (20.5) | .12 |
| | . , | | . , | | . , | |
| 63 | 48.0 (6.8) | 72 | 48.0 (9.3) | 81 | 47.0 (7.5) | .47 |
| 63 | 48.2 (10.1) | 71 | 50.1 (10.7) | 80 | 51.0 (8.7) | .10 |
| 68 | 47.8 (7.7) | 73 | 47.6 (8.4) | 81 | 46.9 (8.4) | .50 |
| | | | | | | .12 |
| | | | | | | |
| 69 | 79.8 (16.0) | 73 | 81.0 (14.4) | 78 | 80.7 (14.7) | .74 |
| | | | | | () | .59 |
| | | | | | | .89 |
| | | | | | | .98 |
| | | | | | | .79 |
| | | | | | | .004 |
| | 50 (00 50) | | () | 02 | 30 (32 100) | .004 |
| Less that | n high school | | | College grad | duate or more | |
| | | | | | | |
| 00 | 14 (50.0) | 00 | 00 (00 E) | 0.4 | 11 (10 1) | <.001 |
| | | | | | | |
| | | | | | | .79 |
| | () | | | | | .14 |
| | | | | | | .050 |
| 28 | 11 (39.3) | 98 | 30 (30.6) | 85 | 17 (20.0) | .090 |
| | | | 47 7 (0 4) | | | |
| | () | | | | | .64 |
| | | | | | | .40 |
| | () | | () | | · · · | .76 |
| 26 | 51.2 (8.7) | 100 | 50.7 (9.3) | 87 | 49.5 (9.9) | .61 |
| | | | | | | |
| 23 | 71.4 (16.1) | 110 | 72.2 (17.1) | 102 | 75.1 (16.1) | .37 |
| 23 | 71.4 (22.3) | 110 | 68.5 (23.7) | 102 | 73.5 (22.2) | .29 |
| 23 | 71.5 (15.3) | 110 | 74.1 (16.3) | 102 | 75.9 (15.0) | .41 |
| 23 | 72.6 (20.4) | 110 | 75.9 (19.8) | 102 | 77.8 (17.9) | .46 |
| | | | | | | |
| 23 | 81.5 (19.2) | 110 | 77.5 (19.3) | 102 | 75.8 (16.9) | .39 |
| | Lowest S 64 64 63 64 64 63 63 68 63 68 63 69 69 67 68 68 69 69 67 68 68 69 69 67 68 68 68 28 28 28 28 28 28 28 28 28 28 28 28 28 | Lowest SES Tertile 64 24 (37.5) 64 30 (46.9) 63 23 (36.5) 64 29 (45.3) 64 23 (35.9) 63 48.0 (6.8) 63 48.2 (10.1) 68 47.8 (7.7) 63 51.0 (9.6) 69 79.8 (16.0) 69 78.0 (20.5) 67 81.4 (14.9) 68 83.4 (17.3) 68 80.7 (16.2) 69 96 (88-98) Less than high school 28 14 (50.0) 28 14 (50.0) 28 14 (50.0) 28 14 (50.0) 28 14 (50.0) 28 14 (50.0) 28 14 (50.0) 28 14 (50.0) 28 14 (50.0) 28 14 (50.0) 28 14 (50.0) 28 14 (50.0) 29 48.5 (6.4) 26 5 | Lowest SES Tertile Middle S 64 24 (37.5) 71 64 30 (46.9) 72 63 23 (36.5) 71 64 29 (45.3) 71 64 29 (45.3) 71 64 23 (35.9) 72 63 48.0 (6.8) 72 63 48.2 (10.1) 71 68 47.8 (7.7) 73 63 51.0 (9.6) 71 69 79.8 (16.0) 73 69 78.0 (20.5) 73 67 81.4 (14.9) 73 68 83.4 (17.3) 73 69 96 (88-98) 72 Less than high school red 28 14 (50.0) 98 28 14 (50.0) 97 28 14 (50.0) 97 28 14 (50.0) 98 28 11 (39.3) 98 26 49.1 (6.5) 101 <t< td=""><td>Lowest SES Tertile Middle SES Tertile 64 24 (37.5) 71 14 (19.7) 64 30 (46.9) 72 32 (15.0) 63 23 (36.5) 71 25 (35.2) 64 29 (45.3) 71 20 (28.2) 64 23 (35.9) 72 21 (29.2) 63 48.0 (6.8) 72 48.0 (9.3) 63 48.2 (10.1) 71 50.1 (10.7) 63 48.2 (10.1) 71 51.5 (9.5) 63 47.8 (7.7) 73 47.6 (8.4) 63 51.0 (9.6) 71 51.5 (9.5) 69 79.8 (16.0) 73 81.0 (14.4) 69 78.0 (20.5) 73 80.5 (17.9) 67 81.4 (13.3) 73 84.5 (15.6) 68 80.7 (16.2) 73 77.2 98 (94-100) Less than high school 97 29 (29.9) 28 14 (50.0) 97 29 (29.9) 28 14 (50.0) 98 34</td><td>Lowest SES Tertile Middle SES Tertile Highest S 64 24 (37.5) 71 14 (19.7) 78 64 30 (46.9) 72 32 (15.0) 78 63 23 (36.5) 71 25 (35.2) 78 64 29 (45.3) 71 20 (28.2) 77 64 23 (35.9) 72 21 (29.2) 78 63 48.0 (6.8) 72 48.0 (9.3) 81 63 48.2 (10.1) 71 50.1 (10.7) 80 63 48.0 (6.8) 72 48.0 (9.3) 81 63 48.2 (10.1) 71 50.1 (10.7) 80 64 7.8 (7.7) 73 47.6 (8.4) 81 63 51.0 (9.6) 71 51.5 (9.5) 80 69 78.0 (20.5) 73 80.5 (17.9) 78 67 81.4 (14.9) 73 81.4 (13.8) 76 68 83.4 (17.3) 73 84.5 (15.6) 77 69</td><td>Lowest SES Tertile Middle SES Tertile Highest SES Tertile 64 24 (37.5) 71 14 (19.7) 78 12 (15.4) 64 30 (46.9) 72 32 (15.0) 78 42 (63.9) 63 23 (36.5) 71 25 (35.2) 78 22 (28.2) 64 29 (45.3) 71 20 (28.2) 77 21 (27.3) 64 23 (35.9) 72 21 (29.2) 78 16 (20.5) 63 48.0 (6.8) 72 48.0 (9.3) 81 47.0 (7.5) 63 48.2 (10.1) 71 50.1 (10.7) 80 51.0 (8.4) 63 51.0 (9.6) 71 81.5 (15.9) 80 48.6 (9.1) 69 78.0 (20.5) 73 81.0 (14.4) 78 80.7 (14.7) 68 83.4 (17.3) 73 81.4 (13.8) 76 81.1 (12.9) 68 80.7 (16.2) 73 77 79.9 (15.3) 69 96 (88-98) 72 98 (94-100) 82 98 (92-100)<!--</td--></td></t<> | Lowest SES Tertile Middle SES Tertile 64 24 (37.5) 71 14 (19.7) 64 30 (46.9) 72 32 (15.0) 63 23 (36.5) 71 25 (35.2) 64 29 (45.3) 71 20 (28.2) 64 23 (35.9) 72 21 (29.2) 63 48.0 (6.8) 72 48.0 (9.3) 63 48.2 (10.1) 71 50.1 (10.7) 63 48.2 (10.1) 71 51.5 (9.5) 63 47.8 (7.7) 73 47.6 (8.4) 63 51.0 (9.6) 71 51.5 (9.5) 69 79.8 (16.0) 73 81.0 (14.4) 69 78.0 (20.5) 73 80.5 (17.9) 67 81.4 (13.3) 73 84.5 (15.6) 68 80.7 (16.2) 73 77.2 98 (94-100) Less than high school 97 29 (29.9) 28 14 (50.0) 97 29 (29.9) 28 14 (50.0) 98 34 | Lowest SES Tertile Middle SES Tertile Highest S 64 24 (37.5) 71 14 (19.7) 78 64 30 (46.9) 72 32 (15.0) 78 63 23 (36.5) 71 25 (35.2) 78 64 29 (45.3) 71 20 (28.2) 77 64 23 (35.9) 72 21 (29.2) 78 63 48.0 (6.8) 72 48.0 (9.3) 81 63 48.2 (10.1) 71 50.1 (10.7) 80 63 48.0 (6.8) 72 48.0 (9.3) 81 63 48.2 (10.1) 71 50.1 (10.7) 80 64 7.8 (7.7) 73 47.6 (8.4) 81 63 51.0 (9.6) 71 51.5 (9.5) 80 69 78.0 (20.5) 73 80.5 (17.9) 78 67 81.4 (14.9) 73 81.4 (13.8) 76 68 83.4 (17.3) 73 84.5 (15.6) 77 69 | Lowest SES Tertile Middle SES Tertile Highest SES Tertile 64 24 (37.5) 71 14 (19.7) 78 12 (15.4) 64 30 (46.9) 72 32 (15.0) 78 42 (63.9) 63 23 (36.5) 71 25 (35.2) 78 22 (28.2) 64 29 (45.3) 71 20 (28.2) 77 21 (27.3) 64 23 (35.9) 72 21 (29.2) 78 16 (20.5) 63 48.0 (6.8) 72 48.0 (9.3) 81 47.0 (7.5) 63 48.2 (10.1) 71 50.1 (10.7) 80 51.0 (8.4) 63 51.0 (9.6) 71 81.5 (15.9) 80 48.6 (9.1) 69 78.0 (20.5) 73 81.0 (14.4) 78 80.7 (14.7) 68 83.4 (17.3) 73 81.4 (13.8) 76 81.1 (12.9) 68 80.7 (16.2) 73 77 79.9 (15.3) 69 96 (88-98) 72 98 (94-100) 82 98 (92-100) </td |

Table V. Neurodevelopmental, quality of life, and functional status outcomes at 3 years by neighborhood SES tertile and maternal education

*P values represent the χ^2 test for n (%), Kruskal–Wallis test for medians, and ANOVA for means.

+Performance on the ASQ was modeled as a dichotomous outcome using the at-risk cutoffs. Performance on all other questionnaires was modeled as a continuous variable.

education was associated with decreased odds of developing problem-solving skill concerns over time. Differences in fine motor and problem-solving trajectories by maternal education persisted after adjustment (P = .002 and .019, respectively). There were similar rates of decline in behavioral symptoms, adaptive skills, and HRQOL across maternal education categories.

Discussion

Previous studies from the SVR trial and its extension studies have compared neurodevelopmental outcomes in children with HLHS to those of a normative sample and found significant differences in nearly all domains examined at 3 and 6 years post-Norwood procedure.^{6,7} We expand on earlier work by exploring developmental trajectories and identifying specific domains in which children with HLHS and low SES or maternal education are most likely to develop deficits over time. Specifically, we found that a significantly greater percentage of patients with low neighborhood SES and maternal education were at risk for delays in communication and problem-solving skills at 3 years of age. From 3 to 5 years, the differences in problem solving by SES became more pronounced, and new differences in fine motor skills appeared.

These findings highlight the importance of early neurocognitive interventions to improve developmental outcomes in children with HLHS, particularly among those from disadvantaged backgrounds. By 3 years of age, there were already notable differences in social and cognitive skills by SES and maternal education, which persisted or became more pronounced over time. Ensuring that families have the resources to care for their child and access to neurodevelopmental support is essential. Many pediatric cardiac centers have developed neurodevelopmental screening and follow-up programs to link at-risk children with appropriate resources; however, these clinics are often not covered by insurance or require significant travel that may be prohibitive for individuals with low SES. Our data highlight the importance of

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| Outcomes | Estimate for year 3-5 trajectory* | P value | Estimate for year 3-5 trajectory* | P value | Estimate for year 3-5 trajectory* | P value | Unadjusted P value | Adjusted P value |
|-----------------------------------|--------------------------------------|----------------|--------------------------------------|----------------|--------------------------------------|----------------------|-------------------------|--------------------------------------|
| Neighborhood SES | Lowest SES te | rtile | Middle SES tertile | | Highest SES tertile | | for time interaction | for time interaction [†] |
| ASQ, OR (95% CI) [†] | | | | | | | | |
| Communication | 1.71 (0.99-2.95) | .055 | 1.83 (1.00-3.37) | .050 | 0.74 (0.40-1.34) | .32 | .043 | .17 |
| Gross motor | 0.82 (0.53-1.28) | .39 | 0.95 (0.61-1.48) | .81 | 0.59 (0.39-0.91) | .016 | .26 | .19 |
| Fine motor | 2.29 (1.46-3.59) | <.001 | 0.90 (0.57-1.43) | .65 | 0.69 (0.45-1.06) | .056 | <.001 | .003 |
| Problem solving | 0.82 (0.52-1.28) | .38 | 0.50 (0.30-0.85) | .010 | 0.27 (0.16-0.48) | <.001 | .005 | .047 |
| Personal-social | 1.45 (0.94-2.22) | .093 | 1.13 (0.72-1.78) | .58 | 0.92 (0.60-1.42) | .71 | .27 | .35 |
| BASC-2, slope (SE) | | | | | 0.02 (0.002) | | | 100 |
| Behavioral symptoms index | 1.04 (0.30) | .001 | 0.79 (0.29) | .007 | 0.73 (0.26) | .006 | .70 | .78 |
| Adaptive skills composite | -1.42(0.32) | <.001 | -1.15 (0.31) | <.001 | -0.67 (0.28) | .000 | .17 | .24 |
| Externalizing problems | 0.52 (0.31) | .092 | 0.57 (0.30) | .054 | 0.69 (0.27) | .012 | .90 | .85 |
| Internalizing problems | -0.14 (0.35) | .70 | -0.66(0.34) | .051 | -0.81 (0.31) | .008 | .28 | .31 |
| Peds-QL, slope (SE) | -0.14 (0.00) | .70 | -0.00 (0.04) | .001 | -0.01 (0.01) | .000 | .20 | .01 |
| Total score | -2.86 (0.53) | <.001 | -2.77 (0.52) | <.001 | -2.20 (0.48) | <.001 | .56 | .59 |
| Physical functioning | -3.66 (0.76) | <.001 | -3.89 (0.76) | <.001 | -3.25 (0.70) | <.001 | .30 | .39 .80 |
| | | <.001 <.001 | | <.001 <.001 | -3.25 (0.70) -1.73 (0.46) | <.001 <.001 | .79 .45 | |
| Psychosocial functioning | -2.52 (0.50) | | -2.22 (0.49) | | () | | | .50 |
| Social functioning | -2.86 (0.62) | <.001 | -2.91 (0.61) | <.001 | -2.14 (0.57) | <.001 | .54 | .60 |
| Emotional functioning | -0.20 (0.61) | .75 | -0.77 (0.60) | .20 | -0.84 (0.56) | .13 | .67 | .82 |
| FS-II (R), slope (SE) | -0.22 (0.35) | .53 | -0.64 (0.34) | .064 | 0.30 (0.32) | .35 | .096 | .13 |
| Maternal education | Less than high so | hool | High school or some college | | College graduate or more | | | |
| ASQ, OR (95% CI) [†] | | | | | | | | |
| Communication | 1.93 (1.09-3.42) | .024 | 1.87 (0.99-3.53) | .053 | 0.80 (0.44-1.45) | .46 | .048 | .19 |
| Gross motor | 0.87 (0.54-1.39) | .56 | 0.90 (0.56-1.45) | .67 | 0.58 (0.38-0.89) | .014 | .26 | .22 |
| Fine motor | 2.34 (1.47-3.73) | <.001 | 0.89 (0.56-1.42) | .62 | 0.71 (0.47-1.09) | .11 | <.001 | .002 |
| Problem solving | 0.89 (0.56-1.41) | .61 | 0.37 (0.20-0.68) | .001 | 0.26 (0.14-0.46) | <.001 | .001 | .019 |
| Personal-social | 1.55 (0.99-2.43) | .056 | 0.93 (0.57-1.52) | .001 | 0.91 (0.59-1.42) | .68 | .13 | .19 |
| BASC-2, slope (SE) | 1.00 (0.00 2.40) | .000 | 0.00 (0.07 1.02) | .11 | 0.01 (0.00 1.42) | .00 | .10 | .15 |
| Behavioral symptoms | 1.01 (0.52) | .055 | 0.88 (0.24) | <.001 | 0.49 (0.25) | .052 | .42 | .52 |
| index | 1.01 (0.32) | .055 | 0.00 (0.24) | <.001 | 0.49 (0.23) | .052 | .42 | .52 |
| | 1 70 (0 55) | .001 | 1.07 (0.05) | - 001 | 0.02 (0.26) | .002 | .28 | .42 |
| Adaptive skills | —1.78 (0.55) | .001 | -1.07 (0.25) | <.001 | -0.83 (0.26) | .002 | .20 | .42 |
| composite | 0 40 (0 50) | 00 | 0.07 (0.05) | 007 | 0.01 (0.00) | | | 50 |
| Externalizing problems | 0.46 (0.53) | .38 | 0.67 (0.25) | .007 | 0.31 (0.26) | .24 | .55 | .58 |
| Internalizing problems | -0.14 (0.60) | .81 | -0.34 (0.28) | .23 | -0.88 (0.30) | .003 | .28 | .28 |
| Peds-QL, slope (SE) | | | | | | | | |
| Total score | -3.86 (0.88) | <.001 | -2.51 (0.44) | <.001 | -2.39 (0.46) | <.001 | .30 | .48 |
| Physical functioning | -4.40 (1.26) | .001 | -3.62 (0.64) | <.001 | -3.39 (0.66) | <.001 | .76 | .85 |
| Psychosocial | -3.50 (0.84) | <.001 | -2.06 (0.42) | <.001 | -1.84 (0.44) | <.001 | .20 | .36 |
| · · · · | | | | | | | | |
| functioning | | | | | | | | |
| functioning Social functioning | -4.10 (1.05) | <.001 | -2.24 (0.52) | <.001 | -2.36 (0.54) | <.001 | .25 | .44 |
| | -4.10 (1.05) 0.63 (1.01) | <.001 .53 | -2.24 (0.52) -0.50 (0.51) | <.001 .33 | -2.36 (0.54) -1.17 (0.53) | <.001 .028 .99 | .25 .22 .82 | .44 .33 .98 |

Table VI. Results of longitudinal model for neurodevelopmental, quality of life, and functional status outcomes from 3

*Estimates provided represent ORs (95% CIs) for the ASQ, which was modeled as a dichotomous outcome using the at-risk cutoffs. All other estimates for continuously modeled outcomes are slope (SE).

†Adjusted for Hispanic ethnicity, nonwhite race, birthweight, prenatal diagnosis, treatment assignment, and genetic condition.

advocacy to ensure that children from low-SES families have access to needed resources.

Similarly, children from middle-class backgrounds may benefit from more intensive neurodevelopmental interventions. In general, children in the middle SES and maternal education categories performed worse on 3-year assessments of communication and problem-solving compared with those in higher SES and maternal education categories, and their trajectories mirrored those of in the lowest SES and maternal education categories. Focusing interventions exclusively on children from low SES backgrounds may omit others who would benefit from more intensive early follow-up.

Lower SES may adversely affect neurocognitive development through prenatal factors, decreased educational

292

stimulation at home, nutrition, environmental exposures, and parental stress.^{17,18} Several programs geared toward children of economically disadvantaged backgrounds in the general population have focused on early cognitive stimulation and addressing the negative consequences of low SES (eg, nutritional supplementation, improving access to medical care).¹⁹⁻²² These programs have shown promising results, but the effectiveness of such programs in children with congenital heart disease remains unknown. Based on these data, programs that target problem-solving and fine motor skills are likely to be most advantageous for reducing disparities in neurodevelopmental outcomes by SES. Creative solutions, such as enhancing the richness of the physical home environment and play materials at home, may be needed to help mitigate some of the differences observed.

Limitations of this study include missing outcome data in 20%-25% of patients, the use of parent-reported rather than self-reported instruments to assess neurodevelopment and HRQOL, and the assessment of maternal education and SES at a single time point without examining changes in these variables over time. However, early-life SES may impact long-term neurodevelopment through prenatal factors, early exposures, and parental stress and involvement in infancy.¹⁸ An additional limitation is the inability to determine whether the differences in neurodevelopmental outcomes by SES observed in our study are specific to children with HLHS or are similarly observed in the general population. Previous studies have found that children from lower SES backgrounds are at increased risk of lower school achievement, cognitive attainment, and language skills compared with children of higher SES.^{23,24} Unfortunately, we lacked a population control group to determine whether the effect of SES on neurodevelopmental outcomes was more pronounced in children with HLHS. Differences in neurodevelopmental trajectories by neighborhood SES and maternal education mirrored each other, likely because these variables are closely related. We evaluated these variables in separate models to avoid issues with collinearity; however, future investigations are needed to determine which socioeconomic factors are most closely related to neurodevelopment.

In conclusion, our data indicate that children with HLHS and low SES or maternal education are at increased risk of early delays in communication and problem-solving compared with patients from higher SES or maternal education backgrounds. Over time, differences in fine motor development and problem-solving skills became more pronounced. Early and targeted neurodevelopmental interventions in all children with HLHS, but particularly those with low SES, are essential for reducing long-term disability in this high-risk population. ■

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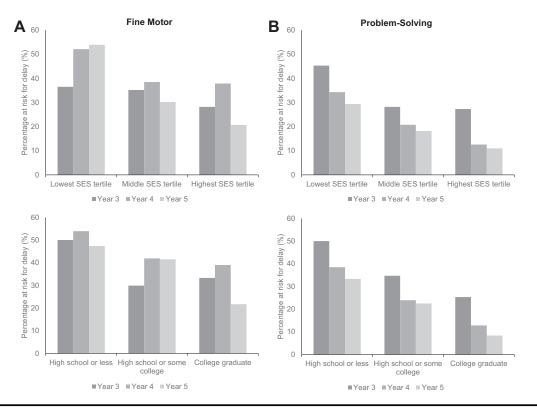


Figure. Percentage of children at risk for delay on **A**, fine motor and **B**, problem-solving components of the ASQ by neighborhood SES and maternal education over time.

| Table I. Sample sizes for neurodevelopmental outcomes | | | | | | |
|---|------------------|----------|----------|----------|--|--|
| Outcomes | Year 3 | Year 4 | Year 5 | Year 6 | | |
| Neighborhood S | SES (N = 285), n | (%) | | | | |
| ASQ | 220 (75) | 253 (86) | 242 (83) | _ | | |
| BASC-2 | 230 (79) | 248 (85) | 239 (82) | 245 (84) | | |
| Peds-QL | 228 (78) | 251 (86) | 240 (82) | 248 (85) | | |
| FS-II(R) | 231 (79) | 251 (86) | 239 (82) | 249 (85) | | |
| Maternal education (n = 274), n (%) | | | | | | |
| ASQ | 211 (77) | 238 (87) | 225 (82) | _ | | |
| BASC-2 | 221 (81) | 233 (85) | 222 (81) | 232 (85) | | |
| Peds-QL | 219 (80) | 236 (86) | 224 (82) | 235 (86) | | |
| FS-II(R) | 222 (81) | 236 (86) | 222 (81) | 236 (86) | | |

| Table II. Parent-completed outcome scales and timing | | | | | | |
|--|--------------------------------------|---|--|--|--|--|
| Outcome | Questionnaire | Timing of assessment | | | | |
| Neurodevelopment Neurodevelopment Quality of life Functional status | ASQ BASC-2 Peds-QL FS-II(R) | Years 3, 4, and 5 Years 3, 4, 5, and 6 Years 3, 4, 5, and 6 Years 3, 4, 5, and 6 | | | | |

| Characteristics | Lowest tertile (N = 84) | Middle tertile ($N = 94$) | Highest tertile (N = 107) | P value* |
|---|-------------------------|-----------------------------|---------------------------|------------------|
| Demographic characteristics | | | | |
| Female sex, n (%) | 32 (38) | 38 (40) | 39 (36) | .85 |
| Hispanic ethnicity, n (%) | 29 (35) | 18 (19) | 7 (7) | <.001 |
| Nonwhite race, n (%) | 25 (30) | 13 (14) | 9 (8) | <.001 |
| Birth characteristics | | | | |
| Prenatal diagnosis, n (%) | 6 (77) | 66 (70) | 93 (87) | .015 |
| Gestational age<37 weeks, n (%) | 5 (6) | 11 (12) | 5 (5) | .16 [†] |
| Birth weight, kg, mean (SD) | 3.10 (0.53) | 3.12 (0.49) | 3.24 (0.51) | .10 |
| Anatomy | () | | | |
| HLHS, n (%) | 74 (88) | 86 (91) | 96 (90) | .76 |
| Norwood procedure | (), | | | |
| Treatment assignment, n (%) | | | | .61 |
| RV-pulmonary artery conduit | 37 (44) | 48 (51) | 49 (46) | |
| Modified BT shunt | 47 (56) | 46 (49) | 58 (54) | |
| Weight z-score pre-Norwood, mean (SD) | -0.51 (1.14) | -0.47 (1.12) | -0.20 (1.08) | .10 |
| Height z-score pre-Norwood, mean (SD) | -0.30 (1.54) | -0.45 (1.51) | -0.52 (1.43) | .63 |
| Head circumference z-score pre-Norwood, mean (SD) | -0.85 (1.40) | -0.70 (1.32) | -0.33 (1.35) | .026 |
| Post-Norwood procedure | . , | | | |
| Age at stage 2 procedure, y, mean (SD) | 0.47 (0.15) | 0.42 (0.21) | 0.43 (0.12) | .057 |
| Age at Fontan, y, mean (SD) | 3.24 (0.95) | 2.87 (0.93) | 2.77 (0.72) | .001 |
| Number of complications through 12 mo, median (IQR) | 4 (2-6) | 4 (2-6) | 3 (1-6) | .67 |
| Hospital characteristics | | | . , | |
| Site volume (patients/y), n (%) | | | | .14 |
| ≤15 | 19 (23) | 11 (12) | 16 (15) | |
| 16-20 | 9 (11) | 24 (26) | 17 (16) | |
| 21-30 | 28 (33) | 29 (31) | 36 (34) | |
| >30 | 29 (33) | 30 (32) | 38 (36) | |

*P values from the χ^2 test for categorical variables and ANOVA or the Kruskal–Wallis test for continuous variables. +P values from the Fisher exact test.

| Table IV. Sociodemographic and clinical characteristics by maternal education (N = 274) | | | | | | |
|---|--------------------------------|--|---------------------------------------|----------|--|--|
| Characteristics | Less than high school (N = 32) | High school or some college (N = 130) | College graduate or more (N = 104) | P value* | | |
| Demographic characteristics | | | | | | |
| Female, n (%) | 8 (25) | 55 (41) | 41 (38) | .23 | | |
| Hispanic ethnicity, n (%) | 20 (65) | 22 (17) | 10 (9) | <.001 | | |
| Non-white race, n (%) | 8 (26) | 19 (14) | 13 (12) | .16 | | |
| Birth characteristics | | | | | | |
| Prenatal diagnosis, n (%) | 21 (66) | 102 (77) | 88 (81) | .20 | | |
| Gestational age <37 wk, n (%) | 3 (9) | 13 (10) | 6 (6) | .41† | | |
| Birth weight, kg, mean (SD) | 3.10 (0.55) | 3.12 (0.49) | 3.24 (0.52) | .13 | | |
| Anatomy | | | | | | |
| HLHS, n (%) | 26 (81) | 118 (89) | 101 (93) | .17 | | |
| Norwood procedure | | | | | | |
| Treatment assignment, n (%) | | | | .42 | | |
| RV-pulmonary artery conduit | 13 (41) | 67 (50) | 47 (43) | | | |
| Modified BT shunt | 19 (59) | 66 (50) | 62 (57) | | | |
| Weight z-score pre-Norwood, mean (SD) | -0.52 (1.17) | -0.48 (1.13) | -0.20 (1.09) | .11 | | |
| Height z-score pre-Norwood, mean (SD) | -0.27 (1.59) | -0.50 (1.43) | -0.51 (1.44) | .52 | | |
| Head circumference z-score pre-Norwood, mean (SD) | -0.85 (1.46) | -0.75 (1.32) | -0.34 (1.36) | .032 | | |
| Post-Norwood procedure | | | | | | |
| Age at stage 2 procedure, y, mean (SD) | 0.47 (0.15) | 0.41 (0.21) | 0.43 (0.12) | .069 | | |
| Age at Fontan, y, mean (SD) | 3.20 (0.92) | 2.88 (0.95) | 2.75 (0.71) | .003 | | |
| Number of complications through 12 mo, median (IQR) | 4 (3-7) | 4 (2-6) | 3 (2-6) | .29 | | |
| Hospital characteristics | | | | | | |
| Site volume (patients/y), n (%) | | | | .043 | | |
| ≤15 | 8 (25) | 20 (15) | 16 (15) | | | |
| 16-20 | 7 (22) | 31 (23) | 18 (17) | | | |
| 21-30 | 15 (47) | 40 (30) | 35 (32) | | | |
| >30 | 2 (6) | 42 (32) | 40 (37) | | | |

**P* values from the χ^2 test for categorical variables and ANOVA or the Kruskal–Wallis test for continuous variables. +*P* values from the Fisher exact test.