

Table. Rates of Cryopreservation Between Patients Assigned Male or Female at Birth

| Method of fertility preservation | No. (%) | |
|---|--|---|
| | Prior to commencing gonadotropin-releasing hormone agonists ^a | Prior to commencing estrogen or testosterone ^a |
| Transgender adolescents assigned male at birth (n = 53) | 23 (43.4) | 30 (56.6) |
| Masturbatory semen collection with sperm cryopreservation | 7 (30.4) | 15 (50.0) |
| Testicular tissue biopsy | | |
| Sperm and testicular tissue cryopreservation | 3 (13.0) | 2 (6.7) ^b |
| Testicular tissue cryopreservation only | 4 (17.4) | 2 (6.7) ^b |
| No fertility preservation | 9 (39.1) | 11 (36.7) |
| Transgender adolescents assigned female at birth (n = 49) | 3 (6.1) | 46 (93.9) |
| Oocyte retrieval and cryopreservation | 0 | 0 |
| Ovarian tissue biopsy and cryopreservation | 0 | 0 |
| No fertility preservation | 3 (100) | 46 (100) |

^a It is important to note that gonadotropin-releasing hormone agonists, estrogen, and testosterone have differential associations with reproductive function. For example, prolonged use of estrogen in patients assigned male at birth has been associated with impaired spermatogenesis, with the reversibility still unclear. Meanwhile, testosterone administration in patients assigned female at birth can similarly impair reproductive function, although this outcome appears reversible. Finally, gonadotropin-releasing hormone agonists can be expected to inhibit reproductive development, and although this should also be reversible, most adolescents who undergo pubertal suppression subsequently proceed to gender-affirming hormones.

^b Three of these individuals had received puberty-blocker therapy prior to commencing estrogen (1 with sperm cryopreservation and 2 with tissue only).

costs for patients who were AMAB at our clinic are relatively affordable (testicular biopsy is free, semen analysis costs approximately \$66 [AU \$100], and annual sperm storage costs approximately \$132 [AU \$200]). Consistent with this, a recent Dutch study in which FP costs were also largely covered by insurance observed that 12 of 32 transgender individuals who were AMAB (38%) froze sperm prior to starting hormones.⁶ Notably, this rate was still considerably lower than ours. One likely reason is that testicular biopsy, which is likely to be less dysphoria-inducing than masturbation and also more suitable for younger adolescents, was not an option for the patients in the Netherlands, highlighting the importance of providing different FP options.

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The Interwoven Nature of Medical and Social Complexity in US Children

Health is strongly influenced by both medical conditions and social determinants of health (SDH). The degree to which challenges in one affect the frequency or magnitude of challenges in the other is not fully understood. Children with medical complexity may be at especially high risk for related social complexity.^{1,2} If so, then children with medical complexity may be even more vulnerable than their underlying illness might

Table. Demographic Characteristics of the Study Population by Complexity of Special Health Care Needs

| Characteristic | No. (%) | | | |
|--------------------|-------------------|---------------------------|-------------------|-------------------|
| | All children | Special health care needs | | |
| | | None | Lower complexity | Higher complexity |
| Overall | 73 424 383 (100) | 60 096 885 (81.8) | 11 417 083 (15.6) | 1 910 415 (2.6) |
| Age, y | | | | |
| 0-1 | 7 699 922 (10.5) | 7 324 816 (12.2) | 342 720 (3.0) | 32 386 (1.7) |
| 2-4 | 12 084 849 (16.5) | 10 655 129 (17.7) | 1 241 489 (10.9) | 188 231 (9.9) |
| 5-12 | 32 926 710 (44.8) | 26 302 300 (43.8) | 5 661 967 (49.6) | 962 442 (50.4) |
| 13-17 | 20 712 902 (28.2) | 15 814 640 (26.3) | 4 170 907 (36.5) | 727 356 (38.1) |
| Sex | | | | |
| Male | 37 542 467 (51.1) | 29 803 477 (49.6) | 6 487 287 (56.8) | 1 251 703 (65.5) |
| Female | 35 881 916 (48.9) | 30 293 408 (50.4) | 4 929 796 (43.2) | 658 712 (34.5) |
| Race/ethnicity | | | | |
| Non-Hispanic white | 37 415 487 (51.0) | 30 794 035 (51.2) | 5 695 824 (49.9) | 925 627 (48.5) |
| Non-Hispanic black | 9 841 673 (13.4) | 7 238 651 (12.0) | 2 185 677 (19.1) | 417 345 (21.8) |
| Hispanic | 18 309 354 (24.9) | 15 358 772 (25.6) | 2 535 935 (22.2) | 414 647 (21.7) |
| Other ^a | 7 857 869 (10.7) | 6 705 426 (11.2) | 999 647 (8.8) | 152 796 (8.0) |

^a Other race/ethnicity included Asian, American Indian, and Pacific Islander.

suggest owing to enhanced risk for SDH challenges. A comprehensive medical-social approach to pediatric complex care may be warranted—one not currently seen in traditional health care practices. To better understand this potential need, we compared the prevalence and types of SDH challenges across children by level of medical complexity.

Methods | We performed a retrospective, cross-sectional study of 21 599 responses representing 73.4 million children aged 0 to 17 years. Data were taken from the 2017 National Survey of Children's Health, which is funded and directed by the Maternal and Child Health Bureau of the Health Resources and Services Administration.³ The screening items of children with special health care needs (CSHCN) were used to categorize children into 3 groups.⁴ Children without special health care needs had none of the following attributes: (1) chronic mental or physical health problems; (2) chronic functional limitations; or (3) the need for therapies, chronic medications, or any health care needs greater than healthy peers. Children with special health care needs were then categorized as having lower medical complexity if they had neither chronic functional limitations nor greater health care needs than their peers. Children with special health care needs with either of those 2 attributes were categorized as having higher medical complexity. Waiver of ethical review for the study and informed consent was granted by the institutional review board of Boston Children's Hospital because the research did not meet criteria for human subjects research.

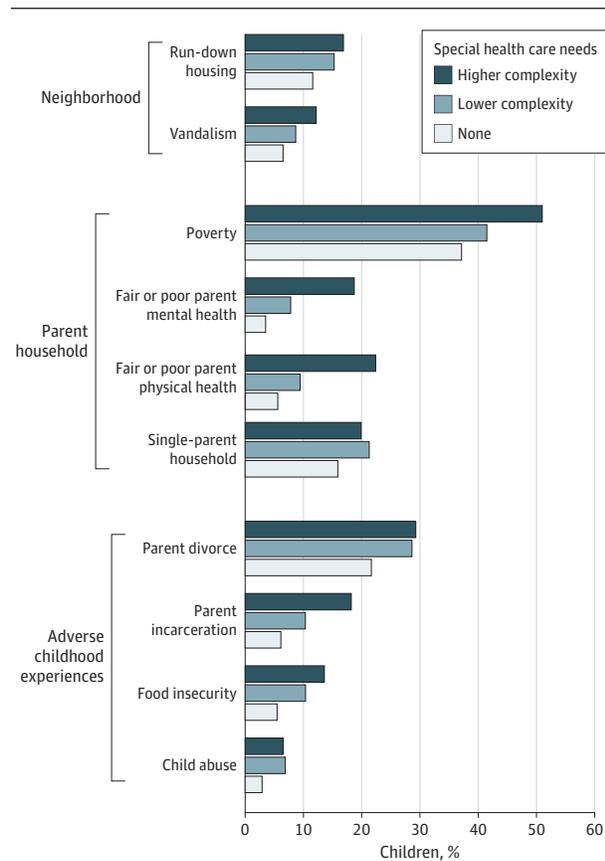
The data analysis was performed between January 1 and December 31, 2017. With the use of the Healthy People 2020 framework,⁵ SDH challenges identified from the survey were organized by (1) neighborhood characteristics, (2) parent or household characteristics, and (3) adverse childhood experiences. The rates of SDH challenges were adjusted by age, sex, and race or ethnicity and compared across groups using design-adjusted logistic regression. Because of the large sample size, the threshold for statistical significance was 2-sided $P < .01$.

All analyses were performed with SAS software, version 9.4 (SAS Institute Inc).

Results | In the study cohort of 73 424 383 children, 37 542 467 (51.1%) were boys and 35 881 916 (48.9%) were girls; 51.0% were non-Hispanic white, 24.9% Hispanic, 13.4% non-Hispanic black, and 10.7% another race/ethnicity. Among children in the cohort, 81.8% had no special health care needs, 15.6% were CSHCN with lower medical complexity, and 2.6% were CSHCN with higher medical complexity (Table). The percentages of children experiencing challenges in the following domains increased with medical complexity (no special health care needs vs CSHCN with higher medical complexity): (1) neighborhood: rundown housing (11.6% vs 16.9%) and vandalism 6.5% vs 12.2%; (2) parent/household: single-parent household (15.9% vs 19.9%), primary parent has fair or poor physical health (5.6% vs 22.4%), primary parent has fair or poor mental health (3.5% vs 18.7%), and income less than 200% of the federal poverty level (37.2% vs 51%); and (3) adverse childhood experiences: parent divorce (21.7% vs 29.3%), parent incarceration (6.1% vs 18.2%), child abuse (2.9% vs 6.5%), and food insecurity (5.5% vs 13.6%) (Figure). All differences were statistically significant ($P < .001$).

Discussion | In the present study, SDH challenges were prevalent and associated with medical complexity. This association suggests that more attention with respect to SDH challenges is needed, especially for children with medical complexity. Because of the problems reflected by many of the SDH challenges, implementation of not only individual-level but also community-level social solutions is probably needed. Otherwise, efforts expended on SDH may remain predominately focused on helping children and families endure these problems rather than helping society solve them. A limitation of the present study is that it could not assess causal associations between SDH challenges and medical complexity. More research is needed to understand when and how medi-

Figure. Social Determinants of Health in Children by Complexity of Special Health Care Needs



Shown are the percentages of children with each social determinant of health measured from the 2017 National Survey of Children's Health.

cal complexity and SDH challenges develop and influence each other. Population-based, longitudinal surveys should consider items that clarify the onset of both special health care needs and SDH challenges to help unravel these temporal relationships.

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Association of Prenatal Opioid Exposure With Precentral Gyrus Volume in Children

Prenatal opioid exposure is associated with delayed locomotor performance at multiple stages of early child development^{1,2} and with smaller neuroanatomical structures, such as the basal ganglia.³ The motor cortex, which controls speech and motor skills, may also be vulnerable to drug exposure, but to our knowledge, this has yet to be assessed. Identifying risks of exposure associated with brain structures is critical for prevention and intervention strategies for cognitive effects that can last long after conception.^{3,4}

Most neuroanatomical opioid-related research has focused on heroin, used smaller samples, and failed to control for social factors that are associated with development. Using data from the Adolescent Brain Cognitive Development (ABCD) study,⁵ we aimed to identify structural differences of the precentral gyrus (motor cortex) among children with reported pre-