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Inequities in Therapy for Infantile Spasms: A Call to Action

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Potential Conflicts of Interest

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Additional supporting information can be found in the online version of this article.

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Abstract

Objective: The aim of this study was to determine whether selection of treatment for children with infantile spasms (IS) varies by race/ethnicity.

Methods: The prospective US National Infantile Spasms Consortium database includes children with IS treated from 2012 to 2018. We examined the relationship between race/ethnicity and receipt of standard IS therapy (prednisolone, adrenocorticotropic hormone, vigabatrin), adjusting for demographic and clinical variables using logistic regression. Our primary outcome was *treatment course*, which considered therapy prescribed for the first and, when needed, the second IS treatment together.

Results: Of 555 children, 324 (58%) were non-Hispanic white, 55 (10%) non-Hispanic Black, 24 (4%) non-Hispanic Asian, 80 (14%) Hispanic, and 72 (13%) other/unknown. Most (398, 72%) received a standard treatment course. Insurance type, geographic location, history of prematurity, prior seizures, developmental delay or regression, abnormal head circumference, hypsarrhythmia, and IS etiologies were associated with standard therapy. In adjusted models, non-Hispanic Black children had lower odds of receiving a standard treatment course compared with non-Hispanic white children (odds ratio [OR], 0.42; 95% confidence interval [CI], 0.20–0.89; $p = 0.02$). Adjusted models also showed that children with public (vs. private) insurance had lower odds of receiving standard therapy for treatment 1 (OR, 0.42; CI, 0.21–0.84; $p = 0.01$).

Interpretation: Non-Hispanic Black children were more often treated with non-standard IS therapies than non-Hispanic white children. Likewise, children with public (vs. private) insurance were less likely to receive standard therapies. Investigating drivers of inequities, and understanding the impact of racism on treatment decisions, are critical next steps to improve care for patients with IS.

There are inequities in the care delivered to people with epilepsy from racial and ethnic minoritized groups compared to white people with epilepsy. Examples include reduced access to subspecialists,[1,2] reduced use of antiseizure medications (ASMs),[3,4] and reduced frequency of surgery for refractory seizures.[5–10] Groups that have been historically marginalized are also underrepresented in epilepsy research trials.[11] Research on inequities in the *pediatric* epilepsy population has focused predominantly on surgical treatments. Black,[6] Hispanic,[12] and non-white[13] children, as well as children from lower socioeconomic status (SES) groups[6,10] were less likely to undergo epilepsy surgery and had a longer wait time before receiving care than white children, although not all findings are consistent.[14]

Infantile spasms (IS) are seizures that usually present in the first year of life and are associated with a severe developmental and epileptic encephalopathy that affects approximately ~2–3.5 per 10,000 children[15] between the ages of 2 months and 2 years of age.[16] While epilepsy and neurodevelopmental outcomes after IS are largely determined by etiology, optimal patient-specific outcomes are only possible with rapid initiation of effective treatment.[17] Consensus documents highlight the selection of 3 treatments – adrenocorticotropic hormone (ACTH), oral steroids, and vigabatrin – as standard first-line therapy for IS.[18–23] Response to treatment should be assessed after 1 to 2 weeks and, if needed, an alternative or additional standard therapy should be given by or before day 14 of treatment.[23,24] Delays in diagnosis, treatment initiation, or assessment of treatment response, as well as the use of non-standard therapies (treatments other than ACTH, oral steroids, or vigabatrin) may lead to worse outcomes.

In this study, we investigated whether children from racial and ethnic minoritized groups who presented with new-onset IS received similar treatment as white children with IS using the National IS Consortium (NISC) registry. The NISC registry is a multicenter prospective observational study of children treated for IS at 25 tertiary care children's hospitals across the United States between 2012 and 2018. Clinicians at NISC centers received suggested treatment regimens for ACTH, oral steroids, and vigabatrin, although patient enrollment did not require the use of these regimens. Since >50% of children with IS require a second treatment due to persistent or recurrent IS, we considered the first two treatments prescribed to each child for IS.[25] We hypothesized that children with IS from historically marginalized groups are less likely to receive standard therapy for IS than white, non-Hispanic children.

Methods

NISC Database

The National IS Consortium (NISC) database is a prospective database of children diagnosed with IS at 25 tertiary care children's hospitals in the United States between 2012 and 2018. The Institutional Review Board (IRB) at each site approved the study and a parent/guardian provided written informed consent. Prospective entry of data obtained via chart review into a Research Electronic Data Capture database (REDCap Consortium; Nashville, TN[26]) was supervised by site investigators, who were all pediatric epileptologists.[25,27–30] IRB approval for follow-up analysis of this dataset was waived.

Children were included in the current analysis if they were between the ages of 2 and 24 months at IS onset and received at least one treatment specifically for IS (Fig). Children were excluded if IS ceased before treatment initiation, initial treatment was delayed greater than 1 year from IS onset, or they were lost to follow-up before 2 weeks. To focus on treatments initiated for recurrence of IS and not new seizure types, we considered second treatments only if they were initiated within 1 year of initial IS therapy.

Coding of Demographic Data

Race and ethnicity, as recorded in the NISC database, were extracted from patient charts. The NISC database included 7 race categories: white/Caucasian; Black/African American; Asian; American Indian/Alaskan Native/First Nations; Native Hawaiian/Pacific Islander; other; unknown/not reported. The NISC database contained 3 ethnicity categories: Hispanic/Latino; not Hispanic; and unknown.

We used the NISC data fields on race and ethnicity to create a combined race/ethnicity variable with 5 categories: (1) non-Hispanic white (white/NH); (2) non-Hispanic Black (Black/NH); (3) non-Hispanic Asian (Asian/NH); (4) Hispanic; and (5) other [including those categorized as other in the NISC database as well as the 4 patients categorized as either American Indian, Alaskan Native, First Nations, Native Hawaiian, Pacific Islander] and unknown. We combined race and ethnicity rather than assessing each separately, as we wanted to assess the impact of being part of an historically marginalized group on treatment, regardless of whether the inequity was secondary to race or ethnic identification. Additionally, the vast majority of Hispanic patients were noted to be white, other, or unknown for race; hence, the ethnicity category provided more definitive information than race for these children with regard to inclusion in a minoritized group. We also recognize that the use of “other” can carry negative connotations, but have preserved this nomenclature to reflect the original dataset. Insurance type was categorized as: (1) public, (2) private, or (3) other/unknown. Similarly, preserving nomenclature used in the original dataset, sex was coded as binary (male/female). Public insurance in the United States is administered by Medicaid programs, which vary by state; for this reason, we aggregated data from study sites within the same state. We combined adjacent regions in two instances (Baltimore with Washington, DC, and Iowa with Minnesota) to ensure that each state contributed at least 9 participants. We entered year of diagnosis as a categorical variable with the following possible values: 2012, 2013, 2014, 2015, 2016, 2017/2018. We combined data from 2017 and 2018 as only 3 subjects were enrolled in 2018.

Coding of Clinical Data

Age at IS onset and time to initial diagnosis were measured as continuous variables. Other clinical data were modeled as categorical values and included: history of premature birth (yes; no); history of seizures prior to IS (yes; no); history of developmental delay prior to IS diagnosis (none/mild; definite/significant; unknown, according to the clinicians’ assessments, as described elsewhere[25,27–30]); history of developmental regression prior to IS diagnosis (none/possible; definite; unknown); etiology of IS (unknown; tuberous sclerosis complex [TSC]; other); and electroencephalogram (EEG) at IS diagnosis (no hypsarrhythmia; hypsarrhythmia; or unknown).

Definition and Coding of Outcomes

Standard therapies were defined as ACTH, oral steroids or vigabatrin, and non-standard therapies were defined as all other treatments.[18–23] Our primary outcome was *treatment course*, which combined first treatment and (if prescribed) second treatment. We focused on the first two treatments for several reasons. First, significant differences in receipt of standard therapy by race or ethnicity had not been previously noted when looking at only the first treatment alone.[27] Additionally, >50% of children require more than one treatment for IS[25] due to failure of the first medication or relapse after initial remission, making choice of second treatment very important. Finally, as there are two main classes of recommended therapy for IS (hormonal therapy and vigabatrin), providers can switch between them if the first medication fails. We defined a *standard treatment course* as: (1) a single treatment with a standard therapy, or (2) two sequential standard therapies. We defined a *non-standard treatment course* as: (1) a single treatment with a non-standard therapy; or (2) two treatments, either or both of which were non-standard therapy (Fig). We also evaluated whether standard therapy was prescribed for treatment 1 and treatment 2.

Analysis

Statistical analyses were performed using SAS OnDemand for Academics (Cary, NC). We first performed unadjusted bivariate analyses to measure the association between demographic, clinical, and treatment response variables with: (1) standard treatment course, and (2) racial/ethnic category. For continuous variables, we applied Wilcoxon rank-sum or Kruskal-Wallis tests. For categorical variables, we applied chi-squared or Fisher exact test. To assess whether the odds of receiving a standard treatment course differed by race/ethnic category, we performed a logistic regression, adjusting for insurance type; state of treating hospital; year of diagnosis; history of prematurity, prior seizures, developmental delay, or regression; head circumference; etiology of IS; and presence of hypsarrhythmia on diagnostic EEG. The choice of covariates was based on our a priori clinical knowledge of patient-specific factors that influence physicians' treatment decisions; these variables were selected before examination of the bivariate analyses. We then replicated these models separately for the first prescribed IS treatment and the second prescribed IS treatment; when modeling the second treatment, we also adjusted for whether or not treatment 1 was standard.

Results

Children and IS Treatments

Of the 629 children enrolled in the NISC database, 555 (88%) met inclusion criteria for this study (Fig). Most infants were white/NH (324/555, 58%), while 10% (55/555) were Black/NH, 4% (24/555) were Asian/NH, 14% (80/555) were Hispanic, and 13% (72/555) were in the other/unknown category. The category of "other/unknown" included 1 child whose family identified as American Indian/Alaskan Native/First Nations, 2 children whose family identified as Native Hawaiian/Pacific Islander, 34 children whose family identified as "other," and 35 children for whom a racial or ethnic group was not recorded.

All 555 infants received treatment for IS: 481 (87%) of the initial treatments were standard therapies (252 received ACTH, 121 oral steroids, and 108 vigabatrin), while 74 (13%) were non-standard therapies (68 received ASM, 6 ketogenic diet). Among 296 infants (53%) who received a second treatment, 199 (67%) received standard therapies (56 ACTH, 39 oral steroids, and 104 vigabatrin) and 97 (33%) received non-standard therapies (86 other ASMs, 10 ketogenic diet, 1 surgery). Of the 481 infants who received standard therapy for treatment 1, 238 did not have a second treatment and 160 received a standard second treatment; this group, representing 72% (398/555) of the initial cohort, was categorized as having received a *standard treatment course*. The remaining 28% (157/555) were categorized as having received a *non-standard treatment course* (21 received non-standard therapy for treatment 1 and no second treatment; 14 received non-standard therapy for both treatments; 83 received standard therapy for treatment 1 and non-standard therapy for treatment 2; and 39 received non-standard therapy for treatment 1 and standard therapy for treatment 2) (Fig).

Demographic Variables Associated with Standard Therapy

Treatment Course: Receipt of a standard treatment course (standard therapy for treatment 1 and, if prescribed, for treatment 2) differed significantly by race, with Black/NH children less likely to receive standard therapy for all treatments (29/55, 53%) than children who were white/NH (240/324, 74%), Asian/NH (19/24, 79%), Hispanic (62/80, 78%), or other/unknown (48/72, 67%) ($p = 0.009$). Children with public insurance were also less likely to receive a standard treatment course (159/242, 66%) than those with private (192/252, 76%) or unknown (47/67, 76%) insurance ($p = 0.02$). Children were more likely to receive a standard treatment course in later years of the study period (41/46, 89% in 2017/2018 vs. 27/42, 64% in 2012). Finally, medication prescription varied by the treating hospital's state, with a range of 44% (4/9) to 89% (41/46) of children receiving a standard treatment course ($p = 0.003$) (Table 1).

Treatment 1 & 2: In follow-up analyses, we examined the association of demographic variables with standard therapy for treatment 1 and treatment 2 individually. Race was not significantly associated with standard therapy for treatment 1 or 2 individually, although Black/NH children were less likely than those from other groups to get standard therapy for treatment 1 (80% of Black/NH children vs. 83–92% for other groups, $p = 0.38$) and treatment 2 (51% vs. 63–72%, respectively; $p = 0.20$). Insurance type was associated with standard therapy only for treatment 1, with 90% (227/251) of children with private insurance and 92% (57/62) with unknown insurance but only 81% (197/242) of children with public insurance receiving standard therapy ($p = 0.006$); insurance type was not significantly associated with therapy received for treatment 2 ($p = 0.35$). Similarly, the location of care, as defined by the treating hospital's state, was significantly associated with the therapy chosen for treatment 1 ($p < 0.0001$) but not for treatment 2 ($p = 0.49$). In general, a higher proportion of children in each state received standard therapy for treatment 1 (range, 50–100%) than for treatment 2 (range, 33–81%). Year of diagnosis was marginally associated with therapy chosen for treatment 1 ($p = 0.09$) and treatment 2 ($p = 0.05$).

Clinical Variables Associated with Standard Therapy

Treatment Course: History of preterm birth ($p = 0.03$), seizures preceding IS onset ($p = 0.005$), pre-existing developmental delay ($p = 0.0006$), developmental regression ($p = 0.005$), and abnormal head circumference ($p = 0.0007$) were associated with a non-standard treatment course (Table 2).

Treatment 1 & 2: Etiology of IS and presence of hypsarrhythmia on the diagnostic EEG were specifically associated with the choice of therapy for treatment 1 but not for treatment 2 or the entire treatment course. Children with an unknown etiology of IS (209/229, 91%) were more likely than those with TSC (32/36, 89%) or other etiologies (240/290, 83%) to receive standard therapy for treatment 1 ($p = 0.02$), but etiology was not associated with treatment 2 ($p = 0.46$) or the treatment course ($p = 0.39$). Children without hypsarrhythmia at IS diagnosis (73/97, 75%) were less likely than those with hypsarrhythmia (366/407, 90%) or with an unknown initial EEG background pattern (42/51, 82%) to receive standard therapy for treatment 1 ($p = 0.0004$), but hypsarrhythmia on the diagnostic EEG was not associated with treatment 2 ($p = 0.11$) or the whole treatment course ($p = 0.13$).

Demographic and Clinical Variables Associated with Race/Ethnicity

Insurance type differed by race, with 60% (33/55) of Black/NH and 76% (61/81) of Hispanic children using public insurance vs. 36% (116/324) of white/NH, 17% (4/24) of Asian/NH, and 39% (28/72) of other/unknown children ($p < 0.0001$). There was also variation in the racial and ethnic backgrounds of children seen across different states ($p < 0.0001$). For instance, although Ohio and Maryland/DC only made-up 16% of the study sample, 40% (22/55) of Black/NH patients received care in these states. Fifty percent (12/24) of Asian/NH patients were treated in California and Massachusetts (responsible for 16% of the study sample), while 54% (43/80) of Hispanic patients received care in Texas, California, or Illinois (states which, combined, contributed 28% of the sample). Year of diagnosis and clinical variables (e.g., etiology, hypsarrhythmia, neurodevelopment) did not differ across racial groups (Table S1).

Impact of Race/Ethnicity on Odds of Receiving Standard Therapy

Treatment Course.

Unadjusted: Logistic regression models compared the odds of receiving a standard treatment course for each race/ethnic category to that of the white/NH group. In an unadjusted model (Model A), children who were Black/NH had a lower odds of receiving a standard treatment course (odds ratio [OR], 0.39, confidence interval [CI], 0.22–0.69) than white/NH children ($p = 0.001$). The odds of receiving standard therapy did not differ for children in the Asian/NH (OR, 1.31; CI, 0.48–3.63), Hispanic (OR, 1.17; CI, 0.66–2.10), or other/unknown (OR, 0.69; CI, 0.40–1.20) groups when compared with children in the white/NH group (Table 3).

Adjusted: We next adjusted the regression models for demographic variables (insurance type, year of diagnosis, treating hospital's state) (Model B) and for both demographic and clinical variables (history of preterm birth, seizures, developmental delay or regression,

abnormal head circumference, IS etiology, or history of hypsarrhythmia) that could be associated with standard therapy (Model C). After these adjustments, Black/NH children still had lower odds of receiving a standard treatment course than their white/NH counterparts (OR, 0.42; CI, 0.20–0.89; $p = 0.02$). No other racial/ethnic groups had significantly different odds of receiving a standard treatment course than the white/NH children, although the data suggest that children in the other/unknown group were also less likely to receive standard therapy. Although this association was not statistically significant, it may be clinically important (OR, 0.57; CI, 0.30–1.12; $p = 0.10$). As some clinicians consider ketogenic diet or surgery a first-line standard therapy, we ran sensitivity analyses reclassifying these therapies as standard (OR, 0.40; CI, 0.18–0.85; $p = 0.02$ for Black/NH vs. white/NH children) and excluding the 17 patients who had received them (OR, 0.36; CI, 0.16–0.78; $p = 0.01$); results did not differ in these analyses (Table 3).

Treatments 1 & 2.

Unadjusted: Black/NH children had lower odds than white/NH children of receiving standard therapy for treatment 1 (OR, 0.57; CI, 0.27–1.18; $p = 0.13$) and treatment 2 (OR, 0.42; CI, 0.20–0.89; $p = 0.02$), although this difference was only significant for treatment 2. Children in the Asian/NH, Hispanic, and other/unknown groups did not have a different odds of receiving standard therapy for treatment 1 or 2 compared to white/NH patients (Table 3).

Adjusted: After adjusting for demographic and clinical variables that could be associated with treatment choice, Black/NH children were less likely than white/NH children to receive standard therapy for treatment 2 (OR, 0.42; CI, 0.15–1.14; $p = 0.09$) at a trend level. The difference between Black/NH and white/NH children for treatment 2 was significant in both the sensitivity analysis recategorizing ketogenic diet and surgery as standard therapy (OR, 0.28; CI, 0.10–0.84; $p = 0.02$) and the analysis excluding patients who received these therapies (OR, 0.29; CI, 0.10–0.87; $p = 0.03$) (Table 3).

Impact of Insurance Type on Odds of Receiving Standard Therapy

Although not the primary focus of this analysis, we noted in our multivariable models that insurance type was strongly associated with standard therapy, even after adjusting for race and other demographic variables, and we present these findings in Table 4. Most notably, even after adjusting for all other demographic and clinical variables, children with public insurance (vs. private insurance) had a significantly lower odds of receiving standard therapy for treatment 1 (OR, 0.42; CI, 0.21–0.84; $p = 0.01$) and trended toward a lower odds of receiving a standard treatment course (OR, 0.66; CI, 0.40–1.08; $p = 0.1$) (Table 4).

Discussion

This prospective, observational multicenter study of prescribing practices for children with newly diagnosed IS suggests treatment inequities. Black children and children with public insurance were much less likely than white children and children with private insurance to receive standard therapy. Inequities were especially pronounced when considering the second treatment prescribed to children with refractory or relapsed IS. Given that rapid

initiation of effective therapy may be the best opportunity to limit neurodevelopmental disability[19] and lower the risk of life-long refractory epilepsy, our findings serve as a call to action. All children, regardless of race/ethnicity or ability to pay, should receive standard therapy for IS.

Prior analyses of the NISC database did not identify associations between the first treatment prescribed and race/ethnicity, but those studies subdivided therapies into 4 categories (ACTH, steroids, vigabatrin, or ASMs), which diminished the statistical power. Given the consensus that only ACTH, steroids, or vigabatrin are acceptable initial therapies for IS,[18,20] we considered any of these three medications as "standard therapy" when assessing for inequities in treatment. The present sample size is also larger than that of the initial NISC manuscripts. A recent analysis of this expanded NISC dataset that dichotomized treatment as standard vs. non-standard found that children with unknown ethnicity were less likely to receive standard therapy for treatment 1.[30] Thus, "unknown" might not be a random assignment of race/ethnicity and should be addressed in future studies. We additionally considered the *treatment course* (treatment 1 and, if prescribed, treatment 2) rather than treatment 1 alone as inequities in either treatment could have significant clinical repercussions. We report that Black/NH children were less likely to receive standard treatment than white/NH children even after adjusting for insurance type, state of treatment, and several clinical variables. When looking at treatment 1 and treatment 2 separately, the inequity is much more pronounced for the second treatment (51% of Black/NH patients vs. 72% of white/NH patients received standard therapy) than for the first (80% vs. 87%, respectively), suggesting that inequity worsens for patients who do not respond completely to initial therapy.

We add to a growing body of literature identifying racial inequities across medical specialties. Black children and adults have reduced access to subspeciality neurology care[31] and are underrepresented in epilepsy surgery cohorts.[5–7,9,10,32] There are also inequities in timing to epilepsy surgery; Black patients experience extended time to temporal lobe surgery compared to white patients.[8] This is especially concerning since the incidence of temporal lobe epilepsy[33] and status epilepticus[34] may be higher in the Black population. Inequities in epilepsy care also exist for other minoritized groups (e.g., longer time to epilepsy surgery for Asian patients and those with lower English proficiency).[8] Furthermore, people with lower SES or without private insurance, who have disproportionately higher incidence of sudden unexpected death in epilepsy (SUDEP),[35] are less likely to have epilepsy surgery.[5–7,9,10,32] Some data on healthcare inequities are conflicting. For example, one study showed that Hispanic ethnicity is associated with poorer epilepsy outcomes and more refractory epilepsy,[12] while another reported that Hispanic children receive epilepsy surgery more quickly, even after controlling for insurance type.[14]

The nature of our study makes it difficult to determine specific drivers of the inequity, which may vary across individual patients or study centers. Race is largely a social construct tied to SES and health outcomes *because of* the effects of racism.[36] Therefore, we must consider the ways that institutionalized racism (structurally driven differences in access to resources and opportunities) and interpersonal racism (individuals' implicit or explicit prejudice and discrimination) contribute to our finding.[36] In this context, the FACETS framework,[37]

developed to understand drivers of inequities for epilepsy surgery, may be applicable to understanding our findings and working to address them. FACETS stands for: (1) fear of treatment; (2) access to care; (3) communication barriers; (4) education; (5) trust; and (6) social support (Table 5). While "access to care" traditionally refers to access to appropriate healthcare providers, this may be less of an issue in our cohort who were all enrolled at tertiary care epilepsy centers. The fact that most children (87%) received standard therapy for treatment 1 suggests that having a protocolized approach to initial infantile spasms treatment protects against inequities in treatment, at least in these tertiary care centers; the community setting may be different. Affordability of care is likely a concern in our cohort, as insurance type was a significant predictor of treatment 1, even after controlling for the effect of race. We can advocate with our own states' Medicaid programs to ensure that standard IS therapies are covered from the onset of the disorder.

IS requires urgent evaluation followed by frequent, time-intensive follow-up. Access to appropriate care and to social support that enables it, thus, are not one-time issues, but rather, ongoing concerns. We posit that greater inequity is seen with the second treatment, because, with each new interaction with the healthcare system, there is added opportunity for racism to shape care. Both hormonal treatments and vigabatrin require monitoring for adverse events, such as gastrointestinal bleeding, opportunistic infection, adrenal insufficiency, and vision loss. Providers may alter treatment recommendations based on their perception of a family's medical aptitude; alternatively, families may choose specific treatments based on fear of side effects, especially if the first medication did not work as hoped. Prescription of the second treatment may coincide with a time when family resources (i.e., financial, occupational, or social) either become depleted or are perceived as such by their physicians. We must consider, study, and resolve institutional barriers both at the state and hospital level that may interfere with treatment (i.e., hours during which care is accessible, availability of telehealth, financial/logistical support to travel to healthcare, availability of paid disability leave). As clinicians, we must deliberately examine how our treatment recommendations might be influenced by a patient's social circumstances. Once identified, we need to explicitly label these barriers and seek resources to close such gaps. As we do this work, we can implement standardized diagnostic and therapeutic algorithms that extend beyond the first treatment for all children with IS.[24, 38]

Patient-clinician interactions – captured by the FACETS framework via fear of treatment, communication, education, and trust – may also contribute to the inequity in IS treatment. Fear of treatment is a near universal experience for families of infants with IS. After diagnosis, families are asked to rapidly initiate therapies with severe and potentially irreversible side effects; suddenly they find themselves administering daily injections, or dealing with inconsolable infants, or signing forms acknowledging risk of permanent vision loss.[39] Fear or suspicion of treatment may be augmented among people from historically marginalized groups, and particularly Black patients, especially those who perceive discrimination in prior healthcare interactions.[40] How clinicians mitigate patients' fear may also differ based on the patient's race and ethnicity. Counseling provided to Black adult patients tends to be less optimistic and less patient-centered than that provided to white patients.[41] Physician implicit bias can reduce the quality of patient-physician interactions and may affect outcomes (for a recent review[42]). While concordance in patient-provider race

may improve trust and satisfaction,[40, 43, 44] the child neurology workforce notably lacks diversity. In 2015, 70–80% of child neurologists identified as white, with few identifying as being from minoritized groups (14–20% Asian, 6–7% Hispanic, 1.6–2.2% Black/African American, 1% American Indian/Alaska native, and 5–8% other).[45] Finally, as outcomes for Hispanic and Asian/NH patients did not diverge from white/NH patients, language differences may not be a primary barrier to care, although NISC lacks information needed to test this. We outline suggestions for studying and addressing patient-provider interactions in Table 5. As authors, we represent a fairly homogenous group, however, and recognize these are merely starting points.

Several limitations warrant discussion. First, race and ethnicity were obtained from patient charts but the method by which they were entered into the medical record (i.e., by patient self-identification vs. staff assumption) was not standardized; potential variation across institutions is not possible to ascertain. Additionally, 13% of our sample had missing data for race and ethnicity. Although the difference did not reach statistical significance, children in the other/unknown category had a lower odds of standard treatment, which suggests that demographic information may not be missing at random. This issue requires further study. Second, race is a social construct whose impact on health may vary with geographic location. While we controlled for hospital state, our data were too sparse to comment meaningfully on regional/site-specific discrepancies. We also did not have a direct measure of SES and, hence, used insurance as a proxy. Third, selection bias may influence our results as our group represents a selected group of patients who sought care at tertiary-care epilepsy centers and consented to the study. Fourth, children may have been lost to follow-up before they received a second IS treatment and, thus, been miscategorized as having a s*tandard treatment course* based solely on their first treatment when in fact they received a non-standard therapy for their second treatment elsewhere. We think this issue is more likely to bias our results toward the null as a significantly larger proportion of Black children did not follow-up at 3 months compared with white children. Finally, switching between standard therapies may not have been a typical course of action at each center when the patients were enrolled. Still, therapy chosen for the second treatment should not vary by race/ethnicity.

Black children with IS did not receive the same level of care as white children, most notably those who required a second treatment. We publish this at a time when best therapy for IS is an evolving concept, with some centers moving toward dual therapy with hormonal therapy plus vigabatrin.[46] Our work highlights an urgent need for us all to assess our management of children with IS and to address barriers to standard therapy on the individual, institutional, and national/state-level.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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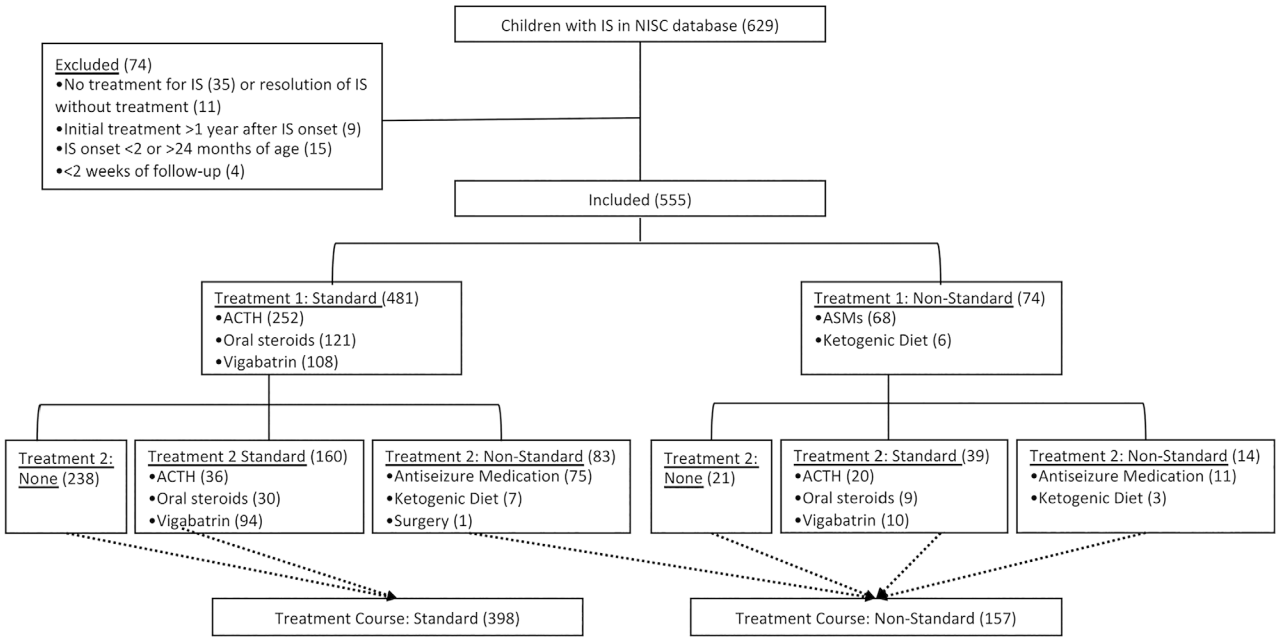

FIGURE:

Participant inclusion and definition of outcome measures. Flow diagram indicating which participants in the National Infantile Spasms Consortium (NISC) database were included in the analysis and illustrating how the primary outcome of treatment course was defined based on therapies received for treatment 1 and treatment 2. Number in parentheses = n for each step.

TABLE 1.

Demographic Variables Associated with Standard Therapy

	Treatment 1 (n = 555) n (%)		Treatment 2 (n = 295) n (%)		Treatment Course (n = 555) n (%)	
	Standard	**Non-Standard**	**Standard**	**Non-Standard**	**Standard**	**Non-Standard**
Sex		$p = 0.69$		$p = 0.69$		$p = 0.89$
Male	261 (86)	42 (14)	111 (68)	52 (32)	218 (72)	85 (28)
Female	220 (87)	32 (13)	87 (66)	45 (34)	180 (71)	72 (29)
Year of Diagnosis		$p = 0.38$		$p = 0.20$		$p = 0.009$
White/NH	283 (87)	41 (13)	124 (72)	49 (28)	240 (74)	84 (26)
Black/NH	44 (80)	11 (20)	18 (51)	17 (49)	29 (53)	26 (47)
Asian/NH	22 (92)	2 (8)	7 (64)	4 (36)	19 (79)	5 (21)
Hispanic	72 (90)	8 (10)	24 (67)	12 (33)	62 (78)	18 (23)
Other/UK	60 (83)	12 (17)	25 (63)	15 (38)	48 (67)	24 (33)
Insurance		$p = 0.006$		$p = 0.35$		$p = 0.02$
Private	227 (90)	24 (10)	97 (71)	39 (29)	192 (76)	59 (24)
Public	197 (81)	45 (19)	82 (63)	48 (37)	159 (66)	83 (34)
Unknown	57 (92)	5 (8)	19 (66)	10 (34)	47 (76)	15 (24)
Race/Ethnicity		$p = 0.09$		$p = 0.05$		$p = 0.03$
2012	38 (90)	4 (10)	12 (52)	11 (48)	27 (64)	15 (36)
2013	108 (79)	28 (21)	51 (67)	25 (33)	89 (65)	47 (35)
2014	173 (88)	24 (12)	67 (65)	36 (35)	142 (72)	55 (28)
2015	62 (87)	9 (13)	23 (61)	15 (39)	49 (69)	22 (31)

	Treatment 1 (n = 555) n (%)		Treatment 2 (n = 295) n (%)		Treatment Course (n = 555) n (%)	
	Standard	**Non-Standard**	**Standard**	**Non-Standard**	**Standard**	**Non-Standard**
2016	58 (92)	5 (8)	21 (72)	8 (28)	50 (79)	13 (21)
2017/2018	42 (91)	4 (9)	24 (92)	2 (8)	41 (89)	5 (11)
Hospital Location		$p < 0.0001$		$p = 0.49$		$p = 0.003$
CO	84 (84)	16 (16)	40 (74)	14 (26)	74 (74)	26 (26)
MI	48 (80)	12 (20)	27 (67.5)	13 (32.5)	37 (62)	23 (38)
TX	58 (98)	1 (2)	14 (52)	13 (48)	45 (76)	14 (24)
CA	49 (98)	1 (2)	19 (73)	7 (27)	42 (84)	8 (16)
IL	46 (100)	0 (0)	22 (81)	5 (19)	41 (89)	5 (11)
OH	44 (90)	5 (10)	14 (70)	6 (30)	39 (80)	10 (20)
PA	23 (79)	6 (21)	9 (64)	5 (36)	18 (62)	11 (38)
MD/DC	28 (76)	9 (24)	12 (52)	11 (48)	20 (54)	17 (46)
IA/MN	14 (74)	5 (26)	8 (62)	5 (38)	10 (53)	9 (47)
NY	11 (100)	0 (0)	1 (33)	2 (67)	9 (82)	2 (18)
VA	9 (90)	1 (10)	3 (75)	1 (25)	8 (80)	2 (20)
OR	22 (81)	5 (19)	7 (78)	2 (22)	20 (74)	7 (26)
WA	5 (50)	5 (50)	4 (67)	2 (33)	5 (50)	5 (50)
MA	33 (85)	6 (15)	16 (67)	8 (33)	26 (67)	13 (33)
AL	7 (78)	2 (22)	2 (40)	3 (60)	4 (44)	5 (56)

Chi-squared test or Fisher’s exact test for association for categorical variables.

NH = non-Hispanic; UK = unknown.

TABLE 2.

Clinical Variables Associated with Standard Therapy

	Treatment 1 (n = 555) n (%) or median (25–75%)		Treatment 2 (n = 295) n (%) or median (25–75%)		Treatment Course (n = 555) n (%) or median (25–75%)	
	Standard	**Non-Standard**	**Standard**	**Non-Standard**	**Standard**	**Non-Standard**
Premature Birth		$p = 0.01$		$p = 0.69$		$p = 0.03$
Full Term	392 (88)	51 (12)	161 (68)	77 (32)	327 (74)	116 (26)
Premature	89 (79)	23 (21)	37 (65)	20 (35)	71 (63)	41 (37)
Seizures Prior to IS		$p = 0.001$		$p = 0.27$		$p = 0.005$
No	396 (89)	49 (11)	160 (69)	73 (31)	331 (74)	114 (26)
Yes	85 (77)	25 (23)	38 (61)	24 (39)	67 (61)	43 (39)
Development Delay		$p = 0.01$		$p = 0.02$		$p < 0.001$
Normal/Minor	205 (92)	19 (8)	83 (77)	25 (23)	181 (81)	43 (19)
Significant Delay	262 (84)	50 (16)	110 (62)	67 (38)	205 (66)	107 (34)
Unknown	14 (74)	5 (26)	5 (50)	5 (50)	12 (63)	7 (37)
Regression		$p = 0.01$		$p = 0.28$		$p = 0.005$
None/Possible	243 (90)	28 (10)	94 (70)	40 (30)	204 (76)	65 (24)
Definite	136 (90)	10 (10)	39 (71)	16 (29)	75 (77)	23 (23)
Unknown	150 (81)	36 (19)	65 (61)	41 (39)	117 (63)	69 (37)
Head Circumference		$p < 0.001$		$p = 0.32$		$p < 0.001$
Normal	344 (91)	36 (9)	136 (69)	60 (31)	291 (77)	89 (23)
Abnormal	116 (80)	29 (20)	49 (60)	32 (40)	90 (62)	55 (38)
Unknown	21 (70)	9 (30)	13 (72)	5 (28)	17 (57)	13 (43)

	Treatment 1 (n = 555) n (%) or median (25–75%)		Treatment 2 (n = 295) n (%) or median (25–75%)		Treatment Course (n = 555) n (%) or median (25–75%)	
	Standard	**Non-Standard**	**Standard**	**Non-Standard**	**Standard**	**Non-Standard**
Etiology of IS		$p = 0.02$		$p = 0.46$		$p = 0.39$
Unknown[b]	209 (91)	20 (9)	79 (63)	46 (37)	166 (72)	63 (28)
TSC	32 (89)	4 (11)	8 (73)	3 (27)	29 (81)	7 (19)
Other	240 (83)	50 (17)	111 (70)	48 (30)	203 (70)	87 (30)
EEG at Diagnosis		$p < 0.001$		$p = 0.11$		$p = 0.13$
No Hyps	73 (75)	24 (25)	40 (77)	12 (23)	65 (67)	32 (33)
Hyps	366 (90)	41 (10)	141 (67)	71 (33)	301 (74)	106 (26)
Unknown	42 (82)	9 (18)	17 (55)	14 (45)	32 (63)	19 (37)
Age at IS Onset[a]		$p = 0.95$		$p = 0.88$		$p = 0.47$
	6mo (5–8)	6mo (4–10)	6mo (4–8)	6mo (4–9)	6mo (5–8)	6mo (4–10)

[a] No significant differences for age of onset across 3 treatment groups.

[b] Other etiologies = acquired, developmental/structural, genetic, other.

Chi-squared test or Fisher's exact test for association for categorical variables; Wilcoxon rank-sum tests for continuous variables.

Hyps = hypsarrhythmia; IS = infantile spasms; mo = months; TSC = tuberous sclerosis complex.

TABLE 3.

Odds of Receiving Standard Therapy by Race/Ethnicity

	Model A: Unadjusted		Model B: Adjusted for Demographic Variables[a]		Model C: Adjusted for Demographic & Clinical Variables[b,c]	
	OR (95% CI)	p-Value	OR (95% CI)	p-Value	OR (95% CI)	p-Value
Racial/Ethnic Group Treatment Course						
White/NH	Reference	--	Reference	--	Reference	--
Black/NH	0.39 (0.22–0.69)	0.001	0.44 (0.22–0.88)	0.02	0.42 (0.20–0.89)	0.02
Asian/NH	1.31 (0.48–3.63)	0.60	1.10 (0.36–3.42)	0.86	1.05 (0.30–3.71)	0.94
Hispanic	1.17 (0.66–2.10)	0.59	1.11 (0.57–2.17)	0.75	1.09 (0.53–2.21)	0.82
Other/UK	0.69 (0.40–1.20)	0.19	0.75 (0.40–1.40)	0.36	0.57 (0.30–1.12)	0.10
Racial/Ethnic Group Treatment 1						
White/NH	Reference	--	Reference	--	Reference	
Black/NH	0.57 (0.27–1.18)	0.13	0.59 (0.23–1.46)	0.25	0.55 (0.19–1.58)	0.27
Asian/NH	1.56 (0.35–6.86)	0.56	0.82 (0.15–4.49)	0.81	1.25 (0.19–8.40)	0.82
Hispanic	1.25 (0.56–2.80)	0.58	0.99 (0.39–2.53)	0.98	0.95 (0.34–2.64)	0.92
Other/UK	0.71 (0.35–1.43)	0.33	0.74 (0.33–1.68)	0.48	0.47 (0.19–1.19)	0.11
Racial/Ethnic Group Treatment 2						
White/NH	Reference	--	Reference	--	Reference	--
Black/NH	0.42 (0.20–0.89)	0.02	0.61 (0.24–1.52)	0.28	0.42 (0.15–1.14)	0.09
Asian/NH	0.70 (0.20–2.48)	0.58	0.74 (0.18–3.12)	0.68	0.50 (0.10–2.45)	0.40
Hispanic	0.80 (0.37–1.72)	0.56	0.79 (0.33–1.91)	0.60	0.71 (0.27–1.82)	0.47
Other/UK	0.66 (0.32–1.37)	0.27	0.69 (0.30–1.60)	0.39	0.58 (0.24–1.43)	0.24

[a] Adjusting for demographic variables of insurance type (public, private, unknown), state of treating hospital, and year of diagnosis.

[b] Adjusting for demographic & clinical variables (history of prematurity, seizures prior to IS, developmental delay, or regression; head circumference; etiology of IS; findings on diagnostic EEG) associated with standard therapy.

[c] The treatment 2 model is also adjusted for whether or not treatment 1 was standard.

NH = non-Hispanic; UK = unknown.

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TABLE 4.

Odds of Receiving Standard Therapy by Insurance Type

	Model A: Unadjusted		Model B: Adjusted for Demographic Variables[a]		Model C: Adjusted for Demographic & Clinical Variables[b,c]	
	OR (95% CI)	**p-Value**	**OR (95% CI)**	**p-Value**	**OR (95% CI)**	**p-Value**
Insurance Type Treatment Course						
Private	Reference	--	Reference	--	Reference	--
Public	0.58 (0.39–0.85)	0.006	0.59 (0.36–0.88)	0.01	0.66 (0.40–1.08)	0.10
Other/UK	0.95 (0.49–1.82)	0.87	1.48 (0.66–3.36)	0.34	1.52 (0.65–3.60)	0.34
Insurance Type Treatment 1						
Private	Reference	--	Reference	--	Reference	
Public	0.44 (0.26–0.76)	0.003	0.40 (0.22–0.74)	0.003	0.42 (0.21–0.84)	0.01
Other/UK	1.16 (0.42–3.17)	0.78	1.88 (0.58–6.09)	0.29	2.47 (0.66–9.19)	0.18
Insurance Type Treatment 2						
Private	Reference	--	Reference	--	Reference	--
Public	0.69 (0.42–1.16)	0.16	0.67 (0.37–1.20)	0.18	0.66 (0.34–1.25)	0.20
Other/UK	0.77 (0.33–1.81)	0.55	1.08 (0.36–3.32)	0.89	1.23 (0.37–4.08)	0.73

[a]Adjusting for demographic variables of race/ethnicity (non-Hispanic white, non-Hispanic Black, non-Hispanic Asian, Hispanic, other/unknown), state of treating hospital, and year of diagnosis.

[b]Adjusting for demographic & clinical variables (history of prematurity, seizures prior to IS, developmental delay, or regression; head circumference; etiology of IS; findings on diagnostic EEG) associated with standard therapy.

[c]The treatment 2 model is also adjusted for whether or not treatment 1 was standard.

UK = unknown.

TABLE 5.

FACETS[a] Analysis for Racial Disparities in Access to Standard Therapy for Infantile Spasms

	Future Research Questions	Quality Improvement Interventions
Fear	- Characterize families' fears (i.e., treatment side effects, prognosis, cost of care). - Assess if clinicians address fears. - Assess for contribution of personal or historical experiences of racism.	- Provide additional time for counseling during to ensure questions are answered. - Provide educational materials on first line therapies in caregivers' language of choice. - Connect families with community resources & as caregiver support groups.
Access	- Characterize racial disparities in access to care & follow-up. - Identify barriers to access, including financial impediments; competing responsibilities (caregiving & employment); & transportation.	- Advocate with public and private insurance providers to ensure that standard therapies are immediately covered. - Remove institutional barriers for IS care; consider copay assistance. - Advocate for legislation that improves access to diagnostics & prescription medications.
Communication Barriers	-Examine language & communication barriers (i.e., misperceptions of clinicians or patients) that arise during medical visits.	- Use professional interpreters. - Standardize guidelines on counselling on first-line medication risks & benefits. - Clearly convey recommendations for first-line therapies to all patients.
Education	-Identify ways in which implicit bias affects clinicians' prescribing practices. -Identify reasons that families may refuse standard therapies.	- Develop clear, visual educational materials on IS treatment for caregivers. - Educate all members of the healthcare team & hospital leadership on implicit bias & institutional/interpersonal racism. - Highlight identified disparities in both provider & patient forums.
Trust	- Assess drivers of caregivers' mistrust of the healthcare system at institutional & interpersonal levels. - Assess drivers of providers' discomfort in prescribing certain therapies to specific patients.	- Improve workforce diversity by recruiting underrepresented minority groups into child neurology healthcare teams. - Elicit & address patient/family concerns fully.
Social Support	- Identify which supports are most necessary to allow families to complete IS treatment. - Assess screening tools that best elicit this information during clinical visits.	- Involve social work & case management. - Use strength-based approaches to identify caregivers' resources. - Facilitate community support (i.e., information nights, support groups).

[a]FACETS framework[37] was created to understand drivers in disparities to epilepsy surgery.