Epilepsy & Behavior 123 (2021) 108282

Contents lists available at ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

Impact of intellectual and developmental disability on quality-of-life priorities in adults with epilepsy

Sharon Chiang [a,*], Robert Moss [b], Mary Anne Meskis [c], Vanessa Vogel-Farley [d], Joseph E. Sullivan [a], Anup D. Patel [e], Vikram R. Rao [a]

[a] Department of Neurology and Weill Institute for Neurosciences, University of California, San Francisco, San Francisco, CA, United States
[b] Seizure Tracker, LLC, Springfield, VA, United States
[c] Dravet Syndrome Foundation, Cherry Hill, NJ, United States
[d] Dup15q Alliance, Highland Park, IL, United States
[e] Department of Pediatrics and Division of Neurology, Nationwide Children's Hospital, Columbus, OH, United States

ARTICLE INFO

Article history:
Received 18 April 2021
Revised 29 July 2021
Accepted 14 August 2021

Keywords:
Patient-reported outcomes
Health-related quality of life
Core outcomes
Intellectual disability
Seizures

ABSTRACT

Objective: Adults living with intellectual and developmental disability (IDD) and epilepsy (IDD-E) face challenges in addition to those faced by the general population of adults with epilepsy, which may be associated with distinct priorities for improving health-related quality of life (HR-QOL). This study sought to (1) conduct a survey of HR-QOL priorities identified by adults with IDD-E and caregivers, and (2) perform an exploratory cross-sectional comparison to adults with epilepsy who do not have IDD.

Methods: This cross-sectional study recruited 65 adults with IDD-E and 134 adults with epilepsy without IDD and caregivers. Using a three-step development process, 256 items from existing quality-of-life scales recommended by the American Academy of Neurology (AAN) were rated by patients/caregivers for their importance as HR-QOL priorities. HR-QOL items identified as critical to the majority of the sample of adults with IDD-E were reported. Health-related quality of life priorities were compared between adults with IDD-E and adults with epilepsy without IDD.

Results: Health-related quality of life was significantly lower in adults with IDD-E. Health-related quality of life domains identified as critical priorities by adults with IDD-E included seizure burden, anti-seizure medication side effects, seizure unpredictability, and family impact. Priorities for improving HR-QOL differed between adults with and without IDD-E, with concerns about family impact, difficulty finding appropriate living conditions, inadequate assistance, and difficulty transitioning from pediatric-to-adult care valued significantly more among those with IDD-E.

Significance: Intellectual and developmental disability is an important determinant of HR-QOL among adults with epilepsy. We report HR-QOL priorities identified by adults with IDD-E and their caregivers. These results may help epilepsy clinicians and researchers develop tailored strategies to address priorities of the patient with IDD-E/caregiver community.

1. Introduction

Adults living with intellectual and developmental disability (IDD) and epilepsy (IDD-E) face challenges in addition to those faced by the general population of people with epilepsy [1]. Higher rates of comorbid physical, psychiatric, sleep, and/or cognitive disabilities [1–4], as well as higher rates of generalized and drug-resistant epilepsies [5], are often present in adults with IDD-E.

Reduction in seizure frequency is the major focus of research and clinical management for people with epilepsy. However, there is increasing awareness that the impact of having epilepsy on health-related quality of life (HR-QOL) extends beyond seizures. Indeed, social stigma, seizure unpredictability, and long-term effects on memory, language, and cognition can be as disabling as seizures themselves. These other domains are affected with increased incidence in people with IDD-E due to higher rates of comorbid disability and drug resistance. Furthermore, due to the higher incidence of drug-resistant epilepsy, seizure control remains elusive for many individuals with IDD-E. For these reasons, attention to other factors contributing to HR-QOL may be particularly salient. While there is work on patient- and caregiver

* Corresponding author at: University of California, San Francisco, Department of Neurology and Weill Institute for Neurosciences, 505 Parnassus Avenue, San Francisco, CA 94143, United States.
E-mail address: Sharon.Chiang@ucsf.edu (S. Chiang).

https://doi.org/10.1016/j.yebeh.2021.108282
1525-5050/

perspectives on HR-QOL priorities in severe pediatric epilepsies and the pediatric populations with IDD-E [6–10], there is a need for a clearer understanding of the priorities of adults with IDD-E [1].

The AAN has defined HR-QOL outcome assessment as a central measure in the 2017 Epilepsy Quality Measure Set [11]. To meet these quality guidelines in the adult population with IDD-E, improved fundamental understanding of HR-QOL priorities among adults with IDD-E, and whether and how priorities differ from adults with epilepsy without IDD, is needed. Measurement of HR-QOL among adults with IDD-E often employs instruments developed for use in the adult population with epilepsy without IDD [12–14] or modification of pediatric scales [6–10,15], which tacitly assumes identical needs of different groups [16]. Defining HR-QOL priorities of the adult population with IDD-E, including clarification of which priorities are unique and which are similar to the adult population with epilepsy without IDD, is needed to optimize interventions aimed at improving HR-QOL.

Here, we hypothesize that the HR-QOL priorities among adults with IDD-E differ from those of the adult population with epilepsy without IDD. To test this hypothesis, we conducted a cross-sectional survey of 199 adults/caregivers of adults with epilepsy, with and without IDD, to gather patient- and caregiver-identified perspectives on HR-QOL priorities in the adult populations with IDD-E and with epilepsy without IDD. We report the HR-QOL priorities identified as critically important by adults with IDD-E and perform a cross-sectional comparison with the adult population with epilepsy without IDD.

2. Methods

This cross-sectional observational study involved survey data collected from adults with IDD-E, caregivers, and adults with epilepsy without IDD.

2.1. Participants

The study was approved by the Institutional Review Board at the University of California, San Francisco (#19-28508). Participants included (1) adults with epilepsy either with or without IDD, who were diagnosed with epilepsy by a physician and had not been diagnosed with nonepileptic seizures, and (2) caregivers of adults with epilepsy with or without IDD. Participants were recruited from SeizureTracker.com, Dravet Syndrome Foundation, Dup15q Alliance, TSC Alliance, LGS Foundation, Gould Syndrome Foundation, My Epilepsy Story, STXBP1 Foundation, and TESS Research Foundation. Participants met the following inclusion/exclusion criteria: (1) self-identification as an adult with epilepsy or caregiver of an adult with epilepsy ($\geq$18 years old), (2) diagnosed with epilepsy by a physician, (3) access to internet, (4) English-speaking, and (5) no prior diagnosis of psychogenic nonepileptic seizures. Survey respondents were shown the definition of IDD utilized by the National Institutes of Health, as "Disorders that are usually present at birth and that negatively affect the trajectory of the individual's physical, intellectual and/or emotional development. Intellectual disability starts any time before a child turns 18 and is characterized by problems with both intellectual functioning or intelligence, which include the ability to learn, reason, problem solve, and other skills; and adaptive behavior, which includes everyday social and life skills. The term 'developmental disabilities' is a broader category of often lifelong disability that can be intellectual, physical, or both" [17]. Respondents were then asked to state whether the person with epilepsy in question had been diagnosed with IDD based on this definition. Both patients and caregivers were included in the respondent sample in an effort to reduce sampling bias against people with severe disability, in order to accommodate increased difficulty communicating preferences that people with IDD may experience. Caregivers were explicitly asked to attempt to respond on behalf of the person with epilepsy to mitigate patient/caregiver differences. Informed consent was obtained from all participants.

2.2. Survey instrument

Respondents used a Likert scale to rate a comprehensive list of items from existing adult epilepsy HR-QOL instruments. The survey development process involved three steps: (1) creating a comprehensive list of items asked in adult epilepsy HR-QOL surveys recommended by the AAN, (2) filling in gaps with qualitative input from adults with epilepsy and caregivers, both with and without IDD, (3) expert input from two epileptologists at different institutions (Fig. S1). First, an item bank was developed via inclusion of all items in the scales that were recommended by the AAN 2017 Quality of Life (QOL) Assessment for Patients with Epilepsy Measure [11]: QOL in Epilepsy (QOLIE)-10, QOLIE-31, QOLIE-AD-48, Personal Impact of Epilepsy Scale (PIES), QOL in Childhood Epilepsy Questionnaire (QOLCE-55), Global Assessment of the Severity of Epilepsy (GASE), Child Health Questionnaire (CHQ), PedsQL Epilepsy Module, and Epilepsy Surgery Inventory 55 Survey (ESI-55). The QOLIE-89 was substituted for the QOLIE-10 and QOLIE-31, as the QOLIE-89 contains similar properties but includes more comprehensive items. Bibliographies of these scales were reviewed and others included based on review, including the Perceived Predictability Index (PPI), Liverpool Seizure Severity Scale (LSSS), Epilepsy Foundation of America Concerns Index, Multidimensional Locus of Control, Modified Impact on Family Scale, GEOS-90 scale [18], TSC-associated Neuropsychiatric Disorders (TAND) behavioral and cognitive section [19], Dravet survey [20], Lawton instrumental activities of daily living (IADL) scale, and Katz activities of daily living (ADL) scales. Questions about healthcare access [21] were added. Redundant or similar items in the item bank were combined and thematically grouped by two independent reviewers (SC, RM) into domains. Second, focus group meetings were conducted with eight adults with childhood-onset and adult-onset epilepsy, and six caregivers of patients with developmental epileptic encephalopathies from the TSC Alliance, Dravet Syndrome Foundation, and SCN8A Alliance, to review the item bank and domain groupings. Focus groups were transcribed and evaluated by two independent reviewers (SC, RM) for thematic content. Items could be combined or added if agreed upon by a consensus in focus groups. The final item bank and description of changes was distributed to focus group participants. Thematic saturation was achieved if focus group participants did not identify any remaining new content to be added by the end of iterative revision. Third, the item list was reviewed by two epileptologists with domain expertise in adult and pediatric epilepsy (VRR, ADP). The final item list included 256 HR-QOL items from the following 20 domains: language, memory, cognition, fear of seizures, seizure unpredictability, seizure semiological characteristics, seizure burden, antiseizure medicine (ASM) side effects, epilepsy technology, healthcare access, healthcare utilization, social activities, social stigma, work/school concerns, family impact, functional independence, mood, behavior, fatigue, and sleep. The wording of all items was reviewed and revised by a health language expert to target a fifth-grade reading level with the final content including <20% complex words.

Surveyed aspects of HR-QOL are shown in Figs. 1–4 and Supplementary Figs. S2–S7. Patients were asked to rate the importance of each item for its importance as a HR-QOL priority. Caregivers were provided a parallel version of the survey and asked to provide responses based on what they believed were the views of the

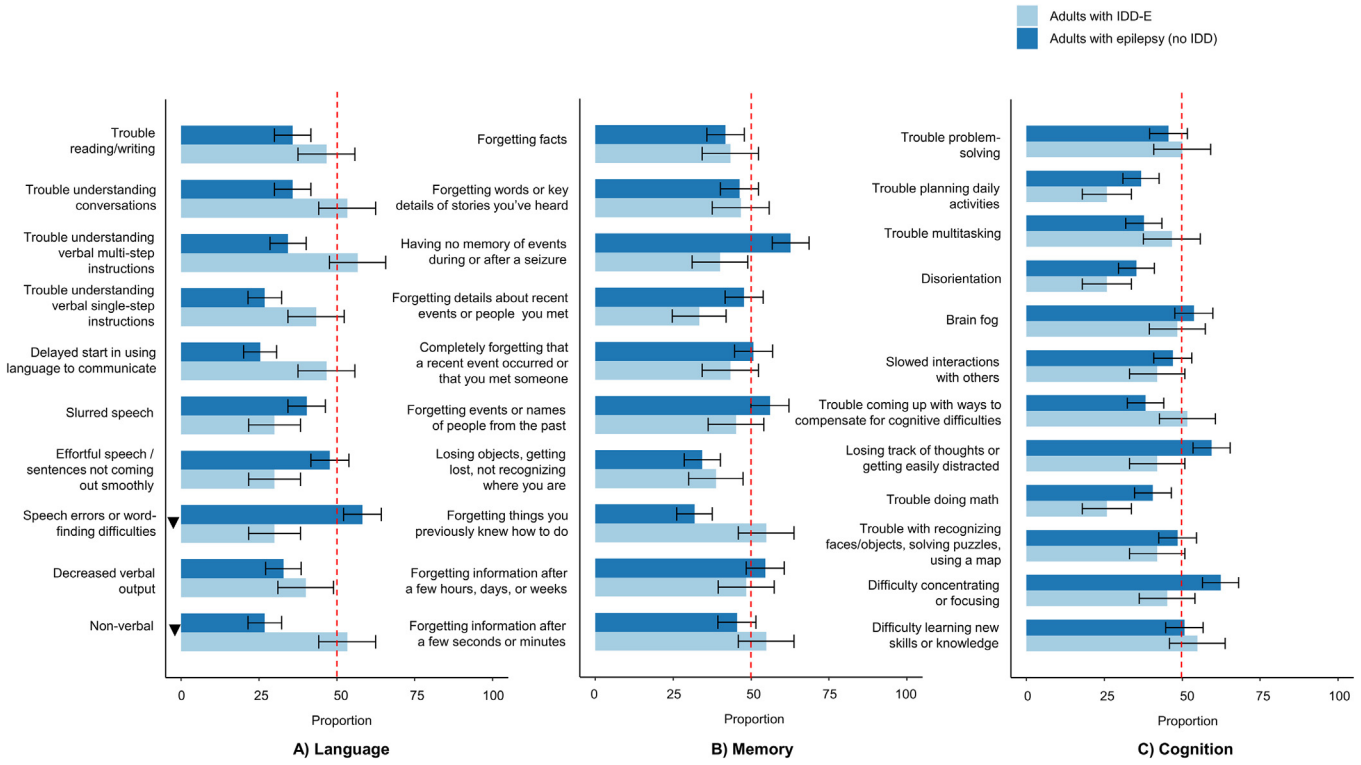

Fig. 1. Health-related quality-of-life priorities in (A) language, (B) memory, and (C) cognition. Proportion of adults with IDD-E and adults with epilepsy without IDD rating each item as "critically important to quality of life" (Likert 7–9) on 10-point Likert scale are shown. Error bars denote standard error. Statistically significant differences after controlling the false discovery rate at the 0.10 level and stratified confounder analysis are denoted with a triangle (▼). There were no statistically significant differences after false discovery rate control at the 0.05 level. *Abbreviations*: IDD-E, intellectual and developmental disability and epilepsy; IDD, intellectual and developmental disability.

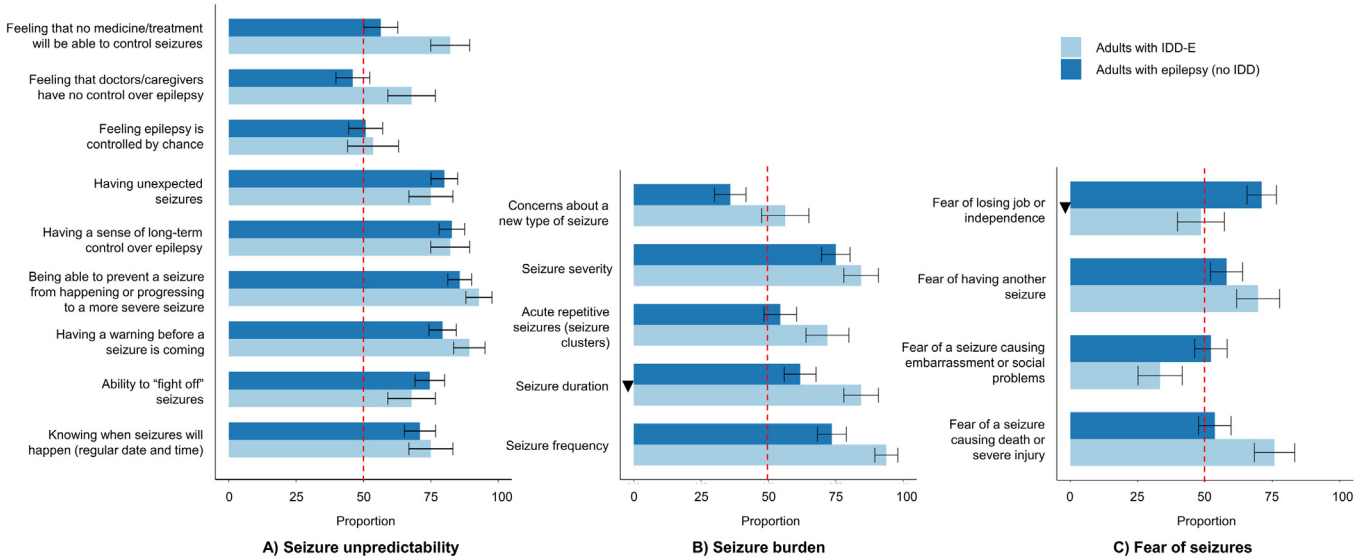

Fig. 2. Health-related quality-of-life priorities in (A) seizure unpredictability, (B) seizure burden, and (C) fear of seizures. Proportion of adults with IDD-E and adults with epilepsy without IDD rating each item as "critically important to quality of life" (Likert 7–9) on 10-point Likert scale are shown. Error bars denote standard error. Statistically significant differences after controlling the false discovery rate at the 0.10 level and stratified confounder analysis are denoted with a triangle (▼). There were no statistically significant differences after false discovery rate control at the 0.05 level. *Abbreviations*: IDD-E, intellectual and developmental disability and epilepsy; IDD, intellectual and developmental disability.

person with epilepsy. The internet-based survey was disseminated over a 4-week period. A second reminder was sent halfway through the data collection period. Respondents were provided with each item in the item bank and asked to rank the importance of each QOL item on a 9-point Likert scale: 1–3 indicating "little to no importance," 4–6 indicating "important but not critical," and 7–9 indicating "critically important." Block randomization (for domains) and item randomization (within each domain) were used

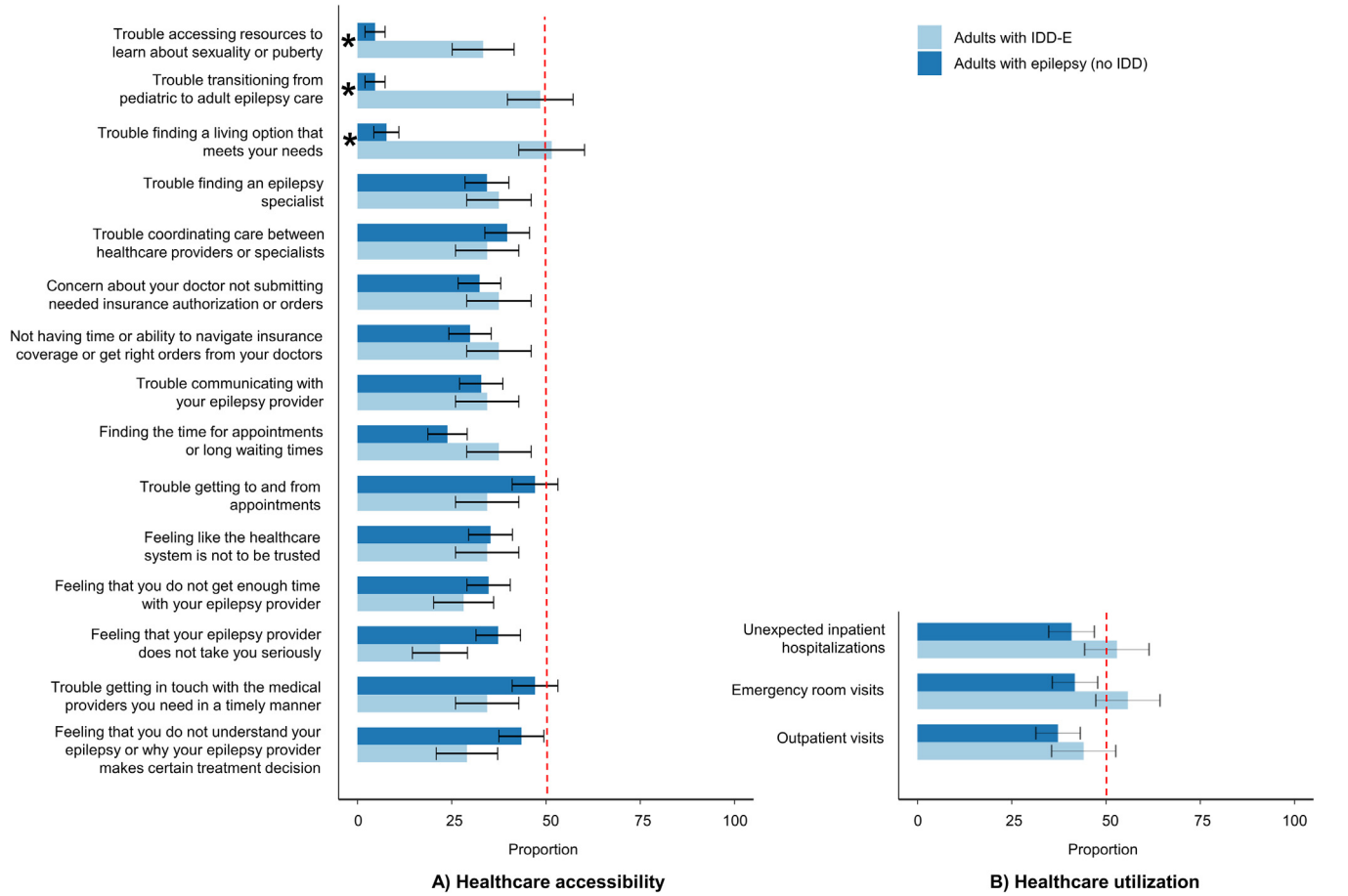

Fig. 3. Health-related quality-of-life priorities in (A) healthcare accessibility and (B) healthcare utilization. Proportion of adults with IDD-E and adults with epilepsy without IDD rating each item as "critically important to quality of life" (Likert 7–9) on 10-point Likert scale are shown. Error bars denote standard error. Statistically significant differences after controlling false discovery rate at 0.05 level and stratified confounder analysis are denoted with an asterisk (*). *Abbreviations*: IDD-E, intellectual and developmental disability and epilepsy; IDD, intellectual and developmental disability.

to minimize effects from testing burden [22]. Data were exported as de-identified, unlinked data using a secure exchange process to a blinded analyst (SC).

2.3. Statistical analysis

R version 3.5.1 was employed for analysis. The percentage of respondents ranking each HR-QOL issue as "critically important" for HR-QOL (Likert 7–9) was calculated. Chi-square tests were performed to evaluate significant differences between adults with and without IDD-E. Fisher exact tests were performed if a cell count was <5 and the Wilcoxon test for continuous variables. Missing data were treated as missing at random. To account for the large number of multiple hypothesis tests, statistical significance of odds ratios (OR) was evaluated after false discovery rate control for multiple comparisons at the 0.05 level [23]. The Haldane-Anscombe correction was applied in ratios with zero cell counts. P-values were reported after multiple testing correction. Stratified analysis comparing crude odds ratios to strata-specific odds ratios was performed for statistically significant differences to evaluate for confounding effects from demographic variables, including patient/caregiver status, sex, age, and age of epilepsy diagnosis. Items regarding impact on family were evaluated for confounding effects from sex, age, and age of epilepsy diagnosis. Confounding effects were identified if the stratum-specific odds ratios both differed from the crude odds ratio by 10% or more, with both odds ratios either less than or greater than the crude odds ratio, and if the variable was associated with both IDD and the outcome of interest. When present, confounding was adjusted for via the exact Cochran-Mantel-Haenszel odds-ratio.

3. Results

3.1. Patient characteristics

A total of 422 responses were collected out of over 4908 e-mail opens over a four-week period (8.9% respondent rate). Of respondents, 226 met inclusion/exclusion criteria, including 65 adults diagnosed with IDD-E and 134 adults diagnosed with epilepsy without IDD. Twenty-six adults were uncertain of whether they had a diagnosis of IDD and were excluded from analysis, resulting in a total sample size of 199. Respondents on behalf of the adult population with IDD-E were largely caregivers (86.1% caregivers, 13.8% patients) and for the adult population with epilepsy without IDD were largely patients (11.9% caregivers, 88.1% patients). HR-QOL was significantly lower among adults with IDD-E compared to adults with epilepsy without IDD (Table 1, $p = 0.002$). Data were analyzed by collapsing across caregiver-reported and self-reported data. Demographic characteristics are in Table 1.

3.2. Language, memory, and cognition

Aspects of language, memory, and cognition were prioritized similarly between adults with epilepsy with or without IDD

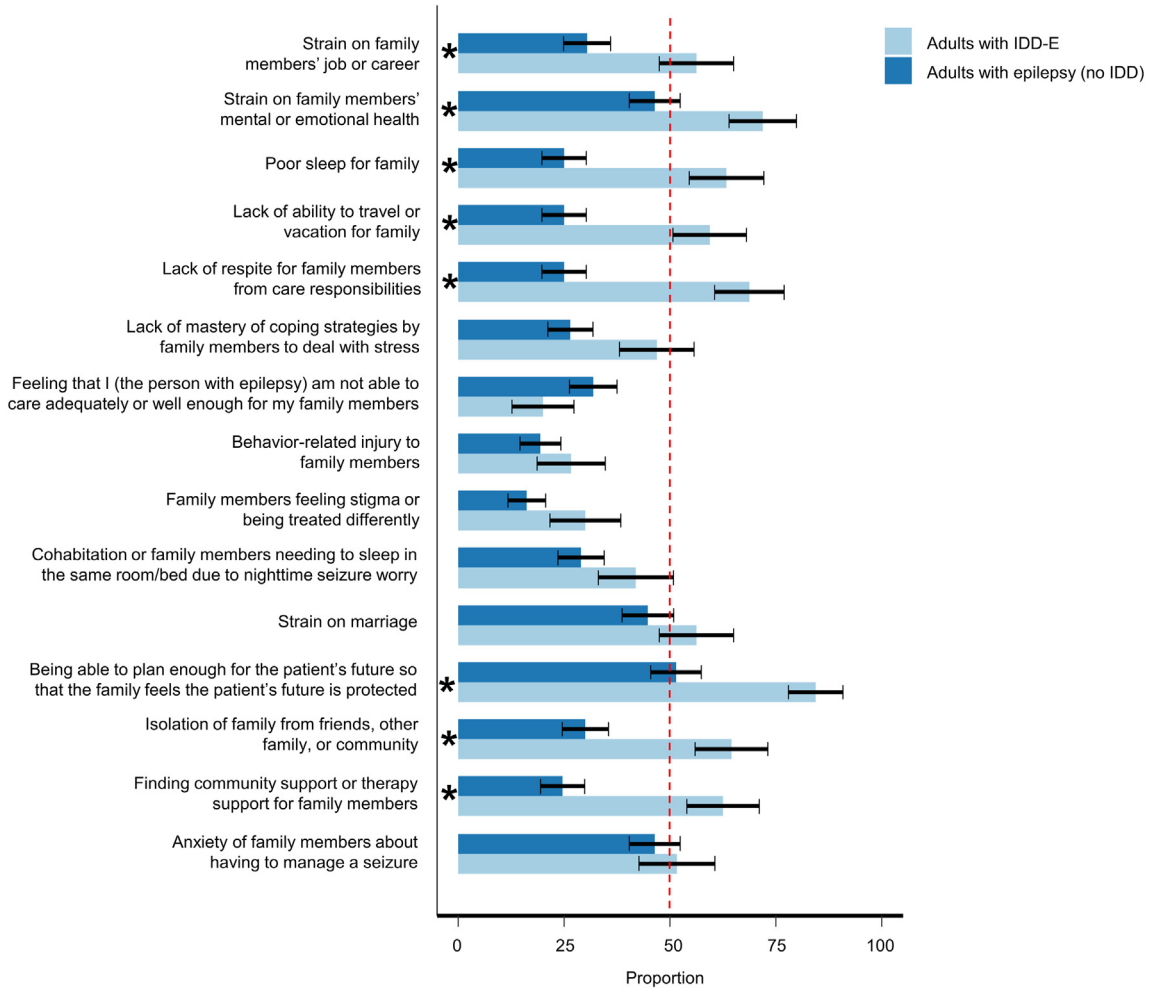

Fig. 4. Health-related quality-of-life priorities in family impact. Proportion of adults with IDD-E and adults with epilepsy without IDD rating each item as "critically important to quality of life" (Likert 7–9) on 10-point Likert scale are shown. Error bars denote standard error. Statistically significant differences after controlling false discovery rate at 0.05 level and stratified confounder analysis are denoted with an asterisk (*). *Abbreviations*: IDD-E, intellectual and developmental disability and epilepsy; IDD, intellectual and developmental disability.

(Fig. 1A–C). Language issues identified as critical to HR-QOL for greater than 50% of adults with IDD-E included nonverbality (53.3%), difficulty understanding multi-step instructions (56.7%), and difficulty understanding conversations (53.3%). These language aspects were critical to a minority of patients without IDD-E (27.9%, 34.4%, and 36.1%, respectively). Being nonverbal tended to be more important for adults with IDD-E (53.3% vs 26.9%, $p = 0.10$), and speech errors or word-finding difficulties tended to be more important for adults with epilepsy without IDD (30.0% vs 58.2%, $p = 0.10$) (Fig. 1A). Aspects of memory that were critically important to >50% of adults with IDD-E included working memory (54.8%) and procedural memory (54.8%) (Fig. 1B). Among other areas of cognition, critical issues for >50% of adults with IDD-E included difficulty learning new skills (54.8%) and the ability to come up with compensatory strategies for cognitive difficulties (51.6%) (Fig. 1C).

3.3. Seizure burden

Across all 256 items surveyed, there were two issues identified as critical to QOL in > 90% of adults with IDD-E, both of which were related to seizures: (1) ability to prevent a seizure from happening or progressing into a more severe seizure (92.9%; Fig. 2A), and (2) seizure frequency (93.8%; Fig. 2B).

The most important aspects of seizure burden for adults with IDD-E were seizure frequency (93.8%), followed by seizure duration (84.4%), seizure severity (84.4%), and acute repetitive seizures (71.9%) (Fig. 2B). Seizure unpredictability was critical in both groups (Fig. 2A). Adults with and without IDD-E rated aspects of seizure burden similarly, although adults with IDD-E tended to be more likely to rate seizure duration as a critical priority (84.4% vs 61.8%, $p = 0.09$) (Fig. 2B).

We queried which aspects of seizures were responsible for causing fear among patients. The most common cause of fear among the community with IDD-E was fear of seizure-related death/injury (75.8%), whereas the most common aspect of seizures causing fear among adults with epilepsy without IDD was fear of the loss of a job/independence (Fig. 2C). Loss of control over internal or external events was similarly prioritized for people with and without IDD-E (Fig. S2).

3.4. Epilepsy technology

False alarms from seizure detection devices (false positives) critically influenced HR-QOL in 40.0% of adults with IDD-E and 16.1% of adults with epilepsy without IDD. False negatives from seizure detection devices critically influenced QOL in 50.0% of adults with IDD-E and 29.5% of adults with epilepsy without IDD.

Table 1
Demographic characteristics of study sample. *Abbreviations*: IDD, intellectual or developmental disability; ADL, activities of daily living; IADL, instrumental activities of daily living. For categorical variables, percentages (sample sizes) are shown. For continuous variables, means (standard deviations) are shown.

	Total (*N* = 199)	Adults with IDD (*N* = 65)	Adults with epilepsy without IDD (*N* = 134)	*p*-value
Demographics				
Patient sex[1]				0.02*
Female	61.8% (*N* = 123)	49.2% (*N* = 32)	67.9% (N = 91)	
Male	38.2% (*N* = 76)	50.8% (*N* = 33)	32.1% (*N* = 43)	
Patient age (%)[2]				<0.001*
18–35 years	43.2% (*N* = 86)	80.0% (*N* = 52)	25.4% (*N* = 34)	
36–65 years	50.3% (*N* = 100)	20.0% (*N* = 13)	64.9% (*N* = 87)	
66 years or older	6.5% (*N* = 13)	0.0% (*N* = 0)	9.7% (*N* = 13)	
Patient/caregiver[1]				<0.001*
Person with epilepsy	63.8% (*N* = 127)	13.8% (*N* = 9)	88.1% (*N* = 118)	
Caregiver	36.2% (*N* = 72)	86.2% (*N* = 56)	11.9% (*N* = 16)	
Age of epilepsy diagnosis[2]				<0.001*
Newborn (birth to 2 months)	1.0% (*N* = 2)	1.5% (*N* = 1)	0.7% (*N* = 1)	
Infancy (2 months to 1 year)	8.5% (*N* = 17)	21.5% (*N* = 14)	2.2% (*N* = 3)	
Toddler (1–3 years)	10.0% (*N* = 20)	24.6% (*N* = 16)	3.0% (*N* = 4)	
Preschool (3–5 years)	7.0% (*N* = 14)	13.8% (*N* = 9)	3.7% (*N* = 5)	
Childhood (6–11 years)	13.6% (*N* = 27)	15.4% (*N* = 10)	12.7% (*N* = 17)	
Adolescence (11–18)	22.6% (*N* = 45)	16.9% (*N* = 11)	25.4% (*N* = 34)	
Young adult (18–25)	17.6% (*N* = 35)	4.6% (*N* = 3)	23.9% (*N* = 32)	
Adulthood (25–65)	18.6% (*N* = 37)	1.5% (*N* = 1)	26.9% (*N* = 36)	
Older adult (65 and older)	5.0% (*N* = 1)	0.0% (*N* = 0)	0.7% (*N* = 1)	
Household income[1]				0.31
Low	27.1% (*N* = 54)	30.8% (*N* = 20)	25.4% (*N* = 34)	
Middle	58.8% (*N* = 117)	49.2% (*N* = 32)	63.4% (*N* = 85)	
High	11.6% (*N* = 23)	13.8% (*N* = 9)	10.4% (*N* = 14)	
Community support level[2]				0.97
Likert 1 (“No support”)	8.5% (*N* = 17)	7.7% (*N* = 5)	9.0% (*N* = 12)	
Likert 2	14.6% (*N* = 29)	13.8% (*N* = 9)	14.9% (*N* = 20)	
Likert 3 (“OK support”)	25.1% (*N* = 50)	26.2% (*N* = 17)	24.6% (*N* = 33)	
Likert 4	21.1% (*N* = 42)	18.5% (*N* = 12)	22.4% (*N* = 30)	
Likert 5 (“Amazing support”)	30.1% (*N* = 60)	32.3% (*N* = 21)	29.1% (*N* = 39)	
Average seizure frequency[2]				<0.001*
Daily	21.6% (*N* = 43)	46.2% (*N* = 30)	9.7% (*N* = 13)	
Weekly	23.1% (*N* = 46)	24.6% (*N* = 16)	22.4% (*N* = 30)	
Monthly	32.2% (*N* = 64)	21.5% (*N* = 14)	37.3% (*N* = 50)	
Yearly	10.0% (*N* = 20)	3.1% (*N* = 2)	13.4% (*N* = 18)	
Less than yearly	12.6% (*N* = 25)	4.6% (*N* = 3)	16.4% (*N* = 22)	
Seizure types[1]				<0.001*
Focal aware	39.2% (*N* = 78)	21.5% (*N* = 14)	47.8% (*N* = 64)	
Focal unaware	57.3% (*N* = 114)	53.8% (*N* = 35)	5.9% (*N* = 79)	
Generalized tonic clonic	50.7% (*N* = 101)	66.2% (*N* = 43)	43.3% (*N* = 58)	
Focal to bilateral tonic clonic	23.6% (*N* = 47)	40.0% (*N* = 26)	15.7% (*N* = 21)	
Absence	31.7% (*N* = 63)	38.5% (*N* = 25)	28.4% (*N* = 38)	
Atonic	9.0% (*N* = 18)	18.5% (*N* = 12)	4.5% (*N* = 6)	
Tonic	15.6% (*N* = 31)	30.8% (*N* = 20)	8.2% (*N* = 11)	
Myoclonic	18.6% (*N* = 37)	26.2% (*N* = 17)	14.9% (*N* = 20)	
History of status epilepticus[1]	18.1% (*N* = 36)	32.3% (*N* = 21)	11.2% (*N* = 15)	<0.001*
History of acute repetitive seizures[1]	28.1% (*N* = 56)	46.2% (*N* = 30)	19.4% (*N* = 26)	<0.001*
History of nocturnal seizures[1]	44.7% (*N* = 89)	56.9% (*N* = 37)	38.8% (*N* = 52)	0.02*
Longest seizure-free period[2]				<0.001*
More than a year	34.2% (*N* = 68)	16.9% (*N* = 11)	42.5% (*N* = 57)	
10–12 months	5.0% (*N* = 10)	6.2% (*N* = 4)	4.5% (*N* = 6)	
7–9 months	5.5% (*N* = 11)	6.2% (*N* = 4)	5.2% (*N* = 7)	
3–6 months	13.1% (*N* = 26)	12.3% (*N* = 8)	13.4% (*N* = 18)	
1–2 months	12.6% (*N* = 25)	10.8% (*N* = 7)	13.4% (*N* = 18)	
A few weeks	15.1% (*N* = 30)	16.9% (*N* = 11)	14.2% (*N* = 19)	
A few days	11.1% (*N* = 22)	24.6% (*N* = 16)	4.5% (*N* = 6)	
Less than a day	3.0% (*N* = 6)	4.6% (*N* = 3)	2.2% (*N* = 3)	
Duration of time since last seizure[2]				<0.001*
More than a year	12.1% (*N* = 24)	6.2% (*N* = 4)	14.9% (*N* = 20)	
10–12 months	2.5% (*N* = 5)	0.0% (*N* = 0)	3.7% (*N* = 5)	
7–9 months	4.5% (*N* = 9)	1.5% (*N* = 1)	6.0% (*N* = 8)	
3–6 months	3.0% (*N* = 6)	3.1% (*N* = 2)	3.0% (*N* = 4)	
1–2 months	12.6% (*N* = 25)	6.2% (*N* = 4)	15.7% (*N* = 21)	
A few weeks	13.1% (*N* = 26)	9.2% (*N* = 6)	14.9% (*N* = 20)	
A few days	23.1% (*N* = 46)	20.0% (*N* = 13)	24.6% (*N* = 33)	
Less than a day	28.1% (*N* = 56)	52.3% (*N* = 34)	16.4% (*N* = 22)	
Epilepsy etiology[2]				<0.001*
Genetic	12.1% (*N* = 24)	29.2% (*N* = 19)	3.7% (*N* = 5)	

Table 1 (*continued*)

	Total (*N* = 199)	Adults with IDD (*N* = 65)	Adults with epilepsy without IDD (*N* = 134)	*p*-value
Congenital structural lesion	7.5% (*N* = 15)	10.8% (*N* = 7)	6.0% (*N* = 8)	
Immune-related	0.5% (*N* = 1)	0.0% (*N* = 0)	0.7% (*N* = 1)	
Infectious	6.0% (*N* = 12)	7.7% (*N* = 5)	5.2% (*N* = 7)	
Metabolic	0.5% (*N* = 1)	0.0% (*N* = 0)	0.7% (*N* = 1)	
Acquired structural lesion	7.0% (*N* = 14)	3.1% (*N* = 2)	9.0% (*N* = 12)	
Traumatic brain injury	7.0% (*N* = 14)	1.5% (*N* = 1)	9.7% (*N* = 13)	
Other	4.0% (*N* = 8)	12.3% (*N* = 8)	0.0% (*N* = 0)	
Diagnosed with genetic mutation[1]	16.1% (*N* = 32)	36.9% (*N* = 24)[†]	5.6% (*N* = 8)[††]	<0.001*
Diagnosed with epilepsy syndrome[2]	13.1% (*N* = 25)	36.9% (*N* = 24)[ʃ]	0.7% (*N* = 1)[ʃʃ]	<0.001*
Epilepsy treatment history				
Number of previously trialed anti-seizure medications[2]				0.14
1	2.0% (*N* = 4)	0.0% (*N* = 0)	3.0% (*N* = 4)	
2	5.0% (*N* = 10)	1.5% (*N* = 1)	6.7% (*N* = 9)	
3	4.0% (*N* = 8)	3.1% (*N* = 2)	4.5% (*N* = 6)	
4	7.5% (*N* = 15)	3.1% (*N* = 2)	9.7% (*N* = 13)	
5	9.5% (*N* = 19)	9.2% (*N* = 6)	9.7% (*N* = 13)	
6 or more	71.4% (*N* = 142)	83.1% (*N* = 54)	65.7% (*N* = 88)	
Number of current anti-seizure medications[2]				<0.001
1	16.6% (*N* = 33)	1.5% (*N* = 1)	23.9% (*N* = 32)	
2	33.7% (*N* = 67)	24.6% (*N* = 16)	38.1% (*N* = 51)	
3	26.1% (*N* = 52)	32.3% (*N* = 21)	23.1% (*N* = 31)	
4	13.6% (*N* = 27)	23.1% (*N* = 15)	8.9% (*N* = 12)	
5	5.5% (*N* = 11)	13.8% (*N* = 9)	1.5% (*N* = 2)	
6 or more	3.0% (*N* = 6)	4.6% (*N* = 3)	2.2% (*N* = 3)	
Neuromodulatory treatment				
Responsive neurostimulation[2]	6.0% (*N* = 12)	7.7% (*N* = 5)	5.2% (*N* = 7)	0.53
Vagus nerve stimulation[1]	28.1% (*N* = 56)	49.2% (*N* = 32)	17.9% (*N* = 24)	<0.001*
Deep brain stimulation[2]	0.5% (*N* = 1)	0.0% (*N* = 0)	0.7% (*N* = 1)	0.99
Prior epilepsy resective surgery[1]	19.6% (*N* = 39)	20.0% (*N* = 13)	19.4% (*N* = 26)	0.99
Functional status				
Needs help with verbally communicating needs to others[1]	34.2% (*N* = 68)	70.8% (*N* = 46)	16.4% (*N* = 22)	<0.001*
Functional independence				
Independent in ADLs and IADLs[1]	52.3% (*N* = 104)	7.7% (*N* = 5)	73.9% (*N* = 99)	<0.001*
Independent in ADLs, dependent in one or more IADL[2]	13.6% (*N* = 27)	6.2% (*N* = 4)	17.2% (*N* = 23)	0.04*
Dependent in ADLs[1]	34.2% (*N* = 68)	86.2% (*N* = 56)	9.0% (*N* = 12)	<0.001*
Quality of life over the past three months, mean (SD)[3,†††]	6.0 (2.2)	5.3 (1.9)	6.4 (2.3)	0.002*

[1] Chi squared test; [2]Fisher exact test; [3]Wilcoxon rank sum test. * = significant at 0.05 level.
[†] TSC1/2 (*N* = 4), SCN1A (*N* = 3), SHANK3 (*N* = 2), BRAF (*N* = 2), SLC25A22 (*N* = 1), Dup15q (*N* = 1), GRIN2B (*N* = 1), KCNT1 (*N* = 1), Lis1 (*N* = 1), PCDA1 (*N* = 1), PURA (*N* = 1), SMARCA2 (*N* = 1), Unknown (*N* = 5).
[††] TSC1/2 (*N* = 3), GGE (*N* = 1), Unknown (*N* = 4).
[†††] Item based on Quality of Life in Epilepsy-89 (QOLIE-89) and Personal Impact of Epilepsy Scale (PIES) quality-of-life question: "Overall, how would you rate your quality of life over the past 3 months? (0 = Worst possible quality of life – as bad as or worse than being dead; 10 = Best possible quality of life)".
[ʃ] Lennox-Gastaut Syndrome (*N* = 16), Dravet syndrome (*N* = 3), Aicardi syndrome (*N* = 1), Dup15q (*N* = 1), Tuberous Sclerosis Complex (*N* = 1), mitochondrial disorder (*N* = 1), BPAN (*N* = 1).
[ʃʃ] Tuberous Sclerosis Complex (*N* = 1).

These aspects of epilepsy technology were prioritized more highly than considerations including short battery life, discomfort from wearable/implantable devices, or feeling bound to the technology (Fig. S3).

3.5. Healthcare accessibility and utilization

Among adults with IDD-E, the greatest healthcare accessibility issues were difficulties with finding appropriate living accommodations (51.5%) and transitioning from pediatric-to-adult epilepsy care (48.8%). Among adults with epilepsy without IDD, the three greatest healthcare accessibility issues contributing to HR-QOL were trouble getting to and from appointments (50.8%), trouble getting in touch with healthcare providers in a timely manner (49.2%), and not feeling like they understood their epilepsy or the rationale behind treatment decisions (42.7%). A significantly greater proportion of adults with IDD-E rated trouble finding living options (51.5% vs 7.7%, $p < 0.001$) and trouble transitioning from pediatric-to-adult care (48.5% vs 4.8%, $p < 0.001$) as critical HR-QOL issues than those without IDD. These differences remained significant after adjusting for confounding variables. Trouble accessing resources to help the person learn about sexuality or puberty was also rated as critical to a greater proportion of the adult community with IDD-E (33.3% vs 4.7%), although the difference did not remain significant after adjusting for patient/caregiver status (Supplementary Table S1). Other aspects of healthcare accessibility were rated similarly by adults with and without IDD-E (Fig. 3A). The impact on HR-QOL of unexpected inpatient hospitalizations, emergency room visits, and outpatient clinic visits was similar for adults with and without IDD-E (Fig. 3B).

3.6. Social activities and social stigma

Adults with and without IDD-E rated trouble with different social activities as priorities in HR-QOL. Social priorities rated as critical to HR-QOL for >50% of adults with IDD-E were lack of interest in or inability to do things with others (70.0%) or by themselves (53.3%), trouble finding a community activity (63.3%), and trouble being social with others (50.0%). Adults with IDD-E were more likely to experience trouble finding community activities to join as a HR-QOL priority (63.3% vs 29.2%), although this difference did not remain significant after controlling for patient age

(Supplementary Table S1). Among aspects of social stigma, feeling isolated was the most common HR-QOL priority among adults with IDD-E (60.6%) (Fig. S4). Social priorities remained similar after subgroup analysis of childhood onset epilepsy (Fig. S4C).

3.7. Impact on family

The impact of epilepsy on the patient's family was directly connected to HR-QOL more so in the population with IDD-E for many issues (Fig. 4): worry about whether the patient's future was protected (84.4% vs 54.0%, $p = 0.01$), availability of community support programs or therapy support for family members (62.5% vs 24.6%, $p < 0.001$), isolation of family from the community (64.5% vs 30.0%, $p = 0.005$), lack of respite from care responsibilities (68.8% vs 25.0%, $p < 0.001$), lack of ability to travel/vacation for family (59.4% vs 25.0%, $p = 0.005$), and poor sleep for family (63.3% vs 25.0%, $p = 0.005$). These differences persisted after adjusting for demographic variables (Supplementary Table S1).

3.8. Functional independence

A significantly greater proportion of the adult community with IDD-E reported difficulty with ADLs and IADLs as critical aspects of HR-QOL (Fig. S5). Inadequate assistance (not having people available when needed) also critically influenced HR-QOL for significantly more adults with IDD-E (58.6% vs. 19.0%, $p < 0.001$). Loss of driving ability was significantly more likely to be important to adults with epilepsy without IDD than to those with IDD-E (31.0% vs 70.8%, $p = 0.002$). These differences persisted after controlling for demographic variables (Supplementary Table S1).

3.9. Behavior, mood, health concerns, and ASMs

Behavioral issues (Fig. S6A), mood (Fig. S6B), health concerns (Fig. S7), and ASM side effects (Fig. S8) were prioritized similarly in groups with IDD-E and without IDD, although behavioral issues contributed to HR-QOL in generally higher proportions in the adult population with IDD-E (Fig. S6A). There was no significant difference in priority rankings for the remainder of HR-QOL domains, including sleep, fatigue, seizure semiology, and work/school concerns (not shown here due to space; available on request).

4. Conclusions

This cross-sectional survey of patient- and caregiver-reported preferences enriches understanding of the priorities of adults with IDD-E for improving HR-QOL. First, we demonstrate that a gap currently exists in overall HR-QOL between the adult communities with epilepsy with IDD-E and without IDD, highlighting the need for continued efforts by the community with epilepsy to develop targeted interventions to address unmet needs. Second, we report HR-QOL priorities that are identified by the adult community with IDD-E. This fills a knowledge gap in an understudied population, complements current recommendations on minimum care standards [1] for the adult population with IDD-E, and informs future research directions, measurement scale development, and resource allocation. Third, we show that while there are many common priorities shared with the community with epilepsy without IDD, the adult community with IDD-E appears to express several distinct HR-QOL priorities, possibly reflecting the unique challenges experienced by adults with IDD-E. This emphasizes the need for unique resources and tools when caring for the adult population with IDD-E.

Our results show that the presence of IDD in adults with epilepsy is associated with lower HR-QOL outcomes. A similar finding has been shown in pediatric populations with epilepsy, where the presence of intellectual disability leads to an independent reduction in HR-QOL [24]. The gap in HR-QOL between the populations with epilepsy with IDD-E and without IDD demonstrates the need for improved understanding by researchers and clinicians of the specific issues that the community with IDD-E identifies as important priorities. The HR-QOL domains for which at least two issues were rated as critical priorities in more than 70% of adults with IDD-E were: (1) seizure burden; (2) ASM side effects; (3) seizure unpredictability; and (4) impact on family. Although the first priority (seizure frequency) is routinely addressed in clinical encounters, the latter aspects are not as routinely incorporated in standard provider documentation [25]. Encouraging incorporation of the patient-identified HR-QOL priorities identified in our study into clinical documentation in the adult population with IDD-E may be one strategy to help increase clinical focus on the unique challenges experienced by the adult population with IDD-E.

Recommendations for modifiable factors based on this study are provided in Table 2, which may help augment minimal care standard for adults with IDD-E [1]. Among distinct HR-QOL priorities expressed by the adult community with IDD-E, lack of social integration, family impact, difficulty finding appropriate living conditions, and difficulty transitioning from pediatric-to-adult care emerged as particularly distinct critical priorities. Failure to adequately address many of these issues has been found to potentially contribute to the increased mortality rates among individuals with intellectual disability [26]. Our findings emphasize the importance of the family unit in IDD-E, including asking about the needs of

Table 2
Recommendations to complement minimum care standards for addressing HR-QOL priorities of the adult patient with IDD-E/caregiver community. These recommendations complement those proposed by Devinsky et al. (2015). *Abbreviations*: IDD-E, intellectual and developmental disability and epilepsy.

Recommendation	Section
Offer Speech Language Therapy resources to work with the patient and family to improve techniques for communication, particularly for nonverbal individuals.	Sec 3.2
Offer Neuropsychological Testing to evaluate cognitive strengths and Occupational Therapy resources to work with the patient and caregiver on developing compensatory strategies for cognitive difficulties.	Sec 3.2
Ask about seizure frequency, seizure duration, anti-seizure medication side effects, and family impact at each clinical visit. Work together to characterize seizure patterns/triggers that may be leveraged therapeutically, in order to reduce seizure unpredictability.	Sec 3.3
When choosing seizure detection devices, consider that adults with IDD-E often prioritize not only false negatives (failure to identify or predict seizures) but also false positives (erroneous alarms in identifying or predicting seizure).	Sec 3.4
Ensure adequate representation of the adult population with IDD-E in trials for seizure detection or prediction devices.	Sec 3.4
Formulate a plan for transitioning from pediatric-to-adult care. Connect families with epilepsy support organizations to provide wrap-around care in formulating transitional plans.	Sec 3.5
Offer resources to help educate the patient about sexuality/puberty.	Sec 3.5
Check with patients/caregivers whether appropriate living options (e.g., group housing) and accommodations (e.g., adaptations to transportation or housing) have been obtained. If not, offer to involve Social Work services in the care plan.	Sec 3.5
Feelings of social isolation, as perceived by the patient or caregiver, should be reviewed along with mental health at every visit.	Sec 3.6
Consider the emotional, interpersonal, and social support needs of family members and actively seek to refer to Social Work for support and connect family members with local and national epilepsy support organizations. Ask family members about concerns about behavioral aggression.	Sec 3.7
Assess the patient's level of needed assistance (e.g. 1:1 assistance) with Physical and Occupational Therapy and evaluate whether needs are being met.	Sec 3.8

family members and whether additional support is needed. Feelings of isolation, anxiety about managing seizures, nighttime seizure worry, and lack of respite for family members are not only detrimental to family members' wellbeing, but may contribute to an overall feeling of being unheard among families and caregivers, which has been identified as a contributory factor to premature death in roughly one-fifth of people with intellectual disability [26]. Other aspects of HR-QOL which matter greatly to adults with epilepsy without IDD, such as loss of a driver's license, may never impact (many) people living with IDD-E, which is important to recognize in developing standard EHR documentation in epilepsy.

The priorities identified in this study suggest that current clinical resources, many of which are developed for the population with epilepsy without IDD-E, may not be adequate to meet needs in the community with IDD-E. Minimum care standards have been proposed, including improving transitions to adult care, considering the needs of family members, and reviewing mental health at every visit [1,27]. In particular, adoption of transitional care clinics to facilitate transitions from pediatric-to-adult care have been shown to improve outcomes [28]. This study highlights the need for increased adoption in the population with IDD-E. Additional workforce training for neurologists and epileptologists may be needed to address unmet care needs. For example, physicians trained primarily to care for individuals without IDD may not be comfortable meeting the needs of patients with IDD-E, or may lack experience with complexities of insurance discrimination or healthcare accessibility. Resources available for the general population with IDD without epilepsy may also not be equally accessible to people with IDD and comorbid epilepsy; for example, epilepsy may provide an additional barrier to community-based supportive housing generally available to people with IDD if onsite caregivers are not comfortable managing seizures.

The adult community with IDD-E in our study emphasized that the fear of seizures causing death or severe injury was a critical concern. This concern is substantiated by the fact that risk factors for SUDEP and seizure-related death—convulsive seizures, high seizure frequency, early age of epilepsy onset, intellectual disability, and polytherapy [29,30]—all occur with high incidence in the population with IDD-E. Greater focus on discussions about SUDEP and seizure-related death with patients/families living with IDD-E is essential to help reduce deaths among adults with IDD-E. FDA-approved seizure detection devices have demonstrated utility of detecting convulsive seizures and may reduce SUDEP [31,32]. Seizure action plans (SAPs), common in the pediatric population [33], may also be useful in adult populations with IDD-E to reduce seizure-related injuries/deaths [34].

Similar to the pediatric population [10], we found that the three most important aspects of seizures for adults with IDD-E were frequency, duration, and unpredictability. Notably, seizure unpredictability contributed to HR-QOL to an extent on par with seizure frequency and ASM side effects. Incorporation of seizure unpredictability measurement into routine clinical assessment and HR-QOL scale development for adults with epilepsy (both with and without IDD) may help improve overall HR-QOL. Aspects of seizure unpredictability identified as particularly important to adults with IDD-E included a sense of long-term control over epilepsy, sense of control over external frightening events, warning/knowledge of when seizures would occur, and feelings of hopelessness about epilepsy. Development of artificial intelligence (AI) to reduce seizure unpredictability, such as seizure detection/forecasting, may be useful for advancing these aspects of HR-QOL [35–38]. We found that reduction of false-positive and false-negative rates were considerations greatly prioritized by adults with IDD-E, more so than aspects such as short battery life or device discomfort. The fear of seizures causing death or severe injury, expressed by over three-quarters of the adult community with IDD-E, highlights the importance of ensuring representation of the adult population with IDD-E in AI studies for seizure detection/forecasting [16].

Lastly, although based on convenience sampling, the demographics of our study sample are consistent with several epidemiological findings in IDD-E. Whereas focal seizures predominated in respondents with epilepsy and normal intelligence/development, generalized seizures predominated in the population with IDD-E [5]. Genetic causes were the most common etiology of epilepsy in adults with IDD-E, highlighting the potential for this population to benefit from research on how genetic variations influence therapy selection and prognosis. Adults with IDD-E in our sample also had higher average seizure frequencies, shorter durations of seizure freedom, more ASM polytherapy, and higher rates of status epilepticus, acute repetitive seizures, and nocturnal seizures, similar to prior research [5]. Patients with IDD-E were younger on average than those without IDD, which may reflect the higher rate of mortality in intellectual disability [26].

There are several limitations to this study. (1) The responses in this survey reflect an 8.9% respondent rate. As this was a convenience sample, selection bias may bias responses toward people who are motivated to participate. Future research is needed to validate priorities in the general population. (2) Caregiver reports and patient self-reports were collapsed in analysis to reduce bias against people with severe disability. The priorities here reflect those identified by the adult community with IDD-E, which, in this study, are predominantly represented by caregivers responding on behalf of the person with epilepsy, as well as a small percentage of direct responses from adults with IDD-E. Thus, the responses of the adult community with IDD-E in this survey are largely reflective of priorities that caregivers believe patients have, which may be distinct from priorities of patients themselves [39–41]. To mitigate this, stratified analysis was used to evaluate potential confounding effects of patient/caregiver status; however, special interviewing techniques may be needed to ascertain the direct views of individuals with severe IDD. (3) Because the survey was distributed online, validation of self-reported information was not possible. (4) People with different degrees of disability may have different priorities, with those with milder levels of IDD likely closer to the population without IDD. Co-existing behavioral health diagnoses, such as autism, may also affect priorities, and future analyses focused on understanding differences across subgroups may help elucidate heterogeneity in priorities. (5) The survey contains items which were identified based on literature review and focus groups, but may not exhaustively cover all important issues to individuals living with epilepsy. Sexual safety and protection from abuse, for example, is an important concern to many families which was not covered in this survey. Future surveys will need to explore ongoing need for expanded outreach and resources in these topics.

This study provides a comprehensive view of HR-QOL and its meaning to adults with IDD-E. The priorities identified by the patient and caregiver community in this study may facilitate adoption of strategies and minimum care measures to improve HR-QOL for adults living with IDD-E.

Disclosure of conflicts of interest

RM is the co-founder/owner of *Seizure Tracker*, LLC, which has received funding from Cyberonics, Courtagen, Engage Therapeutics, Greenwich Biosciences, Neurelis, UCB, Brain Sentinel, Xenon Pharmaceuticals, and grants from Tuberous Sclerosis Alliance. JES serves as a consultant for Encoded Therapeutics, Greenwich Biosciences, Xenon, Epygenix Therapeutics, and the Epilepsy Study Consortium. JES has contracted research with Zogenix, Stoke

Therapeutics, Marinus Pharmaceuticals, and Biopharm and has stock options in Epygenix Therapeutics. JES is chair of the PCDH19 Scientific advisory board, Dravet Syndrome Foundation board member, Medical Advisory Board member, and Epilepsy Foundation of Northern California board member. ADP serves as a consultant for Greenwich Biosciences and serves on the advisory board for Neurelis. ADP has research funding from the Pediatric Epilepsy Research Foundation (PERF) and the National Institutes of Health (NIH). ADP performs webinar and educational development for Medscape. VRR has served as a consultant for NeuroPace, Inc., manufacturer of the RNS System. The remainder of the authors report no disclosures relevant to the manuscript.

Acknowledgements

We thank the people and caregivers living with epilepsy, including those with and without IDD, who contributed to this research. We would like to thank our focus group participants and community partners, including the TSC Alliance, LGS Foundation, Child Neurology Foundation, Dup15q Alliance, Dravet Syndrome Foundation, SCN8A Alliance, Gould Syndrome Foundation, My Epilepsy Story, STXBP1 Foundation, and TESS Research Foundation. This research was funded by the University of California, San Francisco Clinical and Translational Science Institute (UL1 TR001872).

Ethical publication statement

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.yebeh.2021.108282.

References

[1] Devinsky O, Asato M, Camfield P, Geller E, Kanner AM, Keller S, et al. Delivery of epilepsy care to adults with intellectual and developmental disabilities. Neurology 2015;85:1512–21. https://doi.org/10.1212/WNL.0000000000002060.
[2] Turky A, Felce D, Jones G, Kerr M. A prospective case control study of psychiatric disorders in adults with epilepsy and intellectual disability. Epilepsia 2011;52:1223–30. https://doi.org/10.1111/j.1528-1167.2011.03044.x.
[3] Espie CA et al. Psychopathology in people with epilepsy and intellectual disability; an investigation of potential explanatory variables. J Neurol Neurosurg Psychiatry 2003;74:1485–92. https://doi.org/10.1136/jnnp.74.11.1485.
[4] Kotagal S, Gibbons VP, Stith JA. Sleep abnormalities in patients with severe cerebral palsy. Dev Med Child Neurol 1994;36:304–11. https://doi.org/10.1111/j.1469-8749.1994.tb11850.x.
[5] Camfield C, Camfield P, Gordon K, Smith B, Dooley J. Outcome of childhood epilepsy: a population-based study with a simple predictive scoring system for those treated with medication. J Pediatr 1993;122:861–8. https://doi.org/10.1016/S0022-3476(09)90008-7.
[6] Nabbout R, Auvin S, Chiron C, Thiele E, Cross H, Scheffer IE, et al. Perception of impact of Dravet syndrome on children and caregivers in multiple countries: looking beyond seizures. Dev Med Child Neurol 2019;61:1229–36. https://doi.org/10.1111/dmcn.14186.
[7] de Vries PJ, Franz DN, Curatolo P, Nabbout R, Neary M, Herbst F, et al. Measuring health-related quality of life in tuberous sclerosis complex - psychometric evaluation of three instruments in individuals with refractory epilepsy. Front Pharmacol 2018;9. https://doi.org/10.3389/fphar.2018.00964.
[8] Sherman ES, Slick D, Connolly M, Steinbok P, Camfield C, Eyrl K, et al. Validity of three measures of health-related quality of life in children with intractable epilepsy. Epilepsia 2002;43:1230–8. https://doi.org/10.1046/j.1528-1157.2002.03602.x.
[9] Lagae L, Brambilla I, Mingorance A, Gibson E, Battersby A. Quality of life and comorbidities associated with Dravet syndrome severity: a multinational cohort survey. Dev Med Child Neurol 2018;60:63–72. https://doi.org/10.1111/dmcn.13591.
[10] Berg AT, Kaiser K, Dixon-Salazar T, Elliot A, McNamara N, Meskis MA, et al. Seizure burden in severe early-life epilepsy: perspectives from parents. Epilepsia Open 2019;4:293–301. https://doi.org/10.1002/epi4.2019.4.issue-210.1002/epi4.12319.
[11] Patel AD, Baca C, Franklin G, Herman ST, Hughes I, Meunier L, et al. Quality improvement in neurology: Epilepsy Quality Measurement Set 2017 Update. Neurology 2018;91:829–36.
[12] Devinsky O, Vickrey BG, Cramer J, Perrine K, Hermann B, Meador K, et al. Development of the quality of life in epilepsy inventory. Epilepsia 1995;36:1089–104.
[13] Vickrey BG, Hays RD, Graber J, Rausch R, Engel J, Brook RH. A health-related quality of life instrument for patients evaluated for epilepsy surgery. Med Care 1992;30:299–319.
[14] Fisher RS, Nune G, Roberts SE, Cramer JA. The Personal Impact of Epilepsy Scale (PIES). Epilepsy Behav 2015;42:140–6. https://doi.org/10.1016/j.yebeh.2014.09.060.
[15] Buck D, Smith M, Appleton R, Baker GA, Jacoby A. The development and validation of the Epilepsy and Learning Disabilities Quality of Life (ELDQOL) scale. Epilepsy Behav 2007;10:38–43. https://doi.org/10.1016/j.yebeh.2006.10.010.
[16] Shankar R, Rowe C, Van Hoorn A, Henley W, Laugharne R, Cox D, et al. Under representation of people with epilepsy and intellectual disability in research. PLoS ONE 2018;13:e0198261.
[17] U.S. Department of Health and Human Services, National Institutes of Health. Intellectual and Developmental Disabilities (IDDs): Condition Information <https://www.nichd.nih.gov/health/topics/idds/conditioninfo/default> (2016).
[18] Espie CA, Watkins J, Duncan R, Espie A, Sterrick M, Brodie MJ, et al. Development and validation of the Glasgow Epilepsy Outcome Scale (GEOS): a new instrument for measuring concerns about epilepsy in people with mental retardation. Epilepsia 2001;42:1043–51. https://doi.org/10.1046/j.1528-1157.2001.0420081043.x.
[19] de Vries PJ, Whittemore VH, Leclezio L, Byars AW, Dunn D, Ess KC, et al. Tuberous sclerosis associated neuropsychiatric disorders (TAND) and the TAND Checklist. Pediatr Neurol 2015;52:25–35. https://doi.org/10.1016/j.pediatrneurol.2014.10.004.
[20] Villas N, Meskis MA, Goodliffe S. Dravet syndrome: characteristics, comorbidities, and caregiver concerns. Epilepsy Behav 2017;74:81–6. https://doi.org/10.1016/j.yebeh.2017.06.031.
[21] Ross M, Patrick K. Putting patients first: developing and maintaining patient-centered medical practices. Greater Washington Research: Brookings Institution; 2007.
[22] Little TD, Rhemtulla M. Planned missing data designs for developmental researchers. Child Develop Perspect 2013;7:199–204.
[23] Benjamini Y, Yekutieli D. The control of the false discovery rate in multiple testing under dependency. Ann Statistics 2001:1165–88.
[24] Sabaz M, Cairns DR, Lawson JA, Bleasel AF, Bye AME. The health-related quality of life of children with refractory epilepsy: a comparison of those with and without intellectual disability. Epilepsia 2001;42:621–8. https://doi.org/10.1046/j.1528-1157.2001.25200.x.
[25] Jones FJS, Smith JR, Ayub N, Herman ST, Buchhalter JR, Fureman BE, et al. Implementing standardized provider documentation in a tertiary epilepsy clinic. Neurology 2020;95:e213–23. https://doi.org/10.1212/WNL.0000000000009778.
[26] Heslop P, Blair PS, Fleming P, Hoghton M, Marriott A, Russ L. The Confidential Inquiry into premature deaths of people with intellectual disabilities in the UK: a population-based study. Lancet 2014;383:889–95. https://doi.org/10.1016/S0140-6736(13)62026-7.
[27] Camfield PR, Andrade D, Camfield CS, Carrizosa-Moog J, Appleton R, Baulac M, et al. How can transition to adult care be best orchestrated for adolescents with epilepsy? Epilepsy Behav 2019;93:138–47. https://doi.org/10.1016/j.yebeh.2018.12.015.
[28] Colver A, McConachie H, Le Couteur A, Dovey-Pearce G, Mann KD, McDonagh JE, et al. A longitudinal, observational study of the features of transitional healthcare associated with better outcomes for young people with long-term conditions. BMC Med 2018;16:1–14.
[29] DeGiorgio CM, Markovic D, Mazumder R, Moseley BD. Ranking the leading risk factors for sudden unexpected death in epilepsy. Front Neurol 2017;8:473. https://doi.org/10.3389/fneur.2017.00473.
[30] Harden C, Tomson T, Gloss D, Buchhalter J, Cross JH, Donner E, et al. Practice guideline summary: Sudden unexpected death in epilepsy incidence rates and risk factors: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the American Epilepsy Society. Neurology 2017;88:1674–80. https://doi.org/10.1212/WNL.0000000000003685.
[31] Picard RW, Migliorini M, Caborni C, Onorati F, Regalia G, Friedman D, et al. Wrist sensor reveals sympathetic hyperactivity and hypoventilation before probable SUDEP. Neurology 2017;89:633–5. https://doi.org/10.1212/WNL.0000000000004208.
[32] Onorati F, Regalia G, Caborni C, Migliorini M, Bender D, Poh M-Z, et al. Multicenter clinical assessment of improved wearable multimodal convulsive seizure detectors. Epilepsia 2017;58:1870–9. https://doi.org/10.1111/epi.2017.58.issue-1110.1111/epi.13899.
[33] Albert DVF, Moreland JJ, Salvator A, Moore-Clingenpeel M, Haridas B, Cole JW, et al. Seizure action plans for pediatric patients with epilepsy: a randomized controlled trial. J Child Neurol 2019;34:666–73. https://doi.org/10.1177/0883073819846810.

[34] Buchhalter J, Shafer PO, Buelow JM, French JA, Gilchrist B, Hirsch LJ, et al. Preferred practices for rescue treatment of seizure clusters: a consensus-driven, multi-stakeholder approach. Epilepsy Behav 2021;117:107836. https://doi.org/10.1016/j.yebeh.2021.107836.
[35] Proix T, Truccolo W, Leguia MG, Tcheng TK, King-Stephens D, Rao VR, et al. Forecasting seizure risk in adults with focal epilepsy: a development and validation study. The Lancet Neurology 2021;20:127–35.
[36] Karoly PJ, Cook MJ, Maturana M, Nurse ES, Payne D, Brinkmann BH, et al. Forecasting cycles of seizure likelihood. Epilepsia 2020;61:776–86. https://doi.org/10.1111/epi.v61.410.1111/epi.16485.
[37] Goldenholz DM, Goldenholz SR, Romero J, Moss R, Sun H, Westover B. Development and validation of forecasting next reported seizure using e-diaries. Ann Neurol 2020;88:588–95. https://doi.org/10.1002/ana.v88.310.1002/ana.25812.
[38] Chiang S, Moss R, Patel AD, Rao VR. Seizure detection devices and health-related quality of life: a patient- and caregiver-centered evaluation. Epilepsy Behav 2020;105:106963. https://doi.org/10.1016/j.yebeh.2020.106963.
[39] Baca CB, Vickrey BG, Hays RD, Vassar SD, Berg AT. Differences in child versus parent reports of the child's health-related quality of life in children with epilepsy and healthy siblings. Value Health 2010;13:778–86. https://doi.org/10.1111/j.1524-4733.2010.00732.x.
[40] Eom S, Caplan R, Berg AT. Behavioral problems and childhood epilepsy: parent vs child perspectives. J Pediatr 2016;179:233–239.e235. https://doi.org/10.1016/j.jpeds.2016.08.096.
[41] Fayed N, Avery L, Davis AM, Streiner DL, Ferro M, Rosenbaum P, et al. Parent proxy discrepancy groups of quality of life in childhood epilepsy. Value Health 2019;22:822–8. https://doi.org/10.1016/j.jval.2019.01.019.