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Parent-reported histories of adults with trisomy 13 syndrome

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Abstract

Clinical histories and outcome data of long-term survivors with trisomy 13 are rare. The goal of this study was to collect the medical histories of adult individuals (≥18 years old) with apparent non-mosaic trisomy 13/Patau syndrome to help gain further insight in to the clinical course for individuals with this condition and to characterize the manifestations for surveillance and management. We collected 11 families through a contact person with the LWT13 (Living with Trisomy 13) LIFE support group. We performed telephone interviews to gather their medical histories and report these data in system-based summaries, tables, and clinical vignettes. In instances where parents retained copies of genetic testing reports or clinicians currently taking care of the individual with trisomy 13 were able to provide documentation, we confirmed diagnosis. All clinical histories and reported manifestations were consistent with a diagnosis of trisomy 13. We also elicited comments from parents on their personal experiences of raising an individual with trisomy 13.

KEYWORDS
adults with trisomy 13, clinical features in trisomy 13, Patau syndrome, trisomy 13

1 | INTRODUCTION

Patau syndrome, or trisomy 13 syndrome, is characterized by multiple malformations, a high neonatal and infant mortality, and significant cognitive and psychomotor disability. Little information about the clinical course for surviving patients is reported in the literature making it difficult to counsel parents with a new diagnosis in their child about management and expectations for those rare individuals with long-term survival. In recent years, survival at 1 year has been improving: data drawn from the Metropolitan Atlanta Congenital Defects Program, a population-based birth defects surveillance system between the years of 1968 and 1999, documented a median survival of 7 days for a patient with trisomy 13. In that study, 5.6% of patients survived past 1 year (Rasmussen et al., 2003). Other large-scale population studies showed similar results in median and one-year survival (Wu et al., 2013). More recent data show a positive trend in survivorship and expands our understanding of what this means for individuals who live beyond the one-year benchmark. In studies which included individuals where more invasive interventions were offered to patients, 11.5% of individuals with trisomy 13 survived to 1 year and a similar number, 9.7% survived to 5 years of age (Meyer et al., 2016; Nelson et al., 2016; Peterson et al., 2018). Bruns and Campbell (2014) identified nine children with non-mosaic trisomy 13 between 12 and 59 months of age. Imataka et al. (2016) documented eight patients described in clinical reports between the ages of 5 and 14 years old and three patients over 18 years with apparent non-mosaic Patau syndrome as previously reported in the literature. This small number of reports highlights the rarity of this type of clinical data. We conducted this study with the goal of uncovering more information to support clinicians and family members in order to better understand the clinical course of trisomy 13.

2 | MATERIALS AND METHODS

We collaborated with the leader of LWT13 Trisomy 13 LIFE support group (http://www.livingwithtrisomy13.org/), who reached out to families involved in the community with a child over 17 years of age with a diagnosis of apparent non-mosaic ("full") trisomy 13 by clinical testing. Our contact information was relayed to interested families. A telephone encounter was scheduled and electronic copies of the consent were provided to the parent/L.A.R. before the encounter.

Consent took place by telephone. A standard questionnaire about medical history, surgical history, developmental history, and parents' reflections on raising a child with trisomy 13 were asked over the phone (available as Data S1). Families had the opportunity to submit photographs of their family member with trisomy 13 (see Figures 1–7). Data were reviewed with the participating family member to verify some details of their initial report. Growth centiles were estimated based on parental reported data and use of Fenton, 2003 growth charts for preterm and term infants. The history of one individual (Individual 3) has previously been reported. Her history reflects an update of this report, which is specified in her clinical vignette below and noted in the tables of clinical information.

Of note, this study strives to recognize and bring awareness to the inherent uncertainty of historical and current practices in the assessment of mosaicism when making the diagnosis of trisomy 13. Previous data have shown that while mosaicism occurs at a low rate as detected by chromosome analysis performed on cells derived from amniotic fluid, a disproportionate number of individuals with mosaicism detected on chromosome testing make up the clinical reports of long-term survivors giving credence to mosaicism as an important factor in terms of survival (Bugge et al., 2007; Imataka et al., 2016). While it is an important consideration in terms of survivorship for this condition, it is outside of the scope of this study. We did not investigate with further chromosome testing in alternative tissues on any of the participants; thus, it is not possible to completely exclude the presence of low-level mosaicism. Instead, we highlighted the histories of individuals with trisomy 13 where initial chromosome testing did not reveal mosaicism, the families received counseling based on these testing results and found that the outcomes of their loved ones were beyond clinical expectation. We hope that these data will be taken into consideration by clinicians in discussing the diagnosis of trisomy 13 with families.

2.1 | Participants

We enrolled 11 families representing 11 adult individuals with apparent non-mosaic trisomy 13 by parental report, or verified by clinical chromosome testing or clinical documentation when available. Similar studies performed using parental reports have shown the accuracy of parental reporting in the distinction of testing that showed non-mosaic

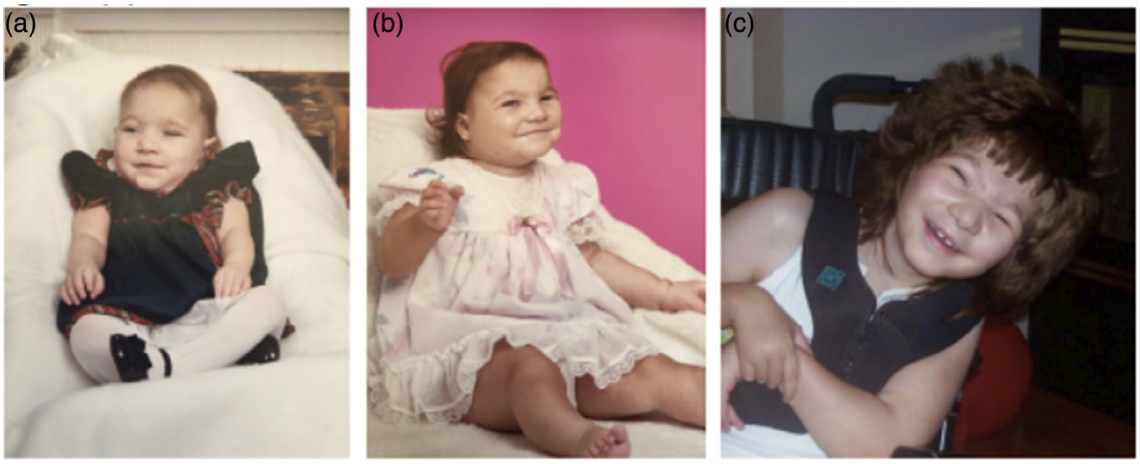

FIGURE 1 (a) Individual 2 at 1 year. (b) Individual 2 at 2 years. (c) Individual 2 as a school-aged girl [Color figure can be viewed at wileyonlinelibrary.com]

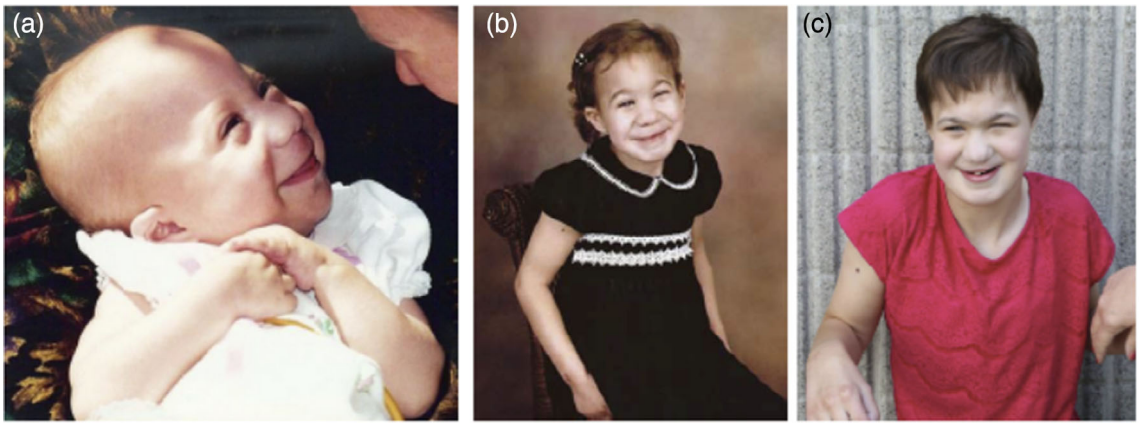

FIGURE 2 (a) Individual 3 at 10 months old. (b) Individual 3 in kindergarten. (c) Individual 3 as an adult [Color figure can be viewed at wileyonlinelibrary.com]

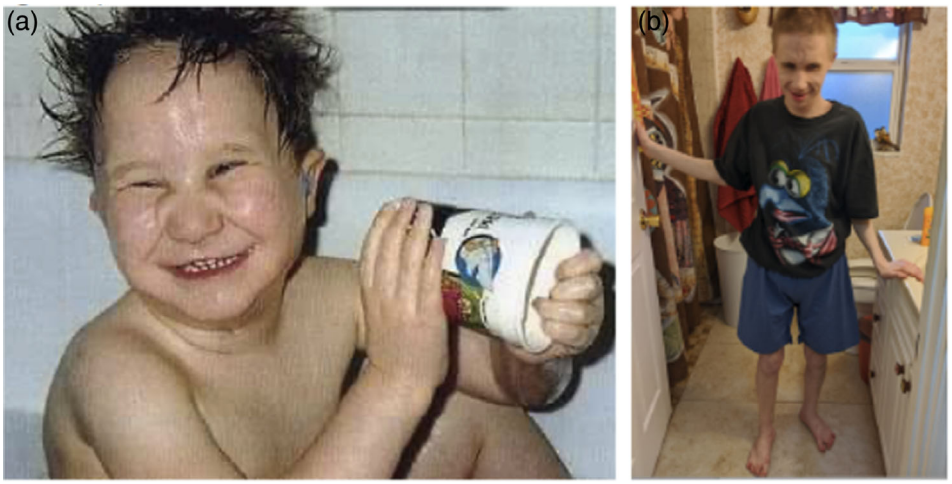

FIGURE 3 (a) Individual 4 as a boy. (b) Individual 4 as a young man [Color figure can be viewed at wileyonlinelibrary.com]

FIGURE 4 (a) Individual 5 as an infant. (b) Individual 5 as an adult [Color figure can be viewed at wileyonlinelibrary.com]

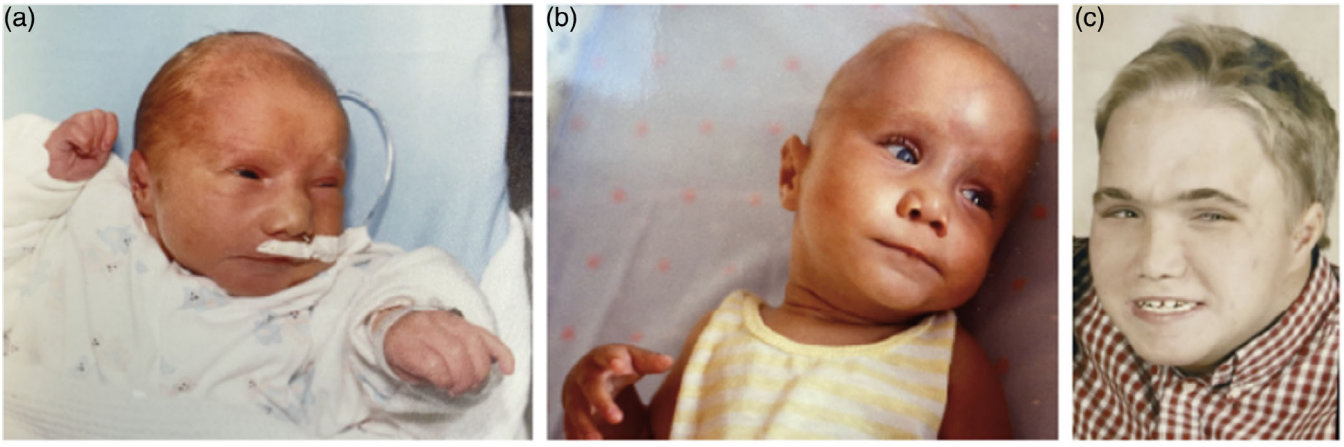

FIGURE 5 (a) Individual 7 as a newborn. (b) Individual 7 at 12-months old. (c) Individual 7 at 18-year old [Color figure can be viewed at wileyonlinelibrary.com]

versus mosaic trisomies, and in medical histories in general (Baty et al., 1994; Bruns & Campbell, 2014; Hansen et al., 2000). Our study included seven women and four men between the ages of 18 years and 35 years old. Three individuals are deceased and reports were given posthumously. We were able to obtain chromosome testing reports or clinical notes verifying testing results for six individuals. No co-

FIGURE 6 (a) Individual 8 as a newborn. (b) Individual 8 as a school-aged girl. (c) Individual 8 at 18 years of age [Color figure can be viewed at wileyonlinelibrary.com]

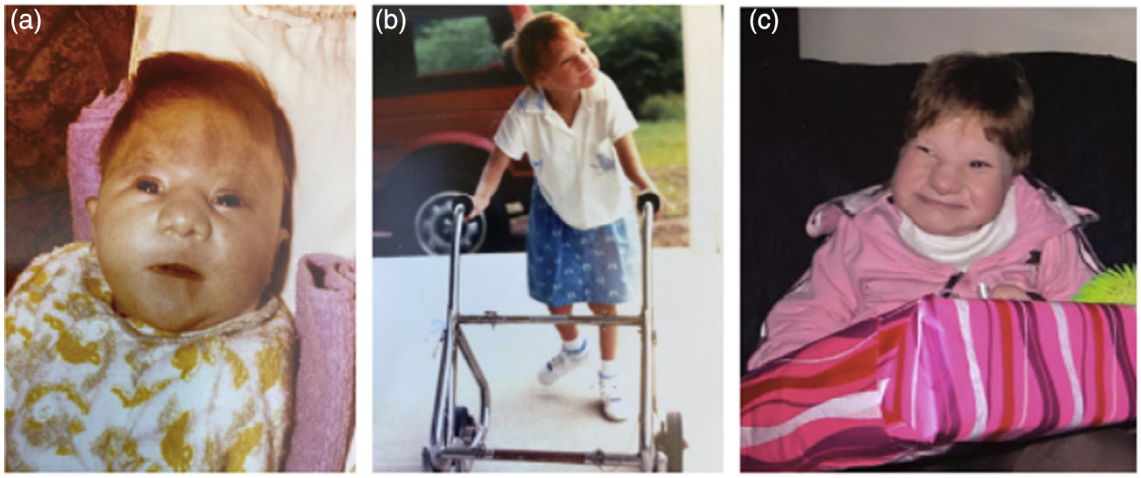

FIGURE 7 (a) Individual 11 at 1 month. (b) Individual 11 at 11 years. (c) Individual 11 at 29 years [Color figure can be viewed at wileyonlinelibrary.com]

occurring genetic diagnoses were reported. The average age of the participants was 24.5 years old. Women in the study had reported adult heights or lengths of 122 cm to 158 cm and were on average about 5.5 standard deviation below the mean height for adult women. Men in the study had reported adult heights or lengths of 135–163 cm, which is about four standard deviations below the mean for adult men. The average BMI for female participants was 23.9 and for male participants was 19.8. The study was approved by the Institutional Review Board of the University of Utah and consent to participate was obtained in all families. No families withdrew participation after consent was obtained.

3 | RESULTS

We have summarized clinical manifestations in system-based summaries below and in Table 1. Prenatal and birth history as well as a summary of medical support in the newborn period are reported in Table 2. Developmental milestones are summarized in Table 3, and Adult-onset Conditions are listed in Table 4. We have included brief descriptions of developmental histories below, whereas more detailed medical and developmental information specific to the individual and the family experiences are featured in 11 vignettes, which are included in Data S1.

3.1 | Cardiovascular findings

In this group of adults, 10 individuals have undergone an echocardiogram. The reported findings included three individuals with isolated atrial septal defect, two individuals with isolated ventricular septal defect, three individuals with both an atrial septal defect and ventricular septal defect, and one individual with dextrocardia and a ventricular septal defect (see Table 1). One person had normal cardiac anatomy on imaging. One individual's cardiac anatomy was unknown, but this person did not experience cardiac symptoms or complications

TABLE 1 Summary of clinical features

ID	Age, gender	Array characteristics, tissue	Height/ length weight BMI	Cardiac	Central nervous system	Apnea	Seizures, onset	Gastrointestinal	Renal urologic	Ears, nose, throat	Eye	Musculoskeletal	Endocrine	Dermatologic
1	35 y F	Non-mosaic, Parental report, Blood.	122 cm 32 kg, (4 ft 70 lbs) 21.5	NR	Brain hemorrhage	Reported, resolved by 7–8 years of life	Myotonic, Within first 12 months	GT, Reflux, Constipation, Abdominal cysts	NR	Hearing loss	Cataracts, Coloboma, Vision loss	Natal teeth, Equinovarus	NR	Cutis aplasia, Skin infections
2	23 y F	**47,XX,+13** 22 cells analyzed, 2 cells karyotyped, Blood.	130 cm 39 kg, (4 ft 3 in 86 lbs) 23.1	Small muscular VSD, Low blood pressure	NR	Apnea with seizures	Myotonic, GTC, 21 months	GT, Umb. hernia, Malrotation, Gallstones, Pancreatitis	VUR, UTI	Dysphagia	Micropth., Coloboma, Cataracts, Vision loss	Scoliosis, Polydactyly	PP, Pancreatic insufficiency	Dermal sinuses
3[a]	19 y F	**47,XX,+13** 50 cells counted, Metaphases counted: 6, 3 cells karyotyped, Blood.	158 cm 47 kg, (5 ft 2 in 103 lbs) 18.8	ASD, VSD	Normal MRI, Contractures	Reported symptoms, Normal sleep study at 5 yo	Infantile spasms 12 months, Cerebral palsy	Reflux, FTT, Malrotation, Umb. hernia, GT, Constipation, "Wandering spleen"	Hydronephrosis, Duplicated ureter, UTI	Cleft lip/palate, Ear tubes, Branch. Cleft cyst, Hearing loss	Cataracts, Vision loss	Scoliosis, Polydactyly	PP, Bone health	Cutis aplasia, Dermal sinuses, Hidradenitis Suppurativa
4	24 y M	Non-mosaic, Parental report, Parental balanced translocation, Blood.	163 cm 52 kg, (5 ft 4 in 115 lbs) 19.6	Normal echocardiogram	MRI: Delayed myelination, Normal structure	NR	NR	Inguinal hernia, Pancreatitis, Malrotation, Constipation	PCK, Unil. Retractile testicle	Cleft palate, Ear tubes, Hearing loss, Aspiration	Micropth., Colobomas, Cataracts, Nystagmus, Retinal dysplasia, Retinal detachment, Lens displacement, Vision loss	NR	NR	Cysts, Boils, CVM
5	27 y F dec.	Non-mosaic, Parental report, Blood.	142 cm 43 kg, (4 ft 8 in 94 lbs) 21.3	ASD, VSD, Cardiac dysfunction	MRI: Atypical position of cerebellum	Reported	NR	GT, Gallstones, Pancreatitis	PCK, Duplicated ureters, VUR, UTI	Intubation at birth. Trach until 8 months Postnatal stridor	Micropth., Cataracts, Coloboma, Vision loss	Polydactyly. Scoliosis, Achilles tendon release	NR	Cutis aplasia
6	28 y M	**47,XY,+13,** Confirmed by neonatal ICU discharge summary, Blood.	135 cm 38 kg, (4 ft 5 in 83 lbs) 20.9	ASD, HTN	NR	Reported symptoms	Yes 8–9 years old	Malrotation	Cryptorchidism	Cleft palate, Nasal polyps, Ear tubes, Aspiration, Hearing loss	Glaucoma, Retinal detachment	Polydactyly	NR	Cutis aplasia
7	18 y M dec.	**47,XY,+13,** Cell count not reported. Blood.	153 cm 58 kg, (5 ft 4 in 125 lbs) 24.8	ASD	NR	Reported	Myoclonic jerks, Absence seizures	Inguinal hernias, Malrotation	Small genitals, VUR, UTI	Cleft palate, Ear tag, Ear tubes	Blindness	Polydactyly	NR	Cutis aplasia, Skin infections

(Continues)

TABLE 1 (Continued)

ID	Age, gender	Array characteristics, tissue	Height/ length weight BMI	Cardiac	Central nervous system	Apnea	Seizures, onset	Gastrointestinal	Renal urologic	Ears, nose, throat	Eye	Musculoskeletal	Endocrine	Dermatologic
8	20 y F	**46,XX,+13,der (13;13)(q10; q10)** Confirmed by physician's note, Initial testing not available, Blood.	147 cm 66 kg, (4 ft 10 in 145 lbs) 30.5	ASD, HTN	Microcephaly	Reported, Developed at 3 weeks	NR	GT, Slow gastric emptying, Eosinophilic esophagitis, Possible Malrotation, Gallstones	VUR, UTI	Ear tag, Aspiration, Ear tubes	Entropion, Coloboma, Hypertelorism	Scoliosis, Contractures	NR	Psoriasis
9	20 y F	Non-mosaic, Parental report, Amniotic fluid	122 cm 43 kg, (4 ft 95 lbs) 28.9	ASD, VSD	NR	NR	GTCs, myoclonic 9 months	GT/GJT, Reflux, Malrotation	PCK, UTI	Ear tubes, Aspiration	Vision loss, Myopia, Lacrimal duct stenosis	Polydactyly, Scoliosis, Limb contractures	NR	NR
10	22 y M	Non-mosaic, Parental report, Amniotic fluid	139 cm 27 kg (4 ft 7 in 59 lbs) 14	Dextrocardia VSD	Holoprosencephaly	Reported	Myoclonic jerks, 1-time GTC	Omphalocele, GT Pancreatitis, Abnormal position of pancreas, SBO	Small genitals, Cryptorchidism PCK UTI	Intubation at birth, Cleft lip, palate, Ear tags	Coloboma, Myopia	Polydactyly, Achilles tendon release	Delayed pubertal progression, Bone health	Cutis aplasia, Cyst, Psoriasis
11	35 y F dec.	**46,XX,+13,** Karyotyped number of cells analyzed: 2, Blood	127 cm 38 kg, (4 ft 2 in 84 lbs) 23.6	VSD	Microcephalic	NR	GTCs, 7 months	Malrotation, Milk allergy GT	Normal imaging	Ear infections	Cataract, Abnormal pupil, Vision loss	Lower extremity contractures, hip dysplasia	Delayed pubertal progress, Osteoporosis	Cutis aplasia, Cysts

Abbreviations: ASD, atrial septal defect; CVM , capillary vascular malformation; dec., deceased; FTT , failure to thrive; GT , gastric tube; GJT , gastrojejunal tube; GTCs, generalized tonic–clonic seizures; HTN , hypertension; micropth., microphthalmia; MRI , magnetic resonance imaging; NR , not reported or work-up not obtained; PCK , cystic kidneys; PP , precocious puberty; SBO , small bowel obstruction; umb., umbilical; unil., unilateral; UTI , urinary tract infections; VUR , vesicoureteral reflux; VSD , ventricular septal defect.

[a]Previously reported in the literature at <18 years.

TABLE 2 Summary of early medical history

ID	Age, gender	Prenatal concerns	Birth history	Known birth parameters	Early support	Time until discharge	Support at discharge
1	35 y F	Hyperemesis, Oligohydramnios	42 weeks SVD	2.72 kg (~1st centile)	Nasal cannula NG	48 hours	Room air, Bottle feeds
2	23 y F	IUGR VUR	36 weeks Induced VD	2.04 kg (~10th centile), 44.5 cm (~20th centile)	Nasal cannula TPN	10 days	Bottle feeds, NG
3[a]	19 y F	Reduced prenatal screening due to parental preference	38 weeks Repeat CS	3.4 kg (~75th centile), 53.3 cm (~97th centile), OFC 34 cm (67th centile)	Nasal cannula NG	11 days	Room air, NG, Bottle feeds, Palate retainer, Suction equipment
4	24 y M	Decreased fetal movement, maternal blood pressure issues	39 weeks Spontaneous onset requiring further induction	2.9 kg (~15th centile) 48.3 cm (~20th centile)	Oxygen hood	Transferred on day 2	Room air Bottle feeds
5	27 y F dec.	Two vessel cord	40 weeks CS due to failure to progress	2.4 kg (~1st centile), 49.5 cm (~35th centile)	Intubated NG	>3 months of life	Tracheostomy (removed at 8 mos) NG
6	28 y M	Maternal edema	39 weeks CS	2.29 kg (~1st centile)	Room air	7 days	Room air Bottle feeding
7	18 y M dec.	None. Normal 1st trimester US	36 weeks SVD	2.72 kg (~50th centile), 53.3 cm (~97th centile)	Nasal cannula NG	5 days	Nasal cannula NG
8	20 y F	Breech	Full term CS	3.147 kg (~30th centile), 48.3 cm (~15th centile)	Room air NG	7 days	Room air Bottle feeds
9	20 y F	Postaxial polydactyly, Abnormal shape and length of kidney	35 weeks SVD	1.53 kg (~2nd centile)	Room air Bottle feeds	3 days	Room air Bottle feeds
10	22 y M	multiple congenital anomalies found on prenatal imaging: holoprosencephaly, omphalocele, postaxial polydactyly, cleft lip and palate, small genitalia, dextrocardia with ventricular septal defect and rocker bottom feet	39 weeks CS	~2.5 kg (~3rd %ile).	Intubated IVF NG	5 days	Nasal cannula GT
11	35 y F dec.	Limited prenatal screening due to practitioner's practice	37 weeks SVD	2.41 kg (~15th centile), 43.18 cm (~5th centile).	Room air NG	4 days	Room air Bottle feeds NG

Abbreviations: Dec., deceased; GT, gastric tube; IUGR, intrauterine growth restriction; IVF, intravenous fluids; NG, nasogastric tube; SVD, spontaneous vaginal delivery; VD, vaginal delivery.
[a]Previously reported in the literature.

later in life. Of all 11 participants, two individuals underwent cardiac surgery (Individuals 5 and 10) for repair of septal defects. The 27-year-old woman (Individual 5) was born with an atrial septal defect and a ventricular septal defect and underwent repair at 4 months of age. She developed a thrombus in her heart at 10–11 years old and was treated for cardiac dysfunction in her twenties. She succumbed to complications of heart failure. Hypertension arose in two individuals. The 28-year old man (Individual 6), who had an atrial septal defect, developed hypertension as an adult, which is controlled with a beta-blocker. The 20-year-old woman (Individual 8), who had an atrial septal defect, developed hypertension at about 9 years of age coinciding with the onset of puberty. Renal imaging performed at that time was normal and laboratory studies did not provide a diagnosis.

TABLE 3 Developmental milestones

Case	ID	Rolling over	Sitting	Pulling to stand	Crawling	Mobility	Communication	Fine motor
1	36 y F	12–24 mo	Supported: 12–24 mo	As a young child	As a young child	With walker, Wheelchair	Smiles, points, says "mama"	Feeds herself finger foods, uses a cup
2	22 y F	12 mo	Unsupported: 24 mo	24 mo	NR	Never walked, wheelchair	Smiles, cries, says "mom"	Could play with toys
3[a]	19 y F	3 yo	Supported: by 24 mo Unsupported: by 3 yo	NR	5 yo	Walked at 29 mo, Walks with walker	Emotions expression, says "mama"	Can grab toys
4	24 y M	7 mo	NR	2.5 yo	NR	Walks with guidance	Had a few words, now uses "mama"	Feeds himself
5	27 y F	2.5 yo	Supported: 2.5 yo Unsupported: 4 yo	6 yo	4 yo	Walks with walker	Expression of emotion, indicating needs by moving through the home	Played with toys, Hold cups
6	27 y M	12–24 mo	Supported: <12 mo Unsupported: 3–4 yo	NR	NR	Wheelchair	Babbling at 3–4 yo, says "dada"	Plays with toys, grabs a spoon
7	18 y M	NR	Unsupported: 3–3.5 yo	Stand supported at 3 yo	NR	Never walked, Wheelchair	A few signs, Mimics words, Emotional expression	Use a cup and spoon
8	20 y F	<12 mo "late"	Unsupported: <12 mo "late"	Stand supported <12 mo	2 yo	Walked at 29 mo	Situational phrases, expressions for "yes" and "no," Some signs	Uses utensils to feed herself, scribbles, pours water
9	20 y F	12–24 mo	Supported: shortly after 12 mo Unsupported: unable	Stand supported ~3 yo	NR	Never walked, Wheelchair	Babbling at 9 mo, "mama" at 12 mo, Expression meaning "no"	Picked up objects at 24 mo
10	22 y M	By 18 mo	Unsupported: 18 mo	Stands with stander	2 yo	Never walked, Wheelchair	Expression of emotion, pointing	Propels his wheelchair
11	35 y F	13 mo		24 months	NR	Walked at 5 years of age, Walks with walker	A few signs, Expression of emotion, Nodding yes and no	Used a spoon to feed herself, open doors, play with toys

[a]Previously reported in the literature.

TABLE 4 List of adult-onset conditions

Case	ID	Adult-onset medical concerns
1	35yF	Failure to thrive, abdominal cysts, worsening seizures, brain hemorrhage
2	23yF	Low blood pressure, recurrent infections, insulin resistance
3[a]	19yF	Low immunoglobulin levels in serum
4	24yM	Retinal detachment, lens dislocation
5	27yF	Congestive heart failure, renal failure secondary to hypoperfusion, gallstones, pancreatitis, urinary tract infections
6	28yM	Recurrent pneumonias, hypertension
7	18yM	Recurrent pneumonias, endocarditis
8	20yF	Asthma, recurrent pneumonias, Low immunoglobulins, possible hemochromatosis
9	20yF	Recurrent pneumonias, sepsis
10	22yM	Surgery to relocate pancreas, treatment of cystic skin infections, repeat occurrences of small bowel obstruction
11	35yF	Ear infections, *Clostridium difficile*, Malrotation, Pneumonia, osteoporosis

[a]Previously reported in the literature.

3.2 | Central nervous system findings

Abnormal brain imaging findings were reported in four individuals. These findings included holoprosencephaly (Individual 10), atypical position of the cerebellum (Individual 5), delayed myelination with otherwise normal structure (Individual 4), and brain hemorrhage without known cause in an adult (Individual 1). Two individuals had normal brain imaging. Six families were not aware of central nervous system findings or the participants had not undergone postnatal imaging.

Seizures arose in eight individuals most with onset within the first 2 years of life. One man had seizures diagnosed at 8–9 years of age. Types of seizures included myotonic seizures, generalized tonic–clonic seizures, infantile spasms, and absence seizures.

3.3 | Respiratory findings

Only two individuals were intubated after birth (Individuals 5 and 10). Individual 10 was extubated to nasal cannula on day two of life after omphalocele repair. Individual 5 underwent tracheostomy, which was later removed at 8 months of life without need for further respiratory support. Five individuals required nasal cannula or oxygen hood in the neonatal period. Four individuals remained on room air after birth.

Symptoms of apnea were reported in seven individuals arising during the first months of life. One person had apnea arising outside of this period coinciding with the onset of seizures. For this individual, symptoms improved after initiation of treatment for epilepsy (Individual 2). Three individuals never had findings or symptoms concerning for apnea. Families who intervened for apneic episodes early on noticed improvement and resolution with time. As adults, one individual will undergo sleep study to evaluate for covert apneic events at night. She is not currently on oxygen or respiratory support for apnea (Individual 8). One individual had a repeat sleep study at 5 years of age, which was normal (Individual 3). Of note, no individuals are on baseline oxygen or positive pressure ventilation during the day or night.

3.4 | Gastrointestinal findings

Six individuals were discharged after birth with a feeding tube (five individuals had nasogastric tubes and one individual had gastric tube). The other five individuals went home with plans to feed by bottle. Surgical feeding tube placement was required in eight individuals with most surgeries taking place during childhood. One individual required revision of a feeding tube at 18 years of age (Individual 9) and one woman underwent feeding tube placement as an adult (Individual 11) (see Table 1).

Eight of the 11 individuals were diagnosed with malrotation. Four individuals had pancreatitis commonly due to gallstones. Other gastrointestinal findings included reflux, constipation, hernias, eosinophilic esophagitis, omphalocele, atypical position of pancreas, pelvic spleen, and milk allergy.

3.5 | Renal and urogenital findings

Seven individuals experienced recurrent urinary tract infections. Vesicoureteral reflux or hydronephrosis were reported in five people, and cystic kidneys were reported in four. Other findings included duplicated collecting duct, cryptorchidism or retractile testicle, and small genital size.

3.6 | Ears, nose, and throat findings

Recurrent ear infections arose in seven individuals. Ear tubes required placement two or more times in three people due to premature expulsion of the ear tubes (Individuals 4, 6, 8). Hearing loss was reported in four people, cleft palate was reported in five, and dysphagia or aspiration was reported in five. Other findings included ear tags, branchial cleft cyst, nasal polyps and suspected laryngomalacia.

3.7 | Ophthalmologic findings

Abnormal eye findings were reported in all participants. These included cataracts in six people and coloboma in seven individuals. Visual impairment likely affected all participants. Other findings included glaucoma, retinal dysplasia, retinal detachment, lens displacement, entropion, microphthalmia, and nystagmus.

3.8 | Musculoskeletal findings

Postaxial polydactyly was found in seven individuals and scoliosis in six. Six individuals had contractures affecting the upper or lower extremities. Other findings included natal teeth, need for subtalar bone fusion, and hip dysplasia.

3.9 | Endocrine findings

Issues with bone health due to osteoporosis is reported in two women (Individuals 3 and 11). Two individuals underwent investigations for delayed onset of puberty. In one of these individuals (Individual 10), a brain MRI to assess the pituitary was normal. He was treated initially with testosterone, which his parents chose not to continue. He now receives zoledronic acid to support bone health. Individual 11 was also evaluated by an endocrine team. Imaging of her uterus was normal. Ovaries were not found on imaging, though parent did not know if this was due to difficulty of exam or confirmed absence of these structures. She had not been on hormonal therapies, but received zoledronic acid, vitamin D and calcium. Precocious puberty was diagnosed by an endocrine team in two individuals (Individuals 2 and 3).

3.10 | Dermatologic findings

Seven individuals had cutis aplasia. Seven individuals had recurrent skin infections involving dermal sinuses, skin abscesses, or cysts. Other findings included psoriasis in two individuals, and a capillary vascular malformation.

3.11 | Early history

Please see Table 2 for details of prenatal, birth history, growth parameters, and early support required in the nursery or neonatal intensive care unit for each person described below. Of note, eight individuals were born after 36 weeks gestation.

3.12 | Vignettes

We provide more detailed accounts of the early history, medical course, and developmental milestones in the Data S1. Below we highlight the developmental histories because few data are available on persons with trisomy 13 over the age of 5 years. Figures 1–7 show photographs at different ages of Individuals 2, 3, 4, 5, 7, and 11.

3.12.1 | Individual 1

This individual is a 35-year-old woman born at term with trisomy 13 diagnosed by postnatal chromosome testing in blood. Her developmental history is summarized in Table 3. Individual 1 turns to sounds and understands warnings from her loved ones if she is near a hazard. She smiles, makes communicative noises, and says "mama." This woman can crawl to her parent and grab the arm to communicate. She feeds herself finger foods and drinks from a cup with a straw. She enjoys music and children's television programming and stories.

3.12.2 | Individual 2 (Figure 1a–c)

The individual is a 23-year-old woman born late preterm, who was diagnosed by prenatal genetic testing and confirmed by postnatal chromosome analysis. Her developmental history is summarized in Table 3. When she was hospitalized for pancreatitis at 8 years of age, she lost many skills including her ability to sit up, pull to stand, and manipulate objects with her hands. Her parent notes that as a child she was able to do summersaults. She enjoys attention, snuggling, feeling hands run through her hair, and sunshine.

3.12.3 | Individual 3 (Figure 2a–c)

This individual is a 19.5-year-old woman born at term and diagnosed by postnatal chromosome analysis. Her developmental history is summarized in Table 3. She can sit and stand on her own, uses a walker several hours per day and can take a few steps on her own. She swipes to grab objects. She understands simple commands, such as "stand," "sit" and can assist her parent with dressing herself. Her parent reports that she functions at the level of a toddler. She is a generally happy and loving woman. She enjoys shows and movies with music. She loves to go outside, use her walker and an adaptive tricycle or tandem bicycle with her parent.

3.12.4 | Individual 4 (Figure 3a,b)

The individual is a 24-year-old man born at term with trisomy 13, translocation type, diagnosed by postnatal chromosome analysis. His developmental history is summarized in Table 3. It is notable that Individual 4 was able to walk independently at 3.5 years. He used a stander for a short period of time when he was acquiring new skills. He can now walk independently in his home, but requires guidance outside of the home due to vision loss. He requires a wide-handled spoon for self-feeding. He was able to make some signs at 2 years of age. He said "mama," and used to have a few more words, but no longer uses them. He uses a communication device (Tec-top) and can ask to go to the bathroom and understands simple commands. He can unzip and pull up his pants. He uses a pull-up during the day and a diaper at night. He demonstrates an awareness of his weekly schedule and likes routine. He can feed himself and eats soft foods, such as pizza and ham sandwiches. The man is currently able to help with bathing, toileting, and dressing himself. He enjoys music, shows, swimming at the beach, and pizza.

3.12.5 | Individual 5 (Figure 4a,b)

This individual was a woman, who died at 27 years of age. She was born at term and was diagnosed by postnatal chromosome analysis. Developmental history is outlined in Table 3. It is notable for playing with toys with her hands at 3 years of age. She would hold cups and put her arms in the sleeves while dressing. After removal of tracheostomy, she started babbling. She was nonverbal and would indicate her needs and desires through expressions and moving through the house to show what she needed by her position. She enjoyed bright, light-up toys, and swimming with her parent's support. As an adult, she used a walker. She was able to feed herself, and carry her cup. She helped with bathing, but required support for toileting and diapering.

3.12.6 | Individual 6

This individual is a 28-year-old man born at term and diagnosed by postnatal chromosome analysis. Developmental history is summarized in Table 3. In addition, he sat supported before 12 months and unsupported at 3–4 years of age. Currently, he uses a wheelchair. He plays with toys and can grab a spoon. He started babbling at about 3–4 years of age and can say "dada." He is otherwise nonverbal, and communicates with sounds and expressions. He requires support for all activities of daily living.

3.12.7 | Individual 7 (Figure 5a–c)

Individual 7 is a man, who passed away during his eighteenth year of life. He was born late preterm and the diagnosis of apparent non-mosaic trisomy 13 was made with postnatal chromosome analysis. His developmental history is summarized in Table 3. It is notable for sitting supported at about three to three and half years of age. At this time, he started to stand with support, but was not able to stand on his own. He used a wheelchair, and could guide his wheelchair by 8 years of age. He was able to hold a bottle within his first year of life and started using a cup and spoon when he was in elementary school. He made a few signs at 11–12 months of age, indicating hunger, thirst and satiation and was able to mimic other's words at 2–3 years of age. For the most part, he would make nonverbal sounds to convey his emotions. He enjoyed milkshakes, bright toys, riding in the car in the carwash, swimming with parental support, swinging, and rides on an adapted bicycle and tricycle. He received some support with feeding. He used a shower chair and support from his parents to bathe. He needed assistance with diapering/toileting and dressing.

3.12.8 | Individual 8. (Figure 6a–c)

This individual is a 20-year-old woman born at term and diagnosed by karyotype with apparent non-mosaic trisomy 13 in the setting of a Robertsonian translocation [46,XX,+13der(13;13)(q10;q10)]. Her developmental milestones are summarized in Table 3. It is notable for walking independently at 29 months of age. She has an abnormal gait, but does not require additional support to ambulate. She can use utensils to feed herself, colors and scribbles, and plays with toys and cards. She can go to the kitchen and get a drink, though she spills when she pours. She babbled until 5–6 years of age. She has situational phrases, such as "I love you," "here's your towel," "take a shower," can name her favorite foods, can say "momma," "dada," and uses words for yes and no, among some others. She uses a communication device at school and can use some signs.

She enjoys socializing, eating out, music and motorcycle rides. She receives support with feeding herself, but manages mostly on her own in this arena. Individual 8 can get in and out of the bath, help clean herself, and assists with toileting. She otherwise requires diapering. She can use a zipper and can start to put on articles of clothing by herself. She washes her own hands.

3.12.9 | Individual 9

This individual is a 20-year-old woman born preterm and diagnosed by prenatal genetic testing obtained via amniocentesis. Amniocentesis was performed at 7 months gestation and chromosome testing showed apparent non-mosaic trisomy 13. Her developmental history is summarized in Table 3. It is notable for sitting with support after 12 months of age and standing supported at 3 years of age. She now gets around with a wheelchair. She developed contractures in her limbs and no longer uses her hands for grabbing. Her family notes that she was able to pick up objects starting at about 24 months. Verbally she can utter sounds indicating "no," and is otherwise nonverbal. She enjoys music, watching birds, car rides, beach sounds, and bright cartoons. She requires support for all activities of daily living.

3.12.10 | Individual 10

Individual 10 is a 22-year-old man born at term and diagnosed with non-mosaic trisomy 13 by amniocentesis. Developmental milestones are summarized in Table 3. Of note he sat on his own at about one and a half years and was able to get around by sitting up and rolling to a new position. He began crawling at 2 years of age. He currently uses a wheelchair, which he self-propels with his hands, and a stander. He uses his hands to pick options that his parent gives him. He is nonverbal but communicates through expression of emotions and tapping on an object. His parent notes that he can follow simple instructions. He enjoys movies, music, laughter, watching children play, and riding in cars or boats.

3.12.11 | Individual 11 (Figure 7a–c)

Individual 11 is a woman, who passed away during her 35th year of life. She was born at term and was diagnosed with apparent non-mosaic trisomy 13 by karyotype. Her developmental milestone history is summarized in Table 3. It is notable for rolling over at 13 months.

She did not learn to crawl, but would scoot on her back with her legs. She sat unsupported at 9 months, stood supported by 24 months and walked with a walker by 5 years of age. She would grab objects by 6 months old. She did not have full control of her hands, but could use her hand to rock and open a doorknob and feed herself with a spoon. She would say "mama," and express herself through emotions and by nodding "yes" and "no." She had some signs that she used to communicate, such as waving to indicate desire to have the lights turned on. Her parent notes that she was at the developmental level of a "wise toddler." She enjoyed interacting with others, exploring, church music, band music, and swimming. She received support with all activities of daily living, but she was able to help with feeding and undressing.

4 | DISCUSSION

This series of adults with trisomy 13 is the largest published compilation of adult individuals with the syndrome. Individuals 1 (currently 35 years) and 11 (lived to 35 years) represent the oldest persons with trisomy 13 documented in the medical literature. A summary of the clinical features of each individual is compiled in Table 1. The constellation of findings is typical of classical trisomy 13 syndrome suggesting that this series is representative of the syndrome and reflects individuals who survived despite the high mortality rate. At this time, there are limited data about risk factors that affect mortality. Some studies have suggested increased survival in infants without heart defects (Rasmussen et al., 2003) and higher mortality in infants with central apnea (Wyllie et al., 1994). According to a multistate population study from 2016, the strongest predictor of mortality in trisomy 13 was prematurity. Increased survival rate was associated with female gender, term birth and residing in a metropolitan area. The presence of heart defects and omphalocele showed a small decreased rate of survival, which was not clinically significant. Association with apneas was not reported (Meyer et al., 2016). While this remains a small group, notable features include a majority of term births (8 of 11) and increased ratio of women to men (seven to four). In addition, only two individuals underwent cardiac surgery. Surprisingly, 7 of 10 individuals had symptoms of apnea in the neonatal period that improved with time. Reflecting on the methods of this study, it is important to highlight that apneic symptoms described by parents could represent other etiologies aside from central apnea, such as obstructive apnea, cyanosis, or seizures. We were unable to verify the etiology of these episodes with clinical documentation.

Other interesting findings include the extent of respiratory support used at birth. Two individuals were intubated. In one of these individuals, the infant needed a surgery and was able to be extubated to nasal cannula and weaned to room air when the surgery was completed (Individual 10). The other person underwent tracheostomy as an infant, but was able to have it removed before 1 year of life (Individual 5). (These two individuals are also the only participants where cardiac surgery was performed for repair of septal defects.) All other postnatal care was limited to oxygen supplementation by nasal cannula or the infant remained on room air.

Feeding by nasogastric tube was common in the neonatal period and varied by parental preference and the infant's immediate need. Eight individuals required permanent placement of a feeding tube for nutrition or medication management after the neonatal period. Dysphagia was common in individuals who take nutrition by mouth. Other complications that have been reported in individuals with trisomy 13, such as reflux, gallstones, pancreatitis, malrotation were common in this group. Notably, three individuals had diagnosis of gallstones, with an additional two who had recurrent pancreatitis without this diagnosis (one individual had the pancreas located beneath the diaphragm that required surgical repositioning). Eight individuals were diagnosed with intestinal malrotation. This finding suggests that intestinal malrotation should be considered in all patients with trisomy 13 presenting at any age with symptoms of gastrointestinal obstruction.

Seizures were reported in 8 of 11 participants with onset predominantly within the first years of life, though one individual developed seizures at 8–9 years of age. Seizure types included myoclonic seizures, generalized tonic–clonic seizures and infantile spasms. Imaging of the brain was reported in five people. Abnormal brain imaging findings included holoprosencephaly, delayed myelination, abnormal position of the cerebellum, and brain hemorrhage. Normal anatomy was found in one individual. In the persons in whom echocardiogram was obtained (10 individuals), septal defects were common and complex cardiac malformations were rare. One individual had normal cardiac anatomy on echocardiogram.

Some degree of vision loss likely affected nearly all participants. Six individuals had cataracts. Glaucoma arose in one individual and retinal detachment occurred in two. Five individuals had cleft palate and three had hearing loss. Cystic kidneys were found in five people, and six individuals required prophylactic management to prevent urinary tract infections. Recurrent skin infections or cystic lesions of the skin were common. Precocious puberty was reported in two people, while two others were evaluated for delayed pubertal onset.

Adult onset conditions included intra-abdominal cysts, spontaneous brain hemorrhage, hypertension, retinal detachment, glaucoma, congestive heart failure, recurrent pneumonias, endocarditis, gallstones and pancreatitis, small bowel obstruction, asthma, low immunoglobulins, possible hemochromatosis, cystic skin lesions and other skin infections. Please see Table 4 for summary of these conditions with respect to reported histories. The finding of low immunoglobulins deserves further study of the immune status of older infants and children with Patau syndrome.

Adult growth parameters were notable for an average height or length of 134.6 cm in women and 149.8 cm in men. Average weight for this group of women was 43.9 kg and for men was 43.3 kg.

Milestone attainment is summarized in Table 3 and varied greatly among the participants. All families reported significant delays in acquisition of milestones and cognitive delays in their adult children. Five adults use a walker or walk independently, while six individuals use wheelchairs. Independent ambulation in the two individuals, while uncommon in the syndrome, has been reported previously (Baty et al., 1994) and indicates that when counseling families of newborns, stating that a child will "never walk" is inaccurate.

Communication varied with most individuals expressing themselves through emotions, pointing, or another use of spatial relationship to convey a need or desire. Five individuals could identify their parent with a name. Some individuals used limited signs, a communication device or situational phrases.

Most individuals could partially assist with activities of daily living, either by walking, using a wheelchair, feeding him- or herself, or partially assisting with dressing, bathing, or toileting.

All 11 adults were reported to have apparent non-mosaic trisomy 13. As we noted previously, mosaicism was not completely excluded with clinical testing in these 11 individuals. The standard chromosome analysis used to diagnose trisomy 13 remains one of the best methods to detect low-level mosaicism, though it is now surpassed by SNP microarray and FISH analysis (Robberecht et al., 2010). Chromosome analysis, however, remains the standard for confirming this diagnosis in clinical practice, which was the case for all of our participants. These individuals' diagnostic stories remain relevant to current practices today.

We asked the parent of each individual to comment on what they would like a family to know who has a new diagnosis of trisomy 13 in their infant. Quotes from their experiences are listed in Table 5 in no particular order. Comments that identified the family with clinical information were left out of this list.

4.1 | Study limitations

The study has several limitations. As acknowledged previously, data come from parent report rather than review of medical records; however, this is becoming a more commonly used method for collecting information about patient outcomes and is supported by the use of such methodologies in previous studies, and routine clinical practice. Furthermore, as discussed previously, standard chromosome analysis cannot completely exclude mosaicism.

In conclusion, we describe 11 adults with Patau syndrome and characterize their medical and developmental histories. Two individuals were able to walk independently, and most showed some skills beyond those typically obtained during the first year of life. The two adults who reached their 35th birthday are the oldest known individuals with trisomy 13 reported in the medical literature.

TABLE 5 Comments from family members

Parent comments
"There is definitely hope." "Don't settle for what the books say." "If I had done what they had told me, she would definitely not be alive."
"You cannot fully listen to what doctors say." "They always give you the worst-case scenario." "Take it day by day." "She reminds me of a toddler; she wants attention and is easy to please."
"First year it is pretty scary." "Living in rural America, there are not too many kids like him around." "I can help—live his life to the best of his ability."
"It's so overwhelming at first, but don't be afraid. Parents are their child's best advocate." "Don't be afraid to take 1 day at a time."
"They're still fun. It's worth the adventure."
"I wish we had a day program to be out in public more." "If you encourage things, they can happen." "Things have gotten a lot easier for us, we've kind of grown up together."
"She definitely fits in to our family." "It is hard if you're in a small area. There are more opportunities in urban areas."
"Fear of the unknown is so powerful, but you can grow with your children." "Even during harder times, you learn to deal with it, you learn to adjust."
"It was difficult to navigate therapies before he got in to school. It took a lot of my time." "There's a grieving period for the child you thought you would have. How can we move forward and make him a part of our family?" "We were his biggest advocate[s]. We brought people on board."
"They know love."

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CONFLICT OF INTEREST

The authors declare none.

DATA AVAILABILITY STATEMENT

Exempt, n/a.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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