ARTICLE

Parental Hopes, Interventions, and Survival of Neonates With Trisomy 13 and Trisomy 18

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Trisomy 13 and 18 are life-limiting conditions for which a palliative approach is frequently recommended. The objective of this study was to examine parental goals/decisions, the length of life of their child and factors associated with survival. Parents of children who lived with trisomy 13 or 18 that were part of English-speaking social networks were invited to participate in a questionnaire study. Participants answered questions about their hopes/goals, decisions regarding neonatal interventions, and the duration of their children's lives. The participants were 332 parents who answered questions about their 272 children (87% response rate based on site visits; 67% on invitations sent). When parents were asked about their hope after the diagnosis, the main themes invoked by parents were the following: meet their child alive (80% of parents with a prenatal diagnosis), spend some time as a family (72%), bring their child home (52%), and give their child a good life (66%). Parents wanted to give them a chance, but also reported their fears were medical complexity, pain and/or life in the hospital (61%). Healthcare providers recommended comfort care at birth to all parents. Life-sustaining interventions "as for any other child" was chosen as a plan of care by 25% of parents. Of the 216 children with full trisomy, 69% were discharged home after birth and 40% lived >1 y. The presence of a prenatal diagnosis was the strongest independent factor negatively associated with longevity: 36% of children with a prenatal diagnosis lived <24 hr and 47% were discharged home compared to 1% and 87%, respectively for children with a postnatal diagnosis ($P < 0.01$). Male gender, low-birth weight, and cardiac and/or cerebral anomaly were also associated with decreased survival ($P < 0.05$). After a prenatal diagnosis, palliative care at birth consisted of limited interventions, whereas after a postnatal diagnosis (median age of 6 days) it consisted of various interventions, including oxygen, ventilation, tube feeding and intravenous fluids, complicating the analysis. In conclusion, the goals of parents of children with trisomy 13 or 18 were to meet their child, be discharged home and be a family. Having a postnatal diagnosis was the independent factor most associated with these goals. Children with a postnatal diagnosis were treated "as any other children" until the diagnosis, which may give them a survival advantage, independent of palliative care. Rigorous transparency regarding specific interventions and outcomes may help personalize care for these children. © 2016 Wiley Periodicals, Inc.

KEY WORDS: trisomy 13; trisomy 18; palliative care; perinatal palliative care; perinatal hospice; prenatal diagnosis; end-of-life decision making

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INTRODUCTION

Trisomy 13 and trisomy 18 are the second and third most common serious chromosomal disorders after trisomy 21. Because of the low survival and the severe disability associated with them, they have long been described as lethal by health care providers. In the past decade, growing evidence has demonstrated that some children with these conditions received interventions

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[Nelson et al., 2012; Meyer et al., 2016] and that some children were prolonged survivors. Families who lived with these children have also reported that despite the challenges, their children were happy and the impact on their lives was positive [Janvier et al., 2012; Kosho et al., 2013]. These studies have led to a more balanced view regarding the management of affected children [Carey, 2012]. However, case reports and case series of long-term survival of infants with trisomy 13 or 18 have been hampered by small numbers, an uncertainty about parental decision-making and the level of care the infants received, as well as the precise nature of any malformations. A recent large population study shows much greater survival rates among chromosomal variants [Wu et al., 2013] as opposed to "full" trisomy, but the potential benefit of interventions for children with "full" trisomy 13 or 18 is difficult to estimate [Janvier and Watkins, 2013; Janvier et al., 2016]. While the current literature suggests that interventions may be beneficial to some children [Muneuchi et al., 2011], others may be harmed and their lives possibly even shortened. Furthermore, parental hopes and goals after a diagnosis and the decision-making regarding levels of care for life-sustaining interventions are generally not reported. [Janvier and Watkins, 2013; Bruns and Martinez, 2016; Janvier et al., 2016]. The objective of this study was to examine parental goals and hopes after a diagnosis of trisomy 13 or 18. Factors associated with survival among families who experienced a live birth were also investigated.

In the past decade, growing evidence has demonstrated that some children with these conditions received interventions and that some children were prolonged survivors. Families who lived with these children have also reported that despite the challenges, their children were happy and the impact on their lives was positive.

METHODS

A computer-assisted self-reported questionnaire was designed using expert opinion, including focus groups and two pilot questionnaires. One of the collaborators in this study is a parent (BF). Our inclusion criteria were: parents of children who live(d) with trisomy 13 or 18 who were part of online (English language) parent-support groups. The 503 potential participants who met inclusion criteria received an email to participate in the study. The general results of this study have been reported, comprising the experiences of 332 parents [Janvier et al., 2012], with a detailed description of the methodology. The name of the affected child was asked at the beginning of the questionnaire and used throughout. Skip logic was used to ensure that insensitive questions would not be asked. For example, if a child lived less than a day, parents were not asked questions about changes in level of care as the child grew older.

For the purpose of this study, the hopes and goals of the parents after the diagnosis were examined, as well as the decisions they made for their child in the perinatal and neonatal period and if/how these decisions changed. Factors associated with survival were also investigated. Parents were asked about the timing of the diagnosis, associated anomalies, the length of life of their child, hospital discharge, and their decisions regarding use of life-sustaining interventions for their child after the diagnosis (i) Full support, or "life-sustaining interventions, as required, as for any baby" or (ii) Some interventions but no life-support, (iii) Comfort care (no interventions to prolong life). Participants also reported the medical interventions their child received. They were asked the following open ended question: "What were your hopes and goals for (*name of child*) after the diagnosis?" After they had reported the level of care they chose and the interventions their children received, they were asked to elaborate on the goals of care and interventions.

When survival was examined, to reduce concerns about how different types of chromosomal rearrangement might impact findings for this publication, only outcomes of children with "full/complete" trisomy 13 or 18 were included (as opposed to genetic variants). For these children, when two parents described factual outcomes about their children, only the mother's answers were used for statistical analysis. For the open ended questions, the answers of both parents were analyzed.

In addition to descriptive statistics, categorical information was analyzed by chi-square and by logistic regression analysis. Open ended questions were analyzed by thematic analysis: the development/description of themes/sub-themes, coding of parental responses (AJ and BF) and the resolution of discrepancies by consensus. NVivo 9 (QSR international) was used to assist with the qualitative analysis, the coding comparison function of NVivo9 was used to ensure an intercoder agreement of 80%.

The questionnaire was anonymous. The first paragraph of the survey included a request for consent. The study was approved by the IRB of CHU Sainte-Justine Research Center.

RESULTS

Parents

All parents satisfying inclusion criteria were invited to participate. Responses to the 503 email requests were received from 332 parents, who answered questions about their 272 children (87% response rate based on site visits, 67% based on invitations sent). A detailed description of the participants can be found in the previous publication [Janvier et al., 2012]. Parents answered questions about 272 children, of whom

216 children had "full" trisomy 13 or 18. The remainder of the results will concentrate on these 216 children and their 261 parents.

The 261 respondents consisted of 202 fathers and 59 mothers, of whom 45% experienced a prenatal diagnosis. The majority of parents (75%) were from the US, 7% from Canada, 7% from the UK, and 11% from 12 other countries. When their child with trisomy 13 or 18 was born, parents' median age was 33 years old and 71% had previous children. The majority (66%) had completed at least one university degree, 83% described themselves as religious.

Children

The majority of the 216 children with "full/complete" trisomy 13 or 18 received their diagnosis after birth, which occurred at a median age of 6 days, whereas the remaining 45% had a prenatal diagnosis (Table I). The majority of children were born after 2000 and many had a low-birth weight or a congenital anomaly (Table I). Survival to 1 year was 40% while survival to age 5 was 21% (Table I).

Parents Hopes and Goals After the Diagnosis

When asked what their goals were after the diagnosis, 80% of parents who experienced a prenatal diagnosis (n = 102/128) mentioned that their goal was to meet their child alive.

The main themes evoked by all parents (n = 261) were the following: (i) bringing their child home (52%); (ii) giving their child a good life (66%); and (iii) being together/a family (72%). Many parents invoked more than one theme in their answers:

- *"I wanted to see Bristol, hold her. Have some good memories, not only grief."*

- *"We hoped we would have a live birth, and bring him home."*

- *"We hoped that we would have time with him alive, even if it was just a short time."*

- *"Our wish was to take Owen home and be a family for a while."*

- *"We knew his life would be short. We wanted to give him the best life possible."*

- *"That she would have as good a life as possible."*

- *"I hoped that we would be able to bring her home and raise her and care for her in our family."*

- *"I wanted her to enjoy a good life as long as she could."*

Many parents also reflected on the tension between doing "too little" and doing "too much." A good life was often defined as one where a child would be happy and loved. On the other hand, many parents also mentioned they feared pain, medical complexity and life in the hospital (61%). They wanted to give their child a chance, but not at the price of burdensome interventions, pain and/or a life in the hospital:

- *"We wanted to give him a good life. We wanted interventions like with any baby but if she was in pain or needed a respirator for a long time my husband and I would make a decision on what to do, give her a chance, but not at the price of pain."*

- *"My biggest hope was that he would not suffer in any way. Naturally I hoped that he would be with us for a long time and have a good life. I wanted to give him a chance."*

- *"I hoped that he would come to live with us. I hoped that he would not suffer. I did not want to keep him alive artificially, but I was willing to give him support to try to make things better."*

- *"We wanted to be sure Eva was not going to be put in significant pain trying to keep her alive and give her a chance."*

Provider Recommendations and Parental Decisions

All parents reported that after the diagnosis, physicians or healthcare teams recommended comfort care. All parents report providers were against any interventions to prolong life:

- *"When I met the perinatologist for the first time he was very negative and told me I'd*

TABLE I. Characteristics of the Children With Full Trisomy 13 or 18

Characteristic	Full T13–18 (n = 216) No. (%)	Full T13 (n = 94) No. (%)	Full T18 (n = 122) No. (%)
Prenatal diagnosis	97 (45)	49 (52)	48 (39)
Birth after 2000	185 (86)	83 (88)	102 (86)
Weight <5 lbs at birth	120 (56)	31 (33)	89 (73)
Gender (females)	152 (70)	50 (53)	102 (84)
Congenital heart anomaly	146 (68)	53 (56)	93 (76)
Brain anomaly	51 (24)	37 (39)	14 (11)
Still alive	79 (37)	25 (27)	54 (44)
Went home after birth	150 (69)	55 (59)	95 (78)
Lived <6 months	118 (55)	64 (68)	54 (44)
Lived > than a year	86 (40)	27 (29)	59 (48)
Lived >5 years	45 (21)	17 (18)	28 (23)
Cardiac surgery	25 (12)	7 (7)	18 (15)

T13-18, trisomy 13 or 18; T13, trisomy 13; T18, trisomy 18; lbs, pounds.

never find anyone to treat my son at birth because they prefer to let nature take its course."

-"We were being repeatedly told she was going to die and nothing was worth treating."

-"The doctor blurted out she was going to die before everyone left the room, even my 4 year old son!"

For parents who received a prenatal diagnosis, the majority (61%) report having been pressured to terminate the pregnancy:

"*The obstetrician encouraged abortion, saying that we would never find any doctors to treat her. We would be doing her a favor by saving her from suffering…"*

-"They definitely disagreed with our decision to continue with the pregnancy and were very outspoken about it."

After the diagnosis, 25% of parents chose full intervention "as for any other child," 27% of parents chose some interventions (no life-support), and 52% chose comfort care (no interventions to prolong life). There was no association between the parents' demographic data and the plan of care. For example, education, age, presence of other children or "religiosity" were not associated with decision-making.

Many parents reported that their decision for level of care had been influenced by the state of their child:

-"We had agreed to expect full interventions should the pregnancy make it to term. Unfortunately, he was born early […]. He could not breathe on his own, so at that point we decided on comfort care."

-"We decided if he showed strong signs of life we would start with the surgery to close his neural tube defect, otherwise keep him close to us."

-"If Hope was fighting we wished to fight with her, however if the prognosis looked poor we didn't want her to go through intensive resuscitation. We wished to make decisions based on her as an individual and not a diagnosis. We did not want her to suffer, which works both ways. […] However we didn't want anything invasive if she wasn't fighting and we wanted to enjoy the little time we had."

"We were willing to fight as long as Krissy wanted to fight. We agreed not to do heroic measures and chose to make each decision as it came based on Krissy's desire to live."

Forty-three percent of parents who chose care beyond "comfort care" agreed with the following statement "I felt judged by the medical providers that the decisions I was making were not in my child's best interest." More parents felt judged after a prenatal diagnosis (67% vs. 25% for postnatal diagnosis; $P < 0.01$).

Factors Associated With Longevity

The single most important factor independently related to mortality before going home or before 1 year, even when correcting for all other factors (including congenital anomalies, interventions, and palliative care), was the presence of a prenatal diagnosis. Other important factors associated with early mortality was gender (male), birth weight <5 pounds and the presence of a heart anomaly (Table II).

With one exception, death in the first 24 hr of life was exclusively seen in children with a prenatal diagnosis ($P < 0.01$, Table II). The proportion of children with a prenatal diagnosis who went home was significantly less (47% vs. 87%, $P < 0.01$), especially if they had a prenatal palliative care consultation (Table II). Children who had a postnatal diagnosis and a plan for palliative care were more likely to go home than children with a prenatal diagnosis and a plan for interventions (90% vs. 58%; $P < 0.01$; still significant after correcting for congenital anomalies) (Table III).

Interventions and Survival

Respiratory support

The need for respiratory support (positive pressure ventilation with bag and mask, CPAP and/or mechanical ventilation) in the neonatal period at birth was not independently associated with a significant decrease in survival. However, neonates with a postnatal diagnosis were more likely to receive ventilator support, complicating the analysis ($P < 0.001$). Among infants with a prenatal diagnosis, ventilator support was associated with increased odds of survival to discharge (OR 2.9; 1.1, 8.1, $P < 0.05$); among infants with postnatal diagnosis, on the other hand, ventilator support was associated with decreased the odds of survival (OR 0.27; 0.07, 0.98, $P < 0.05$) (Table IV). The majority of infants (73%) without a prenatal diagnosis with a birth weight under 4 lb required ventilator support compared to 20% for those over this weight. Of the infants who were ventilated at the time of postnatal diagnosis, 16 had ventilator support withdrawn after a decision for comfort care, 13/16 were discharged home and 6/16 lived >1 year (Table IV).

Cardiac surgery

One hundred and forty-six children had a cardiac anomaly and 25 had heart surgery. Most surgeries (75%) were ventricular septal defect (VSD) repairs performed on children older than 3 months, who had already been discharged home. All 25 children survived to hospital discharge after surgery and 21 children were still living with median survival post surgery of 2.5 years. Of the 86 children who survived more than 1 year, 57 had a congenital heart anomaly (generally a VSD) and the majority (32) did not have surgery.

Abdominal surgery

Eleven infants had abdominal surgery before hospital discharge (Omphalocele, malrotion, etc). Seven infants had abdominal surgery before the diagnosis of trisomy 13 or 18 and 4 after; 6/7 and 3/4, respectively lived >1 year.

Palliative care interventions

Palliative care at birth after a prenatal diagnosis was mainly described by parents as warmth, skin to skin care, medication for comfort and

TABLE II. Factors Associated With Survival in Infants With Trisomy 13 or 18

Characteristic	Survival to go home: OR (95% CI)	Survival for more than 1 y: OR (95% CI)
Postnatal Diagnosis	6.6 (3.4, 12.7)	6.3 (3.4, 11.9)
Birth weight	1.5 (1.2, 1.99)	NS
Sex (girl)	2.1 (1.1, 4.1)	NS
"Full" T13–18	NS	0.16 (0.07, 0.39)
T13 (compared to T18)	NS	NS
No brain anomaly	NS	1.5 (1.1, 2.1)
No heart anomaly	3.4 (1.4, 7.9)	3.1 (1.4, 6.9)
Ventilatory Support during 1 st hospitalization	NS	NS

Ventilatory support: High flow nasal cannula, positive pressure ventilation (bag and mask), CPAP, mechanical ventilation.

bereavement/psychological support. On the other hand, parents of children who chose palliative care after receiving a postnatal diagnosis (n = 52) described the continuation of many interventions such oxygen, intravenous fluids, blood tests (including glucose and bilirubin checks), tube feedings, oximeter, cardiac and/or apnea monitor, caffeine, antibiotics, etc. Parents report these interventions were continued to maximize the comfort of their child.

Changes in goals/level of care after discharge

One hundred and fifty children were discharged home after birth, the initial choice regarding levels of care was frequently revised by parents after home discharge: 67 infants were discharged from hospital with palliative care and half of the parents (n = 35) changed the level of care to "full medical interventions as for any other child." These 35 parents report they changed levels of care because their child did better than expected.

Decisional regret

Parents of children who had died were asked the following question: "Looking back, in terms of medical interventions, I think we did..." In regards to interventions their child received, 75% of parents report choosing "the right amount," 24% "not enough" and only 1% "too much."

DISCUSSION

This study examined the perspectives of a large group of parents who lived with children with trisomy 13 or 18 and has examined factors associated with survival of children with these conditions. To our knowledge, this is the first study examining the hopes and goals of parents, their decision-making regarding interventions and factors associated with the longevity of their children.

Our first finding is that parents have common hopes when they receive a diagnosis of trisomy 13 or 18: they hope to meet their child alive, take their child home, be a family and give their child a good life. They report being torn between giving their child a chance—"doing too little"—versus "doing too much" for their child. Despite these common goals, parents took a variety of decisions regarding level of care for their child, the minority choosing "full intervention as for any other child."

Our first finding is that parents have common hopes when they receive a diagnosis of trisomy 13 or 18: they hope

TABLE III. Length of Survival of Children With Full Trisomy 13 or 18 With or Without Prenatal Diagnosis Versus Postnatal Diagnosis

	Lived <1 d	Went home	Lived >3 mo	Lived >1 yr
Entire cohort (full T13 or T18) (n = 216)	17% (36)	69% (150)	55% (119)	40% (86)
Prenatal diagnosis (n = 97)	36% (35)	47% (46)	28% (27)	19% (18)
Comfort care (n = 52)	56% (29)	38% (20)	23% (12)	15% (8)
Interventions (n = 45)	13% (6)	58% (26)	33% (15)	22% (10)
Postnatal diagnosis (n = 119)	1% (1)	87% (104)	77% (92)	57% (68)
Comfort care (n = 52)	0% (0)	90% (47)	73% (38)	44% (23)
Interventions (n = 67)	1% (1)	85% (57)	81% (64)	67% (45)

TABLE IV. Survival of Children With Trisomy 13 or 18 With or Without Prenatal Diagnosis and With or Without Ventilatory Support

	Total n	Discharged home n (% total n)	Lived >1 y n (% total n)
Prenatal Diagnosis + VS	15	8 (53)	3 (20)
Prenatal Diagnosis, No VS	82	38 (46)	15 (18)
Postnatal Diagnosis + VS	38	29 (76)	16 (42)
−VS withdrawn after Dx	16	13 (81)	6 (38)
Postnatal Diagnosis, No VS	81	75 (93)	52 (64)

VS, ventilatory support: High flow nasal cannula, positive pressure ventilation (bag and mask), CPAP, mechanical ventilation; Dx, Diagnosis.

to meet their child alive, take their child home, be a family and give their child a good life.

Our second finding is that the recommendations parents had from medical providers were homogeneous: comfort care at birth with the plan of not prolonging life was recommended to all parents. These recommendations were probably based solely on the chromosomal diagnosis, as recommended by many position statements, hospital policies and authors who consider that interventions for these conditions are futile [Kumar, 2011; Chervenak and McCullough, 2012a,b]. There are, however, several ways of conceptualizing futility. Quantitative futility implies that interventions do not lead to survival; as these survival statistics (and others) demonstrate, interventions for trisomy 13 and/or 18 do not satisfy this definition of futility. Qualitative futility, in contrast, generally means that interventions are "not worth it": they may prolong a life not worth prolonging. For many providers, these conditions are universally qualitatively futile [Wilkinson et al., 2014; Murray et al., 2016]. In neonatology, even for conditions different to trisomy 13 and 18, for example for prematurity, the desired outcome in many studies has been "intact survival." Life and death decisions are routinely taken with this goal of trying to ensure "intact survival" [Jefferies et al., 2012]. A short or very disabled life has often been portrayed as having little or no value in the neonatal outcome literature. An alternative evaluation of whether interventions are futile for these conditions would examine whether they reach the goals of the patient/family [Schneiderman, 2011]. For families of children with a diagnosis of trisomy 13 or 18, the goals of care are not prolonged and intact survival, nor a cure. Redefining success and goals for these conditions would enable an evaluation of whether specific interventions increase survival to birth, to home discharge and the length of survival. It would also allow an evaluation of whether children have the best life possible by describing the burden of care/pain of these interventions and their quality of life.

Our third finding was that the single most important factor independently related to mortality before going home or before 1 year, even when correcting for all other factors, was the presence of a prenatal diagnosis. Children who had a postnatal diagnosis were treated "as any other child" ("full interventions") until a median age of 6 days, when the diagnosis occurred. This may have given them a survival advantage. After the diagnosis, many of these interventions were withdrawn, mainly the respirator. Our data show that among infants who had a prenatal diagnosis, only a minority of infants had ventilator support or tube feedings. While some children did not need support, others did not receive it because of parental wishes or the decision of physicians. In contrast, this was not true for children with a postnatal diagnosis. Children with a postnatal diagnosis received ventilator support according to their respiratory status only (and not related to decision-making or genetic label). Those who did not need support were probably naturally stronger. Children with a postnatal diagnosis who had good pulmonary function and respiratory drive from the start, and did not require respiratory support, were more likely to survive. After a postnatal diagnosis, many children who had ventilator support removed after a decision for comfort care were able to be weaned from life-support and discharged home. It is likely that the support was withdrawn at an "appropriate time," when children had an increased respiratory drive [Niedrist et al., 2006], some having received caffeine. Other important factors associated with early mortality were gender (male), low-birth weight, and the presence of a heart anomaly. These other factors have also been confirmed by other groups [Wu et al., 2013; Meyer et al., 2016]. It is important for physicians to recognize the scope of presentation of children with these conditions and that survival is possible after a short trial of respiratory support.

Our third finding was that the single most important factor independently related to

mortality before going home or before 1 year, even when correcting for all other factors, was the presence of a prenatal diagnosis.

Our fourth finding is that it appeared unclear to us what consisted palliative interventions and palliative care for these conditions. The aim of palliative care is to give each child with a life-limiting condition the best quality of life [Liben et al., 2008]. We found palliative care was very different when it occurred after a prenatal versus a postnatal diagnosis. We found that palliative care was homogeneous (minimal interventions and no interventions to prolong life) for children with a prenatal diagnosis. On the other hand, palliative care after a postnatal diagnosis seemed more individualized to the child's needs and the family's decisions. Indeed, children with a prenatal diagnosis and a decision for palliative care generally received, at most, warmth, and sometimes sedative and analgesic medications, whereas children with a postnatal diagnosis had a variety of interventions. It seems that palliative care, for children with prenatal diagnosis, is directed to a goal of having as short a survival as possible, with medications being prepared even before delivery [Harlos et al., 2013]. Giving the child an optimal death seemed to be the goal of palliative care after a prenatal diagnosis of trisomy 13 or 18. For children with postnatal diagnosis, palliative care may involve numerous different neonatal interventions, which are described to parents as palliative interventions, given to optimize quality of life: giving the child a good life. These interventions included transfusion for weakness and inability to feed, tube feeds for comfort, CPAP for dyspnea, surgical closure of meningomyelocele, surgery for omphalocele, ventriculo-peritoneal shunt, and even "cardiac surgery for comfort" (symptomatic child with a VSD). It is likely that many pediatricians would not describe such interventions as palliative. Optimizing quality of life and a child's comfort, the goal of palliative care, can be done in very different ways. Children with trisomy 13 or 18 and respiratory failure can receive different kinds of "palliative care": some physicians will recommend oxygen and high flow nasal cannulas to optimize comfort, while others will order comfort medication to manage the respiratory failure [Sibiude et al., 2011]. Similarly, apnea and respiratory distress can be treated with caffeine and/or CPAP/high flow nasal cannula or with opioids/sedatives, generally leading to early death. In children who cannot take all their nutrition by mouth, discomfort and dehydration can be treated with intravenous fluids, drops of milk in the mouth, tube feeds, or their comfort can be addressed with sedatives. All neonates will die without nutrition/hydration. It is important to examine decisions to withhold/withdraw interventions and whether they are in the best interest of neonates, and whether our goal for these children is a good death, or is it a good life?

Our last finding is about the insights regarding parental decision-making and plans of care. Decisions were influenced by the state of the child and whether he was vigorous or weak with parents in general not wanting to impose undue suffering. Parents of almost half the children discharged on comfort care later decided to consider surgical interventions, because their child exceeded expectations. Most parents had been told their child was "incompatible with life" and would live a meaningless life of suffering [Guon et al., 2014] but perhaps experienced the opposite; their baby grew, smiled, and progressed and the family coped and was enriched. A quarter of parents regretted not doing enough interventions.

The implication of these findings is that trisomy 13 and 18 are not homogeneous conditions: interventions may be of benefit to some children and harm others. Based on our findings and the current literature, if a baby is born near term, with a weight above >2.5 kg, without a complex congenital anomaly, the chances of survival to discharge and to 1 year of age are significant. Our data about ventilator support and early survival are important. Poor respiratory drive immediately after birth is common. This support can often be removed after a short time, and allow survival to go home. Sometimes, prolonged survival occurs, especially in neonates without complex cardiac anomalies or other significant adverse associated diagnoses. Infants with a prenatal diagnosis generally do not receive ventilator support, unless parents decide for interventions before birth. On the other hand, when infants with a poor respiratory drive are born without a diagnosis of trisomy 13 or18, they receive interventions solely based on their respiratory status (not on their genetic condition nor according to decision-making). Children who do not need a ventilator are probably stronger children more likely to have a prolonged longevity. In the light of these findings, a short trial of ventilator support for some children may be considered.

The implication of these findings is that trisomy 13 and 18 are not homogeneous conditions: interventions may be of benefit to some children and harm others.

Cardiac surgery seems to be have long-term benefits for older, stable children but is high risk and potentially harmful for others, especially ventilator-dependent neonates or those with comorbidities [Graham et al., 2004; Costello et al., 2015; Janvier et al., 2016]. For other surgeries, such as abdominal procedures, there is very little data, but prolonged survival does sometimes occur [Janvier et al., 2012; Nishi et al., 2014]. On the other hand, some children may have multiple adverse conditions. For these children, interventions may not be advisable. Providers should focus on reaching the goals that are most important to parents,

such as spending time with the child (even in utero), meeting the child alive, or spending time as a family. How these goals are achieved, for children with one or several poor outcome criteria, may require prolonged and repeated discussions with the family. We suggest providers take it one step at the time, and avoid committing to cardiac surgery when a child with complex anomaly is not yet born [Boss et al., 2013; Janvier et al., 2016]. Rigorous research is needed to identify better which infant may benefit from interventions, which specific interventions and the burden of care/pain associated with these interventions.

This study has several limitations. We have no data on individuals who chose to terminate their pregnancy or experienced a fetal loss. Furthermore, this is not a representative sample of children born with trisomy 13 or 18: the survival rate of children in this cohort is higher than described in population based studies, and a small majority of diagnoses were postnatal. Currently, the vast majority of diagnoses of trisomy 13 or 18 are prenatal [Crider et al., 2008; Parker et al., 2010; Irving et al., 2011; Springett and Morris, 2014]. This is also a questionnaire study of self-reported outcomes, which clearly has biases. Despite these limitations, because of our high response rate and large sample size, we are confident that our data provide a good representation of the goals, hopes, and decisions of this community of parents, who likely influence parents with a new diagnosis. Moreover, having data of many children with long-term survival has enabled us to confirm existing factors associated with survival and shed light on the complexity of these analyses as they relate to decision-making and goals of care.

Despite these limitations, because of our high response rate and large sample size, we are confident that our data provide a good representation of the goals, hopes, and decisions of this community of parents, who likely influence parents with a new diagnosis.

Such data are critical to address the increasingly complex ethical issues. The goals of participants were, in general, to meet their child alive, take their child home and be a family. Working with parents towards reaching these goals is feasible, but for some children this will not be possible. The challenge of physicians will often be the same as described by parents: the delicate balance between "giving the child a chance" versus "having the child go through too much." It seems to us that neither a universal imposition of comfort-care nor a universal application of intensive care and invasive surgery is appropriate. A knowledge of the true range of potential outcomes of these children, and a full evaluation of the structural abnormalities present, should permit individualized decision making which is consistent with the infant's and the family's best interest [Janvier et al., 2016]. Further rigorous research about these conditions will enable us to have a balanced approach and avoid extremes, understanding that navigation between doing "too much" or "too little" is often complex and requires an open mind [Janvier and Watkins, 2013].

REFERENCES

Boss RD, Holmes KW, Althaus J, Rushton CH, McNee H, McNee T. 2013. Trisomy 18 and complex congenital heart disease: Seeking the threshold benefit. Pediatrics 132:161–165.

Bruns DA, Martinez A. 2016. An analysis of cardiac defects and surgical interventions in 84 cases with full trisomy 18. Am J M Genet Part A 170:337–343.

Carey JC. 2012. Perspectives on the care and management of infants with trisomy 18 and trisomy 13: Striving for balance. Curr Opin Pediatr 24:672–678.

Chervenak F, McCullough LB. 2012a. Responsibly counselling women about the clinical management of pregnancies complicated by severe fetal anomalies. J Med Ethics 38:397–398.

Chervenak FA, McCullough LB. 2012b. Ethical dimensions of fetal neurology. Semin Fetal Neonatal Med 17:252–255.

Costello J, Weiderhold A, Louis C, Shaughnessy C, Peer S, Zurakowski D, Jonas R, Nath D. 2015. A contemporary, single-institutional experience of surgical versus expectant management of congenital heart disease in trisomy 13 and 18 patients. Pediatr Cardiol 36:987–992.

Crider KS, Olney RS, Cragan JD. 2008. Trisomie s 13 and 18: Population prevalences, characteristics, and prenatal diagnosis, metropolitan Atlanta, 1994-2003. Am J Med Genet A 146A:820–826.

Graham EM, Bradley SM, Shirali GS, Hills CB, Atz AM. 2004. Effectiveness of cardiac surgery in trisomies 13 and 18 (from the pediatric cardiac care consortium). Am J Cardiol 93:801–803.

Guon J, Wilfond BS, Farlow B, Brazg T, Janvier A. 2014. Our children are not a diagnosis: The experience of parents who continue their pregnancy after a prenatal diagnosis of trisomy 13 or 18. Am J Med Genet A 164A:308–318.

Harlos MS, Stenekes S, Lambert D, Hohl C, Chochinov HM. 2013. Intranasal fentanyl in the palliative care of newborns and infants. J Pain Symptom Manage 46:265–274.

Irving C, Richmond S, Wren C, Longster C, Embleton ND. 2011. Changes in fetal prevalence and outcome for trisomies 13 and 18: A population-based study over 23 years. J Matern Fetal Neonatal Med 24:137–141.

Janvier A, Farlow B, Barrington K. 2016. Cardiac surgery for children with trisomies 13 and 18: Where are we now? Semin Perinatol 40:254–260.

Janvier A, Farlow B, Wilfond BS. 2012. The experience of families with children with trisomy 13 and 18 in social networks. Pediatrics 130:293–298.

Janvier A, Watkins A. 2013. Medical interventions for children with trisomy 13 and trisomy 18: What is the value of a short disabled life? Acta Paediatr 102:1112–1117.

Jefferies A, Kirpalani H, Canadian Paediatric Society FaNC. 2012. Counselling and management for anticipated extremely preterm birth. Paediatr Child Health 17:443.

Kosho T, Kuniba H, Tanikawa Y, Hashimoto Y, Sakurai H. 2013. Natural history and parental experience of children with trisomy 18 based on a questionnaire given to a Japanese trisomy 18 parental support group. Am J Med Genet A 161A:1531–1542.

Kumar P. 2011. Care of an infant with lethal malformation: Where do we draw the line? Pediatrics 128:e1642–e1643.

Liben S, Papadatou D, Wolfe J. 2008. Paediatric palliative care: Challenges and emerging ideas. Lancet 371:852–864.

Meyer RE, Liu G, Gilboa SM, Ethen MK, Aylsworth AS, Powell CM, Flood TJ, Mai CT, Wang Y, Canfield MA, National Birth Defects Prevention N. 2016. Survival of children with trisomy 13 and trisomy 18: A multi-state population-based study. Am J Med Genet A 170:825–837.

Muneuchi J, Yamamoto J, Takahashi Y, Watanabe M, Yuge T, Ohno T, Imoto Y, Sese A, Joo K. 2011. Outcomes of cardiac surgery in

trisomy 18 patients. Cardiol Young 21:209–215.

Murray PD, Esserman D, Mercurio MR. 2016. In what circumstances will a neonatologist decide a patient is not a resuscitation candidate? J Med Ethics 42:429–434.

Nelson KE, Hexem KR, Feudtner C. 2012. Inpatient hospital care of children with trisomy 13 and trisomy 18 in the United States. Pediatrics 129:869–876.

Niedrist D, Riegel M, Achermann J, Schinzel A. 2006. Survival with trisomy 18—Data from Switzerland. Am J Med Genet Part A 140A:952–959.

Nishi E, Takamizawa S, Iio K, Yamada Y, Yoshizawa K, Hatata T, Hiroma T, Mizuno S, Kawame H, Fukushima Y, Nakamura T, Kosho T. 2014. Surgical intervention for esophageal atresia in patients with trisomy 18. Am J Med Genet A 164A:324–330.

Parker SE, Mai CT, Canfield MA, Rickard R, Wang Y, Meyer RE, Anderson P, Mason CA, Collins JS, Kirby RS, Correa A, National Birth Defects Prevention Network. 2010. Updated national birth prevalence estimates for selected birth defects in the United States, 2004-2006. Birth Defects Res Part A Clin Mol Teratol 88:1008–1016.

Schneiderman LJ. 2011. Defining medical futility and improving medical care. J Bioethical Inquiry 8:123–131.

Sibiude J, Gavard L, Floch-Tudal C, Mandelbrot L. 2011. Perinatal care and outcome of fetuses with trisomies 13 and 18 following a parental decision not to terminate the pregnancy. Fetal Diagn Ther 29:233–237.

Springett AL, Morris JK. 2014. Antenatal detection of edwards (trisomy 18) and patau (trisomy 13) syndrome: England and wales 2005–2012. J Med Screening 21:113–119.

Wilkinson DJ, de Crespigny L, Lees C, Savulescu J, Thiele P, Tran T, Watkins A. 2014. Perinatal management of trisomy 18: A survey of obstetricians in Australia, New Zealand and the UK. Prenat Diagn 34:42–49.

Wu J, Springett A, Morris JK. 2013. Survival of trisomy 18 (Edwards syndrome) and trisomy 13 (Patau syndrome) in england and wales: 2004–2011. Am J Med Genet A 161A: 2512–2518.