Trisomy 13 and Trisomy 18: A Changing Landscape?

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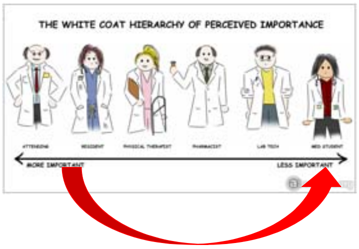
#tbt



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Fellowship Case

- Transport call from adult hospital
- "Can you take a 21 y/o female with Trisomy 13? She's en route here, but we don't take care of that disease."

The Age of Parent Support Groups

Stacy is 36 years old and living with Trisomy 18.

Natalie is 17 years old and living with Trisomy 13.

Phillip is 10 years old and living with a related disorder.

SOFT'S MISSION STATEMENT

SOFT is a network of families and professionals dedicated to providing support and understanding to families involved in the issues and decisions surrounding the diagnosis and care in Trisomy 18, 13 and other related chromosomal disorders. Support can be provided during prenatal diagnosis, the child's life and after the child's passing. SOFT is committed to respect a family's personal decision and to the notion of parent-professional relationships.

SOFT is well known for hosting an annual *Medical/Family* conference that benefits the whole family!

SOFT is a non profit 501(c)(3) all volunteer support organization. Your donations can be directed to operations, research, or conference expenses. A receipt will be provided for your records. Thank You!

Donations can be made electronically on www.trisomy.org using a credit card or PayPal. Mail check donations to: SOFT, 2982 South Union St., Rochester, NY, 14624.

soft

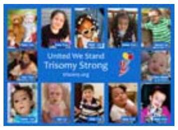
Kari (1977-1988) Trisomy 18
Beloved daughter of Kris and Hal Holladay
Kari's mother is the parent founder of SOFT!

Support Organization for Trisomy 18, 13 and Related Disorders (SOFT)

www.trisomy.org

TRISOMY 13 AND 18

WHAT YOU NEED TO KNOW



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https://www.hopefortrisomy13and18.org/

Hope for Trisomy

let your light shine

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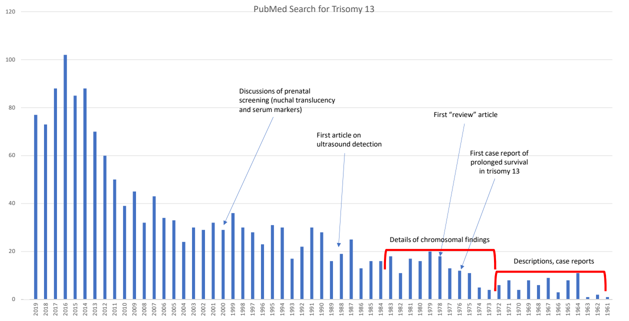


Discussions of prenatal screening (nuchal translucency and serum markers)

First article on ultrasound detection

First "review" article

First case report of prolonged survival in trisomy 13

Details of chromosomal findings

Descriptions, case reports

Mankinen et al. Trisomy 13 in a female over 5 years of age. *J Med Genet.* 1976.
Hodes et al. Trisomy 18 (29 cases) and Trisomy 13 (19 cases): a summary. *Birth Defects Original Article.* 1978

Trisomy 13 (Patau Syndrome)

- Brain and spinal cord anomalies (i.e. holoprosencephaly)
- Heart defects (present in about 80%)
- Profound intellectual disability

Photo credit: nih.gov

Trisomy 13 (Patau Syndrome)

- Cleft lip +/- palate
- Microphthalmia
- Cutis aplasia
- Polydactyly
- Rocker-bottom feet

Photo credits: merckmanuals.com, neoreviews.org, Staso et al. article

Trisomy 18 (Edwards Syndrome)

- Intrauterine growth retardation
- Congenital heart defects
- Severe intellectual disability


[redacted]

Photo credit: pedclerk.uchicago

Trisomy 18 (Edwards Syndrome)

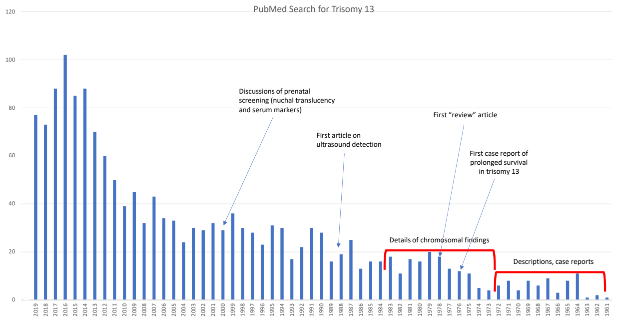
- Clenched fists with overlapping fingers
- Weak cry
- Hypotonia
- Microcephaly

Photo credit: pedclerk.uchicago

Prognosis

- 90-95% mortality in first year
- Miscarriage, termination, or fetal death are common
- Many do not survive the first few days
- Common causes of death: apnea, ductal dependent or cyanotic congenital heart disease, aspiration
- Median survival time
  - Trisomy 13: 7 days
  - Trisomy 18: 14.5 days

Rasmussen et al. Population-based analysis of mortality in trisomy 13 and 18. *Pediatrics*. 2003.



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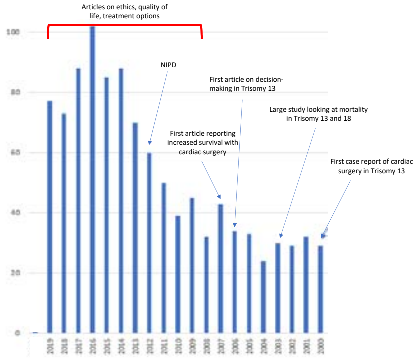
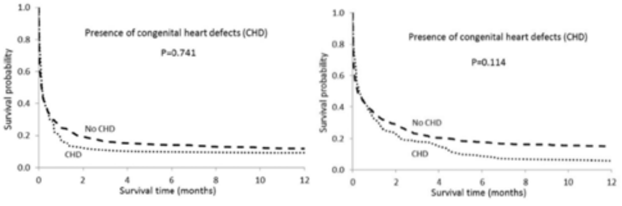


Recent Mortality Studies

- 693 children with T13 and 1113 with T18
- Median survival 5 (T13) and 8 (T18) days
- 9.7 % of patients with T13 survived to 5 years, 12.3% with T18
- In both, children who survived first year had 80% chance of survival to 5 years

Meyer et al. Survival of Children with Trisomy 13 and Trisomy 18: A Multi-State Population-Based Study. *Am Gen Med Genet.* 2016.



Trisomy 13

Trisomy 18

Recent Mortality Studies

	Median survival	1 year survival	10 year survival
Trisomy 13	12.5 days	19.8%	12.9%
Trisomy 18	9 days	12.6%	9.2%

- 174 children with T13 and 254 with T18
- If alive at 6 months, had 50-60% chance of being alive at 10 years
- Increased survival in mosaic or translocation trisomies

Nelson et al. Survival and surgical interventions for children with trisomy 13 and 18. *JAMA*. 2016.

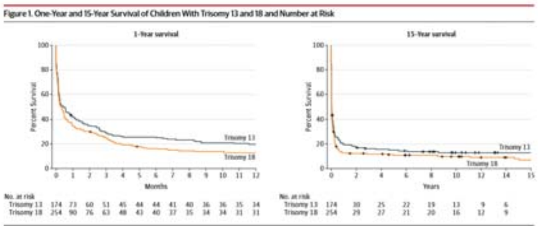


Figure 1. One-Year and 15-Year Survival of Children With Trisomy 13 and 18 and Number at Risk

No. at risk													
Trisomy 13	174	73	60	51	45	44	44	41	40	36	36	35	34
Trisomy 18	254	90	76	63	48	43	40	37	35	34	34	31	31

No. at risk								
Trisomy 13	174	30	25	22	19	13	9	6
Trisomy 18	254	29	27	21	20	16	12	9

What about surgical intervention?

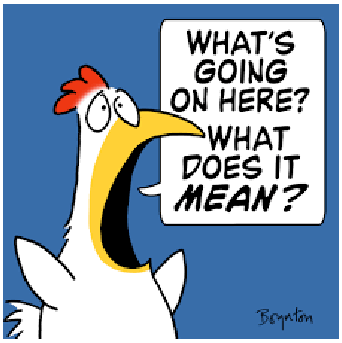
- 23.6% of T13 and 13.8% of T18 patients underwent surgical intervention
- Median survival after first surgery was >1 year expect for ophthalmologic surgery in T13 and cardiac surgery in T18
- Survival rates likely related to both patient selection and surgical benefit

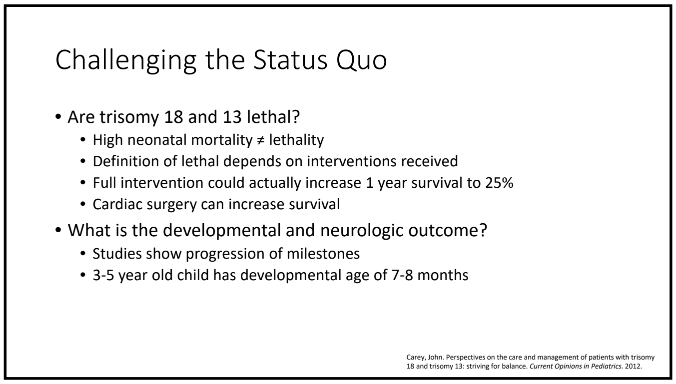
Nelson et al. Survival and surgical interventions for children with trisomy 13 and 18. *JAMA*. 2016.

Cardiac Surgeries

- 73 operations in patients with T13 and 270 with T18
- 70% of centers surveyed will perform surgery in this population
- Types of surgery ranged from VSD repair to single ventricle palliation
- Complication rate higher (55%) than overall population (36%) for both groups
- Mortality rate similar to overall population in T13 (~10%) but higher in T18 (15%)
- Pre-operative mechanical ventilation associated with increased mortality

Cooper et al. Cardiac Surgery in Patients with Trisomy 13 and 18: An analysis of the Society of Thoracic Surgeons Congenital Heart Surgery Database. *Journal of the American Heart Association.* 2019.

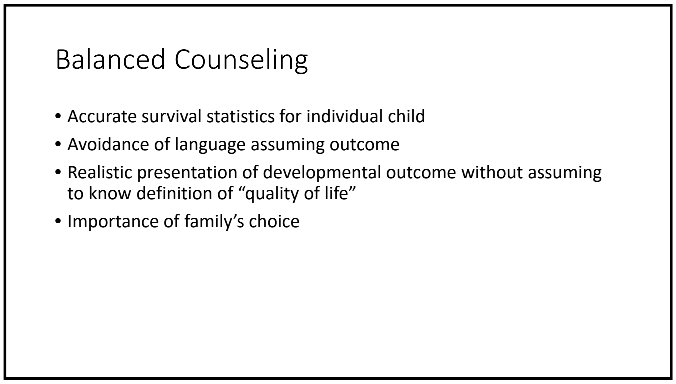




Challenging the Status Quo

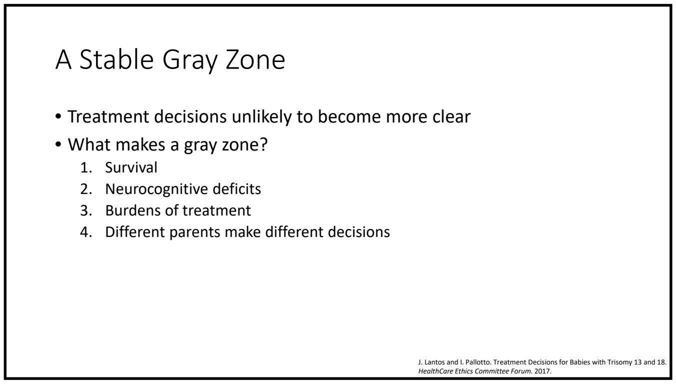
- Are trisomy 18 and 13 lethal?
  - High neonatal mortality ≠ lethality
  - Definition of lethal depends on interventions received
  - Full intervention could actually increase 1 year survival to 25%
  - Cardiac surgery can increase survival
- What is the developmental and neurologic outcome?
  - Studies show progression of milestones
  - 3-5 year old child has developmental age of 7-8 months

Carey, John. Perspectives on the care and management of patients with trisomy 18 and trisomy 13: striving for balance. *Current Opinions in Pediatrics.* 2012.



Balanced Counseling

- Accurate survival statistics for individual child
- Avoidance of language assuming outcome
- Realistic presentation of developmental outcome without assuming to know definition of “quality of life”
- Importance of family’s choice



A Stable Gray Zone

- Treatment decisions unlikely to become more clear
- What makes a gray zone?
  1. Survival
  2. Neurocognitive deficits
  3. Burdens of treatment
  4. Different parents make different decisions

J. Lantos and I. Pallotto. Treatment Decisions for Babies with Trisomy 13 and 18. *HealthCare Ethics Committee Forum.* 2017.

Why Do Doctors Still Struggle?

- Physician belief about quality of life with severe disability
- Allocation of health care resources to patients with high mortality
- Inability to have uniform approach, depends on baby and parents

J Lantos and I Pallotto. Treatment Decisions for Babies with Trisomy 13 and 18. *HEC Forum*. 2017.

Why Do Doctors Still Struggle?

- Definition of futility depends on goal you are trying to achieve
- Difference in perspective between physicians and parents
- Concept of justice: treat equals as equals
- Treatment is ethically permissible and should be offered but not required

Pyle et al. Management options and parental voice in the treatment of trisomy 13 and 18. *Journal of Perinatology*. 2018.

Application to Palliative Care

- May meet these families prenatally or after birth
- Average age of consult 19-25 days
- Followed between 1 to 2,442 days
- Reasons for referral:
  - Diagnosis
  - Decisional support for interventions
  - Transition to hospice
  - Because they lived longer than expected

Mullin et al. Experiences of children with trisomy 18 referred to pediatric palliative care services on two continents. *American Journal of Medical Genetics.* 2019.

Parent Perspective

- 89% reported child’s overall life experience was positive
- 98% reported child enriched their lives
- 82% positive effect on siblings
- 68% positive effect on marriage

Janvier et al. The experience of families with children with trisomy 13 and 18 in social networks. *Pediatrics. 2012.*

Parent Perspective

- 35% felt judged for choosing intervention
- All parents reported recommendation for comfort care
- For prenatal diagnosis, 61% had termination suggested
- Heard phrases like:
  - Incompatible with life (87%)
  - Meaningless life (50%)
  - Life of suffering (57%)
  - Be a vegetable (50%)

Janvier et al. The experience of families with children with trisomy 13 and 18 in social networks. *Pediatrics. 2012.*

Parental Hopes and Fears

- 80% wanted to meet their child alive
- Bring their child home
- Give their child a good life
- Be together as a family
- Fear of pain, life in hospital

Janvier et al. Parental hopes, interventions, and survival of neonates with trisomy 13 and 18. *American Journal of Medical Genetics. 2016.*

Choosing Thomas -- Inside a family's decision to let their son live,...
Facing death can be hardest for a family expecting new life. Follow T.K. and Deidrea Lauxs journey after they learn that their unborn son has a ...
youtube.com

- https://www.youtube.com/watch?v=ToNWquoXqJI&feature=emb_title

What makes a supportive clinician?

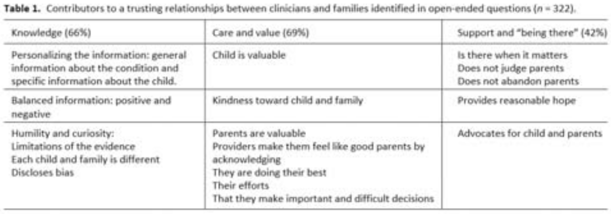


Table 1. Contributors to a trusting relationships between clinicians and families identified in open-ended questions (*n* = 322).

Knowledge (66%)	Care and value (69%)	Support and "being there" (42%)
Personalizing the information: general information about the condition and specific information about the child.	Child is valuable	Is there when it matters Does not judge parents Does not abandon parents
Balanced information: positive and negative	Kindness toward child and family	Provides reasonable hope
Humility and curiosity: Limitations of the evidence Each child and family is different Discloses bias	Parents are valuable Providers make them feel like good parents by acknowledging They are doing their best Their efforts That they make important and difficult decisions	Advocates for child and parents

Janvier et al. Building trust and improving communication with parents of children with Trisomy 13 and 18: A mixed-methods study. *Palliative Medicine.* 2019.

Where do disagreements come from

- 66% felt physicians did not see a unique baby
- 74% felt they had to fight to get therapies their child needed
- 35% felt judged for their decisions
- 42% did not want to be part of end-of-life decisions

PARENTAL RECOMMENDATIONS
Know the name of our child and use it.
Know the details of "our case" (charts and tests) before communicating with us
Personalize the information: tell us what organs are malformed, and which are not, and how these findings may affect the possible outcomes.
It helps us to know there is nothing we could have done to prevent this, to decrease the guilt we may feel.
Tell us about possible outcomes for our child -either in utero or after birth-. Emphasize the spectrum and uniqueness of each child and the lack of control we both have on many of these outcomes.
Balance the information. We need to know that caring for a disabled child is challenging, that experiencing the death of our child will likely be the most difficult time in our lives. But also tell us that our child's life – even if short - can have a positive impact on our family.
Recognize that this is a difficult time for us, that we are doing our best. Empower us as parents by telling us what we are doing well. We need to know that we are stronger than we think.
Words are important: do not tell us our child is a waste of resources and will harm us. Tell us our child has a life-limiting condition, not a lethal condition that is incompatible with life. Do not tell us there is nothing you can do nor ask us if we want "everything done". Be specific and focus on what you will do, not what you do not want to do. Don't use suffering as a means to discourage non-futile interventions.
Give us reasonable hope, as appropriate, for each step in the journey. For example, hope we can spend moments with our child -even in utero-, that we can meet our child at birth, that we can take our child home, that we can raise our child, that our child will eat on his own. Let us live these moments one step at the time.
Personalize decision-making. Tell us that parents are all different, that some want to take life-and-death decisions on their own, some want to take them with the medical team, and some leave that decisions for others -the team, God, Nature, the child- ask us which kind of parents we are and do not pressure us to decide if we don't want to.
Remember you are important to us and our family.
Suggest parents connect with a trisomy support group, such as Support Organization for Trisomy 13/18 (SOFT): http://trisomy.org

Figure 1. Synthesis of recommendations to providers, using the parental voice.

Shared Decision-Making

- Family-centered approach given existence in stable gray zone
- Clinical reasoning should be based on the specific case and not a broad generalization
- Present range of options available
- “some families” approach

Summary

- Not as simple as incompatible with life
- Recent data suggests potential long-term survival, especially if survive beyond 6 months
- Parents and physicians may have different views on quality of life
- Diagnoses live in a gray zone where several options are ethically permissible
- Palliative care can play an important role in supporting parents and helping teams provide care consistent with their goals

Sinclair Suggestions

- Always look up your topic on Twitter, YouTube, Reddit – you get good stories and insights that are different than Google. Consider them search engines like Pubmed and Google.
- Twitter – trisomy palliative – like this one – I didn't know this – birth of pediatric palliative care?
- YouTube This video has 5 million views! https://www.youtube.com/watch?v=ToNWquoXqJI&feature=emb_title