



Establishing a paediatric and adolescent oncofertility program: uptake of procedures and acceptance of fertility decisions in families at The RCH

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Australia : one of the highest incidences of childhood cancer

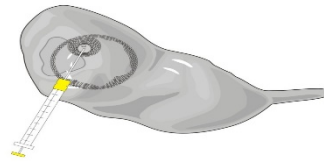


- Survival is excellent
- 1 in 900 aged 16 – 45 years is a childhood cancer survivor
- Fertility a major survivorship consideration
- Childhood cancer survivor study: 10938 survivors 3943 siblings, 27 centres, reduced chance of livebirth compared to siblings:
 - Females 15-29 years 18%;
 - Females 30-44 years 37%;
 - Males 15-44 years 40%; Chow et al Lancet Oncol 2016:
- International guidelines recommend discussing impact of cancer treatment on fertility and potential fertility preservation options (ASCO 2013, NICE 2013. ASRM 2013)

Fertility Preservation

- Females

Oocyte collection



- Experimental:

Ovarian tissue cryopreservation (OTCP) :



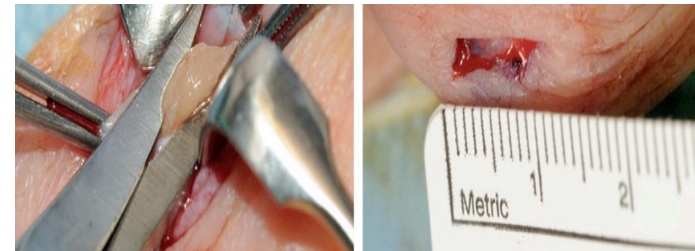
86 live births, 2 from
childhood
30% efficacy

- Males

Sperm collection

- Experimental

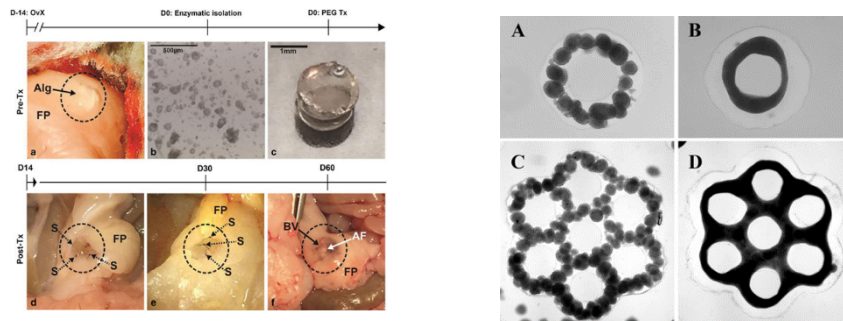
Testicular tissue cryopreservation (TTCP)



FAURE 2016, YOKONISHI 2016

Malignant reseeding leukemia

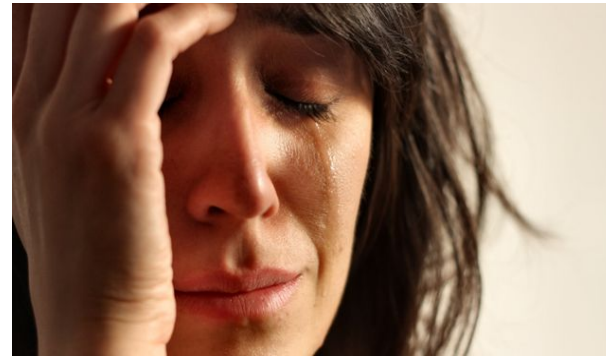
- Tissue can harbour malignant cells
- Research being done : invitro maturation of gametes on Biogel or 3D printed artificial ovary, artificial testis



Soares 2017 Kim 2015, Xiao 2015, Carson 2013, Laronda 2015 YOKONISHI 2016 Dores 2014,

- **Paediatric oncofertility takes clinicians out of their comfort zone**
- Lack of information about fertility : the most unmet information need¹ , 35-64% of survivors are dissatisfied/distressed with quality of fertility information²

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Decision Regret

- Want clinicians to be more proactive so that they can make informed decisions, and instigate coping strategies

Established a Fertility Taskforce in 2012 :

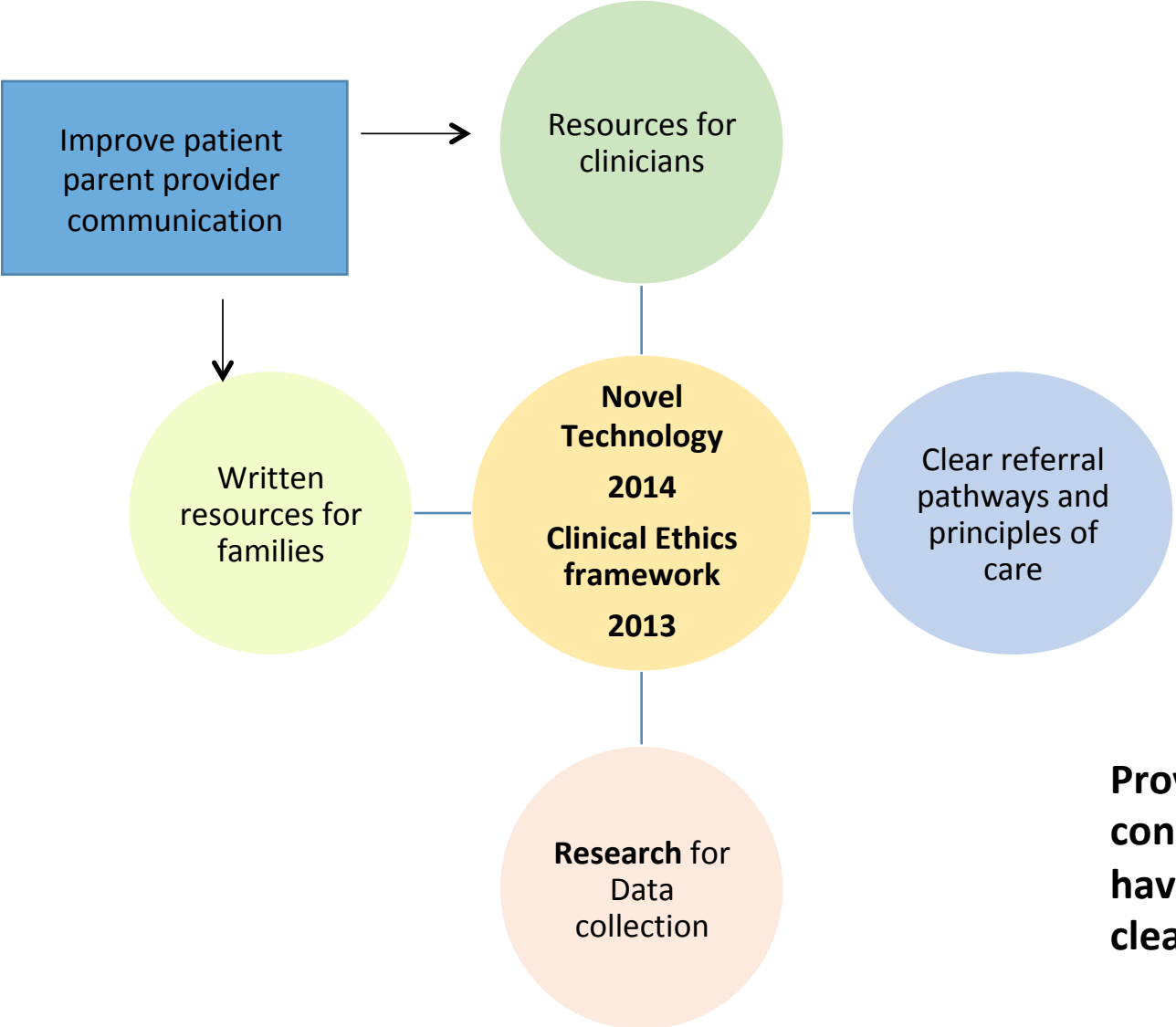


The late Dr Sarah Drew
Thinking about fertility:
Narratives of young adult
survivors of cancer in
childhood or adolescence
(2002)

Aim

1. To describe the establishment of a formalised fertility program at RCH (Aug 2013)
2. The uptake of fertility procedures at The Royal Childrens Hospital since 1987
3. Describe safety and efficacy data
4. Describe decisional regret in families seen since 1987

Setting : 3 levels of governance



Provide education and consultation to all patients having curative treatment in a clear consistent manner

Methods

Families past and present, consent to

1. Use of medical records for research

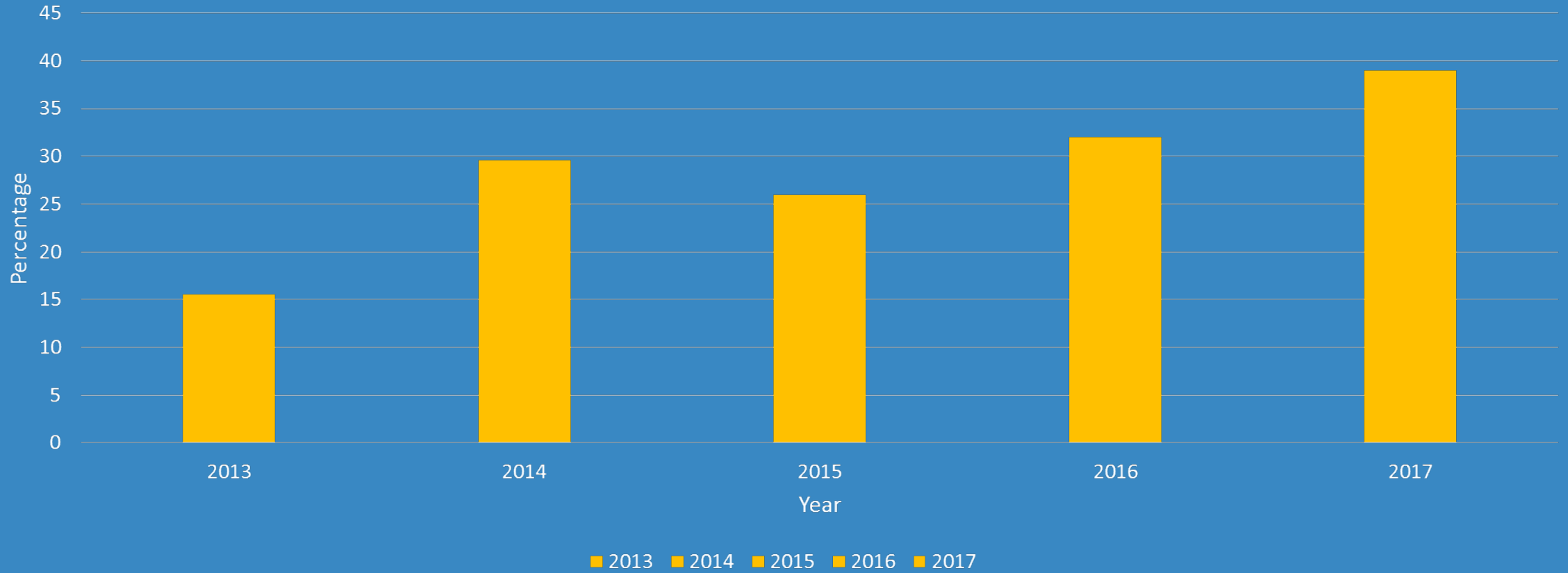
2. Linkage to IVF and register of births

3. Future research: if yes, then a Decision regret survey

was sent to parents and those ≥ 15 years [Validated regret scale

Breuhat et al.]

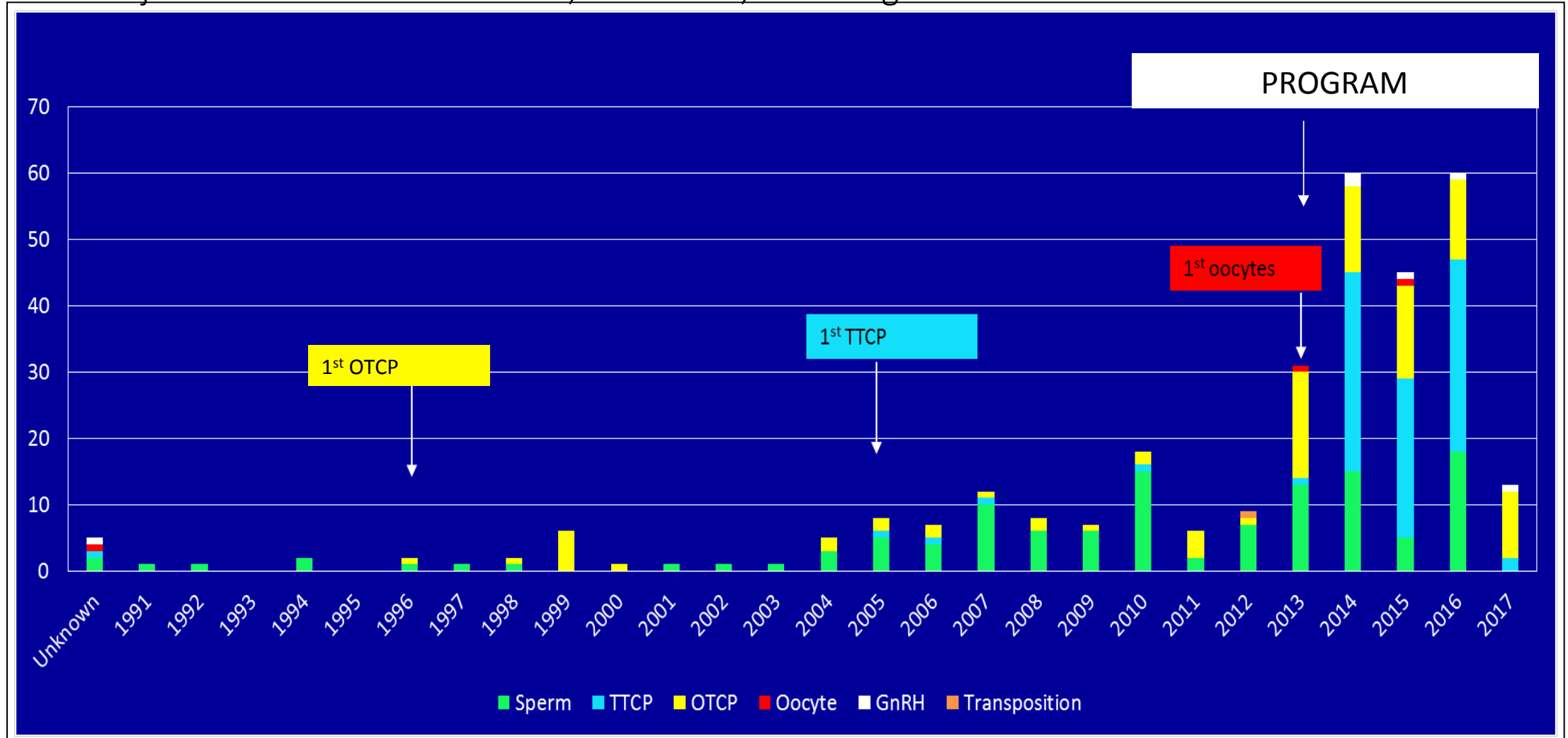
Fertility Discussions documented in chart over time



This is the KPI , not the procedures

Fertility Preservation Procedures Over Time

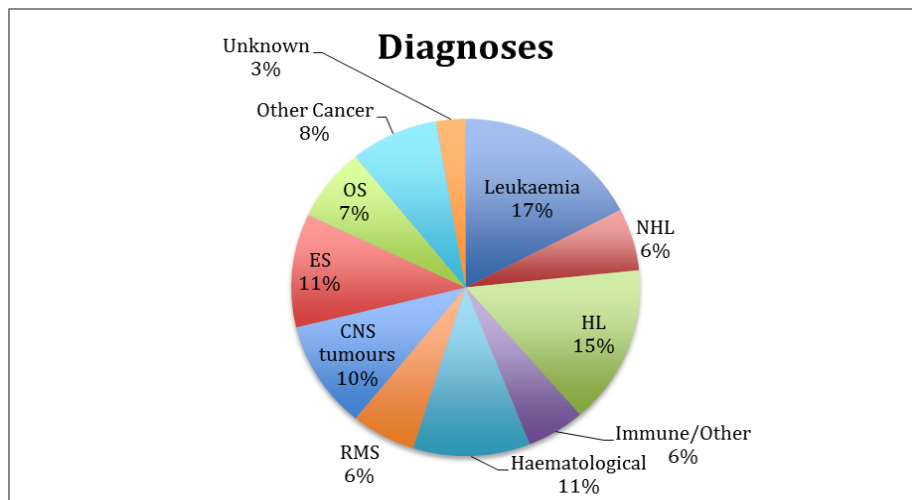
307 subjects consented : 227 had FP, 76 did not, 4 missing



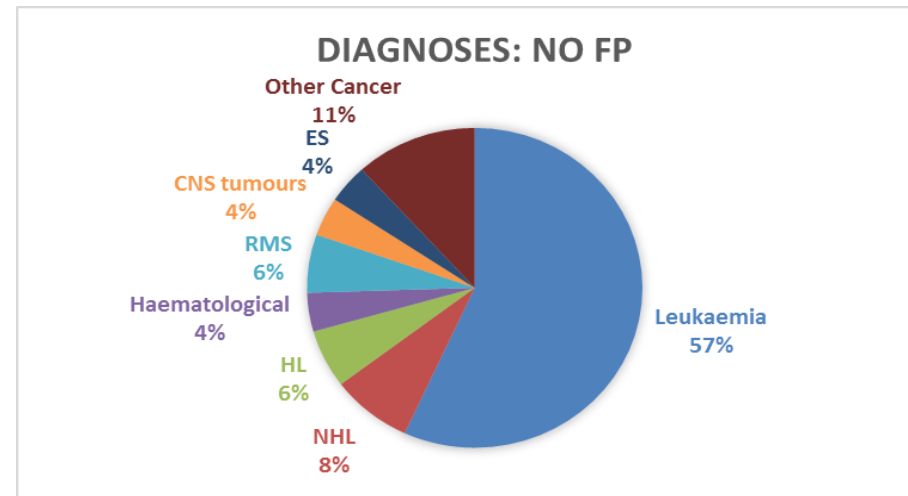
TTCP = Testicular Tissue Cryopreservation
 OTCP = Ovarian Tissue Cryopreservation
 GnRH = Gonadotropin-releasing hormone agonist
 Transposition = Moving one or both ovaries away from a pelvic radiation field

Comparing FP yes versus FP no

- FP yes n=227



- FP no n=75



	FP yes n%	FP no n%	
Median age years	13.9 [IQR 9.1-15.6][range 0.2-18.6]	5.6 [IQR 3.2-5.6][range 0-17]	P<0.001
Male	143 (87.7)	17 (10)	P<0.001, 5.8 [3.1-11.3]
Female	84 (59.2)	58 (40.8)	
Christian	106 (46)	30 (40)	P=0.82
No religion	96 (43)	33 (44)	
Risk to fertility medium or high	197 (86.8)	46 (61.3)	P<0.001, 4.1 [2.2-7.9]

Safety and Efficacy Data

- **OTCP n=78**

- 4 umbilical port infections 5%
- 2 bleeding settled with diathermy 2.5%
- 1 tear bowel serosa 1.2%
- 1 delay to chemo 1.2%

- follicle density of 0.3-134/mm², no malignancy
- 4 had oocytes in tissue
- 14 had prior chemo

- **TTCP n=60**

- 1 scrotal dehiscence 1.6%

- about 25 mm², 2-5 mm slices, no malignancy
- 15 had mature sperm in tissue
- 8 had prior chemo

Follow-up

12% who had FP subsequently passed away due to disease
4 went on to collect eggs

Decision regret



108 parents and 30 patients (76% participation rate), completed a validated decision regret survey about the fertility decision

98% had medium to high risk of infertility,

70% had had Fertility Preservation

50% within 1.5 years of diagnosis

10% could not recall discussion (> 75% leukemia, prepubertal, low risk)

High expectations regarding the success of FP in their lifetime

		Current lifetime
Established	Sperm or oocyte cryopreservation	
	Ovarian Tissue cryopreservation / GnRH analogue	
Experimental	Testicular Tissue cryopreservation	

LEGEND

■ Strongly agree

■ Agree

■ Neither agree or disagree

■ Disagree

RESULTS

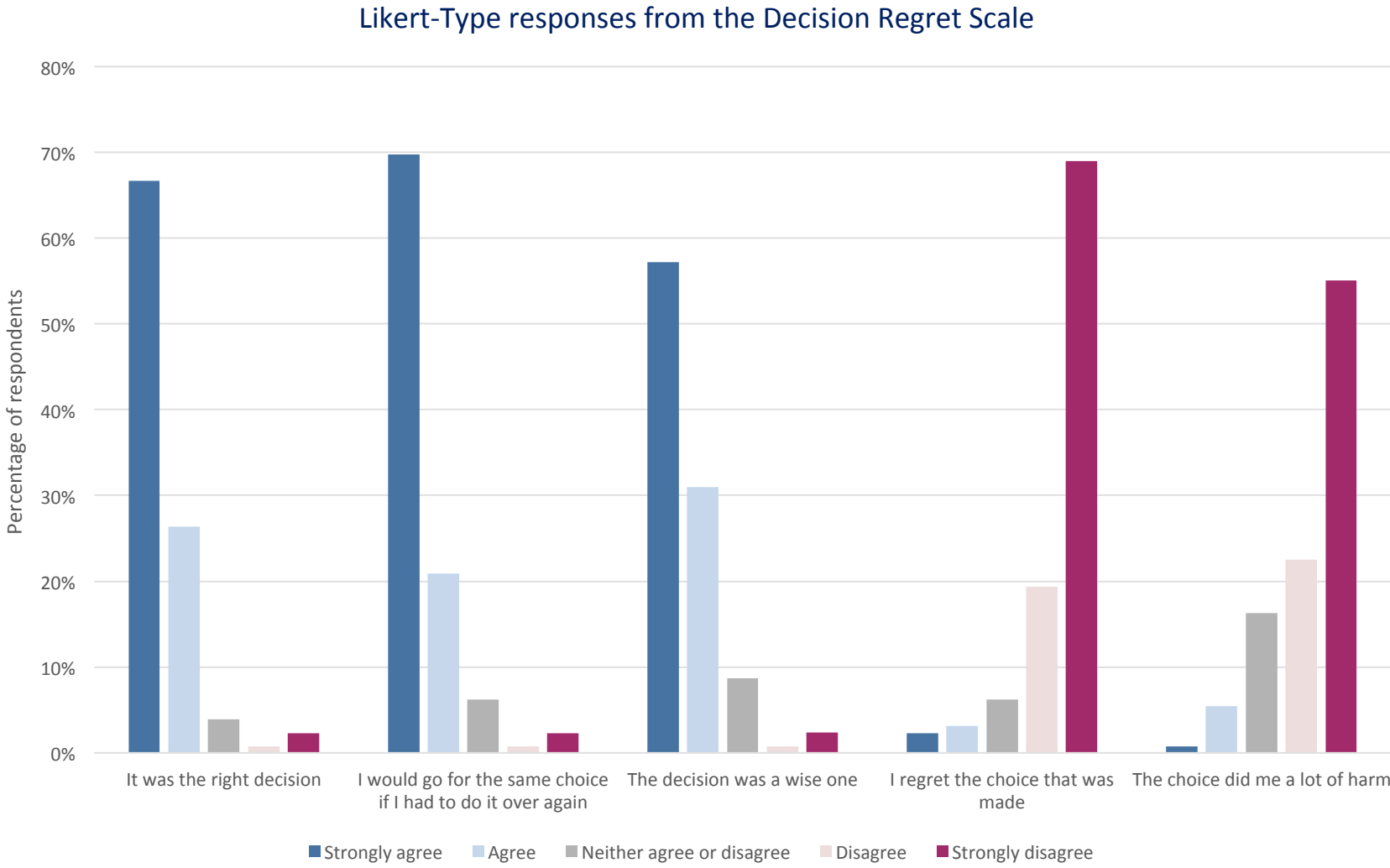


Figure. Item-level analysis of the Decision Regret Scale

RESULTS

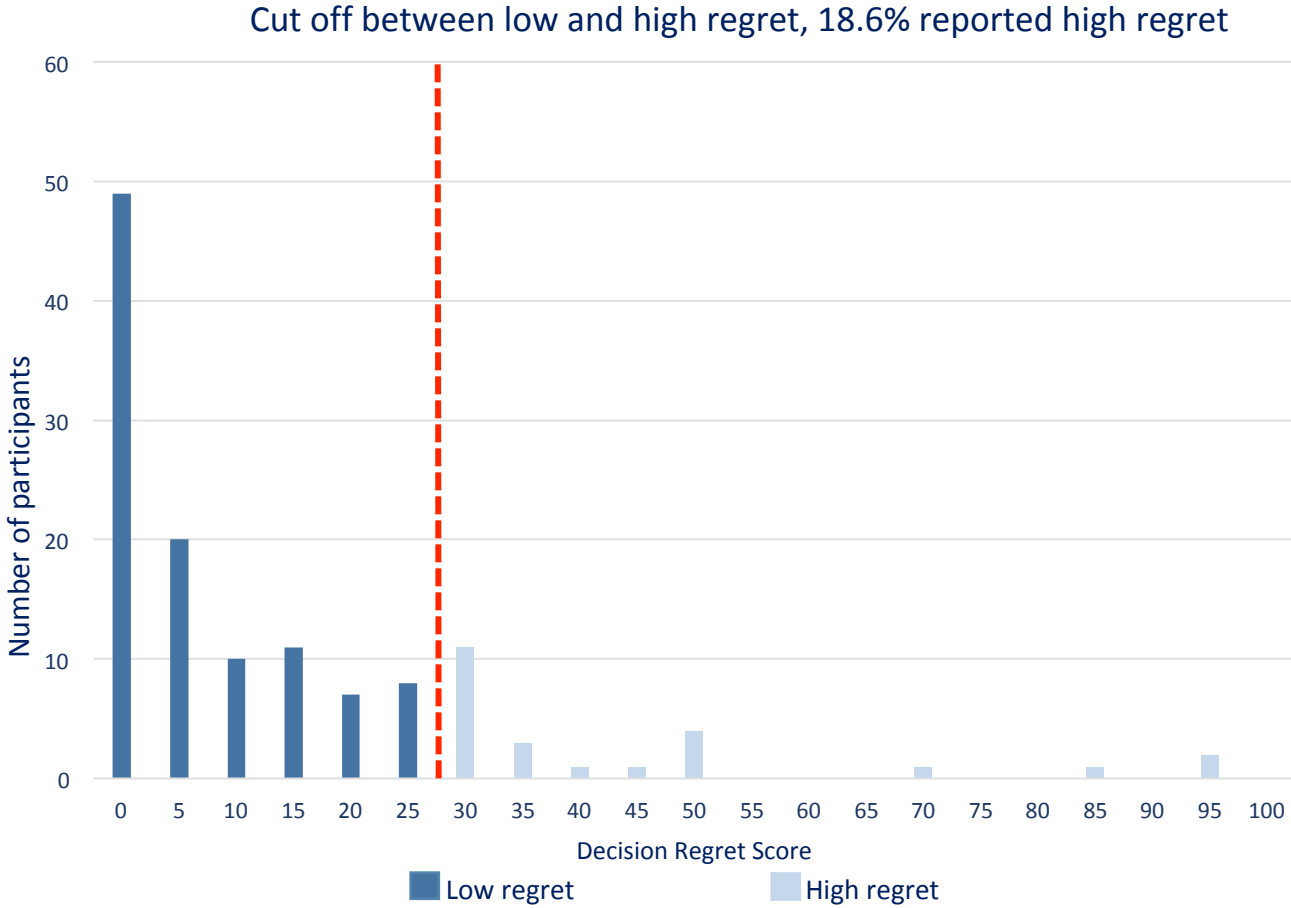
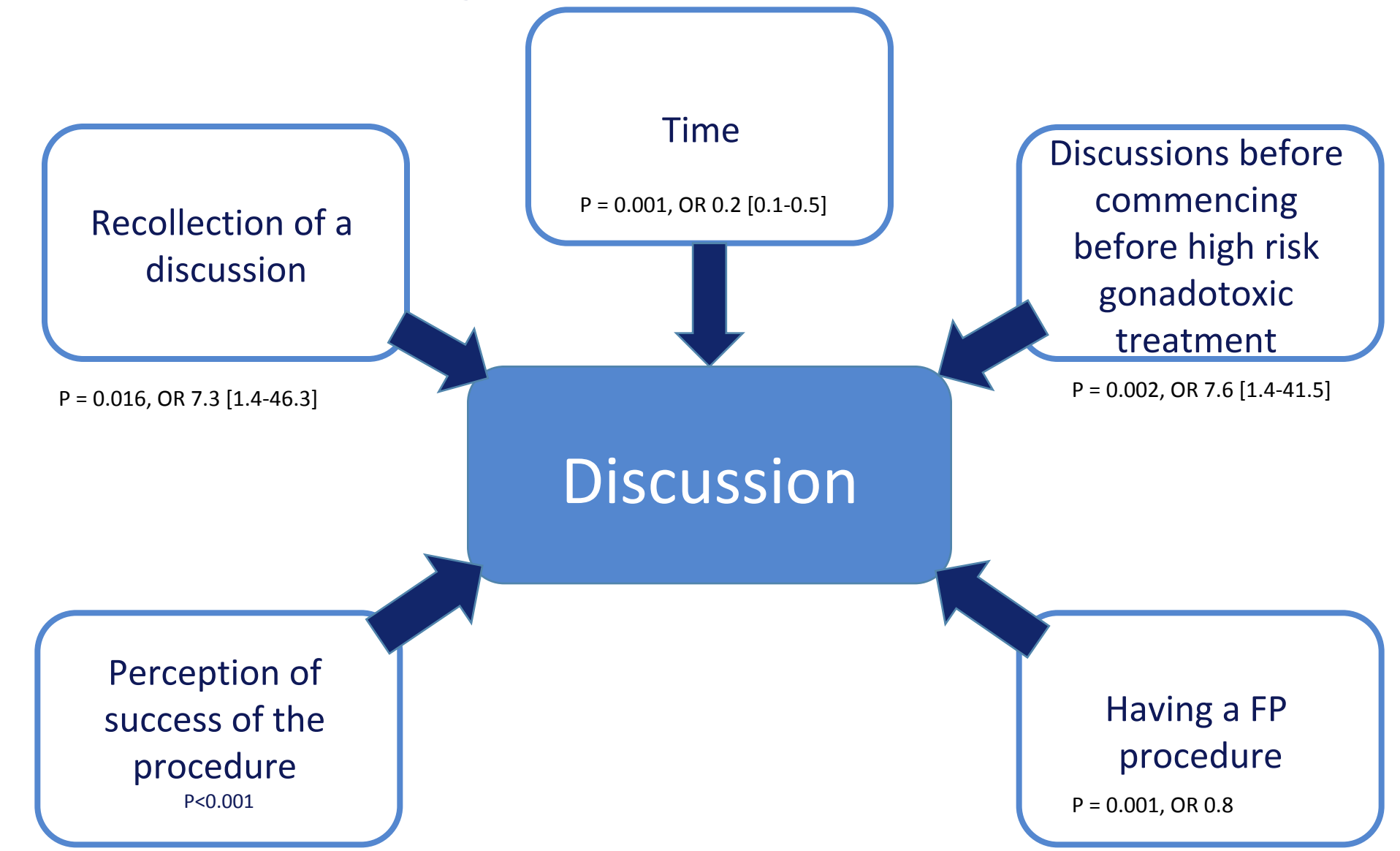


Figure 1. Decision Regret scores at the time of the initial survey for each participant (N=129), calculated using the Decision Regret Scale by Brehaut et al.

What reduces regret?



CONCLUSION:

Childhood cancer can redefine life priorities for families

Formal research-informed oncofertility program

Serve the need of families while bringing it into the safe zone for clinicians

Our friend and colleague, the late Dr Sarah Drew wanted us to act in the right spirit, out of an abiding respect for the autonomy of families

We have a lot of work to do: improve information support, avoid false hope, coordinated care

The plane has not landed

Thankyou 😊

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- Dr In Young Chung
- Students : Catherine Allingham, Meredith Hand, Sadunee Jayasuria, Hannah Clarke, Nancy Li



Results : 76% participation

- 108 parents (mean age 40.0 ±6.7), 82.4% female, 79.6% Australian born
- 30 patients (mean age 20.0 ±6.3), 46.7% female, 86.7% Australian born
- Child demographics at diagnosis: age 8.6 ±6.0, 68.1% female, 98% medium to high risk of infertility, **70% had fertility preservation**
- Time point they received survey:

	FP Yes	FP No	Total (%)	
2 months	13	1	14	(10.1%)
6 months	20	10	30	(21.7%)
12 months	24	4	28	(20.3%)
> 18 months	40	26	66	(47.8%)

Development of RCH Clinical Ethical framework (co-chair Lynn Gillam)

Ethically appropriate to offer the procedure in some circumstances in the absence of proven benefit, within a system of governance because

- the risks of obtaining the tissue are low (in most cases)
- there is an identifiable pathway to achieving the intended benefit (with research work currently being done)
- the value likely to be placed by the patient on fertility in the future is very high.

The clinician has to judge if it is medically safe, and makes usual recommendations to families. Decision is value-laden thus within the zone of parental discretion.

Procedures undertaken 1987-2017, are they appropriate?

	Sperm	Ovarian tissue	GnRH alone	Testicular tissue	Oocyte	Total	%
Prepubertal	0	36	0	37	0	73	32.0
Postpubertal	82	41	5	17	2	147	64.7
Unknown	0	1	0	6	0		3.1
Low risk <20%	5	3 (3.8%)	2	0	0	10	4.4
Medium risk	19	13	2	12	1	47	20.7
High risk ≥80%	49	55	1	44	1	150	66.1
Unknown	9	7	0	4	0	20	8.7
Total	82 (36.0%)	78 (35.0%)	5 (2.2%)	60 (26.4)	2 (1.1%)	227	100 %

12% who had FP deceased now

Wallace et al 2005, Sklar et al 2006 , Barton et al 2013 Stern et al COYAA

In their words

- *'...at the time we had to ask what was availableit was not offered, it could have been missed ...'*
 - *Parent low regret OTCP*
- *'The discussion was at a very late stage, rushed and without [enough] time to adequately address [the] fertility preservation process.'*
 - *Parent sperm collection suboptimal sample, high regret*
- *'As it was ovarian slices, my IVF specialist is hesitant to use them, as they may contain leukaemic cells. Until recently I felt [starting a family] would happen either way, however that is not the case.'*
 - *Patient OTCP in 1996, low regret*
- *At the time of diagnosis I was too young and immature to be making my own decisions about fertility preservation, an option that would have longstanding uses. Thus I am happy a decision was made for me by an older individual.'*
 - *Patient TTCP low regret*
- *'I was very impressed by the initiative taken on my behalf. I was very satisfied.'*
 - *Patient TTCP low regret*
- *"I want my child to know that we did all [we could] "*
 - *Parent OTCP low regret*