


Paediatric and adolescent oncofertility: procedure uptake and family acceptance of fertility decisions

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- Families regard oncofertility care as one of their highest unmet needs
- No consensus on fertility preservation management of paediatric patients
- The rapidly evolving technologies, outpacing clinical guidance, limited efficacy
- Takes clinicians into zone of clinical uncertainty
- Variation in clinical practice, based on clinician preference/parental demand

ASCO 2013, NICE 2013, ASRM 2013, McQuillan JPO 2013,

- Parents surrogate decision makers
- Complex decision in time pressured and vulnerable environment
- Experimental nature is not a deterrent



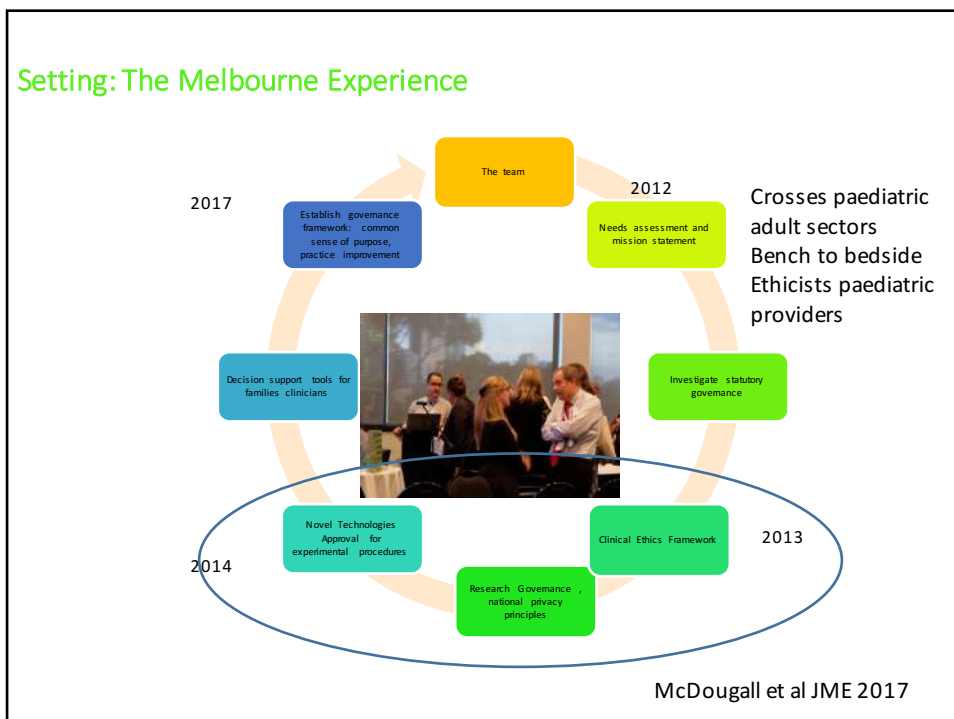
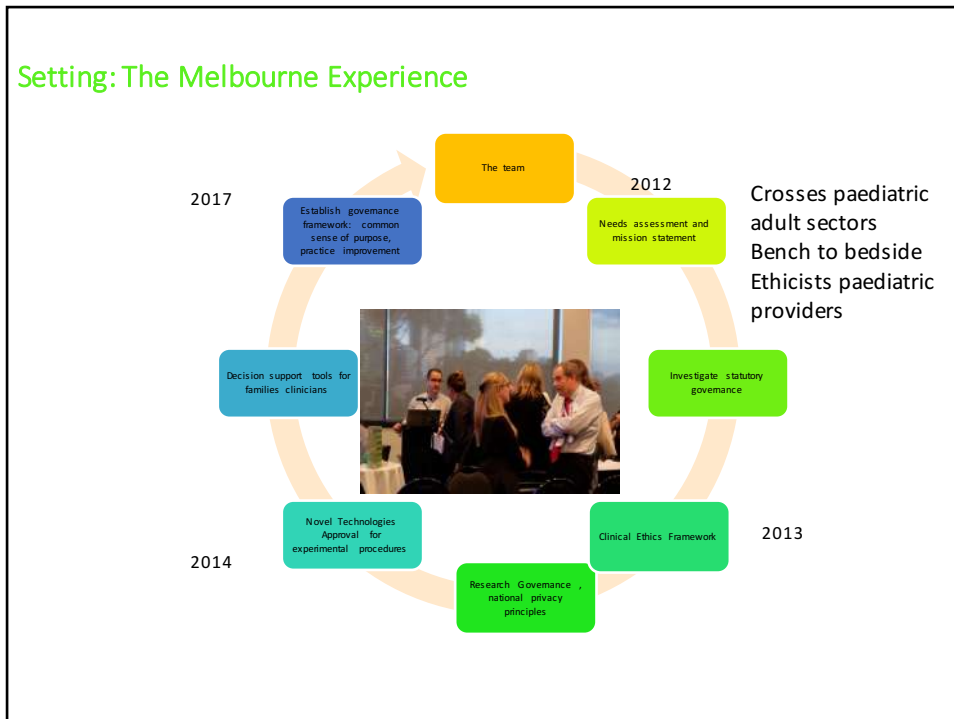
➔ Decision Regret

Connor AM. Medical Decision Making. 1995
Peate et al. BMC 2012, 10(6), 1053-1061
Li et al 2016 JAVAO

Wyns et al., 2015;
Ginsberg et al., 2014.

Aim

1. To describe the establishment of a formalised fertility program at RCH (Aug 2013-2017)
2. The uptake of fertility procedures at The Royal Childrens Hospital (had been doing so ad hoc since late 1980's)
3. Describe safety data
4. Describe decisional regret in families



Setting : The clinical principles

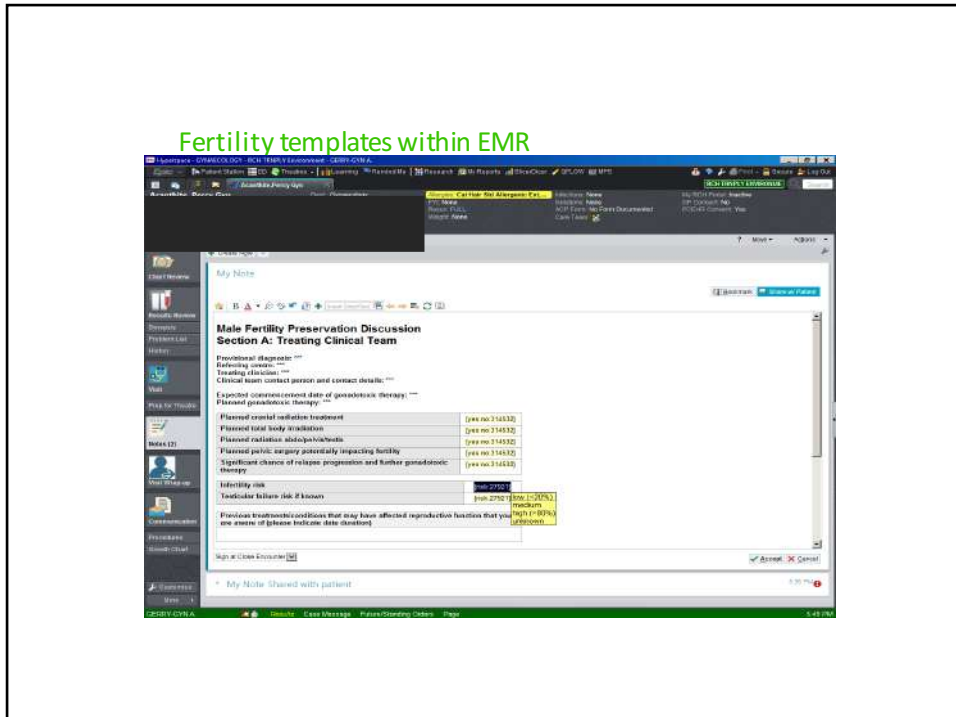


- Real aim is to facilitate informed discussions, decisions and coping mechanisms, irrespective of fertility outcome **as we cannot guarantee future fertility**
- to **all patients and/or families with curative intent** in a clear and consistent manner (by oncology)
- Consider Referral (Paed gynaecology, Endocrinology/ Surg):
 - All pubertal children at any risk of infertility
 - Pre-pubertal children at mod-high risk of infertility
 - At request of patient/family
 - At discretion of oncology team

RGH intranet

The screenshot shows the intranet page for 'Fertility preservation' at The Royal Children's Hospital Melbourne. The page is organized into several sections:

- For health professionals**: This section includes a link to 'Males - Fertility Preservation Documents' and a note that the fertility preservation pathway for males opens in a new tab. It also lists 'General guidance' with links to PDFs for fertility preservation guidance, endocrinology, paediatric endocrinology, and sperm preservation procedures.
- Research treatment forms**: Lists forms for fertility preservation consent for patients under 18, over 18, and adult fertility preservation services.
- Sperm cryopreservation**: Provides information resources for families, including links for storage consent after cancer, sperm storage, and male infertility.
- Storage consent forms and pathology slips**: Lists forms for urology consent, sperm storage, and pathology slips.
- Testicular tissue cryopreservation**: Provides information resources for families, including a link for testicular tissue preservation.
- Storage consent forms**: Lists a form for MZP consent and testicular tissue storage.

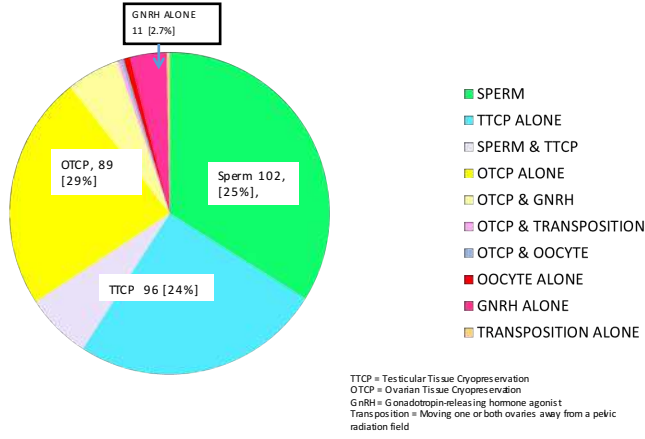


Methods:

Families past and present, consent to

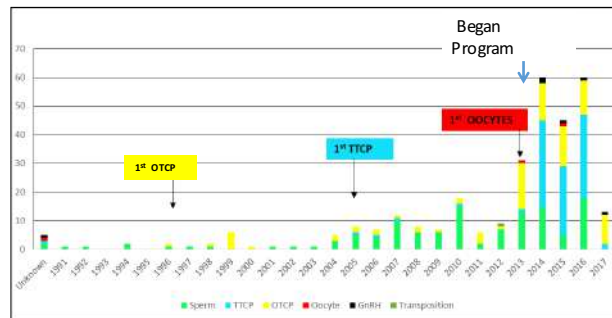
1. Use of medical records for research: collect oncofertility, safety and efficacy data
2. Linkage to IVF and register of births
3. Future research: if yes, then a Decision regret survey was sent to parents and those ≥ 15 years
 [Validated 5 item decision regret scale Brehaut et al. 2003]

Results : number of FP interventions 1987-2016 (n=301)



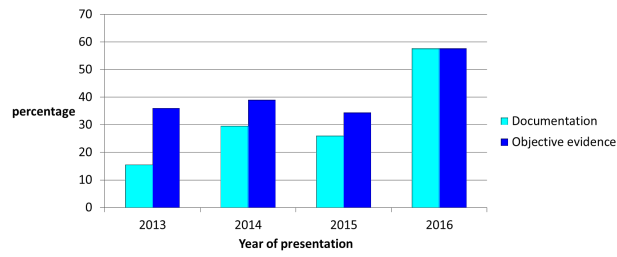
Results :Fertility Preservation Procedures Over Time

306 subjects consented to research: 226 had FP, 76 did not, 3 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

Evidence of discussion about fertility since the formalised program was introduced



This is the KPI , not the procedures

Comparing FP yes versus FP no

• FP yes n=226
n=76

FP no



	FP yes n%	FP no n%	
Median age diagnosis years	11.6 (0.9-19)	7.0 (0-17)	P<0.001
Male	143 (87.7)	17 (10)	P<0.001, 5.8 [3.1-11.3]
Female	83 (59.2)	60 (40.8)	
Christian	106 (46)	30 (40)	P=0.82
No religion	96 (43)	33 (44)	

3 OTCF done in low risk patients

Safety and efficacy

	OTCP n=89	TTCP =96	FP no =75)
complications	4 port infections	1 scrotal dehiscence	
	2 bleeding		
	1 tear bowel serosa		
	1 delay to chemo		
time from referral to be seen	Median 0.5 days [IQR0-5,]	Median 0 days [IQR0-15]	
tissue	Follicle density 0.3-134/mm ² ,	2-5 mm slices	
	No malignancy	No malignancy	
	4 oocytes	15 had mature sperm dissected	
Follow-up	4 collected oocytes		
Deceased	8/77 (10.4%)	5/60 (8.3%)	2.8%

Ho et al Clin Endo 2017

Results 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)

Brehaut et al 2003

Results Decision Regret

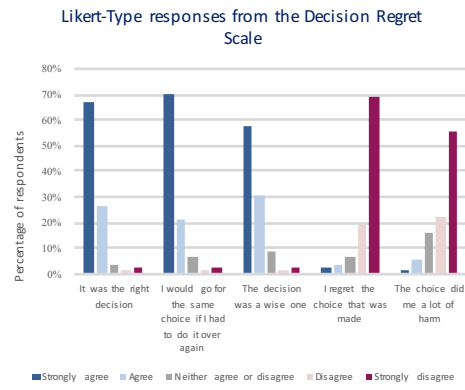
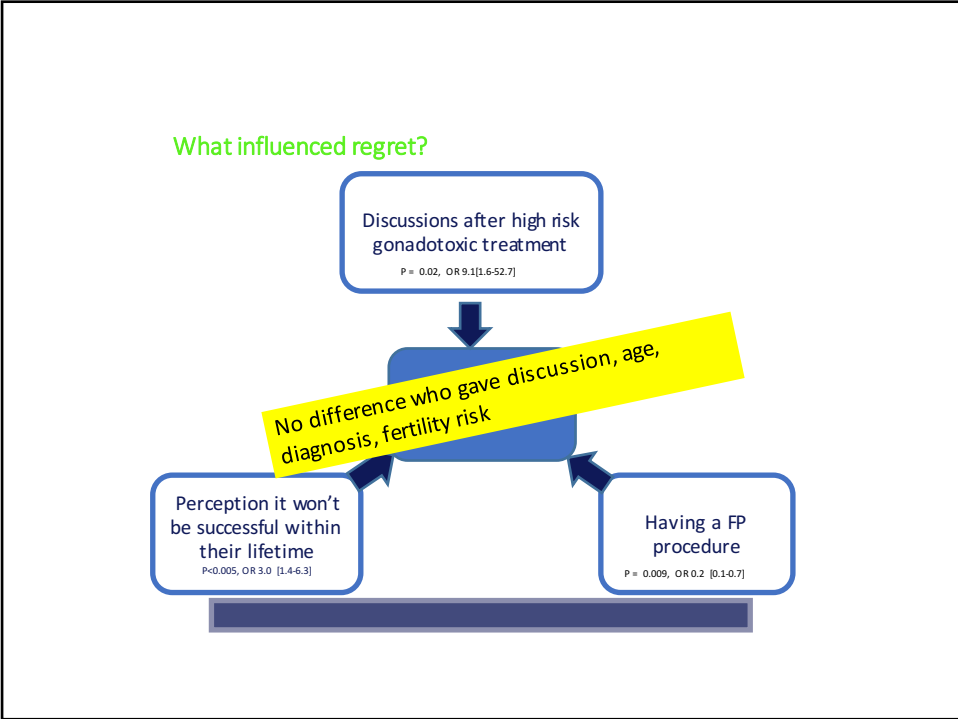
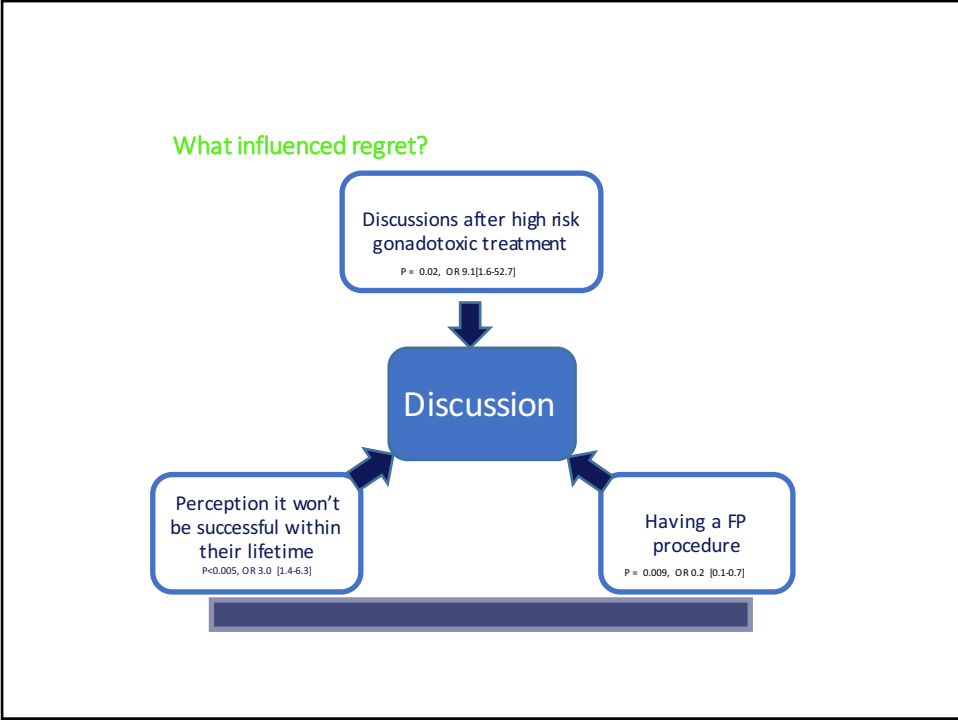


Figure. Item-level analysis of the Decision Regret Scale

Results Decision Regret



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.



Conclusions:

Formal research-informed oncofertility program:
serve need of families while bringing it into
the safe zone for clinicians



Acting in the right spirit:
Needs high levels of ethical oversight, Long term evaluation

Thankyou ☺

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- Studer



VICTORIAN
COMPREHENSIVE
CANCER CENTRE



Victorian
Cancer
Agency



the women's
health research hospital



MONASH University

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.

Clinical Ethics review required

- Prepubertal patients
- Delay to ca treatment
- Not minimal risk
- Low risk of fertility loss
- Significant risk of not leaving one gonad intact
- Discordance
- Parents unwilling to inform the child
- No curative intent
- Unlikely to be able to use the tissue
- Any treating clinician has ethical concerns

McDougall et al JVE 2017

Is it legal?

- Does not need family court approval
- Storage may be for 20 years
- Tissue may never be used for research, even after death
- Tissue can never be used by another person



Setting : Ethical Framework

Primary ethical arguments :

- low risk (with careful selection),
- long lag phase, rapidly advancing research,
- reproductive damage irreparable
- value likely to be placed on future fertility high.



Expected benefits have to be proportionate to the risk

- fertility threatened
- capacity to benefit (ie tissue is healthy, can be retrieved and reimplanted)
- low risk (won't jeopardise cancer treatment, no co-morbidities to increase risks)

Clinical ethics checklist, oversight of individual cases more rigorous than research

McDougal JME 2017

RESULTS – Impressions regarding success of FP

		Within current lifetime	
Established	Sperm or oocyte cryopreservation	12 %	35 %
	Ovarian Tissue cryopreservation	44 %	40 %
Experimental	Testicular Tissue cryopreservation	3 %	62 %

Legend:

- Strongly agree
- Agree

Procedures undertaken 1987-2016, appropriate?

	Sperm	Ovarian tissue n=77	GnRH alone	Testicular tissue n=60	Oocyte alone	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%)	77 (35.0%)	5 (2.2%)	60 (26.4)	2 (1.1%)	226	100%

- *"I want my child to know that we did all [we could] ..."* Mother OTCP low or no DR
- *discussion was at a very late stage, rushed and without [enough] time to adequately address [the] fertility preservation process.* Father, son had sperm collection, high DR
- *'...at the time we had to ask what was availableit was not offered, it could have been missed ...'* Mother, OTCP low or no DR
- *'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 or no DR
- *'I was very impressed by the initiative taken on my behalf. I was very satisfied.'* Patient TTCP low or no DR
- *'As it was ovarian slices, not eggs, my IVF specialist is hesitant to use them, as they may contain leukaemic cells. I wish they had frozen the eggs instead. Until recently I felt [starting a family] would happen either way, however that is not the case.'* Patient OTCP low or no regret