Evidence tables communication considerations fertility preservation

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?			
Anderson et al. Do doctors discuss fertility issues before they treat young patients with cancer? Hum Reprod 2008;23:2246-51			
Study design & Main study objective	**Participants and relevant characteristics**	**Relevant results (per outcome)**	**Additional remarks**
1. Study design Prospective, observational study 2. Main study objective: To investigate current practices of UK pediatrics oncologists regarding fertility preservation discussion and consequent referral patterns 3. Additional study characteristics, if relevant: - Data form for each patient in 12 month period:	1. Type and number of participants: Paediatric oncologists completed forms for 1030 patients *Response rate:* 68% Patients registered in 17 (out of the 22) Children's Cancer and Leukaemia Group (CCLG) Centres 567 (55%) Males 463(45%) Females 2. Age (at diagnosis) of participants: NR 442(78%) Pre-pubertal males 83(15%) Pubertal males 42(7.4%) Post-pubertal males 339(73%) Pre-pubertal	1. Outcome(s) definition: Outcome 1. Discussion of the impact of treatment on future fertility Outcome 2. Discussion of methods for preserving fertility and referral to fertility centers **Results outcome 1:** *1. 1 Barriers to discussing treatment impact on fertility* 382 (37%) patients did not have a discussion with their clinician regarding the impact of treatment on future fertility Reported barriers included patient's infertility risk regarded as 'not significant' (300, 79%); patients seen as too young (93, 15%); patients' poor prognosis 48(13%); severity of patient's illness (19, 5%); unproven fertility preservation techniques (9, 2%); and inadequate facilities and/or funding (2) Pubertal status highly predictive of discussion in girls ($p<0.001$), and boys ($p<0.05$) *1.2. Characteristics of discussing treatment impact on fertility with males* Pubertal/postpubertal boys: discussion with 91 (73%) Prepubertal boys: discussion with 271 (61%) Pre-pubertal boys: 130(76%) were judged not at significant risk, and 55(32%) as too young	Limitations: - Survey response rate 68% (authors argue age/diagnosis distribution is representative of the national cohort) - Risk of reporting bias: form completed by oncologist after seeing patient - Outdated in relation to FP practices (all FP techniques considered experimental except from sperm cryopreservation for postpubertal boys) - Assessment of fertility risk based on oncologist own knowledge and not guidelines (although study outcome is to assess provision of information with risk classification and not if classification is correct) - No detailed reasons for no discussion of impact of treatment in fertility in girls (only reported in boys)

from 1st November 2003 - The study recruited centers, the centers data management resources completed forms	females 75(16%) Pubertal females 49(11%) Post-pubertal females <u>3. Number of participants per diagnosis:</u> NR <u>4. Additional participants characteristics, if relevant:</u> 76% Chemotherapy 23% Radiotherapy 9% Uncertainty as to whether radiotherapy	*1.3. Characteristics of discussing treatment impact on fertility with females* Pre-pubertal: 60%; Pubertal:55%; Postpubertal: 86% Discussion with 286(62%) of girls **<u>Results outcome 2:</u>** *2.1. Barriers to discussing fertility preservation methods* 532(52%) patients did not have a discussion with their clinician regarding fertility preservation methods Barriers to the discussion included that patients were too young (299, 56%), patients 'not at significant risk' (258, 48%), unproven fertility preservation techniques (133, 25%), severity of patient's illness (69, 13%) and unlikely to survive (13, 2.4%), inadequate funding and/or facilities (62, 12%) 274/532 (52%) patients perceived as, and informed to be, at significant risk but no discussion *2.2. Characteristics of discussing FP methods with males and females* - Discussion on FP methods in 116 patients: 78(67%) were males and 38(33%) females - 30% of each sex were at high risk - FP methods were discussed more common among boys than girls (22 vs 13%) - Reproductive specialist provided information for 31 (27%) patients *2.3. Characteristics of discussing FP methods with male* - Topics discussed: Ejaculation (n=78); Electroejaculation and Epididymal aspiration (n=3) - Referral to conception clinic: 83% post-pubertal boys,	

		13(39%) pubertal boys at medium/high risk, 6(15%) at low risk - Pre-pubertal boys: discussed with 20(7.4%); 1 boy referred to conception clinic *2.4. Characteristics of discussing FP methods with females* - Topics discussed: oophoropexy (4, 10%), ovarian tissue cryopreservation (21, 55%), oocyte cryopreservation, (11, 29%), embryo cryopreservation (4, 10%) and hormone protection (3) - Referral to conception clinic: 4(1%); of these 1 high-risk prepubertal and 2 high risk, 1 medium risk postpubertal <u>4. If applicable, results per additional outcomes:</u>. - Discussion about impact of treatment on fertility usually raised by oncologist, but instigated by parent (7%), and patient (2%), - Most cases discussion of impact of treatment on fertility at diagnosis, in 7% of cases during treatment	

NR: not reported; FP: fertility preservation

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?			
Bashore et al. Semen preservation in male adolescents and young adults with cancer: one institutions experience. Clin J Oncol Nurs 2007;11(3):381-6			
Study design & Main study objective	**Participants and relevant characteristics**	**Relevant results (per outcome)**	**Additional remarks**
<u>1. Study design</u> Observational report <u>2. Main study</u>	<u>1. Type and number of participants:</u> 32 male patients with initial and recurrence cancer diagnosis	<u>1. Outcome(s) definition:</u> - Describe who successfully banked sperm (viable semen sample suitable for freezing) - Describe reasons for not successfully banking sperm	<u>1. Strengths:</u> Examined all eligible males in 16- month period when funds were not an issue as institution paid for sperm banking

objective: To describe one institutions experience with semen cryopreservation over 15 month period 3. Additional study characteristics, if relevant: This institution had funds from the now defunct organization Lance Armstrong Foundation to provide sperm banking and storage for ten years	2. Age (at diagnosis) of participants: NR Range age at diagnosis of patients who successfully banked their sperm: 14-22 years 3. Number of participants per diagnosis: (only provided for those who successfully banked) 8(53%) ALL 2(13%) NHL 1(7%) GCT 1(7%) PNET 1(7%) OGS 1(7%) RMS 4. Additional participants characteristics, if relevant Patients included in the study were either initially diagnosed or with a recurrence	2. Results outcome 1: 15(47%) successfully banked (by masturbation) 3. Results outcome 2: *Barriers to sperm banking* 7(22%) patients were too ill to provide sperm sample 2(6%) parents did not consent for sons to be approached to discuss sperm banking: 1 parent due to religious beliefs; 1 parent felt that masturbation was not adequate for their son to perform *Unable to produce sperm sample* 8(25%) patients unable to produce adequate sperm sample; 2/8 (25%) azoospermic 4. If applicable, results per additional outcomes: - Discussions did not always happen privately with the adolescents - Provision of written material provided	2. Limitations: - Did not include data for those unable to bank - Treatment for fertility preservation may be outdated - Single institution study: results have low external validity - No separate results section in article

NR: not reported; ALL: acute lymphoblastic leukemia; GCT: germ cell tumor; NHL: non-Hodgkin lymphoma; OGS: osteogenic sarcoma; PNET: primitive neuroectodermal tumor; RMS: rhabdomyosarcoma

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?			
Clayton et al. Trends in clinical practice and nurses' attitudes about fertility preservation. Oncol Nurs Forum 2008;35:249-55			
Study design & Main study objective	**Participants and relevant characteristics**	**Results (per outcome)**	**Additional remarks**
1. Study design Cross-sectional (surveys) study 2. Main study objective To examine attitude and behaviors of pediatric oncology nurses regarding fertility preservation and evaluate their awareness of ASCO fertility preservation guidelines 3. Additional study characteristics, if relevant Surveys were conducted between 2005 and 2006	1. Type and number of participants 210 pediatric oncology nurses (115 in 2005, 95 in 2006) *Response rate*: 65% in 2005; 67% in 2006 2. Age (at diagnosis) of participants NA 3. Number of participants per diagnosis NA 4. Additional participants characteristics, if relevant	1. Outcome(s) definition Outcome 1: Trends in nurses attitudes toward FP discussions Outcome 2: Trends in impact of patient factors on FP discussions Outcome 3: Potential Institutional barriers for FP 2. Results outcome 1 - Nurses attitudes about FP discussions with pts did not change during the survey period - Majority of nurses felt FP discussions were their responsibility; 91% in 2005 and 81% in 2006 - The majority of nurses reported that they felt pts with cancer at risk for infertility should be offered FP (93% in 2005, 94% in 2006) - The majority of nurses felt that patients must be made aware of their risk for infertility including patients that are less than 18 and regardless of parental consent (72% in 2005 and 68% in 2006) 3. Results outcome 2 - Nurses likelihood to discuss FP with pts with specific characteristics significantly changed over time - FP discussions were just as likely for single pts as they were for those married or recently engaged. - In 2006, however, nurses were more likely to discuss FP options with pts who had at least one child or who had a poor prognosis for survival (5% in 2005 v 22% in 2006). - The majority of nurses indicated that patients factors such	1. Strengths - Highlighted importance of including nurses in any fertility preservation program. They are often at the bedside and can help initiate fertility preservation conversations. - Survey pre-tested in subgroup of healthcare professionals 2. Limitations - Old survey data (2005-2006): much more in literature regarding FP as it pertains to children and young adult compared to when this study was conducted - Survey administered to nurses attending conference so results might not be generalizable - 19% attended conference in 2005 and also in 2006 and completed both surveys - Possible reporting bias (as use of survey)

		as being single, homosexual, <18yrs, HIV positive, no health insurance, poor prognosis would not affect the likelihood of FP discussions Results outcome 3: *Barriers to discussing fertility preservation* Barriers to the discussion included low availability of guidelines for fertility preservation and established links with service providers Barriers did not differ during the study period 4. If applicable, results per additional outcomes Nurses awareness of ASCO guidelines was 5%	

NA: not appropriate; Pts: patients; FP: fertility preservation

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?			
Forman et al. Pilot Survey of Oncologists Regarding Treatment-Related Infertility and Fertility Preservation in Female Cancer Patients. J Reprod Med 2009;54(4):203-7			
Study design & Main study objective	**Participants and relevant characteristics**	**Relevant results (per outcome)**	**Additional remarks**
1. Study design Single center cross-sectional study (survey) 2. Main study objective To quantitatively explore oncologists' practice patterns	1. Type and number of participants 36 oncologist *Original cohort*: 91 oncologists invited, response rate 40% 22(61%) medical oncologists 8(22%) paediatric	1. Outcome(s) definition a) Frequency of discussing the impact of treatment on fertility with patients b) Reasons for not discussing this impact c) Frequency of referring patients to a reproductive specialist d) Reasons for not referring patients to a reproductive specialist e) Knowledge of fertility preservation techniques and of impact of chemotherapy on fertility	Limitations - Low response rate (40%) - Risk of selection bias (no surgical oncologists participated) - No socio-demographic information on respondents reported. - Single center study (results have low external validity)

and attitudes surrounding treatment-related infertility and fertility preservation among women of reproductive age. 3. Additional study characteristics, if relevant - Survey emailed using online survey tool - Survey sent on April 2007	oncologists 6(17%) radiation oncologists 2. Age (at diagnosis) of participants NR 3. Number of participants per diagnosis NA 4. Additional participants characteristics, if relevant All participants were from one single institute (i.e. Duke University Medical Center)	2. Results outcome a 22(61%) always or usually discussed the impact treatment on fertility 3. Results outcome b *Barriers to discussing treatment impact on fertility* Barriers included patient poor prognosis (53%), the need for immediate therapy (24%) and patient already having children (24%) 4. Results outcome c 16(45%) never referred women to reproductive specialists 5(15%) routinely referred 5. Results outcome d *Barriers to referring patients to fertility specialist* Patient disinterest in preserving fertility (39%); limited time because of emergent need to start therapy (13%)	

NA: not applicable; FP: fertility preservation

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?

Burns et al. Attitudes regarding fertility preservation in female adolescent cancer patients. J Pediatr Hematol Oncol 2006;28(6):350-4

Study design & Main study objective	Participants and relevant characteristics	Relevant results (per outcome)	Additional remarks
1. Study design Single center quantitative cross-sectional survey 2. Main study objective To determine whether	1. Type and number of participants 50 families of female adolescents diagnosed with cancer: 39 parent/female	1. Outcome(s) definition 1. Baseline knowledge of infertility and interest in fertility preservation 2. Source of information for baseline knowledge 3. Rate life goals 4. Survey with 4 main topics: **1**. Adolescent has thought about the future; **2**. Someone has talked to them about how their	1. Strengths - 2. Limitations - Due to limited sample size (single center study) results may not be generalizable to the

female adolescents with a diagnosis of cancer and their parents are interested in trying to preserve fertility 3. Additional study characteristics, if relevant: Survey between February 2004-2005	adolescent pairs 3 parent-only 8 female adolescent-only *Response rate*: 93%, 54 families invited Excluded patients known to be infertile at time of study (documented evidence of premature menopause), families not speaking English, and patients with end-stage disease 55.9% of pts off therapy Median nr of months since diagnosis: 22 (1-291) Median nr months off therapy 35 (3 to 168) 2. Age (at diagnosis) of participants NR Median age at time of survey: 15 years (10 to 21) 3. Number of participants per diagnosis Leukemia: 26 (52%) Osteosarcoma: 5(10%) Ewing/PNET: 4(8%) Wilms tumor: 2(4%) Neuroblastoma: 1(2%)	treatment might affect fertility; **3**. They have interest in pursuing research-based fertility preservation techniques; **4**. Willing to wait 1 or more months to start therapy. 2. Results outcome 1 94% answered that they were aware that some people (in the general population) were unable to have children 3. Results outcome 2 61.76% learned from physician; 79.41% told by a parent; 52.94% in school; 47.06% through media (more than 1 answer possible) 4. Results outcome 3 "To have a good health" was ranked significantly higher that items on children, friends, being in love, job, money, own home and travel 5. Results outcome 4 4.1. "Adolescent has thought about the future" Adolescents: 91.42% yes Parents: 96.88% % Agreement Adolescents and adults: 88.89% ns 4.2. "Someone has talked to them about how their treatment might affect fertility" Adolescents: 68.75% yes Parents: 48.97% % Agreement Adolescents and adults: 77.22% ns 4.3. "Interest in pursuing research-based fertility preservation techniques" Adolescents: 80.65% yes Parents: 93.1% yes % Agreement Adolescents and adults: 77.78% ns	general population of female cancer patients and their families (results have low external validity) - Survey not validated - Possible reporting bias (as use of survey) - Study is from 2006, treatment data or FP options might be outdated

	Hepatocellular carcinoma: 1(2%) Brain tumor: 1(2%) Hodgkin lymphoma: 6(12%) Rhabdomyosarcoma: 1(1%) <u>4. Additional participants characteristics, if relevant</u> 46% of patients were exposed to potentially gonadotoxic treatment: 100% received CT; 40% AA CT 32,65% received RT, 8% pelvic, CNS or TBI RT Patients were either on treatment or on follow-up care at time of survey	4.4. "Willing to wait 1 or more months to start therapy" Adolescents: 29.02% yes Parents: 19.23% % Agreement Adolescents and adults: 73.08% ns *Barriers to fertility preservation* Adolescents and parents reported to not be willing to postpone cancer treatment by 1 month or more for research treatments of fertility preservation <u>3. If applicable, results per additional outcomes</u> No statistical difference on any of the 54 outcomes between any of the subgroups: age 10-14 vs 15-21; on versus off therapy; acute leukemia vs other	

pts: patients; ns: not significant; CT:chemotherapy; RT: radiotherapy; AA: alkylating agents; TBI: total body irradiation; CNS: central nervous system

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?			
Campbell et al. Fertility Preservation Counseling for pediatric and adolescent cancer patients. J Adolesc Young Adult Oncol. 2016;5(1):58-63			
Study design & Main study objective	**Participants and relevant characteristics**	**Relevant results (per outcome)**	**Additional remarks**
<u>1. Study design</u> Quantitative cross-sectional study (email survey) <u>2. Main study objective</u>	<u>1. Type and number of participants</u> 1492 health professionals members of the COG: clinicians and investigators dedicated to pediatric	<u>1. Outcome(s) definition</u> Outcome 1: Number of physicians who provided patients with fertility preservation counseling Outcome 2: Limitations to providing counseling <u>2. Results outcome 1</u>	<u>Limitations</u> - Patient sex not specifically delineated.(i.e.study did not report if limitations to providing counselling differed by patient gender)

To evaluate if pediatric oncologists were performing fertility preservation counseling, if the new guidelines were being adopted, and how reproductive endocrinologists can educate this patient population and their providers. <u>3. Additional study characteristics, if relevant</u>: Study between May 2014 and August 2014	cancer research *Response rate:* 234 responded (16%) <u>3. Number of participants per diagnosis</u> NA <u>4. Additional participants characteristics, if relevant</u> 60% female 92% MD Degree Equal distribution among years of clinical practise 93% practised in urban setting 99% cared for pediatric population >50% of pts seen by respondents were diagnosed at reproductive age	95% of providers reported that they mentioned fertility preservation options prior to starting treatment, most commonly including referral to a reproductive endocrinologist (28%) and sperm banking (57%). When counselling patients, 91% of providers spent at least 5 minutes with 54% spending 10 minutes or more <u>2. Results outcome 3</u> *Barriers to discussing fertility preservation* Barriers for not counseling patients were financial (47%), lack of knowledge (39%), perceived poor success rate (35%), lack of current partner (28%), poor patient prognosis (28%), lack of time (12%), and the patient already had children (5%) <u>3. If applicable, results per additional outcomes</u> Males are offered fertility preservation more than females (57% vs 28%) Fertility preservation methods discussed: • Sperm banking (57%) • Referral to reproductive endocrinologist (28%) • Ovarian tissue cryopreservation(15%) • Gonadotropin suppression with gonadotropin-releasing hormone analog (15%) • In vitro fertilization with embryo freezing(8%) • In vitro fertilitzation with oocyte freezing (9%)	- Low response rate (16%) - No validated survey due to time constraints - Possible selection bias of only providers who counsel oncofertility preservation to participate (but authors argue reporting percentages are likely lower estimates) -Possible reporting bias as use of survey

COG: Children's Oncology Group; NA: not applicable; RR: response rate; pts: patients; ASCO: American Society of Clinical Oncology

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?			
Ginsberg et al. Testicular Tissue Cryopreservation in Prepubertal Male Children: An Analysis of Parental Decision-Makin. Pediatr Blood Cancer 2014;61(9):1673-8			
Study design & Main study objective	**Participants and relevant characteristics**	**Relevant results (per outcome)**	**Additional remarks**
1. Study design Qualitative cross-sectional survey (questionnaire) 2. Main study objective To assess the acceptability and safety of testicular tissue cryopreservationin prepubertal male in 3 centers (CHOP in 2008, Seattle Children's Hospital in 2012 and Memorial Sloan Kettering Cancer Center in 2013) 3. Additional study characteristics, if relevant To explore the decision-making influences and mood states at the	1. Type and number of participants 74 patients facing gonadotoxic therapy completed the questionnaire *Response rate:* 89% (66 completed the questionnaire) -> 57(77%) consented to testicular biopsy (accepters) - 48/57(84%) underwent biopsy - 9/57(15.8%) had benign histology or frozen biopsy not consistent with study eligible malignancy -> 17(23%) refused testicular biopsy (refusers) 2. Age (at diagnosis) of participants Accepters:	1. Outcome(s) definition Outcome 1: Factors influencing decision-making to testicular biopsy for testicular cryopreservation Outcome 2: Safety of testicular tissue biopsy 2. Results outcome 1 *Barriers to testicular tissue cryopreservation* - Refusers felt more overwhelmed at the time of the decision (compared to accepters, p=0.0221) - Refusers were more likely to weigh the risks of the testicular biopsy procedure (compared to accepters, p=0.007) *Factors that influenced accepters* - Accepters were more likely to endorse that the science of reproductive medicine will advance so that their son can use the tissue to attempt pregnancy (compared to refusers, P=0.0022) - Accepters were more likely to endorse that fertility is important and worth trying to preserve, even though there are no guarantees (P<0.0001) *Factors that influenced accepters and refusers* - Accepters and refusers were not influenced by religion, ethics or finances - Accepters and refusers felt in control of their decision, and it was made by them without the inappropriate influence of	1. Strengths - Takes into consideration potential barriers to tissue cryopreservation In prepubertal boys: religion, ethics, finances, risks of biopsy procedure, and experimental nature of method - A validated tool that measures strength of control of decision-making is used: Decision-Making Control Instrument - Study population from 3 institutions 2. Limitations - Possible reporting bias (as use of survey - Gap of 5 years between surveys (2008 to 2015) - Unclear how many of participating parents were acceptors or refusers - Unclear how much influence the children (especially between 10-14 y) had on the parents decision.

time point of offering testicular tissue cryopreservation	Mean: 6.7 years (0.2-14.5 years) Refusers: Mean: 7.0 years (0.8-15 years) <u>3. Number of participants per diagnosis</u> Diagnosis of accepters and refusers to testicular biopsy: Neuroblastoma (9, 18.8%)) Rhabdomyosarcoma (7, 14.6%)) Osteosarcoma (5, 10.4%)) Ewing Sarcoma (8, 16.7%)) Sarcoma NOS (7, 14.6%)) Hematological disease (6, 12.5%)) Immunodeficiencies (6, 12.5%)) <u>4. Additional participants characteristics, if relevant</u> Amongst accepters: 45(79%) with a malignant disease 12(21%) with a non-malignant disease No significant differences	others - Accepters and refusers not deterred by experimental nature of the procedure *Other characteristics* 62.3% of parents would not be willing to delay treatment 32.1% of parents would delay cancer directed therapy within reason in order to pursue this option 50.9% of parents were willing to go through a separate operative procedure solely for the testicular biopsy than to delay therapy (32.1%) 41.5% of parents would not allow an additional trip to the operating room just for the testicular biopsy <u>3. If applicable, results per additional outcomes</u> - No intraoperative complication - One postoperative scrotal cellulitis	

	in age of patient, race, religion, or education level between the accepters and the refusers		

NOS: not otherwise specified; CHOP: The Children's Hospital of Philadelphia (CHOP); FP: fertility preservation; DMCI: Decision-Making Control Instrument

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?

Goodwin et al. Attitudes and practices of pediatric oncology providers regarding fertility issues. Pediatr Blood Cancer 2007;48(1):80-5

Study design & Main study objective	Participants and relevant characteristics	Relevant results (per outcome)	Additional remarks
1. Study design Single center cross-sectional (survey) study 2. Main study objective To understand the current practices and attitudes of FP in a pediatric hematology/ oncology clinic 3. Additional study characteristics, if relevant	1. Type and number of participants 30 healthcare providers in pediatric hematology/ oncology department *Response rate:* 93.8% (32 healthcare providers approached) 2. Age (at diagnosis) of participants NR 3. Number of participants per diagnosis NA 4. Additional participants characteristics, if relevant 16 (53.3%) physicians 14 (46.6%) NPs or RNs	1. Outcome(s) definition Outcome 1: Current practices for fertility-related side effects and treatment options Outcome 2: Obstacles to current fertility-related practices Additional outcomes: Outcome 3: Perception of patients beliefs and attitudes 2. Results outcome 1 9(34.6%) of providers routinely sought advice from a reproductive endocrinologist about patient-related fertility Issues; 26(92.8%) of providers routinely discussed cancer treatment effects on potential fertility with patients and families;; 19(63.3%) of providers discussed infertility as a possible side effect with all at risk patients 20(74%) of providers inform patients whose fertility will most likely not be affected are informed that they are not at risk of infertility	1. Strengths Response rate (93.8%) 2. Limitations - Small sample size (single center study) - Possible risk of reporting bias (as use of survey) - Unclear if surgical oncologist are also included as part of physicians. If not, risk of selection bias - Did not include patient surveys (only healthcare providers) - Not validated survey - Outdated study in relation to fertility preservation practices (article from 2007)

		3. Results outcome 2 *Barriers to fertility preservation* More than half of the healthcare providers (18, 64.3%) reported as barrier for fertility-related practices the difficulty in finding for their patients the proper facilities and specialists for fertility preservation 34.4% and 10.3% of providers reported that the success rates for female fertility preservation and for male sperm banking respectively were too low to justify pursuing gamete preservation; 14.8% and 7.1% of providers reported that costs for infertility treatment for females and males respectively were too high to justify; 4. If applicable, results per additional outcomes Outcome 3 24 (85.7%) of providers reported that parents often ask about potential treatment effects on their child's fertility; 16(57.2%) of providers reported that patients themselves ask about fertility issues; 22(79.5%) of providers perceived that older patients and families are more concerned about fertility issues; 3(50%) of providers also perceived that concerns about fertility issues varied according to specific ethnic groups, gender 7(22.4%) and SES 7(22.4%)	

NP: nurse practitioners; RN: registered nurses; SES: socioeconomic status; NA: not applicable; NR: not reported

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?			
Chong et al. A Cross Canada Survey of Sperm Banking Practices in Pediatric Oncology Centers. Pediatr Blood Cancer. 2010;55(7):1356-61			
Study design & Main study objective	**Participants and relevant characteristics**	**Relevant results (per outcome)**	**Additional remarks**

1. Study design Cross-sectional design (survey) 2. Main study objective Describe sperm banking practices in pediatric oncology in Canada and identify perceived barriers 3. Additional study characteristics, if relevant - Two-stage process: first a survey was first completed and after a follow-up survey was administered to rank importance of items using 5-point Likert scale - Phone survey and if this was not possible in writing	1. Type and number of participants 15 medical professionals with an interest in fertility preservation: 14 (93%) pediatric oncologists 1 (6.7%) specialist nurse *Response rate*: 94% (15/16 institutions) 2. Age (at diagnosis) of participants N/A 3. Number of participants per diagnosis N/A 4. Additional participants characteristics, if relevant -Pediatric oncologists (14, 93%) - Specialist nurse (1, 6.7%)	1. Outcome(s) definition Outcome 1: Current practices and facilities for sperm banking Outcome 2: Utilization of sperm banking among male adolescents Outcome 3: Barriers to sperm banking 2. Results outcome 1 - 2/15 (13%) institutions with dedicated FP teams - Institutions with FP policy: 7/15 (formal), 1/15(written) - 2/15 (13%) institutions with adolescent focused educational sessions for staff (none has specific training sessions on how to facilitate/arrange sperm banking in adolescents) - 7(47%) institutions: initial discussion about FP and sperm banking is dependent on the individual providers' practice - 9/15 (60%) institutions with educational pamphlet (generic adults focused) about sperm banking; 1/15(6.7%) adolescents specific - 0/16 institutions with in-house room for sample procurement for patients too unwell to go the sperm banking unit - 10/15 (66%) institutions covered patient's cover costs, 5/15 (33%) institutions partial or full funding available from the institution or local charity 3. Results outcome 2 - Over two years, 50/262 (19%) adolescents in 12 institutions banked a specimen - 49% (85/172) of adolescents from 11 institutions offered to bank, 38/85 (45%) subsequently attempted 4. Results outcome 3 - Main reported barriers: need to start therapy, restricted banking hours (or not accessible weekends/evenings) and lack of appropriate adolescent approach, particularly educational material	1. Strengths Includes all major pediatric oncology centers in Canada 2. Limitations - Cannot verify the objectivity or accuracy of each response (possible risk of reporting bias as use of survey) - Study does not include patient surveys (only medical professional) - Only one survey per institution, small sample size - Not validated survey

		- Cost not perceived as barrier by majority (10/15) <u>5. If applicable, results per additional outcome</u> initiatives to improve sperm banking: • formal education of health care providers in FP practices • financial support to families • adolescent focused approach	

FP: fertility preservation; NA: not applicable

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?			
Köhler et al. Results from the survey for preservation of adolescent reproduction (SPARE) study: gender disparity in delivery of fertility preservation message to adolescents with cancerJ Assist Reprod Genet 2011; 28: 269–277			
Study design & Main study objective	**Participants and relevant characteristics**	**Relevant results (per outcome)**	**Additional remarks**
<u>1. Study design</u> Cross-sectional study (survey) <u>2. Main study objective</u> To assess whether the gap between FP options and practice patterns has narrowed with the advent of ASCOR (fertility preservation recommendations of ASCO) <u>3. Additional study</u>	<u>1. Type and number of participants</u> 180 pediatric oncology health professionals *Response rate:* 12.6% (1428 individuals contacted) 209 initiated the survey, 180 completed the survey <u>2. Age (at diagnosis) of participants</u> NA <u>3. Number of participants</u>	<u>1. Outcome(s) definition</u> Outcome 1: Assessment of barriers to sperm banking Outcome 2: Assessment of general fertility preservation attitudes and practice patterns Outcome 3: Assessment of fertility preservation attitudes and practice: male cancer patients Outcome 4: Assessment of fertility preservation attitudes and practice: female cancer patients Additional outcomes: Outcome 5: Assessment of knowledge of fertility preservation Outcome 6: Assessment of sperm banking <u>2. Results outcome 1</u> *Barriers to sperm banking* - Barriers for not recommending sperm banking was poor survival prognosis, aggressive disease requiring immediate initiation of treatment, and no consent provided by patients'	<u>1. Strengths</u> Nationwide online survey <u>2. Limitations</u> - Limited representation of healthcare providers (healthcare providers are mainly physicians, results not generalizable) - Low response rate - No data on non-responders (unclear if selection bias), authors argue due to anonymous nature of the survey - Risk of selection bias (probably interested physicians answered), knowledge probably overestimated - Risk of reporting bias (as use of survey)

<u>characteristics, if relevant</u> Contact via email, follow-up email four weeks later, Messages left with phone staff encouraging to complete emailed survey Researchers blinded to who did and who did not participate	<u>per diagnosis</u> NA <u>4. Additional participants characteristics, if relevant</u> 167(93%) pediatric oncologists 5(3%) Nurse or nurse practitioners 2(1%) reproductive specialists 6(3%) other or no answer 79% Primarily affiliated with university practice Respondents saw approximately 30 adolescent male and female patients (age 18 and under) per year	parents - Least likely barrier for pediatric oncologists: Discomfort with discussing sperm banking with their pubertal patients *Barriers to sperm banking (according to healthcare professionals)* - Patients/parents desire to initiate treatment as soon as possible, not wanting to be concerned with possible infertility, and not being concerned with parenthood at the time of treatment - Least likely barriers for patients and patients' parents: desire to conceive with fresh sperm and believing that sperm banking is not worthwhile <u>3. Results outcome 2</u> - 81% identified fertility threats major concern to them as physicians; and 84% to the patients' parents - 85% reported that both parents and patients asked about fertility threats 99% felt all pubertal patients should be informed prior to treatment about fertility threats (100% concerning male pubertal patients) - 79% believed pubertal patients should be referred to a fertility preservation specialist prior to treatment - 93% felt all pre-pubertal patients should be informed prior to treatment about fertility threats (94% concerning female pre-pubertal patients) - 36% believed pre-pubertal patients should be referred to a fertility preservation specialist prior to treatment - More respondents thought offering tissue cryopreservation (testicular or ovarian) was useful to pubertal patients than to pre-pubertal patients <u>4. Results outcome 3</u> Fertility preservation attitudes and practice: male cancer	- Did not include patient surveys (only medical professional opinion)

		patients - 86% agreed all pubertal males should be referred to a fertility preservation specialist; 66% report doing this >= 50% of the time - 92% agreed all pubertal males should be offered sperm banking prior to treatment; 85% report doing this >= 50% of the time - 23% agreed that testicular cryopreservation should be offered to males with azoospermia; 10% report doing this >= 50% of the time - 73% agreed all pubertal males should be sent to fertility specialist; 50% report doing this >= 50% of the time - 15% agreed that testicular cryopreservation should be offered to pre-pubertal males; 5% report doing this >= 50% of the time <u>5. Results outcome 4</u> Fertility preservation attitudes and practice: female cancer patients - 73% agreed all pubertal females should be referred to a fertility preservation specialist pre treatment; 23% report doing this >= 50% of the time - 46% agreed all pubertal females should be offered ovarian tissue cryopreservation prior to treatment; 13% report doing this >= 50% of the time - 77% agreed all pubertal females should be referred to a fertility preservation specialist post cancer treatment; 46% report doing this >= 50% of the time - 24% agreed all pre-pubertal females should be offered ovarian tissue cryopreservation prior to treatment; 6% report doing this >= 50% of the time <u>6. If applicable, results per additional outcomes</u> Sperm banking	

		- 121/170 numerical answer to question about youngest age they would offer sperm banking: Mean age 12.6 years, median age 13 years - Remaining respondents offer banking based on pubertal status, Tanner staging, or ability to ejaculate - 75% agree the expense of sperm banking and storage is worthwhile - 36% agree sperm banking is affordable - 85% offer sperm banking within a week after cancer diagnosis - After patients death:46% recommend banked sperm be thawed and destroyed; 37% recommend it being given to the patients parents; 23% recommend donating it to research facility	

NA: not applicable; ASCO: American Society of Clinical Oncology; ASCOR: American Society of Clinical Oncology recommendations on fertility preservation

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?

Overbeek et al. Practice, attitude and knowledge of Dutch paediatric oncologists regarding female fertility. Neth J Med 2014;72(5):264-70

Study design & Main study objective	Participants and relevant characteristics	Relevant results (per outcome)	Additional remarks
1. Study design Cross-sectional study (survey) 2. Main study objective: To assess the current practice, attitudes and the knowledge of Dutch pediatric oncologists	1. Type and number of participants 37 Paediatric oncologists registered with the Dutch Childhood Oncology Group and who had treated at least 5 girls (age 0-18) in the past year *Participation rate*: 58%	Outcome(s) definition Outcome 1: assessment of current practice Outcome 2: assessment of need for information or training Outcome 3: perceived barriers Additional outcomes Knowledge and attitude 2. Results outcome 1 - 75% reported usually or always discuss fertility issues before the onset of treatment with prepubertal girls or their parents, 89% with postpubertal girls	1. Strengths - Questionnaire was adapted from a previous questionnaire based on qualitative studies, survey covered various aspects of the topic of interest - Nationwide study 2. Limitations - Descriptive study, no comparison group - Questionnaire not validated

regarding fertility and fertility preservation options in female childhood cancer patients 3. Additional study characteristics, if relevant	2. Age (at diagnosis) of participants Mean and median age not reported Range: 30years - >60years 18(48.6%) between ages 40-49years 3. Number of participants per diagnosis NA 4. Additional participants characteristics, if relevant 18(48.6%) male Median number of years in practice: 12 years	- 97% discussed the issue with the parents if the patient was a prepubertal girl, 32% discussed it with the girl herself - 84% of the paediatric oncologists discussed the issue with the parents and 97% with the girl herself if the girl was postpubertal - 77% of the paediatric oncologists indicated to spend between 5-15 minutes on fertility issues, whereas 20% spent more than 15 minutes. - 46% often referred their female patients to a fertility specialist, whereas 38% sometimes referred, 3% always referred and 11% never referred 2. Results outcome 2 14% printed resources 41% reported specialized nurses/social workers to discuss FP 30% had a fertility specialist to refer 68% were most likely to use scientific literature to stay updated on FP 89% thought this information was sufficient 4. Results outcome 3 *Barriers to discussing fertility and fertility preservation* 33 (89.2%) of pediatric oncologists cited insufficient time, 12 (32.4%) cited lack of knowledge about fertility preservation, 8(21.6%) cited lack of data, and 9 (24.3%) cited patient's poor prognosis 4. If applicable, results per additional outcomes *Knowledge* Few had moderate/high confidence in FP knowledge (24% ovarian transposition, 19% IVF, 5% oocyte cryopreservation, 14% OTC)	- Small sample size (despite nationwide study) - Risk of selection bias as clinicians more interested/knowledgeable on the topic might have been the ones participating - Nos distinction of pubertal status in perceived barriers to attitude and practice

		Attitude 97% felt it was their responsibility to discuss infertility, 75% to discuss FP, a few responded that at most they would accept a 1-5% lower survival for improved FP	

NA: Not applicable; OTC: ovarian tissue cryopreservation

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?			
Crawshaw et al. Professionals' views on the issues and challenges arising from providing a fertility preservation service through sperm banking to teenage males with cancer. Hum Fertil (Camb) 2004;7:23-30			
Study design & Main study objective	**Participants and relevant characteristics**	**Relevant results (per outcome)**	**Additional remarks**
1. Study design Qualitative study with semi-structured interviews 2. Main study objective To study experiences of care professionals working in the field of assisted conception and paediatric oncology with boys aged under 18 3. Additional study characteristics, if relevant - Study setting: North of England - Methodology analysis: selective transcription	1. Type and number of participants 22 health and social work professionals (from 2 regional centres and 3 associated conception centres) 4 doctors from Assisted Conception Units 6 doctors from Paediatric Oncology Centres 2 nurses from Assisted Conception Units and 4 nurses from Paediatric Oncology Centres 4 scientists from Assisted Conception Units 2 social workers from Paediatric Oncology Centres	1. Outcome(s) definition A. Understanding processes involved in fertility preservation service B. Identification concerns about delivery of this service 2. Results outcome A • No consensus on gender and/or age professional to best discuss FP • Professionals' felt skills such as being clear and honest in information giving, not embarrassed, attuned to the boy's state of mind were important for the discussion of sperm banking *Barriers by health professionals regarding FP discussion* • Difficulties by pediatric oncologists to approach discussion FP with with little prior knowledge of patient/family and no time to establish a relationship with a patient • Difficulties by pediatric oncologists to have discussion FP with time pressure • Difficulties by staff at conception units to complete consent forms and facilitate provision of sample at first visit	Limitations - Small sample size - Selective transcription as methodology - No two independent analyses performed - No quantitative data, only indication given of broad frequency - Outdated in relation to FP practices - Risk of interviewer induced bias

	2. Age (at diagnosis) of participants NA 3. Number of participants per diagnosis NA 4. Additional participants characteristics, if relevant	3. Results outcome B *Barriers to discussing fertility preservation* Barriers for pediatric oncologists included little prior knowledge of patient/family and no time to establish a relationship with a patient and time pressure Barriers for staff at the conception units included difficulties to complete consent forms and to facilitate provision of samples at first visit Many professionals reported ethnicity as a possible barrier when offering sperm banking to Asian men (in relation to marriage-ability) Barriers included difficulties in professionals in building and maintaining a relevant, adequate knowledge and skills base; lack of appropriate training about the legal and consent frameworks 4. If applicable, results per additional outcomes • Lack of clarity in professionals on who should be offered FP and to know best approach in discussing FP (i.e. should the professional be same gender as patient, parents involvement, should the patient be accompanied to assisted conception unit and by whom) • Professionals expressed the wish to have age appropriate written information to assist the consent process	

NA: not applicable; FP: fertility preservation

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?			
De Vries et al. Attitudes of physicians and parents towards discussing infertility risks and semen cryopreservation with male adolescents diagnosed with cancer. Pediatr Blood Cancer 2009;53(3):386-91			
Study design & Main study objective	**Participants and relevant characteristics**	**Relevant results (per outcome)**	**Additional remarks**
1. Study design	1. Type and number of participants	1. Outcome(s) definition	1. Strengths

Qualitative multi-centre study with in-depth semi-structured interviews 2. Main study objective To determine attitudes and preferred roles of physicians and parents towards sperm banking with male adolescents 3. Additional study characteristics, if relevant Interviews took place between January 2005 and August 2007	15 physicians involved in care of male adolescents with a cancer diagnosis 14 parents of male adolescents undergoing cancer treatment 2. Age (at diagnosis) of participants NR Physicians: Mean age: 42.1 years (32–52 years) Parents: Mean age: 42.8 years (36-50 years) at diagnosis of their adolescents (mean 13.8, range 11-17 years) 3. Number of participants per diagnosis Diagnosis of adolescents: 9 hematologic cancers 5 sarcoma 4. Additional participants characteristics, if relevant Physicians: Working in pediatric oncology for a mean of 7.6 years (1.5-20 years) and 7 (46.7%) were male. Parents: 8 fathers, 6 mothers	Outcome 1. Assessment of the current communication practice of paediatric oncologists regarding FP Outcome 2. Explore experiences of physicians and parents regarding their roles in FP communication Outcome 3. Ethical issues involved Four central themes: 1) concerns about the future quality of life, 2) child participation, 3) parental control, 4) timing and approach for fertility discussions 2. Results outcome 1 • Physicians and parents agreed that infertility would have a major impact on the future quality of adolescents' life • All physicians felt that their duty was to bring up FP discussion • Unanimity among physicians that children should participate in decision-making process • 14(93%) physicians would discuss FP with adolescents even if parents refused to give permission to talk to the son • Physicians always talked to the adolescents because of the sensitive nature and the experience that parents sometimes misjudged the stage of maturity of their son 3. Results outcome 2 *Role of parents in fertility preservation communication* More than half of parents (57%) reported that they wanted control whether physicians discussed sperm banking with their child and also what the physician discussed • Parents also agreed that infertility would have a major impact on the future quality of adolescents' life *Barriers to sperm banking* No unanimity among parents with respect to participation in decision-making by their children: - Some parents reluctant for clinicians to have discussion with their child	- Independent coding of the transcripts - Grounded theory - Saturation in data collection achieved 2. Limitations - Small sample size - No data on pre-pubertal adolescents - No interviews to adolescents - Risk of reporting bias - Risk of interviewer induced bias

		because conversations were ill-timed and confronting due to sensitive nature - Some parents felt it is the child who decides because it relates to their own future 4. If applicable, results per additional outcomes 3(20%)parents were surprised of the timing of the discussion i.e. late announcement in fertility preservation and cryopreservation options	

FP: fertility preservation

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?			
Gupta et al. Testicular biopsy for fertility preservation in prepubertal boys with cancer: Identifying preferences for procedure and reactions to disclosure practices Journal of Urology 2016; 196 (1):219-224			
Study design & Main study objective	**Participants and relevant characteristics**	**Relevant results (per outcome)**	**Additional remarks**
1. Study design Cross sectional multi-center study with in-depth interviews 2. Main study objective To measure and compare parent, male cancer survivor and health professional willingness to accept the risk of TBx in pre-pubertal boys and to identify reactions to disclosure practices regarding biopsy 3. Additional study characteristics, if relevant Interviews conducted	1. Type and number of participants 153 parents of pre-pubertal boys with cancer 77 male survivors of childhood cancer 30 pediatric oncology health professionals 2. Age (at diagnosis) of participants Parents (age of their child at diagnosis): ≤12 years, median 4 years Survivors: ≤12 years, median 5 years Health providers: NA 3. Number of participants per diagnosis • Parents (diagnosis of their child):	1. Outcome(s) definition Outcome 1: Measure of desire for information about TBx for FP and Reactions to practices related to disclosure of information Outcome 2: Measure of relative willingness of each group to accept risk associated with TBx and Predictors of relative willingness 2. Results outcome 1 *Desire for information about testicular biopsy for fertility preservation* 90% survivors and 94% parents would have wanted information about testicular biopsy prior to commencement of therapy regardless of whether or not testicular biopsy was available at treating institution Parents reported the preference of having information	1. Strengths - Use of a novel approach to assessing the acceptability of an as yet experimental procedure that may meet needs otherwise unmet - 3 relevant subgroups of participants with good number in each - 3 institutions in Canada included in the study (multicenter) 2. Limitations - Lack of ethnic/cultural diversity in participant groups (identified by authors)

between July 2012 and September 2013 'Threshold technique' used is clearly described in appendices and measured willingness to accept the risks associated with TBx with reference to 4 relevant considerations: 1. Risk of infertility 2. Risk of complications from bx 3. Likelihood of technology developing sufficiently to allow successful future use of tissue 4. Requirement for family to cover costs of storage of tissue until used In-depth interviews were also conducted with a subset of each participant group to explore information disclosure practices. Threshold technique followed by indepth guided interview of subgroup	106(69.3%) leukaemia/lymphoma: 11(7.2%) sarcoma 17(11.1%) brain tumour 19(12.4%) other • Survivors: 53(69.7%) leukaemia/lymphoma 10(13.2%) sarcoma 4(5.3%) brain tumour 9(11.8%) other • Health providers: NA <u>4. Additional participants characteristics, if relevant</u> • Parents: 38(24.8%) Male 103(67.3%) White 26(17%) Asian 5(3.3%) Hispanic 19(12.4%) Other • Survivors: Boys received at least 2 months of cancer therapy and either still receiving therapy, or post-therapy 62(80.5%) White 5(6.5%) Asian 2(2.6%) Hispanic 8(10.4%) Other • Healthcare providers: 15(50%) Female	about testicular biopsy regardless the risk of infertility <u>3. Results outcome 2</u> *Barrier to testicular tissue cryopreservation* Parents and patients perceived a >30% risk of infertility, a >25% chance of complications of testicular biopsy, a >$500 per year storage cost, and a >14% chance that technology will evolve as barriers for testicular tissue cryopreservation Health professionals perceived a >29% risk of infertility, a >13.5% chance of complications, a >14% chance that that technology will evolve, and >$391 storage cost per year as barriers for testicular tissue cryopreservation <u>4. If applicable, results per additional outcomes</u> Predictors: - Survivors more likely to accept TBx with lower risk of infertility or lower chance of technology evolving as they aged (p= 0.05) - Greater household income associated with a lower minimum infertility risk (p= 0.05), and higher yearly costs (p= 0.04) - No demographic variables were associated with TBx desirability scores for HP Choose TBx vs. no biopsy overall: 110(72%) parents 52(67%) survivors 22(73%) HP	- Risk of selection bias: number of those approached who declined to participate is given, but not reason for non-participation - Study undertaken outside of the 'real life' situation in which decisions around fertility preservation are made (identified by authors) - Risk of interviewer induced bias - Risk of reporting bias

	29(96.7%) White 25(83%) physician 2(6.7%) NP 2(6.7%) RM 1(3.3%) SW		

TBx: testicular biopsy; NA: not applicable; NP: nurse practitioners; SW: social worker; HP: health provider

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?			
Murphy et al. Development of a Spanish Language Fertility Educational Brochure for Pediatric Oncology Families. 2014; 27(4):202-209			
Study design & Main study objective	**Participants and relevant characteristics**	**Relevant results (per outcome)**	**Additional remarks**
1. Study design Cross-sectional study: Qualitative face-to-face interviews and focus groups 2. Main study objective Create Spanish language Fertility brochure for cancer patients and families 3. Additional study characteristics, if relevant - In 2011 authors held feedback groups to assess a new pediatric fertility preservation brochure - Brochure could be validated only for English-speaking	1. Type and number of participants 10 cancer patients (undergoing treatment) 10 parents 5 healthcare providers in pediatric oncology Suggestions for revisions were tested with 3 focus groups: 6 cancer patients 10 parents 2. Age (at diagnosis) of participants Patients 12-23 years Parents NA Healthcare providers NA	1. Outcome(s) definition Outcome 1: Design of Spanish language brochure Outcome 2: Readability Outcome 3: Likelihood to read Outcome 4: Overall opinion 2. Results outcome 1 • Parents and male patients preferred more vivid, eye-catching colors while female patients preferred subtler, simplified designs • Busier background perceived to have more information • Some male patients recommended placing an adolescent male on the cover, female patients recommended a nature scene 3. Results outcome 2 • Almost all parents and patients of both	1. Strengths - Patients and parents involved with staff in creation and evaluation of brochures: transcreated and designed using learner verification method - Each moderator utilized a semi-structured interview guide created by the research team 2. Limitations - Risk of selection bias: unclear how many participants were eligible and invited to participate

patients and families, hence current study - After interviews, two independent reviewers abstracted emergent codes and collapsed into larger codes	<u>3. Number of participants per diagnosis</u> Patients 9/16(56%) Leukemia 3/16(19%) Sarcoma 2/16(13%) Brain tumor 2/16(13%) Carcinoma <u>4. Additional participants characteristics, if relevant</u> - All recruited in one center (Miller Children's Hospital) - Ethnicity: Parents and patients: all Mexican HP:3/5 Mexican, 2/5 Caucasian - HP: Spanish speaking pediatric oncologists, nurses and other medical staff - Years in practice of HP: 9+: 1/5 5-8: 2/5 0-4: 2/5	genders wanted the medical language describing fertility and FP options in the brochure and separate options by pubertal status • The majority of patients inquired about their specific risk and requested information be included that attended to determining this risk for individual patients • Parents had substantially more questions they wanted answered on the brochure • Parents and patients also wanted testimonials of other patients who had undergone FP • Some HPs suggested terminology was too complex, while other HPs remarked that Spanish language families want to read the medical language <u>4. Results outcome 3</u> • The majority of parents said they would read the brochure with their child, however the majority of male patients said they would read the brochure alone • The majority opinion of the brochure for all groups was that it should be a directive tool for families, dictating next steps, not solely for education • The majority of males explained they would have been receptive to reading the brochure and having discussions about fertility. Contrastingly, the majority of female patients said that they would have been receptive to reading the brochure at diagnosis, and would have liked to be referred to a reproductive specialist for further discussions <u>5. Results outcome 4</u> *Opinion of an education brochure on fertility risks and fertility preservation*	- Small sample size (single center study), so generalizability difficult - Risk of reporting bias with interviews - Risk of interviewer induced bias

		Half of the parents said the brochure would have encouraged immediate discussion with the physician Majority of patients stated that they would have been receptive to reading the brochure at diagnosis, and females reported that they would have liked to be referred to a fertility specialist for further discussions Some health professionals suggested terminology was too complex, while others remarked that Spanish language families want to read the medical language The majority of health professionals stated that the brochure was likely to prompt families to have discussions with their physician	

NR: not reported; NA: not applicable; HP: healthcare providers

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?			
Murphy et al. Using a patient-centered approach to develop a fertility preservation brochure for pediatric oncology patients: a pilot study. J Pediatr Adolesc Gynecol 2012;25(2):114-21			
Study design & Main study objective	**Participants and relevant characteristics**	**Relevant results (per outcome)**	**Additional remarks**
1. Study design Cross-sectional study: Qualitative face-to-face interviews 2. Main study objective To test the design, readability, likelihood to read	1. Type and number of participants 7 Oncology patients and survivors 11 parents 6 healthcare providers 2. Age (at diagnosis) - Mean/median age at diagnosis of oncology patients and survivors	1. Outcome definition Outcome 1: Design of the pediatric FP brochure Outcome 2: Content comprehension of the pediatric FP brochure Outcome 3: Concerns of the pediatric FP brochure 2. Results outcome 1 *Design of the pediatric FP brochure* • FEMALE brochure - Teens and parents preferred version 1 - Parents wanted to simplify the design	1. Strengths - Moderators had received prior training during qualitative data seminars and mock focus groups - Moderators solicited parents and teens feedback separately - Each moderator utilized a semi-structured interview guide created by the research team

and overall opinion of a pediatric fertility preservation brochure developed using social marketing approach 3. Additional study characteristics Two versions of the brochure assessed: version 1 and version 2. Differences in brochures not reported in the text but figures of each version shown in the article.	not reported - Age at study: range: 12-21 years 3. Number of participants per diagnosis Brain tumor (1, 14%) Papillary Thyroid (1, 14%) Neurofribromatosis (1, 14%) Synovial Cell Sarcoma (1, 14%) Lymphoma (1, 14%) Other (2, 29%) 4. Additional participant characteristics: Healthcare providers Included were reproductive endocrinologists, pediatric oncologists and nurses	• MALE brochure - Majority of parents preferred version 2 - Majority of teens preferred version 1 • HEALTH CARE PROVIDERS - Healthcare providers had a preference on simplified design and 'less for adults' 3. Results outcome 2 *Content comprehension of the pediatric FP brochure* • FEMALE brochure - Discrepancies between parents and teens - Parents felt there was too much information and language too advanced, and teens preferred to see medical terminology - Suggestion from parents to include information on financial assistance for fertility preservation and information on adoption • MALE brochure - Half of parents felt information was appropriate; Other half parents thought teens would find information 'overwhelming' - Parents commented some content confusing i.e. puberty; Teens disagreed with parents and wanted to see medical terminology - Parents wanted to see financial information - Suggestions to add counselors and adoption agencies - Parents wanted to emphasize FP should be done prior to treatment - Adoptions were not concerns for teens - Majority of teens would prefer to read brochure alone and ask questions after • HEALTH CARE PROVIDERS - HP expressed the need to revise the content to be more	2. Limitations - Risk of selection bias (screening log missing): unclear how many participants were eligible and invited to participate - Small sample size (single center study) so generalizability difficult - Risk of reporting bias with interviews - Risk of interviewer induced bias

		'optimistic', 'hopeful' and expressing return to 'normalcy after cancer' - HP expressed need to mention progress and technological advances in FP field - HP expressed the need to encourage in the brochure scheduling a consultation with reproductive endocrinologist <u>4. Results outcome 3</u> *Concerns of the pediatric FP brochure* • Concerns of the FEMALE brochure - Teens did not express concerns - Parents concerned of FP as unsure of success rate and that not options were relevant to their daughter's age or diagnosis - Parents differ on how they wanted to receive brochure (waiting rooms vs with all patient information) • Concerns of the MALE brochure - Teens did not express concerns - Parents expressed brochure made them think of their son's fertility status and not sure if options applied to them - Parents unsure of how they wanted brochure ((waiting rooms vs with all patient information) • HEALTH CARE PROFESSIONALS - Majority of HP indicated that the brochure needs to emphasize the importance of talking to a reproductive endocrinologist - HP were concerned that brochure make families think about future (instead of day to day) - Majority of HP felt information was not presented in 'captivating/exciting' format - Reproductive Endocrinologists felt barriers that prevent uptake of FP methods were not considered in the brochure	

FP: fertility preservation; HP: healthcare provider

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?			
Quinn et al. Fertility Preservation and Adolescent/Young Adult Cancer Patients: Physician Communication Challenges. J Adolesc Health 2009;44(4):394-400			
Study design & Main study objective	**Participants and relevant characteristics**	**Relevant results (per outcome)**	**Additional remarks**
1. Study design Cross sectional study with qualitative semistructured in-depth interviews 2. Main study objective To examine barriers experienced by physicians in discussing cancer-related fertility issues with patients aged 12-18yrears 3. Additional study characteristics, if relevant - Study used a subset of data from a larger study examining knowledge, attitudes, and behaviors of pediatric oncologists - All interviews were tape recorded and transcribed. The transcripts were read	1. Type and number of participants 24 Pediatric oncologists working in 15 clinics in Florida (US) *Response rate*: 41% participated (59 asked to participate) 2. Age (at diagnosis) of participants NA 3. Number of participants per diagnosis NA 4. Additional participants characteristics, if relevant NA	1. Outcome(s) definition Outcome 1: Healthcare system barriers Outcome 2: Perception of parent/patient desire for FP information Outcome 3: Awareness of FP resources Outcome 4: Patient characteristics that may impact FP discussions Outcome 5: Issues unique to adolescent patients 2. Results outcome 1: - Perceptions that the financial costs of FP were too high for most families (FP not covered by insurance) - Combination of lack of resources and lack of training or guidelines for having discussions 3. Results outcome 2: - About half of physicians said the cancer diagnosis is such a shock that an issue like fertility is often put on the ”back burner” - Other half thought that parents and teens do want this information but are either to embarrassed to discuss it or have no background on the topic and do not know how to begin a discussion 4. Results outcome 3: - One third of physicians were aware of sperm banking facilities	1. Strengths Provides information on barriers to discussing FP in pediatric oncology, implying that new methods of communication between all parties must be examined and utilized 2. Limitations - Results cannot be generalized to other pediatric hematology/oncology physicians or other populations - Authors state that interview may have limited the amount of in-depth discussion on any one topic - Risk of selection bias: responders more interested in the topic and more likely to engage in discussions about and/or encourage FP might have been participants - Risk of interviewer induced bias

through and the content analyzed through intuitive analysis. Key themes were identified - Author used theoretical saturation, in which each new participant we recruited refined new theoretical constructs. Midway in the data analysis we ascertained no new information was emerging; thus, we perceived we had reached theoretical saturation and made no further attempts to recruit additional physicians		- Remainder said their facility had no FP resources or they were unaware of resources for females (except oophoroypexy) - Physicians typically had low levels of knowledge about resources to refer patients to for FP procedures or consultations - Few pediatric oncologsist reported that the nationally distributed educational brochure they used was not always relevant to the local level and needed improvement <u>5. Results outcome 4:</u> - Most were comfortable in a general sense - However, many experienced barriers related to patient specific diagnosis or socioeconomic situation (ranged from perceived cultural or religious differences to knowing a family could not afford FP) <u>6. Results outcome 5:</u> - All found that it is an important issue to address for teens who have reached puberty - Most agreed that these conversations were awkward because resources were usually limited and there was a fine line between establishing a sense of trust with the patient, while not excluding parents - Conversations about fertility were related to issues of sexuality, and this was a source of embarrassment for both the patient and parents <u>4. If applicable, results per additional outcomes</u>	

NA: not applicable; FP: fertility preservation

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?			
Quinn et al. Impact of physicians' personal discomfort and patient prognosis on discussion of fertility preservation with young cancer patients. Patient Educ Couns 2009;77(3):338-43			
Study design & Main study objective	**Participants and relevant characteristics**	**Relevant results (per outcome)**	**Additional remarks**
1. Study design Cross-sectional study: Qualitative semi-structured interviews 2. Main study objective To determine if physician's personal discomfort with the topic of FP and a patient's prognosis would have an impact on the likelihood of discussing FP with cancer patients 3. Additional study characteristics, if relevant - Data obtained from two larger qualitative studies that investigated barriers to FP	1. Type and number of participants 26 pediatric oncologists* 28 adult oncologists *Response rate:* 86.7% (26/30, approached 2 pediatric oncologists across 15 centers) 2. Age (at diagnosis) of participants NR 3. Number of participants per diagnosis NA 4. Additional participants characteristics, if relevant Purposive sampling, clinicians all from the state of Florida	1. Outcome(s) definition Outcome 1: Manifestation of "personal comfort" and "patient prognosis" in relation to whether or not physicians discussed or referred for FP 2. Results outcome 1 *Barriers to discussing fertility preservation* Barriers included little relevant training resulting in feelings of not having necessary skills for fertility preservation discussion; patients with limited English skills; belief that the fertility topic would cause additional distress and burden; perception that parents of children would not want to hear about fertility preservation or sterility; financial costs; patients with poor prognosis or with advanced disease Theme 1: Lack of knowledge or training about FP Theme 2: Perceived language/ cultural barriers between clinicians and patients Theme 3: Belief that FP discussion added stress to patient's situation Theme 4:Uncertainty of success and affordability of FP methods Theme 5: Apprehension about discussing with patients with poor prognosis or have advanced disease 2. If applicable, results per additional outcomes *Use of educational material for fertility preservation*	1. Strengths - Provides insight into the situation that allows for: - development of hypotheses - development of mechanisms to facilitate and improve FP discussions - Use of 2 coders for each transcript for reliability and validity - Use of semi-structured interviews for consistency 2. Limitations - Small and local sampling, data unlikely to be generalizable across health care professionals, states, countries, tumour types, genders, or health care systems - Risk of self-selection bias with those who participate more likely to be interested in FP - Clinician perspective only, no insight into patient perspective

discussions among adult and pediatric oncologists: - Quinn 2007(adult study) - Vadaparampil 2007 (pediatric study)* - Authors used grounded theory and crystallizing immersion method - Data were coded within themes and summarized along with the provision of representative quotes		Few pediatric oncologists reported that the nationally distributed educational brochure they used was not always relevant to the local level and needed improvement	- No description of the type of patients clinicians primarily treat - Limited opportunity to explore differences across patients characteristics such as gender, tumour types, years of experience. as limited sample and using data from other studies - Risk of interviewer induced bias

FP: fertility preservation; NR: not reported; NA: not applicable

* See table for study Vadaparampil 2007

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?			
Reebals et al. Nurse Practice Issues Regarding Sperm Banking in Adolescent Male Cancer Patients. J Pediatr Oncol Nurs. 2006;23(4):182-8			
Study design & Main study objective	**Participants and relevant characteristics**	**Relevant results (per outcome)**	**Additional remarks**
1. Study design Cross-sectional (Quantitative survey) 2. Main study objective To identify factors that influence nurses and NP in discussing SB with newly diagnosed adolescent male patients 3. Additional study characteristics, if relevant Clinical questions: - What factors determine whether a newly diagnosed adolescent male patient is offered the option	1. Type and number of participants 27 hematology/oncology nurse practitioners and registered nurses who care for adolescent male cancer patients (from 4 of the main hospital units (inpatients and outpatients) that treat patients aged 14 to 18 years) *Response rate:* 45% (60 individuals invited) 2. Age (at diagnosis) of participants NA 3. Number of participants per diagnosis NA 4. Additional participants characteristics, if relevant 92.6% female	1. Outcome(s) definition Outcome 1: Knowledge of SB before cancer treatment Outcome 2: Attitudes regarding SB Outcome 3: Patient factors influencing nurse/NP willingness to discuss SB Outcome 4. Use of educational material Additional outcomes Outcome 5: Who should address SB 2. Results outcome 1 *Knowledge about sperm banking as barrier to discussing fertility preservation* 92.6% of nurses had a lack of knowledge regarding cost of banking sperm; 70% of nurses had the mistaken impression that a patient needed to collect 3 to 6 semen samples before cancer treatment; almost 52% of nurses believed that birth defects would increase if children were conceived from semen collected during first week of chemotherapy or radiation; 48% were aware that infertility after treatment is more common in boys than in girls Mean score 63% (40-100%) 3. Results outcome 2 • 96.3% - all patients at risk should be offered SB • 85.2% - parental consent not needed to discuss SB with	1. Strengths - The questionnaire was reviewed for appropriateness by a NP in the hematology/oncology clinic, the nurse director of the stem cell transplant unit, and a nurse educator with experience in research - Reinforces other studies indicating nurses believe it is important to discuss SB, but need more knowledge 2. Limitations - Low response rate, so generalizability difficult - Risk of selection bias as nurses more interested/knowledgeable on the topic might have been the ones participating - Study was published 11 years ago and may not represent current knowledge or attitudes - Risk of reporting bias (as use of

of SB before undergoing chemotherapy treatment? - What factors interfere with addressing the topic? - Under what circumstances would one address the topic? - What is an appropriate age for the topic? - What is the participant's knowledge level of the topic? - Whose responsibility is it to address the issue?	85.2% from southeastern US 48.1% < 30 years of age	boys under 19years of age • 62.9% - disagreed that there was not adequate time to discuss SB • 81.4% disagreed or did not know that sperm banking and storage are affordable for most patients • 92.5% disagreed that expense would be so high it would not be worthwhile • 96.3% were in favor of directive to be signed regarding use and disposal of sperm after death <u>4. Results outcome 3</u> *Patient characteristics as barriers to discussing sperm banking* 78% of nurses reported a less likelihood of offering sperm banking to a HIV patient; 40.7% of nurses reported a less likelihood of offering sperm banking to a patient with aggressive disease; 33% of nurses reported a less likelihood of offering sperm banking to a patient open about being homosexual and 11.1% of nurses reported a less likelihood of offering sperm banking to with a patient under 19 years of age <u>5. Results outcome 4</u> *Use of educational material for sperm banking discussion* 67% of nurses/nurse practitioners reported that they would be more likely to offer the option if they had educational materials explaining sperm banking available for the patients and their families <u>6. If applicable, results per additional outcomes</u> Who should address SB: Oncologists and NPS: 100% RNs: 59.2%	questionnaire) - Descriptive study, no comparison group

RN: registered nurses; NP: nurse practitioners; NA: not applicable; SB: sperm banking; NA: not applicable

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?			
Vadaparampil et al. Pediatric oncology nurses' attitudes related to discussing fertility preservation with pediatric cancer patients and their families. J Pediatr Oncol Nurs. 2007;24(5):255-63			
Study design & Main study objective	**Participants and relevant characteristics**	**Relevant results (per outcome)**	**Additional remarks**
1. Study design Cross-sectional (survey) 2. Main study objective To explore attitudes among pediatric oncology nurses towards the discussion of fertility preservation with pediatric patients and their families 3. Additional study characteristics, if relevant - Nurse survey adapted from previous work in the literature. - Final instrument consisted of 45 items.	1. Type and number of participants 115 nurses attendees of pediatric oncology conference *Response rate*: 64% (out of 180 attendees of pediatric oncology conference) Overall 126 (65%) completed the survey, but 9 excluded as not nurses 2. Age (at diagnosis) of participants NA 3. Number of participants per diagnosis NA 4. Additional participants characteristics, if relevant 47% practiced in Florida (where the conference was	1. Outcome(s) definition Outcome 1: Practice characteristics and behaviors Outcome 2: Provider attitudes toward discussion of FP Outcome 3: Impact of patient factors on discussion of FP 2. Results outcome 1 70(68%) discussed risk of infertility =< 10% of the time 74(73%) discussed FP options =<10% of the time 41(42%) of patients families interested in FP 49(49%) of nurses see patients prior to treatment in >50% of the time 3. Results outcome 2 93% of nurses felt that cancer patients at risk for infertility should be offered FP options 91% of nurses felt nurses and/or social workers should discuss FP options with patients 47% of nurses felt "boys under 18years should not be given erotic magazines or videos during semen collection unless parents agree" 72% of nurses disagreed with the statement "patients < 18 years should not be told about FP unless parents give consent" 4. Results outcome 3 *Barriers to discussing fertility preservation* Reported factors that may have decreased the likelihood of discussing fertility preservation were positive	1. Strengths Study among the first to consider factors affecting FP discussions and recommendations among nurses practicing in the area of pediatric oncology 2. Limitations - Relatively small sample - Participants were attendees at a nursing conference specific to pediatric oncology, thus introducing the possibility of risk of selection bias - Data collected prior to ASCO guideline, so these data may reflect nursing attitudes prior to this seminal publication - Some outdated information regarding FP (e.g. "cryopreservation of embryos is the only established option for females" and 'cryopreservation of oocytes is considered

	held), 6.1% from Connecticut and Georgia, respectively, the remainder was distributed among 21 other states 56(52%) practiced in a pediatric hospital 20(19%) worked in an out-patient clinic 18(17%) worked in a non-specified clinic 14(13%) worked in either a medical hospital, cancer center/research institute, university, or other location type Number of years working in oncology: 48(47%) ≤ 5 yrs 35(34%) 6-15 yrs 20(19%) >15 years 12 (10.4%) missing 111 (97%) served a pediatric population 103 (90%) primarily worked in oncology	HIV status (23%), poor patient prognosis (28%), and the inability to delay treatment because of aggressive disease (37%) *Factors increasing FP discussion* 93(83%) of nurses stated that they would be more likely to discuss FP options if the patient initiated the topic and expressed a desire to have children in the future 67(60%) would be more likely to discuss FP if the patient was married or engaged 35(32%) of nurses would be more likely to discuss FP options with patients and families if they had detailed educational materials *Factors not affecting FP discussion* 92% of nurses felt that patient access to insurance would not affect discussion of FP options *Other important factors* The top 3 attitudinal factors rated by nurses impacting FP discussions include the potential of the discussion to upset patient's families, the position that boys < 18 years of age should not be given erotic materials during semen collection without parents' agreement, and difficulty finding convenient FP facilities	experimental" and other references which were appropriate 10 years ago, but are less applicable currently - The study is exclusive descriptive in nature. No statistical tests were performed - Risk of reporting bias (use of survey)

NA: not applicable; FP: fertility preservation

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?			
Ginsberg et al. An experimental protocol for fertility preservation in prepubertal boys recently diagnosed with cancer: a report of acceptability and safety Hum Reprod 2010;25(1):37-41			
Study design & Main study o bjective	**Participants and relevant characteristics**	**Relevant results (per outcome)**	**Additional remarks**
1. Study design Single center cross-sectional survey 2. Main study objective To determine the acceptability and safety of testicular biopsy cryopreservation to families of prepubertal boys with newly diagnosed malignancy 3. Additional study characteristics, if relevant The protocol for testicular cryopreservation was 'qualitatively' evaluated	1. Type and number of participants Parents of 21 prepubertal boys with cancer diagnosis who were approached for testicular cryopreservation 2. Age (at diagnosis) of participants - Age of parents not reported - Mean (SD) age at diagnosis of 21 approached boys: 5.5 (3.9) yrs (3 months to 14 yrs) 3. Number of participants per diagnosis 5(24%) neuroblastoma 4(19%) Ewing sarcoma 5(24%) rhabdomysarcoma 2(9.5%) pleuropulonary sarcoma 5(24%) other	1. Outcome(s) definition Outcome 1. Parents' rate of acceptance of testicular biopsy Outcome 2:Factors influencing the parents' decision to consent to the biopsy or not Outcome 3:Parents' initial reactions to testicular biopsy protocol Additional outcomes: Outcome 4: Safety of this procedure 2. Results outcome 1 16/21 (76%) families consented to the procedure; 14 (86%) actually underwent testicular biopsy 5/21(23.8%) refused testicular biopsy 3. Results outcome 2 *Barriers to testicular tissue cryopreservation* 80% of parents who refused consent to the biopsy reported that they were too overwhelmed by diagnosis to hear about testicular tissue cryopreservation (vs. 31% of parents who agreed to biopsy) 60% of parents who refused biopsy reported that frozen testicular never used in humans to achieve pregnancy influenced their decision (vs. 38% of parents who agreed to biopsy) *Factors that did not influence decision to biopsy amongst*	1. Strengths Pilot project that considers barriers to prepubertal testicular cryopreservation from parents point of view 2. Limitations - The study has an explorative nature, no 'robust' conclusion can be drawn - Small sample size (single center study) - No demographic data on parents - Study with data from 2008, might have outdated fertility preservation methods - Risk of reporting bias (as use of survey)

		parents who refused biopsy - Religion, finance, ethics and the experimental nature of cryopreservation - The experimental nature of the cryopreservation process - Risk of testicular biopsy was *not* considered as a barrier for those who refused biopsy (60%) but was considered amongst those who agreed (88%) <u>3. Results outcome 3</u> 16(100%) parents who consented to the biopsy indicated post biopsy that 'they made the right choice, even if the tissue cannot be used in the future to restore their son's fertility' 68% of parents who consented to the biopsy felt that the possibility of freezing tissue for future use was 'a great idea for my son' 100% of parents who refused the biopsy indicated 'not sure if this is right'	

Yrs: years

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?			
Vadaparampil et al. Barriers to fertility preservation among pediatric oncologists.Patient Educ Couns 2008 Sep;72(3):402-10			
Study design & Main study objective	**Participants and relevant characteristics**	**Relevant results (per outcome)**	**Additional remarks**
<u>1. Study design</u> Qualitative study (semi-structured, in depth interviews) <u>2. Main study</u>	<u>1. Type and number of participants</u> 24 pediatric oncologists *Participation rate*: 45% out of 58 eligible physicians (45% noted in	<u>1. Outcome(s) definition</u> Factors that contribute to communication issues with FP discussion: Outcome 1. Physician factors Outcome 2. Parent factors Outcome 3. Patient factors Outcome 4. Institutional factors	<u>1. Strengths</u> - First study to consider factors affecting FP among pediatric oncologists in the state of Florida - Use of 3 coders for each transcript, after 2 coders for

objective To examine factors that may influence the discussion of FP among pediatric oncologists and patients/families 3. Additional study characteristics, if relevant Interviews took place in person (4) or by telephone (18), missing (2) Inter-rater reliability rate of 90% (assessing the number of potential codes in a given transcripts and examining the degree of concurrence across the raters)	manuscript, but 41% by these calculations) 15(63%) Male 9(37%) Female 21(88%) Pediatric Hematology/Oncology 2(8.3%) Pediatrics 1(4.2%) Stem cell Transplant, pediatric oncology 13 of 15 Florida centers participated (87%) 2. Age (at diagnosis) of participants NA 3. Number of participants per diagnosis NA 4. Additional participants characteristics, if relevant Average number of years practicing=10.6 (range 0.5-35 years) Average number of patients seen/week = 62.1 Mean age of patients	2. Results outcome 1 *Barriers to discussing fertility preservation* • Pediatric oncologists that felt less conformable discussing fertility preservation reported needing better educational materials and more established fertility preservation facilities to make them more comfortable *Factors around discussion of fertility preservation* • Half of physicians said they would like to learn more about FP, especially for females • Physician priority of FP: Most said this varied by the patient and was based on age, sex, and disease stage • Many of the physicians said that sometimes just mentioning the need for FP was seen as a sign of hope for patients and families • Physician perception of treatment delay: while all physicians said their female patients could not delay treatment for the 6-8 weeks necessary for ovarian hyperstimulation, there was a mixed response about treatment delay for males 3. Results outcome 2 and outcome 3 *Parent/patient-related barriers to discussing fertility preservation* Physicians reported that parental emotional status was a barrier to the parent/patient receiving information 75% of physicians reported that patient health status was a barrier when patients were too ill to bank sperm or explore options; 33% of physicians reported that parents' culture/religion regarding masturbation influenced the discussion of fertility preservation	specific categories - Phone and face-to-face interviews 2. Limitations - Risk of selection bias (those interested in FP more likely to participate in study) - Relatively low number of participants (results may not be generalizable to pediatric hematologist oncologists practicing in other states) - Physicians reporting on their perceptions of parent and patient factors which affect FP (as opposed to parents and patients reporting for themselves) - Some outdated information regarding FP (e.g. "One cycle of ovarian stimulation can take up to 8 weeks") - Risk of interviewer induced bias

	treated by interviewed physicians= 9.0 years (range from 0-21years)	5. Results outcome 4 *Institutional related barriers to discussing fertility preservation* 50% of physicians had no established relationship with any type of fertility clinic or specialist 100% of physicians were not aware of guidelines for fertility preservation; Majority of physicians reported that costs were a barrier to initiate fertility preservation and cost of long-term storage; 66% of physicians, who did not give educational material to patients on a regular basis, reported a lack of patient educational materials or felt the current materials available were not appropriate for their patient population	

FP: fertility preservation; NA: not applicable

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?			
Armuand et al. Physicians' self-reported practice behaviour regarding fertility related discussions in paediatric oncology in Sweden. Psychooncology. 2017;26(10):1684-1690			
Study design & Main study objective	**Participants and relevant characteristics**	**Relevant results (per outcome)**	**Additional remarks**
1. Study design Cross-sectional survey 2. Main study objective: To investigate practice behaviours of	1. Type and number of participants: 58 physicians working within pediatric oncology *Response rate:* 52% (out of 111 identified physicians; according to authors 60% of 67	1. Outcome(s) definition: Outcome 1: Practice behavior Outcome 2. Perceived attitudes Outcome 3. Barriers Outcome 4. Confidence in knowledge Outcome 5. Factors associated with discussing oncological treatment's impact on fertility	1. Strengths: - Study population based on total population of physicians working in pediatric oncology in Sweden - Use of multivariable analyses to identify factors associated with discussions about the risk of infertility with patients/ parents

Swedish physicians with regard to discussing the impact of cancer treatment on fertility with paediatric oncology patients and their parents, and to identify factors associated with such discussions 3. Additional study characteristics, if relevant: - A questionnaire was developed based on items from 2 questionnaires used in adult oncology in the United States - Multivariable logistic regression analyses were performed using the backwards method with with the dependent variable "Discussing	physicians responded, but 9 had not worked clinically with the patient group for the last 2 years and were excluded) 2. Age (at diagnosis) of participants: NA 3. Number of participants per diagnosis: NA 4. Additional participants characteristics, if relevant: Median age 53 years (34-72) 67% worked in university hospital 55% Specialized in paediatric oncology 71% Had access to a reproductive medicine clinic that provides FP	2. Results outcome 1 • Physicians often/always talked with their patients/parents about the potential impact of the treatment on fertility (male patients: 62%; female patients: 57%; P= 0.570) • More often with male patients (55% vs 33%) • 9(16%) reported seldom/never discussing treatment impact on fertility; of these N=8 worked in non-academic hospital and they often or always assigned the discussion to another clinic (e.g. the clinic initiating the cancer treatment) 3. Results outcome 2 • 52(90%) agreed that patients/parents consider having children after cancer treatment as important • 51(88%) agreed it was their responsibility as physicians to discuss possible impairment of fertility following treatment 4. Results outcome 3 *Barriers to the fertility related discussions* The most frequently reported barriers included: patient being of pre-school age (50%); poor prognosis (47%); need for immediate treatment start (28%); patient or parent appearing anxious (26%); overwhelmed by the diagnosis (24%); high workload (24%); unclear referral paths for fertility preservation (22%) 5. Results outcome 4 • Low confidence in knowledge about the risk of infertility following cancer treatment (9%-14%) • Low confidence in knowledge about FP methods (15%-68%), especially those methods appropriate to female patients	2. Limitations: - Risk of selection bias (those more interested in FP might be the ones participating) - Risk pf reporting bias (physicians might act differently when facing real situation and not hypothetical) - Not enough power in some analysis so caution needs to be taken into account with interpretation of results

treatment impact on fertility" with male and female patients, respectively (2 models).		6. Results outcome 5 *Multivariate analysis*: Physicians were less likely to discuss the treatment's impact on fertility with patients/parents if: • they worked at a non-university hospital (male patients: OR 11.49, CI 1.98–66.67;female patients: OR 33.18, CI 4.06–271.07) • believed the subject would cause worry (male patients: OR 8.23, CI 1.48–45.89; female patients: OR 12.38, CI 1.90–80.70) perceived parents as anxious (male patients: OR 7.18, CI 1.20–42.85, female patients: OR 11.65, CI 1.32–103.17)	

FP: fertility preservation; NA: not applicable

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?			
Benedict et al. Young Adult Female Cancer Survivors' Unmet Information Needs and Reproductive Concerns Contribute to Decisional Conflict Regarding Posttreatment Fertility Preservation. Cancer 2016;122(13):2101-9			
Study design & Main study objective	**Participants and relevant characteristics**	**Relevant results (per outcome)**	**Additional remarks**
1. Study design Cross-sectional (survey) 2. Main study objective: To characterized the posttreatment fertility information needs, reproductive concerns, and decisional conflict regarding future options for	1. Type and number of participants: 346 YAFC *Response rate*: 96% (out of 359 who met eligibility criteria) 714 respondents accessed the survey, 359 (50%) met eligibility criteria 2. Age (at diagnosis) of participants:	1. Outcome(s) definition: Outcome 1. Reasons for not pursuing FP pretreatment Outcome 2. Unmet information needs* Outcome 3. Reproductive concerns* Outcome 4. Decisional conflict regarding future FP* *Analysis done in subgroup of patients (N=179): women with uncertain fertility status who had not previously undergone/attempted FP and either wanted future children or were unsure. 2. Results outcome 1 *Barriers to fertility preservation* 30% of patients did not know about fertility preservation;	1. Strengths: - First study to examine the decisional conflict of young female survivors when prompted to consider posttreatment FP - Large sample size 2. Limitations: - Internet survey with responses not validated externally - Risk of reporting bias as use of survey

posttreatment FP among YAFC <u>3. Additional study characteristics, if relevant:</u> - Internet survey completed between February and March 2015 - The survey was designed by an interdisciplinary team with input from YAFC survivors	Age at diagnosis of whole cohort: 23.6 years (birth-35) Age at diagnosis of subgroup: 23.4 (birth-34) <u>3. Number of participants per diagnosis:</u> 79(23%) Lymphoma 68(20%) Breast cancer 50(14%) Gynecologic cancer 45(13%) Leukemia 27(8%) Colorectal 23(7%)Sarcoma 13(4%) Brain 54(16%)Other <u>4. Additional participants characteristics, if relevant:</u> Gonadotoxic treatment: 59(17%) Pelvic radiation 285(82%)Chemotherapy 36(10%)Surgery 35(10%) Bone marrow transplant	29% of patients were feeling too distressed or overwhelmed; and 27% of patients reported cost as barrier <u>3. Results outcome 2</u> *Information needs regarding fertility preservation discussion (from subgroup analysis)* Female cancer patients reported unmet information needs regarding fertility risks (58-60%), options to assess and preserve fertility (51-62%), and options for alternative family building (43%) <u>4. Results outcome 3</u> • 64% of respondents were concerned they may not be able to have (more) children • 41% reported it was stressful to think about getting pregnant • 59% were worried about passing on a genetic risk for cancer • 53% of women were concerned their partner or a future partner would be disappointed if they were unable to have children <u>5. Results outcome 4</u> High levels of decisional conflict: • 13% believed they were informed regarding their FP options • 74% were unclear about their personal values related to the decision • 70% believed they did not have enough advice • 35% believed they did not have enough support to make a decision <u>6. Additional outcomes (if applicable)</u> In bivariate analysis:	- Risk of selection bias as those who participated might be different than those who did not

		• Greater decisional conflict was associated with having greater unmet information needs (p<.001) and reproductive concerns (p<.001) • Across all information topics, women who indicated that they had unmet information needs reported higher levels of decisional conflict (p's<0.01) In multiple regression analysis controlling for current age, age at treatment completion, income, relationship status, nulliparity, and prior fertility evaluation: • The relation between greater unmet information needs and higher levels of decisional conflict about future FP remained significant p <0.001 • Greater reproductive concerns were associated with greater conflict at the trend level • Having undergone a fertility evaluation after treatment was found to be related to lower decisional conflict • Unmet information needs and reproductive concerns accounted for 22% of the variance in decisional conflict	

FP: fertility preservation; YAMC: young adult female cancer survivors; NA: not applicable;

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?			
Diesch et al. Fertility preservation in pediatric and adolescent cancer patients in Switzerland: A qualitative cross-sectional survey. Cancer Epidemiol. 2016 Oct;44:141-146			
Study design & Main study objective	**Participants and relevant characteristics**	**Relevant results (per outcome)**	**Additional remarks**
1. Study design Cross-sectional (survey)	1. Type and number of participants: 9 physicians (1 per each of the Swiss pediatric hematology/oncology	1. Outcome(s) definition: Outcome 2. The availability of FP counseling and/or a SOP in FP counseling Outcome 4. The physician's own view of FP 2. Results outcome 2	1. Strengths: First survey report concerned to FP counseling and procedures in pediatric and adolescent cancer patients in Switzerland

2. Main study objective: To evaluate the different practices in FP performed on children and adolescents, and to identify unmet needs in this field 3. Additional study characteristics, if relevant: Quesstionnaire conducted from June 2014 to October 2014 on the counseling and procedures performed between 2009 and 2013 A questionnaire was sent by mail and e-mail to the head of each of the nine pediatric hematology/ oncology departments in Switzerland	centers) *Response rate*: 100% 2. Age (at diagnosis) of participants: NA 3. Number of participants per diagnosis: NA 4. Additional participants characteristics, if relevant:	• An SOP for FP counseling and procedures was available in four out of nine (44%) centers (two for pre and postpubertal patients and two for postpubertal patients alone) • These SOPs were in-house protocols based on the guidelines of American Society of Clinical Oncology (ASCO) (2006) or British Fertility Society (2004) and were written in collaboration with the university-based fertility team • In 4/5 centers without an SOP performed FP counselling • In 7/9 centers (four with an SOP), an FP counseling was conducted at the beginning of the treatment or procedure However in three out of nine centers (all with an SOP) the FP counseling was conducted before performing HSCT procedure • Absence of an SOP for FP did not exclude the possibility of counseling by some centers; however, the counseling was performed by a hematologist alone 4. Results outcome 3 *Most frequently used procedures* In females: use of a gonadotropin releasing hormone agonist (GnRHa) (42%); ovarian tissue cryopreservation (47%) In males: sperm cryopreservation (88%); Testicular sperm extraction was performed in three postpubertal males; No centers performed a cryopreservation of spermatogonial stem cells 5. Results outcome 4 *Barriers to fertility preservation counselling (according to physicians)* Reported reasons for refusal of counseling by parents/ patients were lack of interest (66%), overwhelming nature of	2. Limitations: - The questionnaire was completed by only one professional person per institution, possibly leading to the introduction of some (reporting) bias regarding the representativeness of the institution - Physician's view on the impact of FP counselling (instead of asking patients directly)

		the situation (66%), and psychological distress in a life-threatening situation (55%) *Barriers to discussing fertility preservation* 33% of the physicians reported that lack of time was the most frequently provided reason for the lack of counseling Doctors' views on the impact of FP counseling mentioned potential benefits for patients: • relief of emotional distress (6/9) • greater ability to cope with the diagnosis (3/9) • less of the inquired considered no difference (3/9) In all centers agreement that financial support is crucial; however, 90% of them indicated the need to promote education on the topic of FP and increase the availability of resources <u>6. Additional outcomes (if applicable)</u>	

FP: fertility preservation; NA: not applicable; SOP: standard operating procedure

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?			
Fuchs et al. Pediatric Oncology Providers' Attitudes and Practice Patterns Regarding Fertility Preservation in Adolescent Male Cancer Patients. J Pediatr Hematol Oncol. 2016; 38(2): 118–122			
Study design & Main study objective	**Participants and relevant characteristics**	**Relevant results (per outcome)**	**Additional remarks**
<u>1. Study design</u> Cross-sectional (survey)	<u>1. Type and number of participants:</u> 326 pediatric oncology providers	<u>1. Outcome(s) definition</u>: Outcome 1. Approach to FP discussion Outcome 2. Educational materials Outcome 3. Provider knowledge of FP guidelines and	<u>1. Strengths:</u> Study examines educational materials on FP for adolescent male patients

2. Main study objective: To evaluate pediatric oncology providers' attitudes toward FP, their use of educational materials, their approach to FP discussion, and their FP knowledge specifically pertaining to adolescent males 3. Additional study characteristics, if relevant: - A survey announcement was emailed to individual members registered to a database of US-based pediatric oncology providers, including physicians, APNs, and nurses - A follow-up email reminding	*Response rate*: 10% (out of 3257 individuals invited to complete the survey) 157(48%) physicians 59(18%) APN 54(17%) nurses 56(17%) unknown 2. Age (at diagnosis) of participants: NA 3. Number of participants per diagnosis: NA 4. Additional participants characteristics, if relevant: Practice setting: 197(60.4%) Academic medical center 51(15.6) Community medical center 16(4.9) Private practice 6(1.8) Other 56(17.2) Unknown	technologies 2. Results outcome 1 • Discussion of the impact of cancer treatment on the future fertility of their adolescent male patients "usually" or "always" (76% to 100% of the time): 93.6% of Physicians 74.6% APNs 48.2% Nurses • High levels of comfort with FP discussions (somewhat or entirely comfortable): 78.7% Physicians 81.4%, APNs • Somewhat or entirely comfortable with FP discussions 51.9% of nurses The difference between physician and nurse groups in both of these comparisons were found to be statistically significant ($p<0.05$) 3. Results outcome 2 *Use of educational material for fertility preservation discussion* 51% of physicians, 54.2% of advanced practice nurses and 38.9% of nurses reported 'usually' or 'always' using educational materials Majority of providers reported using printed materials, the next greatest proportion of providers reported using Internet site referrals *Limitations of existing educational material for fertility preservation* 49% of providers stated that adult content, adult language and overall reading level were limitations of existing	2. Limitations: - Questionnaire was not validated - Risk of reporting bias (as use of questionnaire) - Risk of selection bias (probably those more interested in the topic participated) - Low response rate (this was an email survey so authors think it might be related to not having valid email addresses for everyone) - Authors did not offer multiple repeat reminder emails nor did we offer compensation for participation

recipients to complete the survey was sent 3 weeks later; the online survey was closed 5 weeks after the initial notification - Identities of individual respondents were blinded for the extent of the study		educational material Order of most commonly published by: - Fertile Hope/Lance Armstrong Foundation - Institution specific materials - ASCO - Oncofertility Consortium - The Endocrine Society/the Hormone Foundation *(unclear why N for this answer is 330 while total study population is 326)* <u>4. Results outcome 3</u> *Knowledge about fertility preservation as a barrier to discussing fertility preservation* 26% of physicians, 35.6% of advanced practice nurses and 64.8% of nurses reported to be unfamiliar with 2006 ASCO recommendations on fertility preservation 48.7% physicians reported being unfamiliar with ICSI technique, compared with 52.5% of APNs and 81.1% of nurses (P<0.05) <u>5. Additional outcomes (if applicable)</u> Formal training regarding FP in adolescent oncology patients:92.9% of providers received no formal training Formal training on FP would be useful to providers: 84.4% of all providers reported that training would be useful	

FP: fertility preservation; NA: not applicable; APN: advanced practice nurse; ASCO: American Society of Clinical Oncology; ICSI: intracystoplasmic sperm injection

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?
Klosky et al. Provider Influences on Sperm Banking Outcomes Among Adolescent Males Newly Diagnosed With Cancer. J Adolesc Health 2017;60:277-283

Study design & Main study objective	Participants and relevant characteristics	Relevant results (per outcome)	Additional remarks
1. Study design Prospective study with questionnaires (single group quasi experimental study) 2. Main study objective: To examine provider communication and sociodemographic factors which associate with sperm banking outcomes in at-risk adolescents newly diagnosed with cancer 3. Additional study characteristics, if relevant: Study took part from 2011 to 2014 in United States and Canada Before study	1. Type and number of participants: 54 medical providers and 99 of their adolescents at-risk patients from eight leading pediatric oncology centers in North America 45 oncologists 5 nurse practitioners 2 social workers 2. Age (at diagnosis) of participants: 37(37.4) 13-15 years 30(30.3) 16-17 years 32(32.3) 18-21 years 3. Number of participants per diagnosis: 58(58.6)Leukemia/lymphoma 7(7.1) Brain tumors 34(34.3) Solid tumors 4. Additional participants characteristics, if relevant: Provider gender: males: 25(48.8%) females: 26(50.0%)	1. Outcome(s) definition: Outcome 1.Collection attempt Outcome 2. Successful completion of sperm banking 2. Results outcome 1 47(47.5%) adolescents made collection attempts 38 (38.4%) successfully banked No significant difference between provider comfort and adolescent's rating of provider comfort 3. Results outcome 2 *Barriers to collection attempt* • The final multivariate logistic regression model found the likelihood of making a collection attempt was nine times greater among adolescents who attended a specialized fertility preservation consultation relative to those without this encounter: OR 9.01(95% CI 2.54-31.90), p < 0.001 • Providers who rated themselves as being more comfortable in their skills to negotiate barriers to sperm banking with families had patients who were two times more likely to engage in a sperm banking attempt compared to providers rating themselves as less comfortable in their skills during these negotiations: OR 0.95(95% CI 1.03-3.63), p <0 .04 • Adolescents who did not complete a specialized fertility preservation consultation were less likely to bank sperm relative to those with this referral: consultation yes vs no,	1. Strengths: Quantifies influence of providers on sperm banking of adolescents among at-risk adolescents newly diagnosed with cancer (not a descriptive study but use of multivariate regression analyses) 2. Limitations: - Risk of selection bias with oversampling of oncologists which may underestimate the influence of other medical professions - Parental influences on sperm banking not taken into account - Underpower to study other assiociations in the multivariate analyses (e.g. provider and medical team recommendation to bank, fertility risk communication by provider) - Risk of reporting bias (as use of questionnaire)

enrollment, study team members systematically completed daily eligibility checklists for all potentially eligible adolescent patients at their respective institutions. Once the medical record review was completed and initial study criteria was met for a new patient, the adolescent's oncologist was e-mailed and queried regarding the fertility risk status of the adolescent patient in question (fertility risk score ranging 0, no risk, to 3, high risk). Only after the oncologist rated the participant as being at increased risk for	missing 1 Most of the providers had children: 37(71.2%) Eligibility: • Male • newly diagnosed with a first cancer • 13-21 years of age (inclusive) • Tanner stage III, proficient in speaking and reading English or Spanish, and possessing the cognitive capacity to complete study questionnaires • increased risk for treatment-related infertility secondary to impending cancer treatment	OR 4.96(95% CI 1.52-16.00), p <0 .01 <u>4. Additional outcomes (if applicable)</u>	

infertility (e.g., risk score _1) was the patient considered eligible for the study.			

FP: fertility preservation; NA: not applicable

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?			
Panagiotopoulou et al. Fertility Preservation Care for Children and Adolescents with Cancer:An Inquiry to Quantify Professionals' Barriers. J Adolesc Young Adult Oncol. 2017;6(3):422-428			
Study design & Main study objective	**Participants and relevant characteristics**	**Results (per outcome)**	**Additional remarks**
1. Study design Cross-sectional pilot study (survey) 2. Main study objective: To quantify the barriers of fertility preservation care among professionals through the development and use of a survey tool and to analyze which factors influence professionals'	1. Type and number of participants: 48 adolescent and pediatric oncology healthcare professionals *Response rate*: 55% (unclear how many were approached/invited) 26% oncology doctors 65% nurses 9% allied healthcare professionals 87% Female 75% Younger than 50 years of age	1. Outcome(s) definition: Outcome 1. Barriers to FP care Outcome 2. Association of demographic factors with barriers to FP care 2. Results outcome 1 *Barriers to fertility preservation discussion* 85% of healthcare professionals reported patient's age and patient's medical condition to be the most likely reason for not having a discussion on fertility; 82% reported the patient's or family's lack of interest in fertility discussions; and 77% reported their own knowledge gaps Least frequently endorsed as barriers to fertility preservation: Existing infrastructure of fertility and oncology services; Discomfort with discussing fertility issues or FP with their patients care	1. Strengths: Quantification of barriers to FP care with a multidisciplinary study population (and not only physicians) 2. Limitations: - Risk of reporting bias as use of questionnaire - Risk of selection bias (participation more likely by those professionals with an interest in FP) - Unclear who many individuals were approached - Relatively low sample size

adherence to fertility preservation care <u>3. Additional study characteristics, if relevant:</u> First, we drafted a preliminary survey by identifying content domains in previously published studies that were relevant to oncology professionals' barriers to fertility preservation care Subsequently,we convened a panel of three experts to assess content validity and facilitate item reduction The experts were asked to identify any missing relevant items and to evaluate	<u>2. Age (at diagnosis) of participants:</u> NA <u>3. Number of participants</u> per diagnosis: NA <u>4. Additional participants characteristics, if relevant:</u> Recruitment occurred at the pediatric and adolescent oncology Principal Treatment Centre of the North East of England Eligibility: 1) pediatric and adolescent oncology healthcare professional based at the Great North Children's Hospital, United Kingdom (2) respondent filling in the questionnaire for the first time (3) respondent able to understand and consent to the study	Consensus among responders: Low for knowledge gaps (consensus index of 36%) - Information resources (availability of clinical guidelines, protocols, or patient information leaflets (consensus index of 42%-48%) <u>3. Results outcome 2</u> Overall very few demographic variables were associated with barriers to fertility preservation care Nurses and allied healthcare professionals endorsed knowledge or policy gaps as barriers to a greater degree than medical doctors	

included items for significance in identifying professionals' barriers to fertility preservation care. The survey was pretested by four healthcare professionals that included one doctor, one nurse, and two PhD students			

FP: fertility preservation; NA: not applicable

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?			
Klosky et al. Parental influences on sperm banking attempts among adolescent males newly diagnosed with cancer. Fertil Steril 2017;108:1043-1049			
Study design & Main study objective	**Participants and relevant characteristics**	**Relevant results (per outcome)**	**Additional remarks**
1. Study design Prospective observational study (survey) 2. Main study objective: To investigate the influence of parental	1. Type and number of participants: 144 parents of 122 newly diagnosed adolescent males at increased risk for infertility secondary to cancer therapy *Original cohort*: of the 156 enrolled adolescent	1. Outcome(s) definition: Outcome 1. Sperm collection attempt Outcome 2. Factors predicting sperm banking attempt (factors studied: parental sociodemographic factors, parental fertility related communication, parental health beliefs) 2. Results outcome 1 68 (55.7%) adolescents attempted to bank sperm 57 (83.8%) successfully banked	1. Strengths: - Large study 2. Limitations: - Overrepresentation of mothers in parents - Risk of reporting bias (as use of survey)

sociodemographic, communication, and psychological factors on sperm collection attempts among at-risk adolescent males newly diagnosed with cancer 3. Additional study characteristics, if relevant: - The study team members screened daily patient lists of new patients diagnosed with cancer for eligibility requirements. - The patients were approached for study participation and enrolled 1 through 7 days after initiation of cancer therapy (or up to day 14 at our Canadian site). - Once patient was	males, 146 completed surveys 144 caregivers returned the surveys 2. Age (at diagnosis) of participants: Adolescents: 13-21 years Parents: Mean 44.5 years (5.6 SD) 3. Number of participants per diagnosis: 65 (53.3%) Leukemia/ lymphoma 48 (39.3%) Solid tumor 9 (7.4%) Brain tumor 4. Additional participants characteristics, if relevant: 101 (70%) maternal 42 (29%) paternal 1 survey completed by both Caregivers: 142 parents; 2 aunts 101(70.1%) female 100 (69.4%) white 133 (92.4%) christian 103 (71.5%) married or	3. Results outcome 2 *Barriers to sperm banking attempt* Adolescents who did not have a parental recommendation to bank sperm were less likely to make collection attempt relative to those who did have recommendation: parental recommendation yes vs no, OR 3.72 (95% CI 1.18-11.76), p=0.03 Maternal recommendation and paternal recommendation increased the likelihood of making a collection attempt: Maternal recommendation OR 3.0; 95% CI 1.9-4.8; p<0.001 Paternal recommendation OR 8.2; 95% CI 3.0-22.8; p<0.001 Adolescents who did not have a parent who coordinated/facilitated banking were less likely to make a collection attempt relative to those who did have: Parental self-efficacy yes vs no, OR 1.20; 95% CI 1.02-1.41; p=0.02 4. Additional outcomes (if applicable) Parent communication of fertility risk to their sons increased the likelihood of making a collection attempt: OR 8.7; 95% CI 0.9-83.8; p=0.06	

consented, caregivers were invited to participate	living as married		

OR: odds ratio; CI: confidence interval; SD: standard deviation

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?			
Klosky et al. Prevalence and Predictors of Sperm Banking in Adolescents Newly Diagnosed With Cancer: Examination of Adolescent, Parent, and Provider Factors Influencing Fertility Preservation Outcomes. J Clin Oncol 2017;35:3830-3836			
Study design & Main study objective	**Participants and relevant characteristics**	**Relevant results (per outcome)**	**Additional remarks**
1. Study design Prospective observational study (surveys) 2. Main study objective: To estimate the prevalence of sperm banking among adolescent males newly diagnosed with cancer and to identify factors associated with banking outcomes 3. Additional study	1. Type and number of participants: 146 male adolescents diagnosed with cancer at risk for infertility 144 parents/guardians 52 medical providers *Original cohort*: 180 were approached, 156 enrolled, and 146 returned completed questionnaires 2. Age (at diagnosis) of participants: Mean 16.49 years (SD 2.02 years)	1. Outcome(s) definition: Outcome 1. Collection attempt and successful completion of sperm banking Outcome 2. Reasons for not making collection attempt Outcome 3. Factors associated with increased likelihood of a collection attempt (multivariate model) Outcome 4. Factors associated with increased likelihood of sperm banking completion (multivariate model) 2. Results outcome 1 78/146 (53.4%) adolescents attempted to collect sperm 64/146 (43.8%) adolescents with successful completion of sperm banking 64/78 (82.1%) adolescents who attempted to collect sperm had successful completion 3. Results outcome 2 *Reasons for not making collection attempt*	1. Strengths: Study quantifies effects with OR 2. Limitations: - Overrepresentation of mothers in parents - Risk of reporting bias (as use of surveys)

<u>characteristics, if relevant:</u> Participants were enrolled 1 to 7 days postinitiation of cancer therapy. Self-report questionnaire data were collected at that time Before enrollment, study team members systematically completed daily eligibility checklists for potential participants. Once medical record review was completed and initial study criteria were met, an adolescent's oncologist was queried regarding the patient's fertility risk After oncologist rated the adolescent as	<u>3. Number of participants per diagnosis:</u> 82 (56.2%) Leukemia or lymphoma 9 (6.2%) Brain tumor 55 (37.7%) Solid tumor <u>4. Additional participants characteristics, if relevant:</u> *Parents* 101 maternal 42 paternal 1 survey completed collaboratively by borth parents 42 (29.0%) Male 101(69.7%) Female *Medical providers* 45 (84.6) Oncologist 7 (13.4) Other	64/68 (94%) adolescents disclosed their reasons: In 45.3% of adolescents, sperm banking was discussed but the patient or family decided not to perform collection attempt; 40.6% of adolescents did not believe banking was necessary; 14% of adolescents was unsure about what sperm banking was <u>4. Results outcome 3</u> *Barriers to sperm collection attempt (adolescent report)* • Adolescent consultation with a fertility specialist: OR 29.96; 95%CI 2.48 -361.41; p=0.007 • Parent recommendation to bank: OR 12.30; 95%CI 2.01-75.94; p=0.007 • Higher Tanner stage: OR 5.42; 95%CI 1.75-16.78; p=0.003 <u>5. Results outcome 4</u> *Barriers to sperm banking (adolescent report)* • Adolescent history of masturbation: OR 5.99; 95%CI, 1.25-28.50; p= 0.025 • Self-efficacy for banking coordination*: OR 1.23; 95%CI, 1.05 to 1.45; p=0.012 • Parent recommendation (OR 4.62; 95%CI, 1.46-14.73; p=0.010 • Medical team recommendation: OR 4.26; 95% CI, 1.45-12.43; p=0.008 * e.g. confidence in their ability to manually collect a sample Adolescents who did not have a history of masturbation were less likely to bank sperm relative to those who did have a history of masturbation: masturbation yes vs no, OR 5.99	

being at increased risk for infertility was the patient considered eligible		(95%CI 1.25-28.50), p= 0.025 Adolescents who did not have self -efficacy for banking coordination were less likely to bank sperm relative to those who did have self-efficacy: banking self-efficacy yes vs no, OR 1.23; 95%CI, 1.05 to 1.45; p=0.012 Adolescents who did not have parent recommendation to sperm bank were less likely to bank sperm relative to those who did have recommendation: parental recommendation yes vs no, OR 4.62 (95%CI 1.46-14.73) p=0.010 Adolescents who did not have medical team recommendation to sperm bank were less likely to bank sperm relative to those who did have recommendation: medical team recommendation yes vs no, OR 4.26 (95% CI, 1.45-12.43) p=0.008	

OR: odds ratio; CI: confidence interval; SD: standard deviation

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?			
Diesch et al. Fertility preservation practices in pediatric and adolescent cancer patients undergoing HSCT in Europe: a population based survey. Bone Marrow Transplant. 2017;52:1022-1028			
Study design & Main study objective	**Participants and relevant characteristics**	**Relevant results (per outcome)**	**Additional remarks**
1. Study design Survey 2. Main study objective: To analyze different fertility preservation practices in Europe and determine the	1. Type and number of participants: 38 centers reporting 834 patients receiving HSCT: 585 (70%) Malignant disease 241 (29%) Non-malignant disease	1. Outcome(s) definition: Outcome 1. Barriers for physicians for counseling of fertility preservation Outcome 2. Barriers for parents for counseling of fertility preservation 2. Results outcome 1 17/38 (45%) centers did not receive routinely counseling *Barriers to discussing fertility preservation*	1. Strengths: First survey reporting the current practices in fertility counseling and FP practices in children and adolescents who underwent HSCT in EBMT centers 2.Limitations: - Low response rate (21.5%)

possible obstacles barring their broader implementation <u>3. Additional study characteristics, if relevant:</u> Survey was conducted from October 2014 to December 2015	*Original cohort*: 177 EBMT centers transplanting children and adolescents contacted (response rate 21.5%) <u>2. Age (at diagnosis) of participants:</u> <18 years <u>3. Number of participants per diagnosis:</u> NR <u>4. Additional participants characteristics, if relevant:</u> 612 (73%) Prepubertal 203 (25%) Postpubertal	Physicians cited lack of time (59%), refusal by parents (35%), poor prognosis of the primary disease and financial considerations (5.9%) as the most frequently provided reasons for the lack of counselling <u>3.Results outcome 2</u> *Barriers to fertility preservation counselling (according to physicians)* Reported reasons for refusal of counseling of fertility preservation by parents/ patients were psychological distress in a life-threatening situation (53%), overwhelming nature of the situation (50%) and lack of interest (42%)	- The questionnaire was completed by only one professional person per institution, possibly leading to the introduction of some (reporting) bias regarding the representativeness of the institution -Includes 29% patients of the 834 with non-malignant disease - Physician's view on the impact of FP counselling (instead of asking patients directly) - Centers without a relevant program may also have chosen not to answer the questionnaire

NR: not reported

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?			
Ginsberg et al. Sperm banking for adolescent and young adult cancer patients: sperm quality, patient, and parent perspectives. Pediatr Blood Cancer. 2008;50:594-8			
Study design & Main study objective	**Participants and relevant characteristics**	**Relevant results (per outcome)**	**Additional remarks**
1. Study design Survey 2. Main study objective: To evaluate feasibility of offering newly diagnosed male patients the opportunity to bank sperm and, to determine the beliefs and decision-making processes of patients and their parents who considered sperm banking. 3. Additional study characteristics, if relevant: Questionnaires were then administered to patients and	1. Type and number of participants: -50 male patients completed the questionnaire (including 45 who attempted banking) - 45 parents and 1 legal guardian also completed the questionnaire. *Original cohort*: 73 patients attempted to provide semen for analysis (of 81 patients, 8 refused to bank). Samples of 68 patients were included in the semen quality database. 2. Age (at diagnosis) of participants: Mean 17.2 ± 3.0 78.4% between 15-19 years 3. Number of participants per diagnosis:	1. Outcome(s) definition: 1. Initial response to sperm banking discussions 2. Initial reactions to idea of sperm banking 3. Reactions to the timing of sperm banking discussions 4. Who made the decision to bank 5. Concerns about delaying treatment to bank 6. Decision influences: patient versus parent 2. Results outcome 1 Although a larger proportion of patients (56.2%) would have preferred to hear about banking with their parents, 43.8% would have preferred to have initial discussions without their parent present. 3.Results outcome 2 Upon learning of sperm cryopreservation as an option, most respondents thought banking was a ‘‘great idea’’ No parents and only a few patients had the initial reaction that they did not want to attempt banking. Of the four patients who thought, ‘‘no way, I know that I do not want to do this’’, one responder ultimately attempted sperm banking and succeeded; the other three patients never banked. 4.Results outcome 3 Most parents and patients learned about the possibility of sperm banking within 1 week of diagnosis, and this timing was acceptable to the majority	Limitations: -Small sample

parents who had been approached about sperm banking. This eleven-item questionnaire focused on the patients' understanding of the impact of therapy on future fertility, the timing and approach of the clinical staff, the beliefs that influenced the decision process, and the extent of parental involvement in the final decision. Patients who chose to sperm bank were asked nine additional questions regarding their experience with the sperm banking process. Items focused on the patients' expectations, impact of delaying treatment in order	NM Patients scheduled to receive chemotherapy <u>4. Additional participants characteristics, if relevant:</u>	<u>5.Results outcome 4</u> Most parents and patients report that the decision to bank was made jointly. When patients are matched with their own parents, however, there is not a statistically significant agreement on who made the decision. The level of agreement is 61.9% (P¼0.065). The largest area of disagreement was between patients who reported that they made their decision alone, and parents who reported that it was a joint decision. <u>6.Results outcome 5</u> Although parents were likely to consider the impact of treatment delays, delaying treatment was necessary in only 20% of cases. When necessary, parents reported that treatment delays were upsetting. However, all parents and patients experiencing a treatment delay to sperm bank reported that banking was important enough to warrant such a delay. <u>7.Results outcome 6</u> • Parents and patients considered many of the same issues when deciding to sperm bank. • Most adolescents and young adults felt the decision was a personal one and many were influenced by their parent's opinion.	

to sperm bank, their level of comfort with the process (including whether they were adequately prepared about what to expect), and the actual experience of specimen collection. One parent was also asked to complete an identical questionnaire			

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?			
Klosky et al. Patient Factors Associated With Sperm Cryopreservation Among At-Risk Adolescents Newly Diagnosed With Cancer. Cancer. 2018;124:3567-3575			
Study design & Main study objective	**Participants and relevant characteristics**	**Relevant results (per outcome)**	**Additional remarks**
1. Study design Cross-sectional (surveys) study 2. Main study objective: To investigated the	1. Type and number of participants: 146 patients completed all questionnaires *Original cohort*: 181	1. Outcome(s) definition: 1. collection attempt (yes/no) 2. successful sperm banking (yes/no) A collection attempt was considered as such if the patients answered 1) "Yes"; 2) "No, I tried to but wasn't able to provide a sample"; or 3) "No, I provided a	1. Strengths: - large study (8 centres in US and Canada) - identified 100% agreement between adolescent and parent reports regarding sperm banking outcomes

contribution of developmental, communication and psychological factors in affecting sperm banking among at-risk adolescent males. The role that each of these factors plays in this process was tested in association with our 2 primary study outcomes: 1) collection attempt and 2) successful completion of banking sperm. <u>3. Additional study characteristics, if relevant:</u> Sperm banking among newly diagnosed adolescents from 8 pediatric oncology centers in the United States and Canada from December 2010 through January	eligible patients approached, 156 (80.7%)agreed to participate <u>2. Age (at diagnosis) of participants:</u> 16.5 years (standard deviation 2.0) <u>3. Number of participants per diagnosis:</u> 82 (56.2%) Leukemia or lymphoma 64 (43.8%) Brain tumor and Solid tumor <u>4. Additional participants characteristics, if relevant:</u>	sample but there was no sperm to bank in it." Sperm banking was coded as successful only if the response was "Yes." <u>2. Results outcome 1.</u> Descriptive reasons for not attempting banking: • 78/146 (53.4%) patients made a collection attempt • 14/78 (17.9%) patients did not successfully bank: unable to provide a sample (11 patients; 14%) or sample was azoospermic (3 patients; 4%) • Overall: 64/146(43.8%) patients successfully banked sperm • Other reasons for not attempting to bank included a lack of communication from the physician (6 patients; 8.8%), not desiring biological children (4 patients; 5.9%), religious/moral concerns (4 patients;5.9%), prohibitive cost (4 patients; 5.9%), concern regarding delaying treatment (4 patients; 5.9%), and fear of passing down a genetic risk for cancer (1 patient; 1.5%) • 15/68(22.1%) patients did not report a reason for not attempting to bank Results from multivariate logistic regression: • Adolescents who reported that a parent recommended banking were nearly 5 times more likely to make a collection attempt: collection attempt yes vs no, OR 4.88 (95%CI, 1.15-20.71), p=5 .032 • Adolescents with a higher Tanner stage were more likely to attempt banking: collection attempt yes vs no, OR 4.25 (95% CI, 1.60-11.27), p=0.004 • Adolescents who more strongly endorsed the benefits of banking were more likely to attempt banking: collection attempt yes vs no, OR 1.41 (95% CI, 1.12-1.77), p=0.004 • Adolescents who reported greater barriers to banking in their social environment (e.g. friends, siblings) were less likely to make a collection attempt: collection attempt yes vs no, OR 0.88 (95% CI,0.81-0.96), p=0.005	<u>2.Limitations:</u> - Risk of reporting bias (as use of surveys without medical record validation) - Tanner stage of the participant and fertility risk scores were clinically assigned (as opposed to meeting standardized study-based definitions), which can increase the likelihood of variability in classifications.

2014		3.Results outcome 2. Results from multivariate logistic regression: • Provider-reported recommendations were associated with greater likelihood to successfully bank: successful sperm banking, yes v no, OR 2.67 (95% CI, 1.05-6.77) P=0.039 • Adolescents-reported recommendations from a parent were associated with greater likelihood to successfully bank: successful sperm banking, yes v no, OR 3.02 (95% CI, 1.1-8.10) p=0 .029 • Adolescents who reported higher self-efficacy to bank were more likely to be successful: successful sperm banking, yes v no, OR, 1.16 (95% CI,1.01-1.33), p=0 .034 • Adolescents who consulted with a fertility specialist were more likely to successfully bank: successful sperm banking, yes v no, OR 3.44 (95% CI, 1.00-11.83), p=0.050	

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?			
Khalife et al. Parental Attitudes Toward Fertility Preservation in Female Adolescent Cancer Patients in Lebanon. J Pediatr Adolesc Gynecol 2019;3:525-9.			
Study design & Main study objective	**Participants and relevant characteristics**	**Relevant results (per outcome)**	**Additional remarks**
1. Study design Cross sectional Questionnaire survey study 2. Main study objective To shed light on	1. Type and Number of Participants 70 parents of female adolescents who presented for treatment at the St Jude Childhood Cancer Center at the American University of	1. Outcome definitions The knowledge of the parents toward the effect of cancer treatment on fertility, the knowledge about the current FP options, as well as their readiness to have their daughters undergo FP. **Results** Parental knowledge and attitudes about FP options	1. Strengths Did sample Size and Statistical Calculations. Thus enough participant to detect a significance in the result. Used validated questionnaire. Survey was on the basis of a

the barriers that fertility specialists face, as well as the acceptability of invasive procedures such as ovarian tissue and oocyte cryopreservation among parents of female adolescents diagnosed with cancer. To measure parental attitudes toward fertility preservation (FP) in female adolescent cancer patients in a Middle Eastern Country, to understand barriers to decision-making and decisional conflicts. <u>3. Study years</u> February 2018 to September 2018.	Beirut Medical Center (AUBMC) <u>2.Most common Diagnoses</u> Acute lymphoblastic leukemia 29/70 (41.4%) Osteosarcoma 11/70 (15.7%) <u>3. Age of the children of the participants</u> Mean ± SD=12.2 ± 2.67 at diagnosis <u>4. Controls (if applicable)</u> Not Applicable	- 49/70 (70%) parents were concerned about the effect on normal growth and development of their daughters rather than infertility (20/70), when questioned about the side effects of cancer treatment. <u>Reason for not applying for fertility preservation:</u> - It was not necessary: 32 (45.7%) - Risks of hormones on my child's health: 0 (0%) - Difficulty in finding proper facilities: 16 (22.8%) - Time was limited: 9 (12.9%) - Expenses of the procedure: 6 (8.6%) - Poor success rates of fertility preservation options: 1 (1.4%) - Other or unknown: 6 (8.6%) <u>Reason for declining oocyte cryopreservation:</u> - Unsafe procedure (bleeding, infection risks): 18 (25.7%) - My daughter should decide and it's impossible at her age: 5 (7.1%) - Cultural issue related to disruption of hymen: 20 (28.6) - Delay in the chemo treatment until egg collection: 3 (4.3%) - Expensive procedure: 2 (2.9%) <u>Reason for declining ovarian tissue cryopreservation:</u> - Still experimental; no pregnancy is guaranteed: 18 (25.7%) - Unsafe procedure (risks of bleeding, infection), unnecessary: 34 (48.6%) - Risking cancer relapse at future transplantation: 6 (8.6%) <u>Univariate Analysis:</u> - Parents with higher educational levels were more concerned about fertility-related issues of their daughters than parents with lower educational levels.	validated questionnaire proposed to adolescent male cancer patients to measure parental attitudes toward FP <u>2. Risk of bias</u> *1. Selection bias: Low risk* Reason: 70 parents of all female adolescents who presented for treatment at the tertiary care center were included *2. Attrition bias: Low risk* Reason: 70/72 (97.2%). parents who were approached accepted to take part in the study. *3. Detection bias: Unclear* Reason: Unclear if outcome assessors were blinded *4. Confounding: high risk* Reason: No multivariate analysis adjusting for potential confounders

		(Pearson $\varkappa^2$= 76.6; P< .001). - 19/70 (27.2%) parents with at least a bachelor's degree were more aware of the risk of adverse events of cancer treatment on fertility and were more concerned about infertility related to treatment (Pearson $\varkappa^2$ =87.5 [P < .001]; Pearson $\varkappa^2$ =74.1 [P < .001], respectively). - The acceptance rate of parents for vaginal retrieval did not significantly differ between the different age groups (Pearson $\varkappa^2$= 0.184; P = .67). An acceptance rate of 3/11 (27.3%) was observed for patients younger than 11 years old compared with an acceptance of 20/59 (33.9%) for those older than 11 years. - 18/70 (25.6%) of Muslims, 37/70 (52.6%) of Christians, and 19/70 (27.2%) of Druze would accept their daughters to undergo transvaginal egg collection and this was significantly different among the 3 groups (Pearson $\varkappa^2$ =76.0; P < .001). - The educational level of parents, the number of children in the family, monthly income, employment status, or the girl's current health condition were not associated with their acceptance to approve their daughters' undergoing oocyte cryopreservation through the vaginal route.	

SD= Standard deviation, FP= Fertility preservation.

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?			
Takae et al. Fertility Preservation for Child and Adolescent Cancer Patients in Asian Countries Front Endocrinol (Lausanne) 2019;10:655.			
Study design & Main study objective	**Participants and relevant characteristics**	**Relevant results (per outcome)**	**Additional remarks**
1. Study design Cross sectional Questionnaire survey Multicenter study 2. Main study objective To assess the barriers to FP for childhood and adolescent cancer patients by investigating the current status of FP for patients in Asian countries whom are members of the Asian Society of Fertility Preservation (ASFP) 3. Study years November 2018 4.Additional study	1. Type and Number of Participants Medical professionals in 11/14 Asian countries whom are members of the Asian Society of Fertility Preservation (ASFP). Number of medical professionals in the participating countries were not clearly stated.	1. Outcome definitions Barriers that inhibit promotion of FP for childhood and adolescent cancer patients 2. Results Barriers that inhibit promotion of FP ***Current status of FP:*** - Only five countries (Australia, China, Indonesia, Japan, Korea) had organizations or academic societies to promote FP - Only Indonesia, Japan, Korea had most of the time experience with FP for childhood and adolescent cancer patients while other countries said not very often ***Main reasons for not very often FP experience*** - Not enough information for physicians, oncologists, patients and family - Lack of public awareness - The numbers of facilities that can provide FP treatment for patients are limited ***Major barriers that inhibit promotion of FP for cancer patients*** - 9/11 participants identified low recognition among medical staff - 7/11 participants identified low recognition in society - 8/11 participants indicated that Information is insufficient	1. Strengths Multicenter study covering mainly developed countries in Asia. 2. Limitations The study population is not homogeneous in terms of SES, presence of organizations/ academic societies to promote FP and aid funds/insurance for FP. Thus this result cannot be compared and generalized. The participating countries gross national income per capita is very different (five high income countries, three upper-middle income countries, five lower income countries, and one with no data. Only 5/11 had organizations/academic societies to promote FP. Only Korea and Australia has a partial fund for FP.

<u>characteristics, if relevant</u> Study was conducted within the Asian Society for Fertility Preservation which constitutes 14 Asian countries. (Australia, China, Hong Kong, India, Indonesia, Japan, Korea, Philippines, Taiwan, Thailand, Vietnam, Pakistan, Singapore, Turkey)		- 6/11 said there is a problem with the cooperative system with the pediatrics department - 3/11 selected "There is technology, but we don't know how to provide it" - 3/11 said it is economically impossible. - Only one participant from Thailand chose "It is not necessary because the adoption system is popular" - 3 participants from Australia mentioned "weakness of evidence for FP for pediatrics" ***Suggestions to improve the level of FP awareness*** - 3/11 participants (India, Japan, Korea) are providing opportunities for lecture presentations, oral presentations at scientific conferences, and education for parents or patients ***Framework for providing FP treatment for patients:*** - 10/11 included participant responded to framework for providing FP treatment for cancer patients - 5/10 of participants reported that medical doctors could provide FP treatment for cancer patients - 4/5 countries reported that nurses and/or psychologists could collaborate with the medical teams - In Australia, nurses and psychologist are involved as well as patient navigators to assist decision-making and psychological support - Peer supporters including cancer survivors are not involved in FP treatment for individual cases ***Resources for providing information about FP for cancer patients:*** - All participants selected "Oral explanation" for informed assent - "Article" is used for informed assent as supplementary material in China, Japan, Philippines, Vietnam	The number of participants in the each participating countries was not clearly stated. Small sample size because the respondents were the 11 participating countries. <u>3. Risk of bias</u> *1. Selection bias: Low risk* Reason: A survey was sent to all countries representatives of ASFP. *2. Attrition bias: Low risk.* Reason: 11/14 (78.57%) country representatives replied to the survey *3. Detection bias: Unclear* Reason: Unclear if outcome assessors were blinded *4. Confounding: High risk* Reason: Did not perform multivariate analysis and no confounders were adjusted

		- Korea has supplemented oral explanation with animations/movie including sexual education - Only Australia has an online or printed resource and a video a peer supporter did as "other" means	

ASFP = The Asian Society of Fertility Preservation, SES = Social Economic Status

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?			
Wyns et al. Fertility preservation in the male pediatric population: factors influencing the decision of parents and children. Hum Reprod 2015;30:2022-30.			
Study design & Main study objective	**Participants and relevant characteristics**	**Relevant results (per outcome)**	**Additional remarks**
1. Study design Cross sectional study Single-center survey from Belgium 2.Main study objective To critically analyse the multidisciplinary collaborative care pathway (MCCP) in the pediatric population, focusing on factors influencing the decision, and to elucidate and	1. Type and Number of Participants Prepubertal boys and adolescents aged 0-18 years diagnosed with cancer between May 2005 and May 2013. Eligible patients: 348 of which 120 returned questionnaire; only 78 questionnaires included responses to Part 2. Parents gave their answers for 22 patients under 12 years of age and 3 patients aged 12–18yrs	1. Outcome definitions - Factors influencing the FP decision - Feelings of patients and their parents, with a view to better fulfilling their expectations 2. Results Response by patients, parents or both: - Parents considered their child (91.4% of adolescents and 26.2% of children aged <12 years, but >7yr) capable of understanding and participating in the decisional process - Reasons for not understanding and participating in the decision process were immaturity of the child (5.7%), poor general health (2.9%) - No discrepancy between patient and parent decisions was noted, indicating that decisions were essentially made jointly - Information was provided mainly by 64/78 (82%) oncologist, 7/78 (8.9%) GP, 5/78 (6.4%) specialist and 2/78 (2.5%) by nurses; Although nurse support was limited in this study, it appeared to be relevant for 16.6%	1. Strengths A large study. Closed-ended questionaire followed by response options to minimize random errors in the data collection process and allow quantitative interpretation. 2. Limitations Recall bias due to the to the time interval between the actual FP procedure and the survey. Single-center survey, thus does not allow generalizability of results to other places. There is no availability of preexisting validated questionnaires or gold standard for this type of study.

characterize the feelings of patients and their parents, with a view to better fulfilling their expectations. 3. Study years May 2005 to May 2013 4. Follow-up Mean ±SD 3.4 ± 2.3 years (ie) Time from diagnosis to the time of the survey was	2. Age at diagnosis Mean ± SD: 6.05 ± 3.74 years (range 0.1–143 months) for boys aged <12 yr 14.41 ± 1.5 years (range 144–212 months) for boys aged 12–18 yr 3. Number of responded participants per diagnosis Acute lymphoblastic Leukemia 33(27.7%) Acute myeloid leukemia 2(1.68%) Non-Hodgkin's lymphoma 13 (10.9%%) Hodgkin's lymphoma 6(5.0%) Medulloblastoma 3 (2.5%) Nephroblastoma 4 (3.3%) Neuroblastoma 9 (7.6%) Osteosarcoma 9 (7.6%) Retinoblastoma 7 (5.9%) Ewing's sarcoma 6 (5.0%) Rhabdomyosarcoma 6 (5.0%) Hepatoblastoma 4(3.4%) Brain tumor 7 (5.9%) Astrocytosis 2(1.68%)	of adolescents Emotional state of parents during discussion of FP (barrier) - 52% of adolescents and 23.5% of children felt anxious at the time of discussion - Reasons were concern about future fertility, rather than the method of FP, 46% of boys aged 12–18 years considered the FP method challenging because of poor general health, lack of experience with masturbation and its taboo or embarrassing nature - 76% of children and 48% of adolescents considered their health to be more important than the ability to have a family - Family support was considered important for 75% of adolescents and 58% of children, and medical support was considered important for 50% of adolescents and 42% of children; Nursing support was relevant for 16.6% of adolescents. Understanding information: (facilitator) - Majority of boys aged >12 years reported information to be clear (72%), complete (80%) and understandable (90.9%) - Only 33.3% of boys aged <12 years were able to comprehend the information, the youngest being 11 years old (although, respectively, 71.4 and 57.9% of subjects found it to be complete and clear) Satisfaction with information: - 19% was not satisfied with the fertility preservation information content (completeness) Acceptance and refusal rate: (barrier) - One-third of the patients lack information about FP options when seen by the oncologist	3. Risk of bias 1. Selection bias: high risk Reason: 120/348 (34.5%) eligible patients returned their questionnaires (44 patients died, 14 lost to fup, 8 declined to participate, some did not return their questionnaire.) 2. Attrition bias: High risk Reason: A total of 78/120 (65%) gave information on FP issues and have responded to questions on communication, emotional state and perceptions during discussion of FP, reasons for refusal etc. 3. Detection bias: Unclear Reason: Unclear if outcome assessors were blinded. 4. Confounding: High risk Reason: did only bivalent analysis. Thus did not adjust for confounders.

	Ependymoma 1(0.8%) Benign pathologies 7 (5.9%) 4. Additional patients characteristics, if relevant 42 patients (35%) did not receive information on FP issues	- FP acceptance rates were 74% for boys aged <12 and 78.6% for boys 12-18 years - 6/78 (7.7%) adolescents and 13/78 (16.7%) children under the age of 12 years refused to undergo FP procedures - Reasons for refusal were the urgency of cancer treatment, diminished general health, the FP procedure not being a priority or the experimental status of FP before puberty - Wishing to avoid an additional procedure was not an issue for FP acceptance - Satisfaction about completeness of information provided to patients and parents positively impact decision to preserve fertility (p=0.04) - Hope for future parenthood positively impact decision to preserve fertility (p<0.01) - Timing of FP information, healthcare provider who proved the FP information and anxiety were not significantly associated with decision to preserve fertility	

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?			
Skaczkowski et al. Factors influencing the documentation of fertility-related discussions for adolescents and young adults with cancer. Eur J Oncol Nurs 2018;34:42-8.			
Study design & Main study objective	**Participants and relevant characteristics**	**Relevant results (per outcome)**	**Additional remarks**
1. Study design Retrospective observational study Multicenter study 2. Main study	1. Type and Number of Participants 941 AYAs (15–24 years) diagnosed with cancer with 5-year survival rates between 61 and 77% in all six Australian states	1. Outcome definitions Fertility-related documentation Factors associated with documentation 2. Results Fertility-related documentation - 444 (47.2%) patients had a documented fertility	1. Strengths Eligible patients were identified through the population-based cancer registries in all Australian states. Thus a national representative.

<u>objective</u> To examines the level of documentation, and the factors associated with the documentation of fertility-related discussions and FP procedures in the medical care of AYAs (15–24 years) with cancer. <u>3. Study years</u> January 2007-Decmember 2012	<u>2. Diagnoses</u> AML 18.0% ALL 19.2% Soft Tissue Sarcoma 14.1% Primary Bone Cancer 10.1% Ewing's Family Tumour 9.8% CNS Tumour 28.8% <u>3. Age at diagnosis</u> 15-24 years at the time of diagnosis	discussion - 337 (35.9%) had a documented FP procedure <u>Reasons for not having FP:</u> *Male vs female* - Patient declined to proceed with suggested FP plan: 15/333 (5%) vs 15/268 (6%) - Treatment too urgent: 2/333 (0.6%) vs 6/268 (2%) - Treatment had already commenced 1/333 (0.3%) vs 3/268 (1%) - Infertility risk low NR vs 2/268 (0.7%) - No reasons documented in medical record 315/333 (95%) vs 241/268 (90%) <u>Multivariate analysis: factors associated with documentation of fertility discussions (OR (95% CI)):</u> ***Sex*** Female vs Male: 0.63 (0.46–0.88) ***Type of cancer*** AML vs CNS Tumour: 21.84 (12.64–37.73) ALL vs CNS Tumour: 21.89 (12.63–37.93) Soft Tissue Sarcoma vs CNS Tumour: 4.27 (2.50–7.31) Primary Bone Cancer vs CNS Tumour: 21.66 (11.61–40.41) Ewing's Family Tumour vs CNS Tumour: 10.6(1 5.72–19.69) ***Risk of treatment*** Intermediate vs No/Low: 1.69 (0.89–3.22) High vs No/Low: 5.63 (3.77–8.41) ***Type of treatment centre*** Paediatric vs Adult non-AYA: 0.73 (0.45–1.20) Adult AYA vs Adult non-AYA: 1.60 (1.08–2.37) <u>Multivariate analysis: factors associated with documentation of FP procedure (OR (95% CI)):</u>	Large sample size: n= 941 patients Attempts were made to gather information from all treatment centres that a patient attended, including public and private, metropolitan and regional and large and smaller hospitals, thus aiding the generalizability of results. Few missing data in some variable. Total n=933 due to missing data. Total n=929 due to missing data. Data collectors were trained to extract information from electronic and paper-based medical records. Long study period: 5 years Well defined inclusion and exclusion criteria <u>2. Limitations</u> Used logistic regression, but would have used random effect multilevel model to account for correlation since this study involves many centers Examined the documentation of only some cancers that occur in young people. Thus this study should not be generalized to other

		Sex Female vs Male: 0.42 (0.30–0.59) ***Type of cancer*** AML vs CNS Tumour: 10.36 (6.02–17.83) ALL vs CNS Tumour: 14.07 (8.17–24.25) Soft Tissue Sarcoma vs CNS Tumour: 3.57 (2.00–6.39) Primary Bone Cancer vs CNS Tumour: 18.15(9.67–34.08) Ewing's Family Tumour vs CNS Tumour: 6.97 (3.83–12.69) ***Risk of treatment*** Intermediate vs No/Low: 1.43 (0.76–2.69) High vs No/Low: 3.84 (2.64–5.60) ***Type of treatment centre*** Paediatric vs Adult non-AYA: 0.96 (0.58–1.58) Adult AYA vs Adult non-AYA: 1.74 (1.17–2.57) The interaction between sex and treatment centre was not significant for fertility discussions or FP procedure	cancers. <u>3. Risk of bias</u> *1. Selection bias:* Low risk Reason: 941/955 (98.5%) of eligible cases were included. 5 patients died within 30 days of their diagnosis and 9 patients did not have any treatment *2. Attrition bias:* Low risk Reason: 938/941 (99.7%) included eligible patient have documented fertility discussions or FP procedures. (3 patients: 2 patients were transgender and one person was sterile, have no documented fertility discussions or FP procedures) *3. Detection bias:* Unclear Reason: Unclear if outcome assessors were blinded. *4. Confounding: Low risk* Reason: Adjusted for sex, type of cancer, risk of treatment and type of treatment centre**.**

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?			
Jayasuriya et al. Satisfaction, disappointment and regret surrounding fertility preservation decisions in the paediatric and adolescent cancer population. J Assist Reprod Genet 2019;36:1805-22.			
Study design & Main study objective	**Participants and relevant characteristics**	**Relevant results (per outcome)**	**Additional remarks**
1. Study design A mixed-methods cross-sectional study Questionnaire survey Oncofertility data obtained from oncofertility database and the patient's medical record 2. Main study objective To examine decision regret around FP decisions in families who had a fertility discussion at RCH Melbourne, Australia, and to explore contributing factors to the experience of regret.	1. Type and Number of Participants Participants were parents and their children (if currently aged 15 years or older) who participated in a fertility discussion between January 1987 and November 2016. Parents n=108 Patients n=30 Oncology patients were those with a primary oncology diagnosis or those with a non-cancerous disease needing oncological treatment, and under the care of the oncology department. Non cancer patients were only 25/138 (18.1%)	1. Outcome definitions Decision regret assessed as a dichotomous variable. Scores from 0-29 were defined as indicative of low regret, and scores above 30 were indicative of high regret 2. Results **Impression of success:** - 90.5% (124/137) recalled a discussion while 88.4% of the participants had a documented discussion in the medical records - 80% (78/98) of parents and 77% (23/30) of patients strongly agreed or agreed that FP procedures were likely to be successful in their lifetime - (5/6) 83.3% parents whose child had an established procedure (sperm or oocyte collection) or (53/64) 82.81% an experimental procedure (OTP/TTP or GnRHa believed that FP procedures will be successful within their lifetime **Decision regret:** - Mean total DRS score was 13.7 (SD=18.7; range 0-95) - 93.0% (120/129) respondents felt they had made the right decision and 90.7% (117/129) would make the same choice again - 5% (6/129) of the respondents regretted the choice and 6.2% (8/129) felt that the choice caused them harm - There was a discrepancy in the regret category between individuals in 2 of the 10 parent/parent pairs (20%) and	1. Strengths Used oncofertility database and the patient's medical record to obtain oncofertility data (demographics, diagnosis, type of cancer treatment, FP procedure type, infertility risk and complications. Adjusted for time since discussion to minimize presence of recall bias. Included 25 (18%) of those with non-cancerous disease but in need of oncological treatment. 2. Limitations Regret was assessed using a questionnaire. Thus there may be some level of recall bias since regret was self reported after a time frame. Excluded those receiving palliative care, very sick people. Thus outcome would be underestimated.

3. Study years February 2015 and November 2016	2. Age (at diagnosis) Mean ± SD (range) for patients 14.7 ± 2.1 (8.6-18.6) 3. Number of participants per diagnosis *Parent vs patients* Leukaemia 27 (25.0%) vs 7 (23.3%) Lymphoma 9 (8.3%) 11 (36.7%) CNS 10 (9.3%) 0 (0.0%) Sarcoma 29 (26.9%) 8 (26.7%) Other solid cancer 10 (9.3%) 2 (6.7%) Non-cancerous diseasea 23 (21.3%) 2 (6.7%) 4. Age at Survey Mean ± SD (range) Parents: 40.0 ± 6.7 (24-64) Patients: 20.0 ± 6.3 (14-44) 5. Additional patients characteristics, if relevant 47.8% of participants completed the survey at least 18 months after a fertility discussion had occurred	in 3 of the 17 parent/patient pairs (17.6%) - 112/115(97.3%) responses related to satisfaction with the FP decision - 22/115 (19.1%) responses related to regret **Reasons for satisfaction** - The majority of parents and patients (80%; 92/115) expressed hope around having "options", "choices" and "chances" of parenthood - 19 patients also reported satisfaction with decision made based on preferences to have children - Parents reported satisfaction based on low risk of the procedure (n = 10) and their desire to upkeep their duty of care and parental responsibility to act in the best interests of their child (n = 5) - Satisfaction in decision to decline in FP was based on the experimental nature of what was available (n = 7) and risks to their child's health exceeding the expected benefit (n = 4) **Reasons for regret** - Not having fertility issues raised with them in a timely manner (n = 6) - Two parents initiated the discussion themselves and was disappointed over the potential for it to have been "missed" - A patient expressed dissatisfaction over a lack of pretreatment discussion and the potential alternative prospect of infertility - Five parents said that the provision of information was insufficient **Multivariate logistic analysis factors associated with high decisional regret (OR (95%CI)):**	There is no clear definition of success. Thus, definition is subjective to every participant 3. Risk of bias *1. Selection bias: High risk* Reason: 110/(243+37-8 died -3 pallimative) (40.89%) families corresponding to 138 *respondant (*Parent/patient) were finally included *2. Attrition bias: Low risk* Reason: *129/138 (93.48%) responded to decision regret.* *3. Detection bia: Unclear* Reason: Unclear if outcome assessors were blinded *4. Confounding bias: Low risk* Reason: Adjusted for potential confounders: cancer diagnostic sub-class; time

		- Impression that FP procedures will not be successful in this lifetime: 2.958 (1.289–6.789) - Having a fertility preservation procedure: 0.178 (0.050–0.639) - Having a discussion after high-risk therapy has been commenced: 40.532 (2.352–698.6) - Time since diagnosis: 0.830 (0.564–1.221) - Age of patient at time of discussion: 0.998 (0.645–1.544) - Age of patient at time of survey: 1.046 (0.968–1.131)	since diagnosis; time since discussion; provider of the fertility discussion; patient's age at the time of diagnosis, at discussion, at the time of the survey; patient's treatment status at time of survey; participant ability to recall the discussion.

RCH= The Royal Children's Hospital , DRS= Decision regret scale, GnRHa=gonadotropin-releasing hormone analogues, OTP= ovarian tissue preservation , TTP= Testicular tissue preservation

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?

Borgmann-Staudt et al. Fertility knowledge and associated empowerment following an educational intervention for adolescent cancer patients. Psycho-Oncology 2019;28:2218-2225.

Study design	Participants	Intervention	Main outcomes	Additional remarks
<u>1. Study design</u> Multi-center observational intervention study Eleven pediatric-oncology centers in four European countries <u>2. Study years</u> Phase I control group: March	<u>1. Type and number of participants</u> Childhood cancer patients aged 12-19 years at diagnosis Intervention group: - 101 patients - 99 parents Control group: - 113 patients - 111 parents	<u>Intervention group:</u> Patients and parents received an information flyer at initial diagnosis in addition to standard patient education <u>Control group:</u> Standard patient education according to treatment-optimising protocols for the respective adolescent cancers	<u>1. Outcome definitions</u> Measured by questionnaires at 3 (t0) and 6 (t1) months after initial diagnosis: - Knowledge about fertility impairment and preservation when supportive informational material was implemented: sufficient knowledge was considered when >50% were answered correctly - Empowerment - Influence of study on patient fertility consultation practice <u>2. Results</u> <u>Knowledge about fertility impairment and</u>	Used binary logistic regression, but would have used random effect multilevel model to account for correlation since this study involves many center Small sample size. Did sample size calculation but unable to achieve enrolment goal as per sample calculation. Questionnaire survey study and might be subjected to

2014 - January 2016; Phase II intervention group: April 2016 - October 2017 <u>3. Additional study characteristics, if relevant</u> None	<u>2. Diagnoses</u> Control vs. intervention group: - Leukemia 18 (15.9%) vs. 20 (19.8%) - Lymphoma 44 (38.9%) vs. 45 (44.6%) - Brain tumors 5 (4.4%) vs. 5 (4.9%) - Bone tumors 22 (19.5%) vs. 13 (12.9%) - Soft tissue tumours 8 (7.1%) vs. 6 (5.9%) - Germ cell tumours 13 (11.5%) vs. 10 (9.9%) - Others 3 (2.7%) vs. 2 (2.0%) <u>3. Age at diagnosis</u> - Intervention group: Median 16 (range 12-18) yrs - Control group: Median 16 (range 12-19) yrs <u>4. Age at follow-up</u> Not reported <u>5. Additional participant characteristics, if relevant</u> -		<u>preservation:</u> - Educational intervention non-significantly increased knowledge in both patients and parents compared to control group; mean difference: 1.62 (95% CI -0.73−3.96) at t0 and 2.17 (95% CI -0.38−4.72) at t1 for patients; 2.24(95% CI -0.108−4.583) at t0 and 2.19 (95% CI -0.22−4.616) at t1 for parents <u>Multivariable analyses for determinants of *patient* knowledge at t0:</u> - Education with vs. without intervention: NS - Age in years: OR 1.26 (95% CI 1.14 -1.53) - Female vs. male: OR 3.27 (95% CI 1.84-5.81) <u>Multivariable analyses for determinants of *patient* knowledge at t1:</u> - Education with vs. without intervention: NS - Age in years: NS - Female vs. male: OR 2.19 (95% CI 1.24-3.9) <u>Multivariable analyses for determinants of *parent* knowledge at t0:</u> - Education with vs. without intervention: OR 1.95 (95% CI 1.03-3.71) - Patient age in years: OR 1.32 (95% CI 1.07 - 1.62) - Patient gender female vs. male: OR 3.27 (95% CI 1.84-5.81) - Parent gender female vs. male: NS - Parent educational status: OR 6.21 (95% CI 2.11-18.3)	recall bias. Did not mention what they mean by low, middle and high education level of parents. <u>Selection bias:</u> Low risk Reason: 101/134 (75.4%) patients and 99/134 (73.9%) parents were included in the intervention group; 113/142 (79.6%) patients and 111/142 (78.2%) parents were included in the control group. Gender, age, and cancer diagnosis were comparable between participants and non-participants. <u>Attrition bias:</u> Unclear Reason: Unclear if for all patients and parents the outcomes were complete. <u>Detection bias:</u> High risk Reason: Participating investigators were aware that patients and parents were evaluating fertility counselling within the survey. <u>Confounding:</u> Low risk Reason: Analyses were adjusted for patient education

			Multivariable analyses for determinants of *parent* knowledge at t1: - Education with vs. without intervention: NS - Patient age in years: NS - Patient gender female vs. male: NS - Parent gender female vs. male: NS - Parent educational status: NS Empowerment - Significantly improved in both patients (p = 0.046, d =0.27) and parents (p = 0.046, d = 0.48) in the intervention group Multivariable analyses for determinants of *patient* empowerment at t0: - Age in years: OR 1.35 (95% CI 1.06-1.72) - Estimation of infertility risk high vs. low: OR 0.27 (95% CI 0.09-0.87) - Prior infertility information yes vs. no: OR 6.59 (95% CI 2.12-20.49) - Gender, highest educational degree, diagnosis, country in which treated, information regarding prophylactic measures: NS Multivariable analyses for determinants of *patient* empowerment at t1: - Age in years: OR 1.45 (95% CI 1.09-1.91) - Female vs. male: OR 0.42 (95% CI 0.12-0.95) - Information on prophylactic measures yes vs. no: OR 5.55 (95% CI 1.92-15.98) - Highest educational degree, diagnosis, estimation of infertility risk, country in which treated, recall of risk information	(with/without intervention), gender, and patient age in patient model. Parent gender and highest educational degree were additionally included in the model regarding parent outcomes.

			before treatment: NS <u>Multivariable analyses for determinants of *parent* empowerment at t0:</u> - Patient gender female vs. male: OR 0.165 (95% CI 0.072-0.378) - Prior infertility information yes vs. no: OR 4.544 (95% CI 1.351-15.28) - Information on prophylactic measures yes vs. no: OR 30.53 (95% CI 6.41-145.39) - Patient age, patient gender, parental gender, highest educational, degree, diagnosis, estimation of infertility risk, country in which treated: NS <u>Multivariable analyses for determinants of *parent* empowerment at t1:</u> - Patient age in years: OR 1.38 (95% CI 1.05-1.831) - Prior infertility information yes vs. no: NS - Information on prophylactic measures yes vs. no: OR 6.49 (95% CI 2.17-19.40) - Patient gender, parent gender, highest educational degree, diagnosis, estimation of infertility risk, country in which treated: NS <u>Medical consultation</u> - 12/13 (92.3%) investigators stated that participation in PanCareLIFE patient education had influenced their medical consultation practices concerning fertility issues - Information supported study physicians in educating themselves	

			- Implementation of new standard operating procedures (SOPs) in some centers - 3/11 (27.3%) centres established fertility cryopreservation programmes for girls during the course of the study	

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?				
Balcerek et al. Determinants of utilization of cryopreservation of germ cells in adolescent cancer patients in four European countries. Eur J Pediatr 2020;179:51-60.				
Study design	**Participants**	**Intervention**	**Main outcomes**	**Additional remarks**
1. Study design Multi-center observational intervention study 2. Study years Phase I control group: March 2014 - January 2016; Phase II intervention group: April 2016 - October 2017 3. Additional study characteristics, if relevant	1. Type and number of participants Childhood cancer patients aged 12-19 years at diagnosis Intervention group: n=101 patients Control group: n=113 patients 2. Diagnoses Control vs. intervention group: - Leukemia 18 (15.9%) vs. 20 (19.8%) - Lymphoma 44 (38.9%) vs. 45 (44.6%) - Brain tumors 5 (4.4%) vs.	Intervention group: Patients and parents received an information flyer at initial diagnosis in addition to standard patient education Control group: Standard patient education according to treatment-optimising protocols for the respective adolescent cancers	1. Outcome definitions Utilization of cryopreservation 2. Results Utilization of cryopreservation: - Control group: 37/113 (32.7%) - Intervention group: 37/101 (36.6%) - Difference not statistically significant Rates of cryopreservation showed no statistically significant differences between the groups according to treatment Multivariable analyses for predictors of utilization of cryopreservation (OR (95% CI): *Control group* - Gender (female vs. male): 0.100 (0.023–0.427) - Age of patient (in years): 1.559 (1.077–2.258)	Small sample size. Did sample size calculation, but did not reach the required sample size. Wide confidence interval in some estimates. Study was a multicenter study and analysis was done using binary logistic regression instead of mixed effect model. Questionnaire study which might be prone to bias. Selection bias: Low risk Reason: 101/134 (75.4%) patients were included in the intervention group;

None	5 (4.9%) - Bone tumors 22 (19.5%) vs. 13 (12.9%) - Soft tissue tumours 8 (7.1%) vs. 6 (5.9%) - Germ cell tumours 13 (11.5%) vs. 10 (9.9%) - Others 3 (2.7%) vs. 2 (2.0%) <u>3. Age at diagnosis</u> Control vs. intervention group - 13–15 years: 52 (46.0%) vs. 46 (45.5%) - 16–17 years: 52 (46.0%) vs. 51 (50.5%) - ≥18 years: 9 (8.0%) vs. 4 (4.0%) <u>4. Age at follow-up</u> Not reported <u>5. Additional participant characteristics, if relevant</u> -		- Diagnosis (brain tumours vs. haematological malignancies): 0.765 (0.035–16.917) - Diagnosis (solid tumours vs. haematological malignancies): 0.733 (0.223–2.415) - Country of attending clinic (cz vs. Germany): 0.337 (0.094–1.210) - Country of attending clinic (pl vs. Germany): 0.156 (0.018–1.369) - Country of attending clinic (at vs. Germany): 0.237 (0.035–1.602) - Estimated risk for fertility (medium vs. low): 2.400 (0.652–8.826) - Estimated risk for fertility (high vs. low): 1.196 (0.284-5.032) - Information on prophylactic measures (yes vs. no): 33.663 (2.100-539.574) - Risk information before treatment – including fertility impairment (yes vs. no): 0.599 (0.041–8.710) *Intervention group:* - Gender of patient (female vs. male): 0.093 (0.026–0.330) - Age of patient (in years): 1.027 (0.696–1.516) - Diagnosis (brain tumours vs. haematological malignancies): 1.688 (0.124–22.936) - Diagnosis (solid tumours vs. haematological malignancies): 1.024 (0.305–3.432) - Country of attending clinic (cz. vs. Germany): 0.635 (0.184–2.193) - Country of attending clinic (pl. vs. Germany): 1.267 (0.207–7.771)	113/142 (79.6%) patients were included in the control group. <u>Attrition bias:</u> Low risk Reason: 98/101 (97.0%) of the intervention group and 106/113 (93.8%) of control group were followed-up at 6 months. <u>Detection bias:</u> High risk Reason: Participating investigators were aware that patients and parents were evaluating fertility counselling within the survey. <u>Confounding:</u> Low risk Reason: Analyses were adjusted for potential confounders.

			- Country of attending clinic (at. vs. Germany): 1.550 (0.190–12.642) - Estimated risk for fertility (medium vs. low): 2.503 (0.691-9.071) - Estimated risk for fertility (high vs. low): 43.665 (2.157–883.974) - Information on prophylactic measures (yes vs. no): 10.712 (0.629–182.396) - Risk information before treatment – including fertility impairment (yes vs. no): 4.608 (0.585–36.329)	

Cz: Czech Republic, pl: Poland, at: Austria

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?				
Hand et al. A clinical decision support system to assist pediatric oncofertility: a short report. J Adolesc Young Adult Oncol. 2018;7:509-513				
Study design	**Participants**	**Intervention**	**Main outcomes**	**Additional remarks**
1. Study design Cross sectional single-center questionnaire study 2. Study years March - September 2016 3. Additional study	1. Type and number of participants 39 clinicians involved in paediatric oncofertility care at the Royal Children's Hospital, Melbourne, and collaborating centers - 10 (27.7%) nursing staff - 22 (61.1%) medical staff - 7 (19.4%) allied health or	Clinician decision support system (CDSS) Created by the Fertility Preservation Taskforce at The RCH, Melbourne, a collaborative association of oncologists, fertility specialists, gynecologists, and pediatric providers Main components:	1. Outcome definitions - Involvement in fertility care - Clinician usability and acceptance of pediatric oncofertility CDSS 2. Results Fertility discussions involvement - 23 (72%) often discussed the impact of cancer treatment on fertility - 7 (17.9%) had involvement in >100 fertility discussions - 10 (25.6%) were involved in 11 to 50	Cross sectional design which is a weak design because it cannot assess whether knowledge gained is retained over time and whether it helped in decision-making. n=36, few participants. Questionnaires survey which might be subject to reporting bias.

characteristics, if relevant None	supportive care staff 2. Diagnoses Not applicable 3. Age at diagnosis Not applicable 4. Age at follow-up Not applicable 5. Controls (if applicable) None 6. Additional participant characteristics, if relevant - All participants were educated and trained on the concept, contents, and use of the clinician decision support system - 28 (73.7%) had been involved in fertility care for less than 10 years - 31 (79.5%) females	- Electronic clinical oncofertility pathway, in the form of two comprehensive and interactive flowcharts, one each for male and female patients - Step-wise guidance within the electronic medical record, directing clinicians through the oncofertility pathway, including systematic grouping of relevant steps and orders to be worked through, providing guidance through a fertility discussion; prompts for referrals to relevant hospital departments; and template fertility discussion notes	fertility discussions - 22 (56.4%) were involved in <10 fertility discussions Perceptions on acceptability and efficiency - 33/35 (91.7%) would like to improve their ability to discuss and provide fertility resources to families - 37 (94.9%) said the aims of the CDSS were clear - 30 (83.3%) agreed that the CDSS was created to encourage clinicians to discuss fertility with their patients - 37/38 (97.4%) reported understanding of the overall fertility pathway and CDSS components - 92% stated the CDSS format was clear and understood the steps specific to their role - 96.2% reported the willing to lead fertility discussions using the CDSS - 29/35 (82.9%) of participants thought the CDSS was of appropriate length Impact on clinical practice - 32/37 (86.5%) felt the CDSS would enable adherence to consistent clinical pathways - 30/37 (81.1%) felt the CDSS would enable adherence to policy and standards of care - 17/37 (45.9%) felt the CDSS would help improve clinician satisfaction - 65% felt the CDSS would increase clinician knowledge, improve patient and family understanding and improve their decision marking	Selection bias: Low risk Reason: All clinical staff involved in oncofertility care at the participating centers were invited to participate Attrition bias: High risk Reason: 39/63 (61.9%) recipients responded. Detection bias: Unclear Reason: Unclear if outcome assessors were blinded Confounding: High risk Reason: No multivariate analysis adjusting for potential confounders

			Weaknesses: 3/21 (14.3%) reported incomplete integration of the CDSS into electronic medical record with some components of the CDSS only accessible outside of the electronic medical record system	

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?				
Kemertzis et al. Fertility Preservation Toolkit: A clinician resource to assist clinical discussion and decision making in pediatric and adolescent oncology. J Pediatr Hematol Oncol. 2018;40:e133-e139.22.				
Study design	**Participants**	**Intervention**	**Main outcomes**	**Additional remarks**
1. Study design Longitudinal study Single center Questionnaires survey-based study 2. Study years Phase 1: April to June 2014 Phase 2: June to August 2014 Phase 3: June to August 2016 3. Follow-up Phase 1: no follow up;	1. Type and number of participants All clinical staff involved in the care of oncology patients at the RCH Melbourne and trained on the use/content of Toolkit 2. Number of participants at study phase **Phase 1: April-June 2014** Eligible: n=104 Responded: n=59/104 Nurse: 41/59 (69.49%) Medical staff: 3/59 (22.04%) Allied health: 5/59 (8.47%) **Phase 2: June-August**	Newly developed FP toolkit consisting of clinician instruction booklet, checklist, referral forms, reference information regarding fertility risk of cancer treatments, and handouts for patients and families	1. Outcome(s) definition Outcome 1 Participants' confidence levels in discussing FP, their satisfaction with the current system, and their understanding of and predicted benefits and weaknesses of the proposed toolkit Outcome 2 Clinicians' attitude to the toolkit after 8 weeks of clinical use: clinicians perception on understanding and satisfaction level of patient/parents. The time required for preparation and discussion Outcome 3 The actual impact of toolkit on FP clinical practice after 2 years of use	Selection bias: low risk Reason: All clinical staff involved in the care of oncology patients were eligible to participate Attrition bias: high risk Reason: 59/ 104 (56.7%) of eligible participants in phase 1 responded. 38/65(58.5%) of eligible participants in phase 3 responded. Detection bias: unclear Reason: Unclear if outcome assessors were blinded. Confounding bias: high risk Reason: No multivariate

participants were assessed immediately after education session Phase 2: 8 weeks after introduction of toolkit Phase 3: 2 years after introduction of toolkit	**2014** 26 newly diagnosed patients were reported in which only 11 used toolkit **Phase 3: June to August 2016** Eligible:: n=65 Responded: n=38/65 Nurse: 10/38 (26%) Medical staff: 22/38 (58%) Allied health: 6/38(16%) <u>3. Number of patients per diagnosis</u> 4 (36.4%) diagnosed with a solid tumor <u>4. Age at diagnosis</u> 0-16 years <u>5. Age at follow-up</u> Not Reported <u>6.Controls (if applicable</u> Not applicable <u>7. Additional participants characteristics, if relevant</u> Phase 2: 11/26 (42.3%) patients had information on the use of toolkits		<u>2. Results</u> <u>Participants' confidence levels and roles in providing FP information pre toolkit implementation (phase 1):</u> - 55/59 (93.3%) of participants had some prior involvement in FP discussions - 23/57 (40.4%) felt confident in providing FP information to parents and families (13/13 medical staff and 11/41 nurses staff) - 54/56 (96.4%) had desire to improve in discussing FP with parents and patients - 12/13 (92%) medical staff and 6/41 (14.6%) nursing staff indicated to take a helping role on FP discussion - 4/13 (30.8%) medical staff and 27/41 (65.9%) nursing staff indicated to take a leading role on FP discussion <u>Perceived toolkit impact after participant attained education and training on the use of toolkits (phase 1):</u> - 50/58 (87.2%) understood the toolkit components - 58/59 (98.3%) understood how to use the toolkit in FP discussions - 58/58 (100%) agreed to use and promote the toolkit - 23/57(40.4%) felt confident in providing up to date FP information to parent/patient - 8/58 (14%) often/always provided written information - 20/58 (34.5%) often/always provided verbal information	analysis. Confounders were not adjusted. <u>Additional remarks:</u> <u>Strengths</u> Provided reason for change in number of participatants. (participants did not answer certain questions) <u>Limitations</u> - Few participants - Short follow up period. 8 weeks for phase 2 and only 11 patients were assessed by clinicians - No adequate participation rate - Did not provide information if there is important difference between eligible patients who responded and those that did not respond

	6/11 (54.5%) patients in phase 2 were prepubertal 7/11 (63.6%) discussions were in an outpatient setting. Phase 3 5 (50%) of the nurses were registered nurses 5 (50%) were clinical nurse specialists. Medical staff were 1 endocrinologist, 1 urologist, 2 nephrologists, 10 oncologists, and 8 gynecologists. Higher number of medical staff involved in phase 3 than in phase 1.		<u>Reasons for dissatisfaction before implementation of toolkit (phase 1):</u> - 16/48 (33.3%) were satisfied with the FP system before toolkit implementation <u>Participants opinion on the expected impact of the toolkit on clinical practice & FP discussion (phase 1):</u> - An increase in FP discussion rates - Improving the quality of FP discussions - Providing easy access to relevant information <u>Healthcare provider reported satisfaction 8 weeks after toolkit implementation (phase 2):</u> - In 7/11(63.6%) of FP discussions, the clinician was satisfied with the toolkit - In 11/11 (100%) of FP discussions, the clinician was extremely satisfied with the FP discussion - In 10/11 (90.9%) of patients/parent, clinicians perceived they well understood FP discussion - In 11/11(100%) of patients/parent, clinicians perceived they were satisfied with FP discussion - Clinicians reported 10-20 min discussion time and 20-70 min FP discussion Reason for dissatisfaction with the toolkit *8 weeks after implementation* - missing documents within the toolkit	

			- organization of the documents within the toolkit - too much written information which are not relevant for patient <u>Actual impact of toolkit on FP clinical practice after 2 years of use (phase 3):</u> **Healthcare provider reported satisfaction** - 28 (73.7%) participants had involved before in FP discussions - 20/37 (54.1%) were satisfied with the FP toolkit system - One participant reported a great improvement in clinical practice since the use of toolkit Reason for dissatisfaction: - inefficient - some aspects needed tweaking. **Participants' roles and confidence levels in providing FP information after 2 year implementation:** - 26/37 (70.3%) felt confident in providing up to date FP information to parents/parents - 21/31 (67.7) often/always provided verbal information - 11/31 (35.5%) often/always provided written information **Comparison between study populations of phase 1 (pre-toolkit) and phase 3 (2 yr post toolkit)** - Always/often/sometimes involved in FP	

			discussions: OR 0.5 (95% CI 0.2-1.4) - Satisfaction levels: OR 0.4 (95% CI 0.2-1.1) - Confidence levels: **OR 0.3 (95% CI 0.1-0.9)** - Provision of verbal information (Always/often): **OR 0.3 (95% CI 0.1-0.7)** - Provision of written information (Always/often): **OR 0.3 (95% CI 0.1-0.96**)	

SD= Standard deviation, DA= Decision aid, VCE=Web-based Values Clarification Exercise

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?				
Allingham et al. Fertility preservation in children and adolescents with cancer: pilot of a decision aid for parents of children and adolescents with cancer. JMIR Pediatrics and Parenting 2018;1:e10463.				
Study design Treatment era Years of follow-up	**Participants**	**Intervention**	**Main outcomes**	**Additional remarks**
1. Study design Cross-sectional Pre-post survey design Single center study 2. Study years December 2010 and December 2015	1. Type and number of participants 24 clinicians and 34 parents of patients with cancer (aged 0-18 years) diagnosed between December 2010 and December 2015 at The Royal Children's Hospital, Melbourne 34/74 (45.95%) completed	Web-based DA for parents of children and adolescents with cancer developed according to the International Patient Decision Aid Standards.	1. Outcome(s) definition - Acceptability, usability and feasibility of the Web-based FP DA - Fertility knowledge and decision regret - Clinician acceptance of the DA by its perceived usefulness 2. Results **Parents reported satisfaction with the decision aid design:** - 10/15 (67%) reported reading the DA thoroughly from beginning to end with a	Strengths Collected information on those lost to follow up. 19 parents withdrew after completing survey 1 because of time constraints (n=5), or did not respond to follow-up (n=14) Limitations Small sample size (11/24 clinicians and 15/34 parents)

3. Follow-up Not applicable	the pre-DA survey 15/34 (44.12%) completed the pre- and post-DA surveys 2. Age of participants Mean age for completed the pre-DA survey = 41.5 (SD: 11.1) Range = 27-57 Mean age for completed the pre- and post-DA survey = 42.6 (SD: 7.0) Range = 31-49 3. Diagnosis of the children of the participants who completed the pre- and post-DA survey Leukemia 6 (60%) Rhabdomyosarcoma 3 (60%) Ewing's Sarcoma 1 (20%) Central nervous system 1 (33%) Hodgkin's Disease 1 (50%) Osteosarcoma 1 (33%) Other solid cancers 2 (40%)		median time of 25 minutes (range 15 to >60 minutes) - All parents considered the length to be about right - 8/15 (53%) reported that the DA was very appealing to look at - 11/15 (73%) mentioned that it was very clearly presented - 9/15 (60%) were satisfied with the website format - 5/15 (33%) said they would also like a booklet - 1/15 (7%) stated they would have liked a video **Parents reported satisfaction with content:** - 13/15 (87%) reported that the information in the DA was balanced and fair - 2/15 (13%) reported that the DA was in "favor of FP" - 12/15 (80%) felt that the information was "sufficiently detailed" - 1/15 (7%) found the DA to be confusing - 13/15 (87%) reported that it clearly presented their child's fertility choices - 12/15 (80%) reported that the information would have been quite/very relevant when considering FP for their child **Parents reported expectations of the DA:** - 11/15 (73%) were "satisfied" and 4/15 (27%) "very satisfied with the DA - 1/15 (7%) reported that the DA would	and no sample size calculation was done. Thus results should be interpreted with caustion The distribution of infertility risk differed markedly between those who were lost to follow up after completing the pre-DA survey and those who completed the pre- and post-DA survey. Those who were lost to follow up were classified mainly as medium and high infertility risk. Thus there may be underestimation of outcome. Cross sectional design which is a weak design. Outcome was measured immediately after DA review. Thus cannot assess whether knowledge gained retained over time and whether it helped in decision-making or if regrets increased months/years later since results showed non significant increase in regret immediately after review. Questionnaires survey which might be subject to bias

	Non-Hodgkin's 0 (0%) <u>4. Mean age at diagnosis</u> 9.3 (SD: 6.4) Range (1.5-19.2) <u>5. Age at follow-up</u> Not applicable <u>6.Controls (if applicable</u> Not applicable <u>7. Additional participants characteristics, if relevant</u> There was a significant difference between those who were lost to follow up after completing the pre-DA survey and those who completed the pre- and post-DA survey Those who reviewed the DA (n=15) were more likely to be in part-time or full-time employment and have a higher level of education compared to those who were lost to follow up The distribution of infertility risk differed markedly between the 2 groups; Those who were		not have helped them cope with their situation - The DA met the expectations of parents (11/15, 73%) and exceeded the expectations of parents (4/15, 27%) **Parents emotional impact of the DA:** - 47% (7/15) reported having "somewhat" thought about the information since reading the DA - 40% (6/15) reported feeling worried/concerned about the information - 1/15 parent was "worried for her (child) as preservation was not an option for her and another was "not so much worried but just sad," indicating that worry was linked to concerns about the future impact of treatments on fertility. **Perceived Usefulness as a Decision-Making Tool:** - 86% (13/15) of parents reported that the DA would have been helpful for their child's treatment decision making - 86% (13/15) reported helpful in making decisions about FP and would recommend the DA to other families facing an FP decision - 53% (8/15) parents who completed the VCE reported it is helpful to some extent when making decision. - Reasons for non-completion were time constraints, inaccessibility, and unclear instructions	Included parents of very young patients ie from 0 year up. This population of parents might have a different feeling to FP . Patients were less likely to attempt a PF if they were younger. This might explain why 47% (7/15) parents reported having "somewhat" thought about the information since reading the DA and 40% (6/15) reported feeling worried/concerned about the information. <u>Risk of bias</u> <u>Selection bias:</u> high risk Reason: 34/74 (45.95%) families that were eligible for participation, consented to participate and completed the pre-DA questionnaire. 11/24 (46%) clinicians that were eligible for participation, consented to participate in this study and completed a post-DA review survey. <u>Attrition bias:</u> high risk Reason: 15/34 (44.12%) parents reviewed the DA and completed the post-DA questionnaire.

	lost to follow up were classified mainly as medium and high infertility risk.		Fertility knowledge and decision regret **Improvements in Knowledge and Understanding** - Parents reported that "most" (2/15; 13%) or "some" 74% (11/15) or "none" (2/15;13%) of the information was new to them - Parents reported the DA helped improve their understanding of cancer treatments, infertility, and FP procedures to some degree - Knowledge scores increased significantly by 1.50 (average of 5.21/10 to 6.71/10 FP knowledge question correctly) after reviewing the DA (*P*<0.04) - FP knowledge scale increased from 21% (3/14) prior to reviewing the DA to 64% (9/14) after DA review in parents who scored >70%. **Expectation of success of FP experimental procedure** - 73% (11/15) agreed that FP would be successful in lifetime of their children - Expectation of the FP success decreased to 46% (7/15) after DA review - Expectations of success in this lifetime decreased in parents of boys and increased in parents of girls **Decision regret scale scores from pre to post DA** - There was a non-significant increase in score	Detection bias: unclear Reason: Unclear if outcome assessors were blinded. Confounding: high risk Reason: No multivariate analysis adjusting for potential confounders.

			- All parents 14/14 = 16.5 (SD: 18.6) to 18.5 (SD:19.4) p.value=0.54 - Parents of boys (n=6) 5.8 (SD: 12.0) to 10.0 (SD: 16.7) p.value=0.32 - Parents of girls (n=8) 25.7 (SD: 19.0) to 25.7 (SD: 19.7) p.value=1.0 <u>Clinician acceptance of the DA by its perceived usefulness</u> - All clinicians reported that they would recommend the DA to patients - They thought that the DA was well designed and easy to use; the DA was a good information source; and there is a need for more information and resources for patients and parents beyond the DA - Clinicians reported satisfaction (excellent and well structured) with the design and usability of the DA website - Regarded as a valid and relevant source of information for clinicians, patients, and their families **Perceived need for information and patient resources** - 36% (4/11) of the interviewed clinicians highlighted a lack of patient/ parent resources regarding infertility, FP procedures, and processes. - One clinician noted that she had observed more adolescents, especially boys making FP decision, noting that there are very few resources tailored toward adolescent and parents of adolescents .	

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?				
Bradford et al. Improvements in clinical practice for fertility preservation among young cancer patients: results from bundled interventions. J Adolesc Young Adult Oncol 2018;7:37-45.				
Study design Treatment era Years of follow-up	**Participants**	**Intervention**	**Main outcomes**	**Additional remarks**
1. Study design Multi-center observational intervention study Retrospective cohort study for pre intervention Prospective cohort study for post intervention Five tertiary cancer centers in Queensland, Australia 2. Study years Pre-intervention= 2012–2014 Post-intervention 2015–2016	1. Type and number of participants AYA cancer patients aged 14-25 years at the time of a cancer diagnosis during the years 2012–2014 Pre intervention n=260 Post intervention n=216 2. Age at diagnosis *Pre vs post intervention* 14–19 yrs: 121 (47%) vs 102 (47%) 20–25 yrs: 139 (53%) vs 114 (53%) 3. Number of participants per diagnosis *Pre vs post intervention* Leukemia 50 (19%) vs 39 (18%) Lymphoma 60 (23%) vs 63 (29%) Brain cancer 35 (13%) vs	Bundled intervention: - Establishment of quality indicators for youth cancer fertility addressing if the patients were provided with written and verbal FP information, referred to a fertility specialist, undergone FP and what preservation method used. Quality indicators were prospectively collected and entered into web-based data system (QOOL) - Delivery of targeted education sessions for medical and senior nursing clinicians - Provision of gender-specific patient resource packs to newly diagnosed patients - Development of fertility	1. Outcome(s) definition - Clinical practice of documenting risk of infertility discussion, referral for fertility preservation, and outcomes of fertility preservation - Influence of age, gender and disease on fertility preservation practices in post-intervention cohort 2. Results Univariable analysis for documented risk of infertility discussion pre vs post intervention: *Gender* Males RR:1.35 (95%CI:1.19–1.5) Females RR:1.70 (95%CI:1.39–2.08) *Age group* 14–19 yrs RR:1.45 (95%CI:1.22–1.71) 20–25 yrs RR:1.48 (95%CI:1.29–1.70) *Disease* Leukemia RR:1.32 (95%CI:1.07–1.62) Lymphoma RR:1.27 (95%CI:0.99–1.63) Brain cancer RR:2.15 (95%CI:1.03–3.62) Bone sarcoma RR:1.32 (95%CI:1.03–1.69) Soft tissue sarcoma RR:2.60 (95%CI:1.17–5.78) Germ cell tumor RR:1.49 (95%CI:1.16–1.91)	Strengths Review of medical record of AYA patients. Patients identified using ICD-10 codes for a cancer diagnosis for pre intervention and from QOOL, a state-wide clinical database in the post-intervention Limitations Used different database during pre and post intervention. So information in medical records may be different to that of the other database. It is likely that some infertility discussion might not be documented because in the pre-intervention cohort, there were five patients with lymphoma, treated with gonadotoxic

3. Follow-up Not reported	23 (11%) Bone sarcoma 26 (10%) vs 27(13%) Soft tissue sarcoma 18 (7%) vs 18 (8%) Germ cell tumor 37 (14%) vs 29 (13%) Carcinoma 24 (9%) vs 13 (6%) Other 10 (4%) vs 4 (2%) 5. Age at follow-up Not reported 6.Controls (if applicable Not reported 7. Additional participants characteristics, if relevant Characteristics of both cohorts were comparable for proportions of age group, sex, cancer diagnoses but there is sign different for treatment type:. pre-intervention cohort were more likely to be treated with surgery or localized radiotherapy and patients in the post-intervention cohort were more likely to be treated with chemotherapy or multimodal therapy	referral pathways, procedure, and work instruction forms	Carcinoma RR:1.58 (95%CI:1.09–2.30) Other RR:3.75 (95%CI:0.96–14.65) All patients RR:1.47 (95%CI:1.12–1.63) - Patients in the post intervention were significantly more likely to have evidence of risk of infertility discussion compared to pre-intervention - In post intervention group a significant improvement in documented risk of fertility discussion was observed across all patient variables in both age groups, both males and females, and in all diseases except lymphoma Univariable analyses documented referral to fertility specialist pre vs post intervention: *Gender* Males RR: 1.44 (95%CI:1.17–1.77) Females RR: 1.82 (95%CI:1.15–2.89) *Age group* 14–19 years RR: 1.41 (95%CI:1.03–1.93) 20–25 years RR: 1.63 (95%CI:1.27–2.11) *Disease* Leukemia RR: 0.90 (95%CI:0.52–1.54) Lymphoma RR: 1.33 (95%CI:0.98–1.81) Brain cancer RR: 1.96 (95%CI:0.85–4.51) Bone sarcoma RR: 1.84 (95%CI:1.12–3.01) Soft tissue sarcoma RR: 2.33 (95%CI:0.71–7.62) Germ cell tumor RR: 1.35 (95%CI:0.86–2.12) Carcinoma RR: 2.37 (95%CI:1.15–4.88) Other RR: 6.60 (95%CI:0.32–135.38) All patients RR: 1.53 (95%CI:1.26–1.87) Univariable analyses documented outcomes of	treatment, who did not have a documented risk of infertility discussion, but who did have documented fertility preservation outcomes. Clinicians may be aware of medico-legal consequences. since there was legal case study in 2014 just before post intervention. Thus have been more vigilant with documentation and clinical practice regarding risk of infertility in the post-intervention cohort. Risk of bias Selection bias: low risk Reason: 260/283 (92.86%) of the patients identified during the pre intervention phase were included. Attrition bias: low risk Reason: Data were reviewed for 260 patients included in the pre intervention period. Data were reviewed for all 216 patients' records in the post intervention period. Detection bias: unclear

	% of patients in pre vs post intervention <u>Gender</u> Males 68% vs 91% Females 51% vs 88% <u>Age group</u> 14–19 yrs 60% vs 86% 20–25 yrs 63% vs 93%		<u>fertility preservation pre vs post intervention:</u> *Gender* Males RR: 2.89 (95%CI:2.05–4.09) Females RR: 1.90 (95%CI:1.08–3.33) *Age group* 14–19 years RR: 2.01 (95%CI:1.16–3.48) 20–25 years RR: 2.60 (95%CI:1.82–3.71) *Disease* Leukemia RR: 1.43 (95%CI:0.70–2.90) Lymphoma RR: 2.16 (95%CI:1.32–3.54) Brain cancer RR: 2.13 (95%CI:0.77–5.91) Bone sarcoma RR: 3.08 (95%CI:1.32–7.18) Soft tissue sarcoma RR:5.00 (95%CI:0.66–38.65) Germ cell tumor RR: 2.71 (95%CI:1.37–5.38) Carcinoma RR: 3.69 (95%CI:1.10–12.39) Other RR: 6.60 (95%CI:0.32–135.38) All patients RR: 2.56 (95%CI:1.19–3.44) <u>Influence of age, gender, and disease on fertility preservation practices</u> - In the pre and post intervention, there were no significant differences associated with age categories for documented risk of infertility discussion or referral to fertility specialists - In the post intervention, patients aged 14–19 were 0.50 (95% CI 0.35–0.72) times as likely to have documented outcomes of FP compared to those aged 20–25 years - In the pre intervention, males were more likely to have documented risk of infertility discussion compared to females (RR 1.37, 95% CI 1.11–1.68) - In the post-intervention cohort, males were significantly more likely to be	Reason: Unclear if outcome assessors were blinded. <u>Confounding:</u> high risk Reason: No multivariate analysis adjusting for potential confounders.

			referred to fertility specialists (RR 1.83, 95% CI 1.37–2.46) and to have documented fertility preservation outcomes (RR 2.06, 95% CI 1.44–2.96) - In the post-intervention cohort, germ cell tumors were 1.10 (95% CI 1.01–1.20) times as likely to have documented risk of infertility discussion compared to sum of all other diseases - Patients diagnosed with acute leukemia were less likely to be referred compared to sum of all other diseases (RR 0.59, 95% CI 0.38–0.92) - Patients with lymphoma and bone sarcomas were significantly more likely to be referred (RR 1.29, 95% CI 1.02–1.63) and RR 1.47, 95% CI 1.15–1.87 respectively) - No differences were found with documented fertility preservation outcomes associated with disease	

AYA= Adolescence and Young Adults. FP=Fertility preservation

What are facilitators of and barriers to the communication of treatment-related fertility risks and fertility preservation options?				
Saraf et al. Examining predictors and outcomes of fertility consults among children, adolescents, and young adults with cancer. Pediatr Blood Cancer 2018;65:e27409.				
Study design	**Participants**	**Intervention**	**Main outcomes**	**Additional remarks**
1. Study design Retrospective observational study 2. Study years Not Reported 3. Follow-up Not Reported	1. Type and Number of Participants 161 patients (69 underwent consultation and 92 no consult) with a new cancer diagnosis over 18 months 2. Diagnoses *Consult vs non consult* Sarcoma 16 (23%) vs 14 (15%) Leukemia/Lymphoma 36 (52%) vs 46 (50%) Embryonal 7 (10%) vs 10 (11%) Neuro-oncology 10(15%) vs 22 (24%) 3. Age at diagnosis: Mean age: 8 years (range <1–31 years, SD 6.7). Median age for Consult vs non consult 12 (<1–31) vs 5 (<1–20) 4. Age at follow-up Not Reported	Opt-out implementation: "nudge intervention" in that the default results in an automatic consult order, providing the opportunity for more patients to receive counseling and consider FP Initially, there was a stand-alone order; however, midway through the study, the consult order became automatically preselected in a bundle of orders for new oncology patients. The order would have to be deselected if deemed inappropriate (i.e., an "opt-out")	1. Outcome definitions - Predictors of completed fertility consultation - Demographic differences before and after implementing intervention - Predictors of FP attempt after consultation 2. Results Predictors of completed fertility consultation (OR (95%CI); unclear if multivariable analyses): - Age at Dx: 1.11 (1.06–1.17) - Female gender: 0.78 (0.41–1.49) - Race (white vs other races): 1.17(0.57-2.42) - Opt-out mechanism: 3.64 (1.84–7.22) - Leukemia/Lymphoma vs Sarcoma: 0.69 (0.30–1.59) - Embryonal vs Sarcoma: 0.61 (0.18–2.04) - Neuro-oncology vs Sarcoma: 0.40 (0.14–1.12) Impact of the opt-out as a confounding variable in univariate analysis: - There were no demographic differences before and after implementing intervention - While no statistically significant	1. Strengths Retrospective medical record review was performed at a large pediatric academic center. 2. Limitations No well-defined inclusion criteria. No information about original cohort, which country and hospital this study was performed. Period of recruitment/ year of study was not described. No reported time for implementation of intervention. Small sample size and may lack statistical power to detect a difference or association No reasons for "opting out" or not completing a consult that was ordered ,

	5. Controls (if applicable) Not Applicable 6. Additional study characteristics, if relevant Not Applicable		differences were observed among disease teams, patients with sarcoma were most likely to complete a consult Predictors of FP attempt after consultation (OR (95%CI); unclear if multivariable analyses): - Age at Dx: 1.12 (1.03–1.22) - Female gender: 1.51 (0.51–4.46) - Race (white vs other races): 3.60 (0.74–17.60) - Opt-out mechanism: 0.48 (0.15–1.51) - Leukemia/Lymphoma vs Sarcoma: 1.67 (0.39–7.12) - Embryonal vs Sarcoma: 1.73 (0.22–13.67) - Neuro-oncology vs Sarcoma: 4.33 (0.74–25.29)	3. Risk of bias *1. Selection bias:* Unclear Reason: Just indicated that 161 patients met inclusion criteria. No information about the inclusion criteria was stated. No information about original cohort. *2. Attrition bias:* Low risk Reason: All the included patient were assessed using consult order (table 1 shows 69 patients went to consult and 92 patients no consults, giving a total of 161 patients included). *3. Detection bias:* Unclear Reason: Unclear if outcome assessors were blinded. *4. Confounding:* Unclear Reason: Not sure of the type of analysis conducted, if analysis were crude or adjusted ie if bivariate or multivariate analysis.

SD= Standard deviation, FP= Fertility preservation, OTC= ovarian tissue cryopreservation, TTC= testicular tissue cryopreservation, GnRHa= gonadotropin releasing hormone analogues, TESE= self-stimulation/testicular sperm extraction. DX= Diagnosis.