


# How can we improve oncofertility care for patients? A systematic scoping review of current international practice and models of care

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**BACKGROUND:** Fertility preservation (FP) is an important quality of life issue for cancer survivors of reproductive age. Despite the existence of broad international guidelines, the delivery of oncofertility care, particularly amongst paediatric, adolescent and young adult patients, remains a challenge for healthcare professionals (HCPs). The quality of oncofertility care is variable and the uptake and utilization of FP remains low. Available guidelines fall short in providing adequate detail on how oncofertility models of care (MOC) allow for the real-world application of guidelines by HCPs.

**OBJECTIVE AND RATIONALE:** The aim of this study was to systematically review the literature on the components of oncofertility care as defined by patient and clinician representatives, and identify the barriers, facilitators and challenges, so as to improve the implementation of oncofertility services.

**SEARCH METHODS:** A systematic scoping review was conducted on oncofertility MOC literature published in English between 2007 and 2016, relating to 10 domains of care identified through consumer research: communication, oncofertility decision aids, age-appropriate care, referral pathways, documentation, training, supportive care during treatment, reproductive care after cancer treatment, psychosocial support and ethical practice of oncofertility care. A wide range of electronic databases (CINAHL, Embase, PsycINFO, PubMed, AIEPT, Education Research Complete, ProQuest and VOCED) were searched in order to synthesize the evidence around delivery of oncofertility care. Related citations and reference lists were searched. The review was undertaken following registration (International prospective register of systematic reviews (PROSPERO) registration number CRD42017055837) and guidelines of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).

**OUTCOMES:** A total of 846 potentially relevant studies were identified after the removal of duplicates. All titles and abstracts were screened by a single reviewer and the final 147 papers were screened by two reviewers. Ten papers on established MOC were identified amongst the included papers. Data were extracted from each paper and quality scores were then summarized in the oncofertility MOC summary matrix. The results identified a number of themes for improving MOC in each domain, which included: the importance of patients receiving communication that is of a higher quality and in different formats on their fertility risk and FP options; improving provision of oncofertility care in a timely manner; improving access to age-appropriate care; defining the role and scope of practice of all HCPs; and improving communication between different HCPs. Different forms of decision aids were found useful for assisting patients to understand FP options and weigh up choices.

**WIDER IMPLICATIONS:** This analysis identifies core components for delivery of oncofertility MOC. The provision of oncofertility services requires planning to ensure services have safe and reliable referral pathways and that they are age-appropriate and include medical and psychological oncofertility care into the survivorship period. In order for this to happen, collaboration needs to occur between clinicians, allied HCPs and executives within paediatric and adult hospitals, as well as fertility clinics across both public and private services.

Training of both cancer and non-cancer HCPs is needed to improve the knowledge of HCPs, the quality of care provided and the confidence of HCPs with these consultations.

**Key words:** fertility preservation / oncofertility / survivorship / models of care / late effects / systematic review / communication / training

## Introduction

Oncofertility care includes fertility preservation (FP) discussion and management, as well as the management of sexual dysfunction, hormonal dysfunction, complex contraception and fertility-related psychosocial support (Anazodo, Ataman-Millhouse, Jayasinghe and Woodruff, 2018; Burns *et al.*, 2018). The field has undergone rapid advancements in recent years, improving effectiveness and increasing demand for access from patients and HCPs (Anazodo *et al.*, 2018; Burns *et al.*, 2018).

The ability to bear children is important to a majority of people and procreation is a basic human instinct, so the inability to bear a child can be devastating for most individuals. FP has been cited as one of the top five unmet needs for adolescent cancer patients, along with health, work/school, romantic relationships and close friends (Klosky *et al.*, 2015). FP raises increasingly important medical and quality of life issues for cancer survivors. Therefore, wherever possible, oncofertility care should be an integral part of cancer care from diagnosis through to survivorship.

Despite international evidence about the importance of, and effective ways to deliver, oncofertility care and the availability of 20 different high-level guidelines or models of care (MOC) to steer practice (Multi-disciplinary Working Group convened by the British Fertility Society, 2003; Physicians, 2007; Fallat and Hutter, 2008; Pentheroudakis *et al.*, 2009; French Association for the Care of Oncological Support, 2011; National Comprehensive Cancer Network, 2011; von Wolff *et al.*, 2011; Cardoso *et al.*, 2012; Kim *et al.*, 2012; AYA cancer fertility preservation guidance working group, 2013; Hoog-Labouret and Merlet, 2013; Loren *et al.*, 2013; Martínez *et al.*, 2013; National Institute for Health and Care Excellence, 2013; Scottish Intercollegiate Guidelines Network, 2013; Sudour-Bonnange *et al.*, 2013; 'Fertility preservation for AYAs diagnosed with cancer: Guidance for health professionals,' 2014; Joshi *et al.*, 2014; network, 2014; Roberts *et al.*, 2015; Yasmin *et al.*, 2018; Practice Committee of American Society for Reproductive Medicine, 2014), FP care is often under-implemented. Several barriers have been found to thwart the implementation of comprehensive and equitable FP practice. These include: (i) a lack of referral pathways and MOC for oncofertility services and collaboration between cancer and fertility doctors to deliver services; (ii) inequitable access based on cost; (iii) health literacy; (iv) a lack of trained staff who can deliver these services; and (v) no consensus about the best way to deliver information to patients (Vadaparampil *et al.*, 2008b; Panagiotopoulou *et al.*, 2015).

Available guidelines fall short of providing adequate detail to inform real-world application and lack of effective strategies to reduce or avoid key implementation barriers. To ensure that all patients are sufficiently empowered to make fully informed FP decisions and receive adequate reproductive follow-up care after cancer treatment, together with access to fertility-related psychosocial support, it is important that an inclusive MOC be developed that reflects current

evidence and experiential knowledge across this multifaceted and largely complex domain.

Healthcare providers who are skilled in fundamental competencies and effective health service processes, such as reliable MOCs and referral pathways, underpin high quality oncofertility care. The findings, garnered from systematically characterizing appropriate oncofertility care, will be used as a first step in the development of an oncofertility competency framework to facilitate comprehensive education and professional development in this field.

## Aims

The aim of the current study is to systematically review the literature on the components of oncofertility care for paediatric, adolescent and adult cancer patients, as defined by patient and clinician representatives, and then identify the barriers, facilitators and challenges of these components so as to improve the implementation of oncofertility services.

## Methods

As the components of oncofertility are broad and complex, and the literature includes studies with different methodologies, a systematic scoping review was undertaken following registration (International prospective register of systematic reviews (PROSPERO) registration number CRD42017055837) and guidelines of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).

The preliminary stage of any review is a clear identification of the problem being investigated. A focus group consultation with 50 consumers (patients, partners and parents) was undertaken prior to the review to identify areas they considered were valuable or missing from their oncofertility care experience. Eight strategies (domains) were identified: (i) communication; (ii) oncofertility decision aids; (iii) age-appropriate care; (iv) referral pathways; (v) documentation; (vi) oncofertility training; (vii) reproductive survivorship care; and (viii) fertility-related psychosocial support. The consumer-identified domains were augmented with two further areas identified by Australian clinical researchers as being important from a medical perspective: (i) ethical practice of oncofertility care; and (ii) provision of medical care during FP treatment. This review considered all studies in which at least one of the 10 identified strategies were addressed and reported from the clinician or patient perspective. No restrictions were made on clinician type or speciality, with all studies reporting on an oncofertility MOC strategy included.

A comprehensive literature search strategy was devised and performed in October 2017 (Table I) with suitable studies identified for the period of 2007–2016 by searching of electronic databases PubMed, EMBASE, PsycINFO and CINAHL, alongside the screening of relevant reference lists. Education databases (AEIPT, Education Research Complete, ProQuest and VOCED) were also searched but did not yield any relevant papers. Oncofertility practice was defined in 2007 (Woodruff, 2007) and since then significant investments in clinical and research practice have resulted in the availability of increasing evidence about medical and

**Table 1 Search terms used across electronic databases.**

	<b>PubMed (627)</b>	<b>Embase (467)</b>	<b>CINAHL (12)</b>	<b>PsycINFO (67)</b>
		English language, Humans, published 2007–2016		
	Neoplasms [MeSH] OR cancer OR tumour/tumour OR oncology	Neoplasm [Emtree] OR cancer OR tumour/tumour OR oncology	Neoplasms [subject] OR cancer OR tumour/tumour OR oncology	Neoplasms OR cancer OR tumour/tumour OR oncology
	Fertility preservation [MeSH] OR cryopreservation [MeSH] OR semen preservation [MeSH] OR 'fertility preservation' OR oncofertility OR 'sperm banking' OR 'oocyte cryopreservation' OR 'ovarian cryopreservation' OR 'testicular cryopreservation'	Fertility preservation [Emtree] OR cryopreservation [Emtree] OR sperm preservation [Emtree] OR 'fertility preservation' OR oncofertility OR 'sperm banking' OR 'oocyte cryopreservation' OR 'ovarian cryopreservation' OR 'testicular cryopreservation'	Fertility preservation [subject] OR cryopreservation [subject] OR semen preservation [subject] OR 'fertility preservation' OR oncofertility OR 'sperm banking' OR 'oocyte cryopreservation' OR 'ovarian cryopreservation' OR 'testicular cryopreservation'	'Fertility preservation' OR cryopreservation OR 'semen preservation' OR oncofertility OR 'sperm banking' OR 'oocyte preservation' OR 'ovarian preservation' OR testicular preservation'
<i>Domains</i>				
Communication skills	Communication [MeSH] OR communication (76)	Interpersonal communication/ [Emtree] OR communication (59)	Communication [subject] OR communication (9)	Communication/ OR communication (19)
Decision aids	Decision Support Techniques [MeSH] OR 'decision aid' (8)	'decision aid' (12)	Decision Support Techniques [subject] OR 'decision aid' (1)	'decision aid' (1)
Provision of age-appropriate care	'age-appropriate care' OR 'provision of care' (2)	'age-appropriate care' OR 'provision of care' (1)	'age-appropriate care' OR 'provision of care' (0)	'age-appropriate care' OR 'provision of care' (1)
Referral pathways	Referral and Consultation [MeSH] OR referral (104)	Patient referral/ [Emtree] OR referral (137)	Referral and Consultation [subject] OR referral (0)	Professional referral/ OR referral (8)
Documentation	Documentation [MeSH] OR documentation (23)	Medical documentation/ [Emtree] OR documentation (22)	Documentation [subject] OR documentation (0)	Documentation (0)
Training	Education [MeSH] OR training (145)	Training/[Emtree] OR Education/[Emtree] (63)	Education [subject] OR training (0)	Education/OR training (10)
Supportive care	'supportive care' (5)	'supportive care' (15)	'supportive care' (0)	'supportive care' (3)
Reproductive care in survivorship	'reproductive care' (5)	'reproductive care' (5)	'reproductive care' (0)	'reproductive care' (0)
Psychosocial support	psychosocial (39)	Psychosocial care/[Emtree] OR psychosocial (14)	psychosocial (2)	psychosocial (18)
Oncofertility models of care	'model of care' OR program (124)	'model of care' OR program (114)	'model of care' OR program (0)	'model of care' OR program (3)
Ethics	ethics (96)	Ethics/ [Emtree] (25)	Ethics (0)	Ethics (4)

psychosocial oncofertility care. Therefore, oncofertility MOC that were developed in the first 10 years of this new sub-specialty were evaluated. All titles and abstracts were screened and to ensure inter-rater reliability, two reviewers reviewed the full text of the included studies to confirm eligibility. Discrepancies between ratings of inclusion on studies were discussed between the two reviewers until a consensus was reached. As studies were expected to be heterogeneous, a narrative synthesis was planned.

## Quality analysis and data extraction

The quality of the final studies was assessed using the Mixed Methods Appraisal Tool (MMAT) (Pluye, Gagnon *et al.*, 2009; Pace, Pluye *et al.*, 2012), a valid instrument for testing mixed method reviews and utilized worldwide (Pace *et al.*, 2012). Scores on the MMAT vary from 25% (one criterion met) to 100% (all criteria met) with quality assessed according to four criteria related to either qualitative or quantitative enquiry. Data were extracted from each individual paper and are summarized in Supplementary Table S1 with the MMAT score. Conventional content analysis was used to analyse the cancer and fertility papers and draw out the themes for reproductive concerns from each paper. These themes were then grouped and coded accordingly to assess group differences and trends.

## Results

### Study characteristics

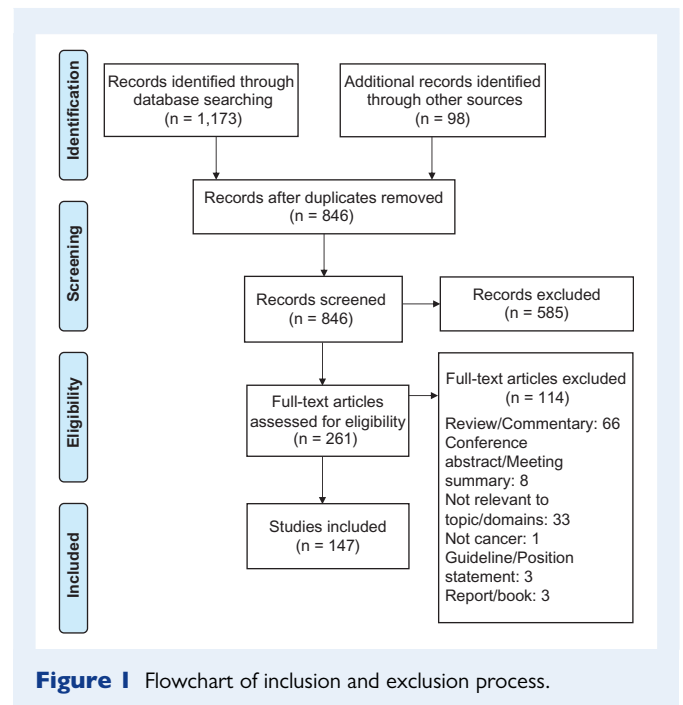
The literature search identified 846 potentially relevant studies after the deletion of duplicates (Fig. 1). Full text review of 261 studies was completed and 147 studies met the eligibility criteria. Of the 147 studies included, 102 were quantitative, 40 were qualitative utilizing discourse, content and thematic analyses, and five utilized mixed methods. All studies were of reasonable quality (50–100%) by MMAT score and were therefore included in this review. The studies were first published between 2007 and 2016, and were conducted across 20 countries representing middle and high-income nations and a range of clinical disciplines. While 42 papers focussed on female patient data or experiences, 32 were on both male and female patients and 12 were on males only. Three papers included paediatric patient data only, although several included paediatric and adult data. Papers reported on patients who had been recently diagnosed (within a few weeks) through to surviving patients (several years post diagnosis). There were 64 papers which summarized the views of healthcare professionals (HCPs) or institutional factors.

Information from the 147 papers was examined in relation to the 10 domains and summarized below. A systematic analysis with two coders (Table II) is presented as well as a summary of the impact, challenges and barriers to delivering oncofertility practice and policy.

### Domain I: communication

The review identified six themes on communication: timing of FP discussion, role of HCPs in communicating about oncofertility care, type of communication, age-appropriate communication, quality of communication and communication between colleagues.

There were 28 papers providing information on the timing and initiation of FP discussion (Table II, section 1a) with significant variation



**Figure 1** Flowchart of inclusion and exclusion process.

reported in timing of such discussions. In one study, as few as 9% of patients reported receiving any information on fertility risk or FP options (Goldfarb *et al.*, 2016), while in another study 22% of patients were counselled on FP before, 6% during, and 7% after cancer treatment (Hohmann *et al.*, 2011). In another study, of those counselled, 78% had FP discussions before treatment (Chin *et al.*, 2016). Cancer survivors and nurses believe the clinician should initiate the conversation about FP (Gorman *et al.*, 2012; Murray *et al.*, 2016), however, between 23 and 50% of discussions were initiated by the patient or a family member or friend (Rabah *et al.*, 2010; Scanlon *et al.*, 2012; Yee *et al.*, 2012b; Chin *et al.*, 2016; Yee, 2016). A study of 115 paediatric oncology nurses showed that low rates of fertility discussion was associated with them not wanting to upset patients and families, not wanting to give out erotic material to male minors and not having appropriate resources (Vadaparampil *et al.*, 2007) (Table II, section 1a).

In a Delphi study of HCPs, all agreed that patients should be given clear and objective information about FP shortly after diagnosis and this should be followed up with more detailed information from a fertility expert later on (Garvelink *et al.*, 2012). Patients, irrespective of age and sex, indicated their preference to receive fertility information around the time of diagnosis (Crawshaw *et al.*, 2009; Lee *et al.*, 2011a). Parents have also indicated that they would have liked more information about fertility at the time of their child's diagnosis (Stein *et al.*, 2014; Ellis *et al.*, 2016).

There were 21 papers discussed the role of staff in communicating about FP (Table II, section 1b). The majority of cancer physicians believe it is their role to raise questions of fertility with patients and, to a lesser extent, FP options (Duffy *et al.*, 2012; Overbeek *et al.*, 2014). Despite this, one study found that 40% of clinicians thought that patients should bring up the topic (Ghorbani *et al.*, 2011). Clinicians who believe discussing FP is their responsibility are twice as likely to discuss it (Takeuchi *et al.*, 2017). Clinicians who attend FP

**Table II Summary table showing illustrative examples of oncofertility model of care strategies.**

Domain	Illustrative examples of relevant findings
1. Communication skills	<p>a. Timing of FP discussion 40% of clinicians thought patients should bring up the topic of FP (Ghorbani et al., 2011). Many of a group of oncology nurses surveyed felt that oncologists should be responsible for initiating FP discussions (Murray et al., 2016). Among adult survivors of childhood cancer, 22% were counselled on FP before, 6% during and 7% after cancer treatment (Hohmann et al., 2011).</p> <p>b. Role of staff In a Delphi study, experts agreed that patients should be given clear and objective information about FP shortly after diagnosis and more detailed information from a fertility expert later on (Garvelink et al., 2012). Half of the oncology nurses reported discussing FP with patients (King et al., 2008b).</p> <p>c. Type of communication A survey of oncologists found that 97% used only verbal communication (Yee et al., 2012c). Brochures were found useful by 96% of male and 93% of female young adult patients (Tam et al., 2016).</p> <p>d. Age-appropriate nature of communication Covered in 3a.</p> <p>e. Quality of communication Covered in 3e.</p> <p>f. Communication between staff HCPs had difficulties communicating between professionals of the same speciality (Shimizu et al., 2015) or different specialities (Shimizu et al., 2015; Abe et al., 2016). This was echoed from the patient perspective, that clinicians should communicate more effectively with each other (Garvelink et al., 2013).</p>
2. Oncofertility decision aids	<p>Patients who received a decision aid showed higher knowledge and lower regret at 12 months and were more likely to discuss FP with their oncologist and to be referred to a fertility specialist (Peate et al., 2012). Parents and healthcare providers had concerns about content and readability of decision aids for younger patients (aged 12–21) (Murphy et al., 2012).</p>
3. Provision of care	<p>a. Age-appropriate care Young adult cancer patients showed high ratings of importance for information on treatment effects on fertility, FP, treating infertility and other parenting options (Gupta et al., 2013). Adolescent patients (12–17 years) showed eagerness to receive information about their fertility (Stinson et al., 2015). Both young patients and their parents felt that FP services should be age-appropriate and accessible (Stinson et al., 2015). Adult cancer survivors suggested that information should be tailored to the patient's age (Corney and Swinglehurst, 2014). Only 27% of female child and AYA cancer patients reported receiving enough information on FP options (Kim et al., 2016).</p> <p>b. What patients want from their care Patients want detailed, verbal and written information on options, risks, benefits, side effects and success rates of FP (Wilkes et al., 2010; Hershberger et al., 2013; Bastings et al., 2014a; Richter et al., 2016). Adolescent male patients felt less stressed when staff were informal, friendly and not embarrassed, and when they spoke clearly and directly to them (Crawshaw et al., 2008).</p> <p>c. Who should be involved in consultations Patients should be involved in fertility discussions, from 7 years of age (Wyns et al., 2015). Clinicians treating adolescent patients wanted to provide care to adolescents without the parents present (Bashore, 2007; de Vries et al., 2009). When male survivors were asked their preference for the initial FP conversation, 56% would have liked their parent to be present and 44% would have preferred their parent not to be present (Ginsberg et al., 2008).</p> <p>d. Clinician comfort and scope of practice 60% of clinicians rarely or never gave any FP educational materials to patients (Quinn et al., 2012). Clinicians reported low levels of discomfort with discussions about infertility and FP for paediatric and adolescent patients (Fuchs et al., 2016).</p> <p>e. Quality of verbal and written information 73% of female survivors of paediatric and AYA cancers did not feel they had received sufficient information on FP options at diagnosis from their cancer team (Kim et al., 2016). Young male patients reported that receiving fertility information was a straightforward process and they felt satisfied with having a choice about FP (Crawshaw et al., 2009). Two-thirds of patients reported satisfaction with the quality and length of fertility discussions (Scanlon et al., 2012).</p> <p>f. Institution factors In a US study, only four out of 30 centres (13%) had a policy on provision of FP information (Clayman et al., 2013). 75% of clinicians indicated a need for FP guidelines in their institution (Vadaparampil et al., 2008a).</p>
4. Referral pathways between cancer and fertility doctors	<p>a. Rates of referral Paediatric oncologists reported a high referral rate for older boys (83% of those at high/medium risk of infertility), but not for girls (1%) or younger boys (39%) (Anderson et al., 2008). Referrals to a reproductive specialist occurred in 28% of adult female breast cancer patients (Vu et al., 2017).</p>

Continued

**Table II** *Continued*

Domain	Illustrative examples of relevant findings
	<p>Oncologists report higher referral rates for adult male patients compared with female patients (Arafa and Rabah, 2011; Yee et al., 2012c).</p> <p>One study found that referrals were most commonly from academic centres (64%) (Lee et al., 2011a).</p> <p>b. Processes for referral</p> <p>In a study of 28 centres, 18% had a referral protocol for FP in place (Warner et al., 2016).</p> <p>In institutions with an established referral pathway including standard referral forms, and sometimes a patient navigator to assist with the process, referrals are more streamlined (Johnson and Kroon, 2013).</p> <p>c. Factors affecting referral</p> <p>Referrals are increased when alliances are formed between cancer and fertility specialists (Dyer and Quinn, 2016).</p> <p>In institutions with an established referral pathway including IT system prompts and referral forms, and sometimes a patient navigator to assist with the process, referrals are more streamlined (Ogle et al., 2008; Reinecke et al., 2012; Johnson and Kroon, 2013).</p> <p>Patients are more likely to be referred when they have a decision aid (Peate et al., 2012) or received other additional information about FP, such as on risks and options (Kelvin et al., 2016).</p> <p>Low rates of discussion and referral are associated with institutional factors such as difficulties finding facilities or specialists to refer patients to (Goodwin et al., 2007; Yee et al., 2012c; Dyer and Quinn, 2016; Mahajan et al., 2016), lack of FP information and problems integrating FP with routine cancer care (Preaubert et al., 2016).</p> <p>Distance to specialist had no impact on whether patients were referred (Lee et al., 2011a; Goodman et al., 2012).</p>
5. Documentation of oncofertility discussions, decisions and procedures	<p>a. Extent of documentation</p> <p>Low levels of oncofertility documentation are seen amongst both haematologists (38%) and oncologists (26%) even when processes were in place within their institution for recording the discussion of fertility issues with patients (Gilbert et al., 2010).</p> <p>Around three-quarters of breast cancer patients had documented FP discussions prior to treatment (Srikanthan et al., 2016).</p> <p>b. Extent of documentation by age</p> <p>Of patients aged 18–45 years, those aged 18–30 years were significantly more likely to have documentation of infertility risk discussion, FP options and referral (Quinn et al., 2015).</p> <p>c. Factors affecting documentation</p> <p>Patient records regarding FP before and after oncofertility program formalization showed that, of 18–40 year olds, 23% were offered FP before and 43% were offered FP after the program was developed (Sheth et al., 2012).</p> <p>Access to a fertility navigator or coordinator of FP lead to increased documentation (Gilbert et al., 2010; Salsman et al., 2016).</p>
6. Training of cancer and fertility healthcare professionals to deliver oncofertility care	<p>a. Level of training and knowledge of cancer clinicians</p> <p>Of 54 oncologists, the majority had received little or no training in FP and this affected their ability to discuss the topic with patients (Quinn et al., 2009b).</p> <p>Clinicians with favourable attitudes towards FP (Quinn et al., 2009a; Shimizu et al., 2013), more knowledge (Quinn et al., 2009a; Shimizu et al., 2013), and who have these discussions more frequently (Forman et al., 2009; Louwé et al., 2018) have improved rates of referral for FP.</p> <p>b. Level of training and knowledge of non-cancer clinicians</p> <p>Gynaecologists had good knowledge and felt confident providing advice and referral for FP, before, during and after cancer treatment (Duncan et al., 2011).</p> <p>A survey found a lack of training of haematologists about FP (Gilbert et al., 2010).</p> <p>c. Level of training and knowledge of allied health professionals</p> <p>Social workers have been shown to have limited knowledge of FP resources and clinics (King et al., 2008b).</p> <p>21% of allied health professionals had undertaken training relating to fertility in cancer patients, compared with 37% of doctors and 31% of nurses (Ussher et al., 2016).</p> <p>d. Types of education and tools</p> <p>The ENRICH online training program showed positive outcomes, including that most trainees improved their knowledge and initiated change to facilitate FP within their institution (Vadaparampil et al., 2016).</p> <p>In a successful FP program, training for medical or fertility clinicians was both formal and informal, and ongoing (Ogle et al., 2008).</p> <p>Types of education include Grand Rounds (Quinn et al., 2011) and internal education sessions (Forman et al., 2009).</p> <p>e. Clinician comfort and scope of practice</p> <p>Covered in 3d.</p>
7. Medical supportive care during fertility preservation: No relevant literature found.	
8. Reproductive care in survivorship	<p>a. Patients' fertility status following cancer treatment</p> <p>Many cancer survivors were found to have incorrect beliefs about the extent of their fertility problems, which did not reflect the information received (Crawshaw and Sloper, 2010).</p> <p>b. Fertility investigations following cancer treatment</p> <p>15% of female survivors of childhood or AYA cancer had a fertility consultation following cancer treatment (Kim et al., 2016).</p>

*Continued*

**Table II** *Continued*

Domain	Illustrative examples of relevant findings
9. Fertility-related psychosocial support	<p>Males were less likely to attend for fertility follow-up if they had negative experiences with the sperm banking process (Pacey et al., 2012).</p> <p>c. Survivorship Information needs Both male and female patients want individual information about their fertility post cancer (Armuand et al., 2015). Many survivors have incorrect beliefs about the extent of their fertility problems (Crawshaw and Sloper, 2010). See also: 1. Communication skills and 3. Provision of care.</p> <p>d. Survivorship emotional needs and views about care Female patients reported frustration with the quality of care and lack of reproductive continuity of care amongst different clinicians in survivorship, and not getting a 'big picture' view of their fertility (Gorman et al., 2012).</p> <p>a. Negative emotions The threat of temporary or permanent infertility was associated with psychological distress, such as depression and anxiety, in both males and females (Lawson et al., 2015; Ellis et al., 2016). Cancer patients experience negative emotions when they lack fertility information and support (Perz et al., 2014). Sufficient information on FP options leads to less distress, fear and decision regret (Hohmann et al., 2011; Letourneau et al., 2012; Peate et al., 2012; Bastings et al., 2014a).</p> <p>b. Psychosocial support Participants felt emotional support was important at all stages of treatment and recovery (Corney and Swinglehurst, 2014). Counselling is useful at many time points due to the complexity of FP decision making (Gardino et al., 2010). With appropriate support, patients experience less distress and decision regret, and feel more positive about the future (Letourneau et al., 2012; Benedict et al., 2015; Lawson et al., 2015). Who provides support—see 9c.</p> <p>c. Role of professionals, family and friends Cancer survivors reported it helpful to discuss oncofertility issues with spouses, friends and family who could provide emotional support and assist with decision-making (Kim et al., 2013). Patients felt oncologists and gynaecologists were most useful (Tschudin et al., 2010). The presence of a psychologist can help improve communication between doctor and patient (Razzano et al., 2014). Patients have stated that nurses are helpful with discussing options and making decisions (Kelvin et al., 2016).</p> <p>d. Seeking support and information Young adult patients want written or web-based information about FP (Wilkes et al., 2010). Young patients raised the need for support from peers of around the same age (Stinson et al., 2015). See also: 1. Communication skills and 3. Provision of care.</p>
10: Ethical practice of oncofertility care: No relevant literature found.	

education sessions are more likely to consider FP routinely in treatment planning (Forman et al., 2009).

Resident doctors were found very likely to discuss FP with female patients (Yu et al., 2015), as were nurses and general practitioners (Pacey et al., 2013), and over half of paediatric endocrinologists stated that they held these conversations (54%) (Miyoshi et al., 2016). Similarly, half of a group of oncology nurses reported discussing FP with patients, and similarly to doctors, reported knowledge and comfort level as barriers to discussions (King et al., 2008a). The importance of nurses (Vadaparampil et al., 2007; Nagel et al., 2009), gynaecologists (Duncan et al., 2011) and social workers (Ogle et al., 2008), being included in FP discussions have all been emphasized across different studies. One study described the benefits of social workers to facilitate the discussion once it has been initiated, as their skills lie in providing emotional support and assisting patients to find resources (King et al., 2008b).

There were 17 papers which included themes on the type of communication (see Table II, section 1c). In one study, clinicians reported that patients and parents are usually given printed resources, then directed to certain websites for further information (Fuchs et al., 2016). While referral to written and online resources occurs (Reinecke et al., 2012; Pacey et al., 2013; Besharati et al., 2016), other studies indicate that clinicians are not consistent in providing comprehensive

information (Buske et al., 2016) and clinicians generally only use verbal communication (Gilbert et al., 2010; Yee et al., 2012c). In fact, one study found that 60% of clinicians rarely or never gave any FP educational materials to patients (Quinn et al., 2012). From the patient perspective, one study of male patients found that 58% later recalled having seen written information about sperm banking (Pacey et al., 2013), while a second study of 20 female patients showed that none received any FP information prior to treatment (Karaöz et al., 2010).

There was an overlap in research findings about communication and provision of care and these results are discussed under domain 3 (Table II, sections 1d and 3a).

There were 27 papers including themes on the quality of both verbal and written information (Table II, sections 1e and 3e) and these showed wide variation in the quality of oncofertility discussions and verbal information. The first FP consultation is improved if written materials are given (Dahhan et al., 2015). In one study, around two-thirds of patients reported satisfaction with the quality and length of fertility discussions (Scanlon et al., 2012) and other studies have shown patients to be generally satisfied with the information presented (Wilkes et al., 2010; Hill et al., 2012; Garvelink et al., 2013; Kelvin et al., 2016).

Many patients, parents and partners reported frustration that information given was incomplete or misleading (Gorman et al., 2012;



Corney and Swinglehurst, 2014; Wright *et al.*, 2014; Banerjee and Tsiapali, 2016; Ellis *et al.*, 2016), that information was presented too quickly (Garvelink *et al.*, 2013) or that there was a lack of written materials (Hill *et al.*, 2012). Different studies of female patients have shown that 73% did not receive sufficient information (Kim *et al.*, 2016) and 54% sought further information on their own (Scanlon *et al.*, 2012). Male patients have been found to be more satisfied with the fertility discussion than female patients in some instances (Crawshaw *et al.*, 2009; Yeomanson *et al.*, 2013).

Several factors had a negative impact on the quality of communication, such as communication being too fast or too late or there being an overload of information (Garvelink *et al.*, 2013). Several papers showed that patients felt ill-informed (Gorman *et al.*, 2012; Niemasik *et al.*, 2012; Wright *et al.*, 2014; Ellis *et al.*, 2016), had unanswered questions (Corney and Swinglehurst, 2014), or did not have the risks explained sufficiently (Niemasik *et al.*, 2012; Banerjee and Tsiapali, 2016; Dyer and Quinn, 2016). Even when the discussion had taken place, not all patients could recall it later (Hohmann *et al.*, 2011; Shnorhavorian *et al.*, 2015).

Three papers described difficulties experienced by HCPs in communication with professionals of the same speciality (Shimizu *et al.*, 2015) or different specialities (Shimizu *et al.*, 2015; Abe *et al.*, 2016). This was echoed by the patient perspective that clinicians should communicate more effectively with each other (Garvelink *et al.*, 2013).

## Domain 2: oncofertility decision aids

Nine studies included themes on decision aids (Table II, section 2) that provided assistance to understand FP options and to weigh up the advantages and disadvantages. These took the form of decision trees (Gardino *et al.*, 2010), web-based or electronic educational tools (Huyghe *et al.*, 2009; Merrick *et al.*, 2012; Garvelink *et al.*, 2013) or brochures/booklets (Devin Peate *et al.*, 2011; Murphy *et al.*, 2012; Peate *et al.*, 2012; Tam *et al.*, 2016).

Patients, parents, partners and HCPs have reported high levels of usefulness or satisfaction with the material (Nagel and Neal, 2008; Peate *et al.*, 2011; Tam *et al.*, 2016) and found that decision aids were clear and understandable (Garvelink *et al.*, 2013) and that use resulted in less FP decisional conflict (Huyghe *et al.*, 2009; Peate *et al.*, 2012). In a non-randomized trial, patients aged 18–40 years who received a decision aid also showed trends towards having higher knowledge and lower regret at 12 months and being more likely to discuss FP with their oncologist (98 vs 93% who did not receive a decision aid) and to be referred to a fertility specialist (62 vs 56% of those without decision aids), but the perceived differences did not reach statistical significance (Peate *et al.*, 2012).

Patients wanted information to take to a fertility consultation (Hershberger *et al.*, 2013), preferred to receive both written and verbal information (Tam *et al.*, 2016) and desired information personalized to their specific situation. The information patients suggested should be included in a decision aid, and which would be useful to the decision-making process, concerned medical procedures, risks, benefits, success rates and costs (Hershberger *et al.*, 2013). Gardino *et al.* (2010) demonstrated the importance of counselling at several points in the decision-making process and by several different care providers.

Despite this, patients, parents and healthcare providers held concerns about the content and readability, and parents felt there was too

much medical terminology and too much information in general (Murphy *et al.*, 2012). Some patients found the information upsetting (Peate *et al.*, 2011). An assessment of internet resources about sperm banking showed the reading age of all material to be 'considerable', while the topics presented and their quality varied (Merrick *et al.*, 2012).

## Domain 3: provision of care, including age-appropriate care

The review revealed six themes on provision of care: age-appropriate care, what patients want from their care, who should be involved in consultations, clinician comfort and scope of practice, quality of verbal and written information and institutional factors. No papers discussed the best methods of delivery or digital platforms.

There were 23 papers which discussed age-appropriate care (Table II, section 3a). A study of adolescent young adult (AYA) patients showed high ratings of importance for information on treatment effects on fertility risk, FP and other parenting options (Gupta *et al.*, 2013). Only one centre in a study of 15 had an adolescent-specific brochure (Chong *et al.*, 2010) despite AYA patients (12–17 years) being eager to receive information about their fertility (Stinson *et al.*, 2015) and wanting detailed, verbal and written information on options, risks, benefits, side effects and success rates of FP (Wilkes *et al.*, 2010; Hershberger *et al.*, 2013; Bastings *et al.*, 2014a; Richter *et al.*, 2016), as well as printed information on specific fertility clinics and financial resources (Tam *et al.*, 2016).

Successful paediatric programs that feature multi-disciplinary teams and streamlined processes for delivery of care (Johnson and Kroon, 2013; Blough *et al.*, 2014) have been developed. The proportion of children for whom a FP discussion occurs is unclear; however, one study reported that 63% of oncologists routinely discussed FP with parents of pre-pubertal male patients (Rabah *et al.*, 2010). It has been recommended that children should be involved in fertility discussions, from 7 years of age (Wyns *et al.*, 2015) and this requires having HCPs with expertise in caring for patients of all ages and good support systems.

There were 21 papers discussing patient preferences concerning provision of care (Table II, section 3b). Survivors have suggested that information should be tailored to the patient's age (Corney and Swinglehurst, 2014) and particular life stage, relationships and fears (Wilkes *et al.*, 2010) and personal story (Murphy *et al.*, 2014). It is important that patients feel respected and listened to (Kirkman *et al.*, 2013). Adult patients wanted information about different parenthood options and assisted reproductive technology (Corney and Swinglehurst, 2014; Richter *et al.*, 2016). Young patients wanted more age-appropriate content and a lower reading level or felt they had been given too much information (Murphy *et al.*, 2012; Fuchs *et al.*, 2016). Adolescent male patients felt less stressed when staff were informal, friendly and not embarrassed, and when they spoke clearly and directly to them (Crawshaw *et al.*, 2008). While it may not be practicable to prepare different information for each different patient group, it has been suggested that basic facts could be included along with information about further resources and contacts (Lee *et al.*, 2011a). In one study 43–62% of female patients reported unmet information needs across a variety of FP topics (Benedict *et al.*, 2016).

In addition, males have been found to receive information about the impact of treatment on fertility and on FP options more often

than females (Anderson et al., 2008; Mancini et al., 2008; Armuand et al., 2012, 2015; Barbour et al., 2013). Of females, those with no children have been more likely to receive fertility information (Goldfarb et al., 2016). Receiving this information gives hope and can improve quality of life (Letourneau et al., 2012; Goldfarb et al., 2016).

There were 14 papers discussing the types of HCPs who should be involved in oncofertility consultations (Table II, section 3c) and 18 papers discussing comfort and scope of practice of HCPs (Table II, section 3d). Clinicians have reported conflicting information about the levels of comfort with FP discussions; low levels of discomfort with discussions about infertility and FP for paediatric and adolescent patients are reported (Vadaparampil et al., 2008b; Fuchs et al., 2016), although clinicians can find these consultations difficult, especially if they are used to directing the discussion through parents rather than communicating directly with young patients (Vadaparampil et al., 2008b). Two studies reported a preference amongst clinicians treating AYA patients to discuss provision of care without the parents being present (Bashore, 2007; de Vries et al., 2009). Private discussions have not always been possible to provide but have been proposed as a means of reducing embarrassment and helping the patient to feel more comfortable in asking questions (Bashore, 2007). Some parents wished to have control over the content of FP discussions in order to protect their child (de Vries et al., 2009) and some felt that fertility information put their child under strain (Stinson et al., 2015). In a study of paediatric endocrinologists in Japan, 13% said the explanation of FP was only given to guardians and older adolescents (Miyoshi et al., 2016). No cultural differences in the expectations of clinicians or patients were noted.

Clinicians have also reported negative feelings about provision of FP care, including feeling unprepared (Nagel and Neal, 2008), being embarrassed (Quinn et al., 2009a), lacking confidence (Peddie et al., 2012) and feeling uncomfortable (Quinn et al., 2009b). In one study, 43% of oncologists considered communication about FP to be difficult and 25% considered it a burden (Buske et al., 2016), and in another, oncologists felt that their explanations to patients about fertility were not sufficient (Abe et al., 2016). Clinicians felt that conversations with younger patients were awkward because of parental presence (Quinn et al., 2009a) and it was not always possible to maintain privacy (Bashore, 2007).

The papers that explored patients' perspectives identified that these consultations can make AYA patients feel anxious or embarrassed (Wyns et al., 2015) and survivors have reported that clinicians can seem uncomfortable or dismissive (Chapple et al., 2007; Gorman et al., 2012). When male survivors were asked their preferences, 56% would have liked their parent to be present, with the remaining 44% preferring their parent not to be present during the initial conversation about FP (Ginsberg et al., 2008). Patients with partners reported that they would like their partner to be present for FP discussions (Richter et al., 2016). A study examining views on written information found that young male patients would rather read the brochure alone, while females would rather read it with a parent (Murphy et al., 2014).

There were 15 papers discussed institutional issues associated with the provision of oncofertility MOC (Table II, section 3f). The majority of centres do not have a policy on provision of FP information. In a US study, only four out of 30 centres did (13%) (Clayman et al.,

2013) and in another, 75% of clinicians felt guidelines were needed for their institution (Vadaparampil et al., 2008a).

#### Domain 4: referral pathways between cancer and FP services

The review identified three themes on referral pathways: rates of referral, processes for referral and factors affecting referral.

There were 30 papers which investigated rates of referral (Table II, section 4a). Clinician referral rates to fertility specialists varied substantially: 15% 'routinely' referred (Forman et al., 2009), 20% referred (Rabah et al., 2010), 29% 'routinely' referred (Mahajan et al., 2016), 38% 'actually' referred (Abe et al., 2016), 46% 'often' referred (Overbeek et al., 2014), 47% 'routinely' referred (Quinn et al., 2009c), 54% 'regularly/always' referred (Louwé et al., 2018) and 86% did not refer females at all (Rabah et al., 2012). However, FP referral rates have been shown to increase over time (Dearing et al., 2014; Sigismondi et al., 2015; Ben-Aharon et al., 2016), and this may reflect clinical practice or uptake of FP. For example, a study of male patients found that only 56% of those given the opportunity to bank sperm actually did so (Pacey et al., 2013).

Oncologists report higher referral rates to fertility specialists for adult male patients compared with female patients (Arafa and Rabah, 2011; Collins et al., 2011; Yee et al., 2012c) and paediatric centres have higher rates for boys rather than for girls (Anderson et al., 2008) but only 36% of oncologists felt that pre-pubertal patients should be referred (Köhler et al., 2011). Uptake of sperm banking was found to be high when oncologists arranged the referral process in the same way as they arranged blood tests and scans (Eiser et al., 2011).

There were 11 papers which reviewed the process for referral, showing that oncofertility referral pathways (Table II section 4b) are clearly lacking. In a study of 30 cancer centres, 26% had a referral program (Clayman et al., 2013), while in another study of 28 centres, only 18% had a referral pathway (Warner et al., 2016). Of 306 clinicians in one study, 62% were aware of an established referral pathway to a local fertility unit (King et al., 2012). In another, 30% did not know where to refer male patients (Rabah et al., 2010). A paper which examined referral sources showed that referrals are most often from academic centres (64%), followed by oncologists (28%) and patients (6%) (Lee et al., 2011b).

There were 36 papers examining different factors which affect referral pathways (Table II, section 4c). Referrals are increased with collaboration between cancer and fertility specialists (Dyer and Quinn, 2016), when FP is seen as just another part of the treatment process (Eiser et al., 2011), and by having an established referral pathway including IT system prompts and referral forms, and sometimes a patient navigator (care navigator) to assist with referrals (Ogle et al., 2008; Reinecke et al., 2012; Johnson and Kroon, 2013). Referral rates have been shown to increase over time in paediatric patients (Ben-Aharon et al., 2016) and in males (Shnorhavorian et al., 2012) and females (Srikanthan et al., 2016). Patients are more likely to be referred when they have a decision aid (Peate et al., 2012) or received other additional information about FP, such as risks and options (Kelvin et al., 2016).

One paper found referrals were more likely if the patient initiated the discussion about FP (Campbell et al., 2016). Between two-thirds to as many as 97% of oncologists have stated that they refer patients

who expressed concern about their future fertility (Adams *et al.*, 2013; Buske *et al.*, 2016). A study of female patients found that 52% of those referred had requested their referral (Kim *et al.*, 2013).

Certain healthcare provider characteristics improved referral pathways: having a female clinician (Quinn *et al.*, 2009c; Shimizu *et al.*, 2013; Bastings *et al.*, 2014b), clinicians having favourable attitudes towards FP (Quinn *et al.*, 2009a; Shimizu *et al.*, 2013), clinicians with more knowledge (Quinn *et al.*, 2009a; Shimizu *et al.*, 2013) and clinicians who had these discussions more frequently (Forman *et al.*, 2009; Louwé *et al.*, 2018).

Certain patient characteristics were associated with high rates of discussion and referral for FP (Table II, section 4c): male patients (Arafa and Rabah, 2011; Yee *et al.*, 2012c), specific types of cancer (more common in breast cancer or lymphoma and less common in gynaecologic, haematologic and gastrointestinal cancers) (Goodman *et al.*, 2012; Bastings *et al.*, 2014a), age (generally patients 20–34 years referred most) (Goodman *et al.*, 2012; Bastings *et al.*, 2014a), having no children (Goodman *et al.*, 2012) and showing high decisional conflict (Mersereau *et al.*, 2013).

Low rates of FP discussion and referral were associated with institutional factors such as difficulties finding facilities or specialists to refer patients to (Goodwin *et al.*, 2007; Yee *et al.*, 2012c; Dyer and Quinn, 2016; Mahajan *et al.*, 2016), lack of FP information and problems integrating FP into routine cancer care (Preaubert *et al.*, 2016).

Having access to fertility care navigation by HCPs (nurses, counsellors, psychologists or fertility navigators) plays an important role in coordination and referral of oncofertility care (Gilbert *et al.*, 2010; Scott-Trainer, 2010). The use of checklists or prompts in electronic medical records, chemotherapy prescribing systems or paper files has also improved referral practices (Reinecke *et al.*, 2012; Sheth *et al.*, 2012; Salsman *et al.*, 2016). Two studies found distance to the specialist had no impact on whether patients were referred (Lee *et al.*, 2011b; Goodman *et al.*, 2012).

## Domain 5: documentation of oncofertility discussions, decisions and procedures

The review revealed two themes on documentation: extent of documentation and factors affecting documentation.

Ten studies covered the extent of documentation (Table II, sections 5a and 5b). One study found that 58% of patients had a documented discussion about reproductive health at the first consultation (Wang *et al.*, 2016). Low levels of oncofertility documentation were seen amongst both haematologists (38%) and oncologists (26%) even when processes were in place within their institution for recording the discussion of fertility issues with patients (Gilbert *et al.*, 2010). In studies examining documentation in medical records, the notes were more likely to be those of the cancer clinician than the nurse or patient navigator. Documentation was better in patients with early stage cancer (Salsman *et al.*, 2016), in patients receiving radiation treatment (Kumar *et al.*, 2012), and in patients with some tumour groups (e.g. 75% of breast cancer patients had documentation in one study) (Srikanthan *et al.*, 2016).

Fertility discussions were less likely to be documented for older patients (Kumar *et al.*, 2012; Quinn *et al.*, 2014; Banerjee and Tsiapali, 2016; Salsman *et al.*, 2016) or for young patients, with only

26% of male and female AYA patient records documenting a discussion about the risk of infertility, 24% documenting a discussion of FP options, and 13% documenting a referral to a fertility specialist (Quinn *et al.*, 2014). Documentation was equally low for patients who have already had children (Quinn *et al.*, 2014; Banerjee and Tsiapali, 2016) and for patients with no children (Quinn *et al.*, 2014).

The level of documentation has increased over time with the development of oncofertility programs and use of IT strategies to improve referral pathways (Sheth *et al.*, 2012; Salsman *et al.*, 2016), but on the whole, documentation levels are still low. Findings regarding likelihood of having a documented discussion and patient gender have been mixed, with one study showing female patients being more likely (Salsman *et al.*, 2016), one study showing male patients being more likely (Quinn *et al.*, 2014), and another showing no difference (Kumar *et al.*, 2012).

Seven papers reviewed factors which improved documentation (Table II, section 5c). Centres with oncofertility programs (Reinecke *et al.*, 2012; Sheth *et al.*, 2012) have improved documentation across ages and genders (Blough *et al.*, 2014). However, one paper found that implementation of a FP program was associated with higher fertility discussion and FP referrals, but not better documentation (Srikanthan *et al.*, 2016). Access to care navigators coordinating care also resulted in increased documentation (Gilbert *et al.*, 2010).

## Domain 6: training of cancer and fertility HCPs to deliver oncofertility care

The review revealed five themes on training: level of knowledge and training in cancer clinicians, level of knowledge and training in non-cancer clinicians, level of training in nurses and allied health professionals, types of education and clinician comfort and scope of practice. It was noted that many specific training programs would not appear in the peer-reviewed literature if they were not evaluated.

There were 30 papers addressing cancer clinician knowledge and training (Table II, section 6a) and 20 papers addressing knowledge and training in non-cancer clinicians (Table II, section 6b). Almost half of oncologists in one study were not aware of any FP options for female patients and a study of oncologists showed that the majority had received little or no training in FP which affected their ability to discuss the topic with patients (Quinn *et al.*, 2009b). Similarly, in a large US survey of paediatric oncologists and nurses, 93% of respondents reported that they had received no training on FP (Fuchs *et al.*, 2016). A national study in Canada, of 25 fertility clinics, found that only 13 (52%) held training on female FP (Yee *et al.*, 2012b).

Related to training is the clinicians' comfort level. Patients have perceived that clinicians were uncomfortable or dismissive (Gorman *et al.*, 2012). However, in some studies, high levels of comfort have been reported by clinicians (Gilbert *et al.*, 2010; Fuchs *et al.*, 2016). This may relate to how regularly clinicians have these discussions as comfort level is viewed by clinicians as an important facilitator (Besharati *et al.*, 2016).

Knowledge gaps are also reported in nurses and allied health professionals (Ussher *et al.*, 2016) (Table II, section 6c) and in most cases, it is the cancer clinicians raising the issue of FP with the patient.

Eight papers reviewed educational programs (Table II, section 6d). HCPs want more educational materials (Nagel and Neal, 2008; Gilbert et al., 2010; Fuchs et al., 2016) and training on FP techniques and referral options (Quinn et al., 2007, 2009b; King et al., 2008a; Gilbert et al., 2010; Arafa and Rabah, 2011; Köhler et al., 2011; Duffy et al., 2012; Peddie et al., 2012; Rabah et al., 2012; Adams et al., 2013; Overbeek et al., 2014; Campbell et al., 2016; Fuchs et al., 2016; Louwé et al., 2018; Takeuchi et al., 2017).

An important component of successful FP programs is the education of multi-disciplinary HCPs to provide oncofertility care (Ogle et al., 2008; Nagel et al., 2009; Quinn et al., 2011; Reinecke et al., 2012; Sheth et al., 2012; Shnorhavorian et al., 2012; Johnson and Kroon, 2013).

Oncofertility communication skills training greatly improves the knowledge and confidence of clinicians with FP discussions (Vadapampil et al., 2016), and online oncofertility training programs for nurses have been developed covering fertility risks, FP options and sexual function (Vadapampil et al., 2016), leading to improved knowledge and change in practice locally (Vadapampil et al., 2013, 2016). A small pilot study demonstrated the benefits in allied health professionals undertaking the same training (Quinn et al., 2016).

### Domain 7: medical supportive care during FP

A review of the literature did not locate any data about requirements or differences in medical supportive care for cancer patients undergoing FP despite these patients being more likely to have complex medical needs. These may include pancytopenia; increased risk of bleeding or infections; mediastinal, abdominal and pelvic masses; or medical problems which make an anaesthetic for oncofertility care more complex or contraindicated.

### Domain 8: reproductive care in survivorship

The review revealed four themes on reproductive survivorship care: the patient's fertility status, follow-up fertility investigations, and information needs and emotional needs in survivors.

Ten papers highlighted a lack of understanding that survivors have about their fertility status (Eiser et al., 2011; Wright et al., 2014), lack of importance placed on follow-up (Eiser et al., 2011), limited fertility follow up (Pacey et al., 2012; Kim et al., 2016) (Kim et al., 2016) and a lack of fertility-related support in survivorship (Perz et al., 2014). Only four studies reviewed fertility investigations following cancer treatment (Table II, section 7b) with very low numbers of clinicians (28%) always/often checking patients' fertility parameters (hormonal tests or sperm analysis) in survivorship and the other 72% rarely or never checking or informing their patients (Preaubert et al., 2016).

Four papers looked directly at survivorship information needs (Table II, section 7c) and this overlapped with the themes on communication and provisions of care. Patients want to have individual information about their fertility after cancer treatment (Perz et al., 2014; Armuand et al., 2015). Many survivors had incorrect beliefs about the extent of their fertility problems, which did not reflect the information received (Crawshaw and Sloper, 2010), or reported frustration with the quality of care and lack of reproductive continuity of care (Gorman et al., 2012) or the lack of pregnancy planning and support (Gorman et al., 2011). This can lead to more anxiety, especially for patients who have normal fertility parameters when finally tested.

On the other hand, some female survivors were focused on survival and did not wish to take risks with their health by attempting to conceive, particularly those who already had children (Lee et al., 2011a).

### Domain 9: fertility-related psychosocial support

The review revealed four themes on psychological support. There were 14 papers which discussed the negative emotions patients faced, 14 papers which explored fertility-related psychological support, five papers which focussed on the role of professional/family support, and six papers which examined the types of psychological support patients sought (Table II, sections 8a–d).

A patient's fertility potential has been shown to have an impact on their identity, well-being and life plans (Crawshaw et al., 2009). The majority of patients felt overwhelmed by FP information and options (Kim et al., 2016). The threat of temporary or permanent infertility has been shown to be associated with psychological distress, such as depression and anxiety, in both males and females (Lawson et al., 2015; Ellis et al., 2016) and this has an effect on patients' self-esteem, confidence, quality of life and relationships. Loneliness was reported by both male and female patients facing fertility loss, even those with good support (Goossens et al., 2015). One study found that 50% of young cancer patients (18–45 years) who wished to have children in the future required some psychological care with regard to fertility and parenthood (Geue et al., 2014).

Patients experience negative emotions when they lack fertility information and support (Perz et al., 2014). Female patients wanted more support (Mancini et al., 2008; Gorman et al., 2012; Penrose et al., 2012) and more opportunities to ask questions and process their feelings (Crawshaw et al., 2009). They were also more likely to be dissatisfied with information and have higher levels of distress (Mancini et al., 2008; Crawshaw et al., 2009; Yeomanson et al., 2013; Armuand et al., 2015). Several studies found that the lack of time to make decisions was associated with negative experiences of FP or increased stress (Yee et al., 2012a; Bastings et al., 2014a) and a feeling of being left with unanswered questions (Corney and Swinglehurst, 2014). Females tend to experience more distress than males during decision-making due to the lack of services for FP (Crawshaw et al., 2009). With appropriate support, patients experience less distress, fear and decision regret, and feel more positive about the future (Hohmann et al., 2011; Letourneau et al., 2012; Peate et al., 2012; Bastings et al., 2014a; Benedict et al., 2015; Lawson et al., 2015).

In a qualitative study of fertility-related experiences of female cancer survivors, participants felt that emotional support was important at all stages of treatment and recovery (Corney and Swinglehurst, 2014), not just at time of diagnosis, which is the point of focus for most studies. Counselling was found to be useful at many time points due to the complexity of FP decision-making (Gardino et al., 2010).

Cancer survivors have reported that they found it helpful to discuss their oncofertility choices with spouses, friends and family who could provide emotional support and assistance with decision-making (Kim et al., 2013). Female patients felt that, of the range of oncofertility HCPs, the most useful were oncologists and gynaecologists (Tschudin et al., 2010). The presence of a psychologist could also be beneficial and help to improve communication between doctor and

patient and reduce anxiety (Razzano *et al.*, 2014), while patients have also stated that nurses are helpful with discussing options and making decisions (Kelvin *et al.*, 2016). Younger cancer survivors, aged 16–30 years, reported that both professional and parental support assisted them to cope with receiving fertility-related information at diagnosis (Crawshaw *et al.*, 2009).

Our review did not find any literature discussing the benefits of support groups or talking with other patients in similar situations. However, one research paper did report on the benefits of fertility discussions from data collected at a support group conference for cancer patients aged 14 years and over (Yeomanson *et al.*, 2013).

### Domain 10: ethical practice of oncofertility care

The review had limited literature on the ethical practice of oncofertility care, as reviews and book chapters on ethical dilemmas and legal parameters of FP and assisted reproduction technology did not fit within the PROSPERO inclusion criteria.

### Summary of established MOC

Amongst the papers included in this review, eight described an oncofertility MOC (Table III) but they did not present criteria for their measurement of success in terms of implementation or patient satisfaction with these models. Three of the models were tailored specifically to AYA patients (Ogle *et al.*, 2008; Nagel *et al.*, 2009; Shnorhavorian *et al.*, 2012; Johnson and Kroon, 2013). All of the models included access to patient educational materials, collaborations or partnerships and standard processes for referral. Five of the models had implemented electronic notifications within their IT systems to remind clinics of the need to discuss FP. Psychological counselling was not a common feature of these MOC.

### Discussion

Despite a number of international recommendations and a consumer charter for FP care (Anazodo *et al.*, 2016), overall, this large

**Table III** Established examples of oncofertility models of care and their key components.

Model	Patient Sex	Pt Age	Pt educational material <sup>A</sup>	Healthcare Professional Education <sup>B</sup>	Referral form/ Established referral process <sup>C</sup>	Patient navigator <sup>D</sup>	Collaboration/ Partnerships <sup>E</sup>	Electronic notification of eligible patients <sup>F</sup>	Psychological counselling <sup>G</sup>
1. Colorado Oncofertility Program (Blough <i>et al.</i> , 2014)	M/ F	All	*	–	*	X	*	*	*
2. Dana-Farber Cancer Institute (Campos <i>et al.</i> 2012)	M/ F	Adult	*	X	*	*	*	*	*
3. Seattle Children’s Hospital (Shnorhavorian <i>et al.</i> , 2012; Johnson and Kroon, 2013)	M	AYA	*	*	*	*	*	X	–
4. McMaster Children’s Hospital (Nagel <i>et al.</i> , 2009)	M	AYA	*	*	*	X	*	X	–
5. Children’s Hospital of Philadelphia (Ogle <i>et al.</i> , 2008)	M	AYA	*	*	*	Some	*	X	X
6. H. Lee Moffit Cancer Centre (Quinn <i>et al.</i> , 2011)	M/ F	Adult	*	*	*	X	*	*	–
7. Fertile Hope Centres of Excellence Program (Reinecke <i>et al.</i> , 2012) <sup>h</sup>	M/ F	All	*	*	*	some	*	*	–
8. Northwestern University (Oncofertility Consortium) (Sheth <i>et al.</i> , 2012; Vu <i>et al.</i> 2017)	M/ F	All	*	*	*	*	*	*	–

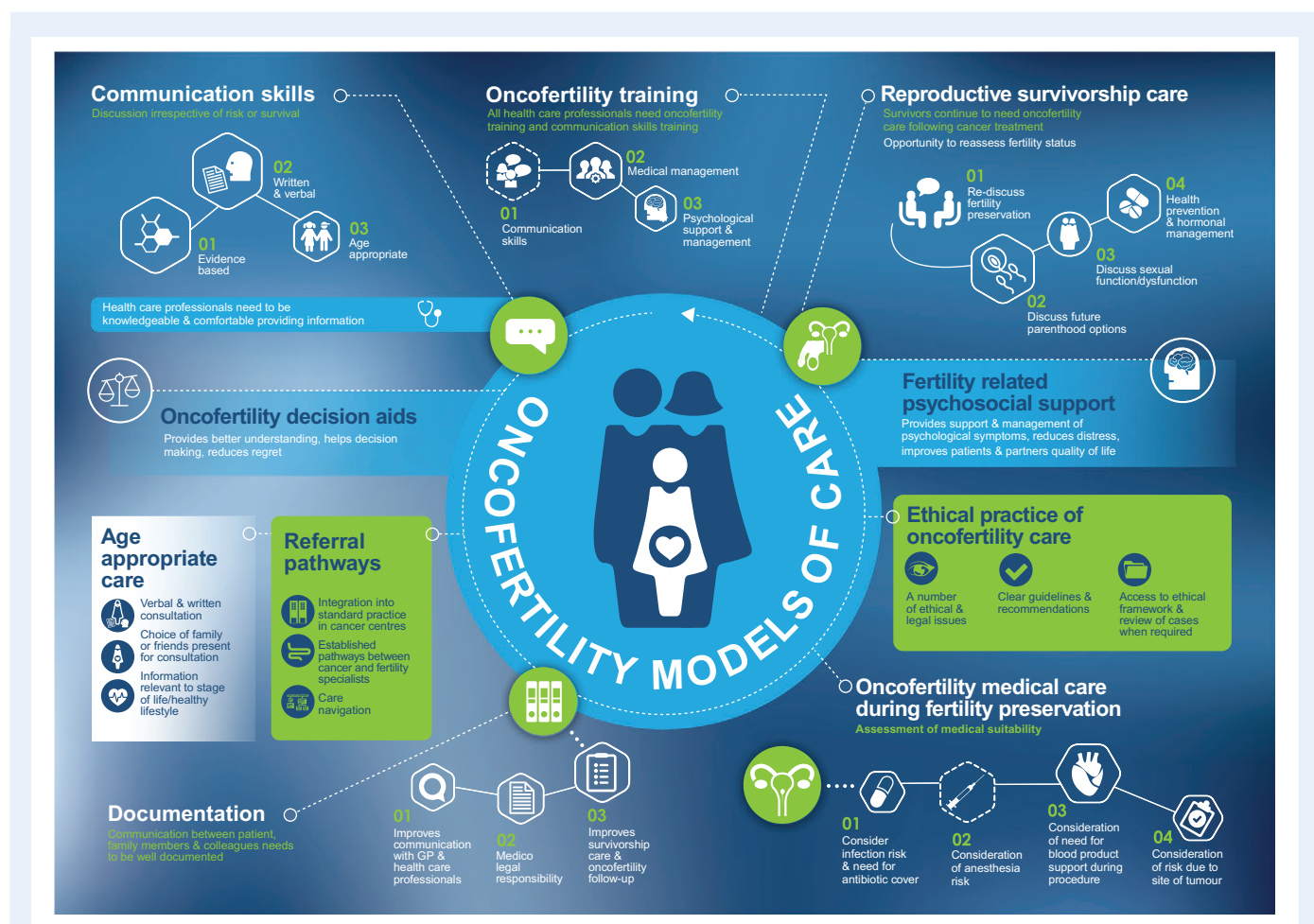
<sup>h</sup>Program has characteristic; X: Program does not have characteristic; –: Not clear whether program has characteristic.  
 A: Patient educational materials: brochures or audio visual material to provide information to the patient/parents. B: Clinician education: staff information or training sessions on FP, grand rounds. C: Referral form/established process: forms/paperwork for referral, guidelines or documented process for referral. D: Patient navigator role (sometimes referred to as patient advocate): nurse or social worker who is readily available, can provide detailed education on FP (options, location of services, costs), answer questions, assist patient to make appointments or facilitate contact with fertility specialists (Johnson and Kroon, 2013; Scott-Trainer, 2010). E: Collaboration/partnerships: established internal team and/or external contacts (e.g. reproductive specialists, sperm banking clinics). F: Electronic notification of eligible patients: an automatic email or other system notification set up to remind the clinician to speak to the patient about FP. G: Psychological counselling: a psychologist available to provide emotional counselling/support for the patient.

systematic scoping review has found that internationally the uptake and utilization of FP remains unacceptably low and the quality of FP care is variable, especially for younger patients of reproductive age. This review aimed to provide an overview of current strategies for oncofertility MOC and the strategies required to ensure that patients not only get access to services but that these services meet the needs of patients, partners and parents in a safe and timely manner. The review identifies a number of strategies within each domain with some of these overlapping across domains. Fig. 2 summarizes the important components of oncofertility MOC.

Patients of different ages and genders and their family members were found to have similar expectations about provisions of oncofertility care. They expect to be informed about fertility risk and FP options and they want complete, tailored information in order to make a reproductive decision in a timely manner. Understandably, patients do not want to find out about the reproductive risk of cancer treatment after treatment has started or to have to advocate for this information themselves (Vvyns et al., 2015). The emergence and subsequent growth in the need for patient and family-centred care will continue to drive policy and practice changes across clinical areas including FP care (Baker, 2001). Forward looking and robust strategies that ensure sustained collaborations among care and support providers are needed to ensure that FP genuinely meets the

expectations of those impacted and does not become fragmented or lost in the responsibility gap between primary and acute, and public and private care systems. Agreed health system-wide international guidelines will support acceptable practice and commitment. Such guidelines will also create a worldwide clinical and academic network to monitor and advance the field.

An essential component of a successful oncofertility service is a coordinated referral pathway with a clear referral process that highlights the proposed treatment and risks of gonadotoxicity. These features provide an increase in routine and timely referrals. Many cancer centres are not fortunate to have access to FP services on the same campus. This adds to the complexity of care for patients, especially when they are unwell, in rural centres which require a long transfer, or have a number of staging and toxicity investigations which also need to be organized prior to starting treatment. IT system alerts may help to improve FP discussions and their documentation, and ultimately, the number of patients who will have the opportunity to preserve fertility. Tele-health platforms can also help provide care to patients who are in rural and remote centres as well as those patients who are too unwell to be transferred for a fertility consultation. Advancing scientific research on human fertility and reproductive life-span may support more widespread availability of reproductive services (Anderson and Telfer, 2018).



**Figure 2** Successful components of an oncofertility model of care.

Economics was a topic that was mentioned across a range of papers, mostly as an issue or barrier to FP. Papers did not generally discuss finance or health insurance coverage, however, affordability is an important factor. As FP is not universally covered by hospitals or insurance companies, finances pose a significant barrier internationally (Rashedi *et al.*, 2017). The World Health Organization provides advice and techniques to study and realize equity in healthcare in different contexts (Niëns, 2014) and more research is needed to ensure that countries have equitable oncofertility practices.

Young patients and their parents believe that FP services should be age-appropriate and accessible (Stinson *et al.*, 2015) and older patients feel that the service should cater for their differing needs. Provision of oncofertility care includes the availability and access to care that meets individual patients' needs irrespective of age, gender and other sociodemographic features. This includes provision of an age-appropriate consultation space, appropriate expertise of HCPs, written and verbal information, and age-appropriate medical and psychological support. Oncofertility care in children is complex and requires a family-centred approach with the development of specialized pathways which may require consideration for the component of care delivered in adult centres. As oncofertility care in pre-pubertal patients is experimental research, governance should be provided and care should be delivered within an agreed ethical framework.

Both cancer and fertility services have experienced nurses and allied HCPs who have an essential role in providing patient care. Care navigators ensure that patients have information to make informed choices and actively participate in care. They provide a vital communication link among clinicians and other care providers, address questions, concerns and clinical issues, and advocate for the patient through their cancer journey into survivorship. Although our review highlighted the benefits and success of oncofertility care navigation, it also showed that HCPs often felt they lacked the skill set and training and were unsure of their role. It is important that all clinical staff, and possibly also non-clinical staff, who are involved in the care of cancer patients are provided with oncofertility training which includes developing oncofertility communication skills training. Clinicians who are more knowledgeable about FP are more likely to discuss FP with their patients and refer patients (Louwé *et al.*, 2018).

A recent study identified a negative trend for care coordination across health service types due to growing complexity and fragmentation of the healthcare system. It identified that a shared understanding of the roles and contributions of different health professional groups, organizations and systems is required to improve the situation. Training in system-literacy was proposed as a potential solution through a specialized care coordination workforce (Naccarella *et al.*, 2016). Monitoring, linking into and leveraging off general health service innovations may be a useful approach to ensure that FP is properly embedded in care delivery.

Internationally, there is wide variation in the FP documentation amongst individual cancer clinicians and services (Skaczkowski *et al.*, 2018). This includes variation in both the documentation of an FP consultation and discussion about FP options provided to patients, partners and parents and variation in documentation of the oncofertility care provided. Documentation about complications and plans for follow-up care are also poor. The documentation of consultation and procedures is essential for communication with patients and HCPs,

provides a record for reproductive follow up and survivorship care, and reduces potential litigation about infertility after cancer treatment.

While papers in this review covered seventeen countries only two papers were available from middle income countries (Iran and India) (Ghorbani *et al.*, 2011; Mahajan *et al.*, 2016). These papers showed similar findings, with oncologists and gynaecologists being familiar with international oncofertility guidelines (67–81%), comparable with doctors in developing countries. The barriers and challenges to oncofertility care for services in middle income countries were also similar to those in high-income countries (Karaöz *et al.*, 2010; Peate *et al.*, 2012) with no service availability, high costs of FP and fears of delaying treatment being barriers in both countries. However, fewer clinicians (40–42%) discussed the gonadotoxic risk and options of FP than the average shown in the studies from high-income countries (0–92%). It must also be noted that limitations in oncofertility care existed in high-income countries and there was wide variation in practice worldwide based on the same barriers to care discussed in this review.

It is clear that patients want to be supported during and after cancer treatment. Fertility-related support and care provides an opportunity to improve knowledge and patient satisfaction, and provides hope (Logan *et al.*, 2018). The support process should be as streamlined as possible and should include both practical, financial and psychological support. Psychosocial support for cancer patients is important throughout the cancer journey and this includes the FP decision-making and procedure period as well as the survivorship period. Advocating for oncofertility care to be covered by public health and insurance systems will reduce the inequity that cancer patients face.

Overall, decision aids were found to be highly useful and lead to more discussions about FP and less decisional regret, and therefore the use of these tools should be encouraged. Oncofertility decision support systems aids have been developed for use in paediatric and adolescent patients (Hand *et al.*, 2018) and they are likely to be as useful if they can overcome the challenge of differing reproductive knowledge and health literacy.

Cancer patients are often left with little information or insight into their reproductive potential which causes uncertainty and worry (Chapple *et al.*, 2007). Once cancer treatment has finished, there is an opportunity for clinicians to re-summarize reproductive health information that provided during the treatment phase and give recommendations for reproductive health after treatment. This is especially important for those patients who did not have FP at diagnosis, for those who were too young or too unwell to participate in the conversations about FP, and those with a high chance of having reproductive complications, including infertility.

### Areas where no relevant literature was found

Despite the absence of robust data on FP supportive care, it is important to think about patient suitability and the medical supportive care needs of patients prior to recommending FP (Cakmak *et al.*, 2013; Shapira *et al.*, 2015). Although this review did not identify studies looking at FP supportive care in cancer patients, clinicians need to be aware that the risk of patients undergoing FP depends on the site

and size of the tumour, the side effects of ovarian stimulation on the tumour or patients' symptoms, the risk of bleeding and infection, and any anaesthetic risks.

There is a distinction between general and specific ethical aspects of oncofertility care, another domain for which no relevant studies were found. Basic ethical principles apply to both care and the necessary prior step of information for all patients at risk of loss or diminished reproductive ability when facing a cancer diagnosis and its treatment. Such principles include: the respect of patients' autonomy with specific aspects concerning information and consent of a child; the balance of beneficence and maleficence relating mostly to the safety of the cryopreservation technique offered and the possible danger of postponing the cancer treatment as well as the fact that some techniques may still be considered research (Patrizio et al., 2005); and (the societal aspect of) justice and equity which includes access to treatment and funding by the state or insurance companies. More specifically, the justice and equity aspects necessitate that interventions to preserve the ability to have a child should be funded publicly. This funding should be considered in a structured way including efficiency, safety and equity to avoid unjustified discrimination. Practitioners have a moral obligation towards their patients and the healthcare system to reduce the cost of treatment as far as reasonably possible (Pennings et al., 2008). Other more specific ethical aspects include the timely renewal of consent during the storage period, posthumous treatment, donation of stored gametes or tissues to others or for research, and the importance of interdisciplinary consulting (Eshre Task Force on Ethics Law, 2004).

In addition, none of the included papers looked at the impact of support groups which may provide practical and psychological benefits to patients, parents and partners.

## Strengths and limitations

The academic literature is a useful source of information on change in an emerging key domain like FP. Comparing the literature between the first and second time periods that this review covers, i.e. 2007–2011 and 2012–2016, shows that promising advancements in FP are being made. The first is the considerable growth in research in this field (102 papers in 2012–2016 compared with 45 in 2007–2011), representing a growing number of countries (17 vs 13). Furthermore, there has been an increase in the proportion of quantitative studies in the 2012–2016 period along with the necessary increase in the number of study participants. It is fair to suggest that the ability to conduct research on larger numbers of patients implies that an increasing proportion of patients are now involved in FP. Secondly and encouragingly, the review found an increase in the use of decision aids in clinical practice and an increase in health professionals receiving oncofertility education and training. The range of HCPs, including social workers, now involved in FP discussions also appears to be increasing. This may signify growing consideration for patient and family needs in this highly sensitive area. Finally, HCP education and training in this field has become more widespread and papers on specific training programs have recently been published (Quinn et al., 2016; Vadaparampil et al., 2016). This training has been shown to improve both the knowledge and confidence of HCPs (Vadaparampil et al., 2016) which, in turn, improves communication. There has been a 5-fold increase in the number of studies emphasizing the importance of documentation of FP

in the latter half of the review time. Coverage and improvements in rates of oncofertility documentation have been described in the last 5 years (Sheth et al., 2012; Vu et al., 2017).

This review is strengthened by the strong focus on consumer engagement which preceded the review. Identifying strategies that care recipients and providers perceive to be important for effective oncofertility medical and psychological care to inform the search strategy was considered the best approach to identifying key relevant domains. It is also strengthened by the comprehensive nature of this large review linking together these domains which will help in the future implementation of oncofertility services. A diverse range of countries were included in this review so it is likely that the results represent diversity in clinical practices and available resources in caring for patients' oncofertility. The review also includes a wide range of patient (childhood cancer, AYA and older adult) perspectives and clinician (paediatric and adult cancer) perspectives from different HCPs, although the majority of feedback was from doctors. This is very important as multi-disciplinary oncofertility care is required for cancer patients, from childhood to adulthood, with many different tumour types.

A potential limitation of this research was the inclusion of only scholarly peer-reviewed papers which met the PROSPERO criteria. The grey literature would be expected to include information relevant to several of the domains, particularly with regard to specific oncofertility programs and training and ethical frameworks. The review also only included papers published in English which may result in missing some relevant papers. It is important to note that many changes have occurred during the last 10-year period and some of these initiatives may not have been published as yet. This review is limited to the papers that were identified relating to the specified domains, using MeSH terms and key words, as well as reference lists of relevant studies. The detail summarized in each of the domains is limited to the information available in the current publications and may have excluded some features of successful programs or some important strategies. Some of the domains have more relevant papers than others, which reflects the lack of current data. A large number of included studies are retrospective recollections by clinicians or patients and hence are limited in their ability to accurately determine the exact benefits and quality of each strategy. We did not exclude studies based on participant numbers so as not to lose the benefit of those studies covering qualitative interviews and research with specific groups of HCPs, though with limited data.

While the review included data from seventeen countries, only two middle income countries are included and so this review is limited in its ability to make oncofertility recommendations for low and middle income countries. However, it must be noted that: limitations in oncofertility care exist in some high-income countries; there is wide variation in practice worldwide; and the barriers identified are the same in developing and developed countries (Rashedi et al., 2017; Salama et al., 2018).

Paediatric, adolescent and adult cancer patients will report different oncofertility needs, are able to access only certain FP services dependent on pubertal status and represent a diverse range of cancer types. As such this review is limited in its ability to draw out specific differences required for the development of oncofertility MOC in different populations. Other relevant information for the development of services such as the impact of health literacy and cultural



components have not been considered in this review and need to be considered in the development of services.

## Conclusion

This review shows that there are many components of a successful model of oncofertility care and many of the strategies within these components overlap or are repeated in the referral pathway, such as clear age-appropriate communication. The findings of this review contribute to our knowledge about best practices in oncofertility MOC and form the basis for the knowledge required for the development of an oncofertility competency framework. Competencies are used by healthcare services and HCPs to ensure that they develop the knowledge, skills and processes to deliver services of a high standard, and this includes suitable MOC and referral pathways (Gonczy and Hager, 2010). Competency frameworks are based on the hypothesis that HCPs need to have the skills to turn the available knowledge into service development and reliable outcomes. The availability of oncofertility competencies would allow HCPs to define how oncofertility care should be developed in line with international guidelines and outline clearly the specific competency for each deliverable component of care. Oncofertility training and service development would be instrumental in developing and maintaining the skills and knowledge needed for oncofertility care of a high standard.

## Supplementary data

Supplementary data are available at *Human Reproduction Update* online.

## Authors' roles

A.A. is the lead author; A.A. was responsible for the study plan and design, analysis, critical discussion and drafting of this article. P.L. is the project manager; P.L. jointly reviewed and analysed all off the papers and was involved in critical discussion and drafting of the article. All of the other authors were involved in discussion about the study plan, in discussions about the results and analysis and in reviewing the drafted article.

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## Conflict of interest

None to declare.

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