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Decision on fertility preservation in cancer patients: development of information materials for healthcare professionals

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Keyword:	Chemotherapy, Fertility, Late Effects, Oncofertility, Supportive Care
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Abstract:	<p>Infertility is a potential side effect of cancer chemotherapy. As the number of AYA-aged survivors increases, future fertility becomes an important issue. However, many patients are not adequately informed and oncologists point the lack of information as a barrier to discussion. Our aim was to produce information materials, tailored to oncologists' needs to promote and support discussion on infertility risk and fertility preservation with AYA-aged patients.</p> <p>After literature review, information materials were successfully developed and are currently being distributed to healthcare professionals, in Portugal, with the collaboration of several national organizations. These information materials will contribute to shared, informed decisions regarding fertility preservation in AYA-aged patients.</p>

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For Peer Review Only/Not for Distribution

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5 **2 materials for healthcare professionals**
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34 **Running head (maximum 60 characters)**

35 Oncofertility: information for healthcare professionals

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37 **Keywords:** fertility preservation, oncofertility, information materials, decision support

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3 **50 Abstract**
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6 51 Infertility is a potential side effect of cancer chemotherapy. As the number of AYA-aged
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10 53 are not adequately informed and oncologists point the lack of information as a barrier to
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14 55 to promote and support discussion on infertility risk and fertility preservation with AYA-
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16 56 aged patients.
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20 57 After literature review, information materials were successfully developed and are
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22 58 currently being distributed to healthcare professionals, in Portugal, with the collaboration
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26 60 informed decisions regarding fertility preservation in AYA-aged patients.
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73 Introduction

74 Infertility is a recognized potential adverse effect of several cancer treatments. In
75 relation to chemotherapy, the degree of gonadal toxicity is influenced by several factors
76 such as the nature of antineoplastic agents, total dose administered and patients'
77 age.^{1,2} Additionally, the number of AYA-aged survivors is increasing, as a consequence
78 of earlier diagnosis and significant progresses in cancer treatment.^{1,3} Besides the
79 repercussions of the disease, these patients will have additional concerns related with
80 the effects on their future fertility. Several studies document that future fertility is an
81 important issue for cancer patients and survivors⁴⁻⁶ and, therefore, shared decision
82 concerning fertility preservation (FP) must take place at the time of diagnosis. In this
83 context, oncofertility, a term created in 2006 by Professor Teresa Woodruff, has
84 emerged as a multidisciplinary field with the purpose to fulfil the needs of AYA-aged
85 patients regarding their reproductive potential.⁷

86 According to the recommendations of international organizations on cancer care,
87 namely the *European Society of Medical Oncology* (ESMO)⁸ and the *American Society*
88 *of Clinical Oncology* (ASCO)⁹, healthcare providers should address infertility risks with
89 all cancer patients treated during their reproductive years. Moreover, they must be
90 prepared to discuss FP options or to refer potential patients to reproductive medicine
91 specialists. Despite the above recommendations, several international studies indicate
92 that professionals caring for cancer patients do not address these issues and a
93 considerable proportion of AYA-aged patients is not informed on the possibilities
94 regarding FP.¹⁰⁻¹³ The main reasons reported by health professionals were the lack of
95 knowledge, access to reproduction specialists and information on FP options, especially

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3 96 those remaining experimental. Patient-related factors such as bad prognosis, terminal
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5 97 disease or the need to postpone treatments were also pointed to contribute.¹¹
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8 98 In Portugal, the oncofertility area is taking its first steps. Nevertheless, a variety of
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10 99 techniques for male and female FP are available at a few specialized institutions of the
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12 100 National Healthcare System, including the *Centro para a Preservação da Fertilidade*
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14 101 (Centre for Fertility Preservation) of CHUC, EPE, in Coimbra.

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17 102 Recently, the *Sociedade Portuguesa de Medicina Reprodutiva* (Portuguese Society for
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19 103 Reproductive Medicine) endorsed the organization of the 1st and 2nd Portuguese
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21 104 Oncofertility Meetings, with the purpose of implementing an integrated national practice
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23 105 concerning FP for cancer patients. In this process, the *Centro para a Preservação da*
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25 106 *Fertilidade* (Centre for Fertility Preservation) of CHUC, EPE, in Coimbra, has been at
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27 107 the front line, actively promoting awareness of this new field and disseminating
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29 108 information regarding infertility risks and FP options, both to AYA-aged patients and
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31 109 healthcare professionals. One specific objective of this information program was the
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33 110 production of information materials for Portuguese cancer care professionals, tailored to
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35 111 the respective reported information needs, in order to promote and support discussion
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37 112 with AYA-aged patients on the topics of infertility risks and FP.
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46 114 **Methods**

47 115 Assessment of information needs

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50 116 In order to identify worldwide reported information needs, a literature search was
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52 117 conducted on Medline, through PubMed, combining the following MeSH terms:
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54 118 *Neoplasms, Antineoplastic Agents/adverse effects, Fertility/drug effects, Fertility*

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3 119 *Preservation, Sperm banks, Health Knowledge, Practice and Attitude of Health*
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6 120 *Personnel*. Quantitative studies reporting oncologists' information needs concerning
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8 121 infertility risks and FP, or barriers to FP implementation were selected and critically
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10 122 evaluated.
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15 124 Production of information
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17 125 Information contents were selected to accomplish two main objectives: 1) to alert for the
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20 126 need to discuss infertility risks with patients and to help healthcare professionals
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22 127 estimating those risks; 2) to promote knowledge on the available male and female FP
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24 128 options. The latest published evidence on infertility risks associated with cancer
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26 129 treatments was identified through literature search, namely regarding mechanisms and
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29 130 adverse effects of cancer treatments on fertility, factors associated with infertility risk
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32 131 and tools available for risk calculation. Regarding FP techniques, current evidence-
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34 132 based information on clinical indications, time requisites, success rates, risks and
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36 133 advantages/disadvantages of each FP technique was gathered, also by literature
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38 134 search. Published clinical guidelines on FP in cancer patients were also identified.

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41 135 A main booklet directed to clinicians working with cancer patients with comprehensive
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43 136 contents was prepared. This professional group presents the greatest information needs
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46 137 as they have the responsibility to initiate FP discussion with patients and referencing
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48 138 them to FP specialists. A booklet with summarized contents was also produced and
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50 139 intended to inform other healthcare professionals working in the cancer setting. This
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52 140 resumed booklet is also intended to primary care professionals, which many times make
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3 141 the first contact with AYA cancer patients, so that they can promote awareness of the
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5 142 FP subject.
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10 144 **Results**

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15 146 Information needs

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17 147 Twelve (12) published articles were selected and analyzed.¹³⁻²⁴ Data on methods and
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19 148 relevant results (reported information needs, gaps in knowledge or barriers to FP
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21 149 discussion) was collected from each individual article (Table 1).
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27 151 Information contents

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29 152 All the identified information topics were included in the main booklet, named
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31 153 “Oncofertility. Fertility Preservation in Cancer Patients”. Information contents were
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33 154 organized in 4 main sections:
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36 155 **Section 1. Why the need for fertility preservation in cancer patients?**

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38 156 In this first section the relevance of oncofertility in the present context is discussed.
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40 157 Moreover, information on the topics of fertility outcomes of cancer survivors, evaluation
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42 158 of reproductive potential and (in)fertility markers, risk factors for infertility in cancer
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44 159 patients and infertility risks associated both with cancer and cancer treatments is also
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46 160 provided.
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50 161 **Section 2. How can cancer patients’ fertility be preserved?**

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52 162 This section includes the following sub-sections: Preserving fertility: which patients and
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54 163 when?; Male fertility preservation techniques; Female fertility preservation techniques
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3 164 (organized according to their classification as established and experimental); Other FP
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6 165 procedures (ovarian transposition, GnRH agonists administration). For each FP
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8 166 technique information is provided regarding procedure, classification as
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10 167 established/experimental, indications (for whom and when), time requisites, success
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12 168 rates, risks for man/woman and offspring, ideal time for conception/pregnancy, using
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15 169 the cryopreserved cells/tissue and costs.

17 170 **Section 3. Questions & Answers**

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20 171 For the most frequently reported topics, information was reinforced in a series of
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22 172 Questions & Answers (total of 15). Some examples are FP in estrogen-positive breast
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24 173 cancer (Which FP techniques are available for hormone-sensitive tumors?), FP in pre-
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26 174 pubertal patients (Which FP techniques are available for pre-pubertal patients?), time
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28 175 requisites for FP (Is there a need to postpone cancer treatments to allow for FP
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30 176 procedures in a cancer patient?), available guidelines (Are there national or
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32 177 international guidelines on FP in cancer patients?), patient referral (What is the
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34 178 procedure for referencing patients to a FP consultation?) or established *versus*
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36 179 experimental techniques (Which FP techniques are acknowledged as established
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38 180 medical practice?),

43 181 **Section 4. Information Tools**

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46 182 A variety of practical tools were developed and included in this last section, including a
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48 183 compilation of electronic tools to estimate infertility risks, the infertility risk tables
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50 184 published by ASCO in 2013 (translated and adapted to Portuguese), a list of published
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52 185 international guidelines regarding FP in oncology and a comparative table of the female
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186 FP techniques. In addition, a list of recommended e-books and review articles was
187 prepared.

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189 The smaller booklet, called “Fertility Preservation in Cancer Patients” presents a similar
190 general organization but summarized contents.

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192 Information dissemination
193 The materials produced are being distributed with the collaboration of the *Liga*
194 *Portuguesa contra o Cancro* (LPCC; Portuguese League Against Cancer), a nonprofit
195 cancer patients organization, the *Sociedade Portuguesa de Medicina Reprodutiva*
196 (SPMR; Portuguese Society of Reproductive Medicine), the *Sociedade Portuguesa de*
197 *Oncologia* (SPO; Portuguese Society of Oncology) and the *Ordem dos Farmacêuticos*
198 (OF; Portuguese Pharmaceutical Society). The LPCC published the summarized
199 booklet and is disseminating both materials to primary care and cancer care health
200 professionals, through its website and promotion campaigns. This smaller booklet is
201 also being distributed to the Portuguese hospital and community pharmacists through
202 the efforts of the OF. The comprehensive information booklet was printed with the
203 support of the SPMR and is being distributed in cancer care institutions and to
204 oncologists with the collaboration of the SPO. Moreover, all information contents of the
205 produced materials are available through the website of the Centre for Fertility
206 Preservation of CHUC, EPE (www.centropreservacaofertilidade.pt), in Portuguese.

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3 209 **Discussion**
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6 210 It is important to note that information materials directed to AYA-aged cancer patients
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8 211 were also developed in the context of this program, including decision aids to support
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10 212 the decision of preserving fertility (or not) and the choice of the FP technique (results to
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12 213 publish). Moreover, we would like to highlight the multidisciplinary context in which it this
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14 214 project has been out, involving oncologists, reproductive medicine physicians,
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16 215 pharmacists, psychologists and the professional societies from the mentioned areas.
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18 216 This cooperation will certainly contribute to a wider dissemination of the developed
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20 217 information materials to the various intervenients in the process of cancer care and to a
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22 218 more effective clinical implementation.
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27 219 Although the present information materials have been developed based on the
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29 220 internationally reported needs, the identified information topics are in accordance with
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31 221 the results from a locally applied questionnaire to a sample of 37 oncologists from two
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33 222 hospitals in the center region of Portugal (unpublished results). In this survey, topics
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35 223 regarding *types of cancer treatments associated to greater infertility risk, interference of*
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37 224 *FP techniques with cancer* and the *available FP techniques* were considered the most
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39 225 important information needs.
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43 226 The developed information materials will support the role of cancer care professionals
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45 227 as patients' educators, increasing their participation in clinical decisions. Additionally,
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47 228 health professionals working in primary care settings can significantly raise awareness
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49 229 of this relevant subject, as they are in a privileged position to disseminate information to
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51 230 the general population.
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3 231 The next step will be to disseminate these materials to other Portuguese language
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6 232 countries and the translation to English and French. Moreover, it is our intention to
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8 233 perform, in cooperation with the SPO, an evaluation study of cancer care clinicians'
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10 234 perceptions on the relevance, reliability and completeness of contents and on the
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12 235 usefulness of this information for their clinical practice.
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17 237 **Conclusions**

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20 238 The opportune information of AYA-aged cancer patients on their risk of infertility and the
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22 239 possibilities concerning FP is recognized as a highly relevant issue, in the context of
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24 240 cancer survival quality of life. Our work confirms the significant information needs of
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26 241 oncologists on these subjects and, by fulfilling those needs, contributes to timely,
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28 242 shared and informed clinical decisions on FP.
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34 244 **Acknowledgments**

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43 248 **Author Disclosure Statement**

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45 249 The authors state that there is no competing financial interest.
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330 Tables

331
332 Table 1. Studies concerning information needs, gaps in knowledge and barriers to FP
333 implementation used on the present work.

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Ref.	Title	Methods (sample)	Information needs / gaps in knowledge / barriers to FP identified
13	Oncologists' Attitudes and Practices Regarding Banking Sperm Before Cancer Treatment	A postal survey was sent to 718 oncology staff physicians and fellows (n=162).	FP options costs; FP facilities; risk of infertility in male versus female patients; treatment delay needed for FP
14	Fertility preservation in cancer survivors: a national survey of oncologists' current knowledge, practice and attitudes	National online survey of oncologists (n=100).	FP options, specially testicular cryopreservation and ovarian cryopreservation; FP techniques success rates; FP in patients with hormonally sensitive malignancy
15	Do doctors discuss fertility issues before they treat young patients with cancer?	Paediatric oncologists prospectively completed a data form for each new patient registered over a 12 month period (n=1030).	FP options in pre-pubertal patients; Experimental/established FP techniques; facilities available for FP
16	Strategies for Fertility Preservation after chemotherapy: Awareness among Irish cancer specialists	Online questionnaire to cancer specialists (n=50).	Success rates; low awareness of published guidelines; available facilities for FP; treatment delay needed for FP; FP in patients with estrogen receptor (ER) positive disease
17	Oncologists' confidence in knowledge of fertility issues for young women with cancer	National sample of medical oncologists, hematology/oncologists, radiation oncologists and gynecologic oncologists (n=344).	Infertility risk estimation; risks of pregnancy for the woman and the fetus; surgical techniques to protect the ovaries from radiation; new IVF stimulation protocols with less delay of cancer treatment or less estrogen exposure; cryopreservation of ovarian tissue and oocytes
18	A nationwide survey of oncologists regarding treatment-related infertility and fertility preservation in female cancer patients	Email survey to a database of oncologists at the top 25 cancer hospitals as ranked by U.S. News & World Report (n=249).	Risk of gonadotoxicity from specific regimens
19	Who should be offered sperm banking for fertility preservation? A survey of UK oncologists and haematologists	Post questionnaire to all members of the Royal College of Radiotherapists' Faculty of Oncology and the British Society for Haematology (n = 499).	Need to offer sperm banking to patients before they go through chemo- or radiotherapy; treatment delay needed for FP

20	Attitudes and Practices of Pediatric Oncology Providers Regarding Fertility Issues	Survey to healthcare providers in a pediatric hematology/oncology clinic (n=30).	Risks of infertility in boys versus girls; risks of ovarian failure in pre-pubertal versus post-pubertal girls; FP techniques in pre-pubertal girls; risk of cancer or birth defects in the offspring of cancer survivors
21	Fertility Preservation in Women Undergoing Treatment for Breast Cancer in the U.K.: A Questionnaire Study	Online questionnaire to surgeons, oncologists, and clinical nurse specialists who manage patients with breast cancer in the United Kingdom (n=306).	Treatment delay needed for FP; FP in patients with estrogen receptor (ER) positive disease; FP options available; interference of FP with the success of cancer treatment
22	Results from the survey for preservation of adolescent reproduction (SPARE) study: gender disparity in delivery of fertility preservation message to adolescents with cancer	Survey by email to all members of a nationwide pediatric oncology subspecialty group (n=180).	FP in pre-pubertal patients; low awareness of published guidelines
23	Fertility preservation among patients with cancer: report of a French regional practical experience	Prospective survey amongst oncologists working in Provence Alpes Côte d'Azur region (n=225).	FP options available and indications
24	Fertility Preservation Practices Among Ontario Oncologists	Questionnaire to Ontario physicians with specialties in medical oncology, radiation oncology, gynecologic oncology, and urology (n=152)	FP specialists for referral; FP costs

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