

ORIGINAL ARTICLE

## Oncologists' practice and attitudes regarding fertility preservation in female cancer patients: a pilot study in the Netherlands

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### Abstract

**Purpose:** The aim of this study was to assess oncologists' practice and attitudes regarding treatment-related infertility and fertility preservation in female cancer patients of reproductive age.

**Participants and methods:** Recruitment letters with a 7-item questionnaire were sent to 454 oncologists.

**Results:** Two hundred and six of the 454 physicians (45%) responded and 96 questionnaires were used for analysis. The sample included 28 (29%) gynaecologists, 22 (23%) medical oncologists, 19 (20%) surgeons, 16 (17%) radiotherapists and 11 (12%) haematologists. Sixty-two percent of the physicians took action to protect ovarian function before or during gonadotoxic therapy. The most important reason for not offering fertility preservation was "factors concerning the disease". About one-third of the oncologists did not discuss fertility issues. Nearly half of the physicians (43%) would offer fertility preservation options, if they were standardized. High importance was given by almost all physicians (96%) to quality of life in general after gonadotoxic therapy and to the provision of information about fertility preservation options (81%). However, when asked about the importance of infertility after a malignancy, a smaller majority of the physicians (59%) gave it high importance.

**Conclusion:** Most physicians considered infertility to be a major issue to be discussed, and most intended to take action to protect ovarian function before or during gonadotoxic therapy.

### Keywords

Cancer, chemotherapy, cryopreservation, fertility, fertility preservation, oncology, quality of life, radiotherapy

### History

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### Introduction

Improvement in the quality of cancer treatment has resulted in higher survivor rates. However, female survivors of child-bearing age are confronted with possible damage to reproductive organs by radiotherapy or chemotherapy [1,2]. Loss of fertility is an adverse effect of cancer treatment negatively influencing quality of life. The combination of improved survival and advances in reproductive medicine provides hope of fertility preservation after cancer treatment in women [3]. The impact of cancer treatment on fertility should be discussed with all cancer patients of reproductive age, according to the guidelines of the American Society of Clinical Oncology (ASCO) [4], the American Society for

Reproductive Medicine (ASRM) and the Dutch Association of Comprehensive Cancer Centers (ACCC).

Fertility preservation methods available before treatment starts are used to achieve a pregnancy after treatment for and recovery from the disease. These methods include cryopreservation of embryos, cryopreservation of ovarian tissue, vitrification of oocytes and transposition of the ovaries. The few studies that investigated oncologists' practice regarding fertility preservation in female cancer patients were nearly all conducted in the USA, and show that though the effect of cancer treatment on fertility is often discussed [5–11], more than half of oncologists rarely refer patients for fertility preservation treatments (see Table 1).

In the Netherlands, 2400 women under the age of 40 are diagnosed with cancer every year [12]. Although discussion of treatment-induced impairment of fertility is also a topic in several Dutch oncological guidelines, there seems to be only a small group of patients that is referred for information about fertility preservation [13]. Little is known about oncologists'

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Table 1. Studies concerning attitude, practice and knowledge in fertility preservation in female cancer patients of reproductive age.

Study	Country	Regarding female (1) male (2) cancer patients			Attitude (1) practice (2) knowledge (3)	Surveys sent (n)	Estimated eligible (n)	Participants (n)	Total response rate (%)	Disciplines#	Positive knowledge of FP options (%)	Discussion of FP options (%)	Referral (%)
		1	2	3									
Louwe et al. [2013]	The Netherlands	1		1,2	454	206	96	45	1,2,4,5,6	55	43	46	
Yee et al. [10]	Canada	1,2*		1,2,3	641	641	152	24(24)**	2,3,5,7	18–61	66	30	
Duffy et al. [9]	USA	1		1,3	2032	1088	344	17(32)**	2,3,5,6	55	60	<14	
Arafa et al. [7]	Saudi Arabia	1,2		1,2,3	180		103	57	2	>90	57	82	
Forman et al. [6]	USA	1		1,2,3	1701		249	15	2,3,5,8,9	>85	95	55	
Forman et al. [8]	USA	1		1,2,3	91		36	40	2,5,8,9		61	47	
Quinn [11]	USA	1,2*		1,2,3	1979	1930	516	32**	2,3,5,6,9,10				

\*It was not possible to differentiate the study results for gender, therefore the combined study findings for female and male cancer patients are reported here; \*\* response rate eligible/participants (%); # 1 Gynecology, 2 Medical Oncology, 3 Gynecologic Oncology, 4 Surgery, 5 Radiotherapy, 6 Hematology, 7 Urology, 8 Pediatric Oncology, 9 Surgical Oncology, 10 Musculoskeletal Oncology.

practice and attitudes regarding treatment-related infertility and fertility preservation in the Netherlands.

The aim of this study is to investigate the practice and attitudes of Dutch physicians regarding fertility preservation in female cancer patients of reproductive age.

## Participants and methods

Recruitment letters were sent via post to a selected group of physicians who were members of Oncologic Working Parties (gynecology, surgery, medical oncology, radiotherapy and hematology) in two regional Comprehensive Cancer Centers in the Netherlands. The letter was accompanied by a 7-item questionnaire in Dutch and referred to a link to complete the questionnaire alternatively online. Four weeks later, a reminder was sent to all non-responders. Respondents were excluded if they were retired or had otherwise left the hospital, if they did not complete the questionnaire, and if they saw fewer than five patients annually who were being treated for cancer and were within the reproductive age group.

The questionnaire was introduced by three questions to characterize and to select participants: “What is your current position?,” “How long have you practiced your current specialty?” and “How many new patients (women younger than 45 years in need of *gonadotoxic therapy*) do you see each year?”

Practice and attitudes were investigated using the following four questions:

- (1) “Do you do anything to protect the ovarian function in your patients before/during gonadotoxic therapy?” (Possible responses were “No” or “Yes” with multiple affirmative options: referral, medication, cryopreservation of ovarian tissue, cryopreservation of embryos, other.)
- (2) “When you do NOT protect ovarian function, what is the most important reason for this decision?” (Possible responses were: age, social factors, disease factors, fertility preservation-related factors, other.)
- (3) “If FP were standardized, to what percentage of your patients would you offer fertility preservation options?”
- (4) “How important do you consider the following to be, for your own patients? Quality of life after gonadotoxic therapy; Infertility after a malignant disease; Providing information about fertility preservation options”. (Responses were given with a 7-point Likert scale: 1. very unimportant, 2. quite unimportant, 3. rather unimportant, 4. neutral, 5. rather important, 6. quite important, 7. very important).

Statistical analysis was performed with SPSS version 17 (SPSS Inc., Chicago, IL) for Windows. Prior to analysis, data were examined for accuracy of data entry, missing values and fit between their distributions and the assumptions of analysis. Cases with missing values on four or more variables were deleted. Descriptive statistics were calculated for all variables. Chi-squared tests were used to compare categorical variables between disciplines and one way ANOVA tests were used to compare continuous variables between disciplines. Where significant differences were found between disciplines, *post-hoc* analyses were performed using the Bonferroni statistics. A value of  $p < 0.05$  was considered significant.

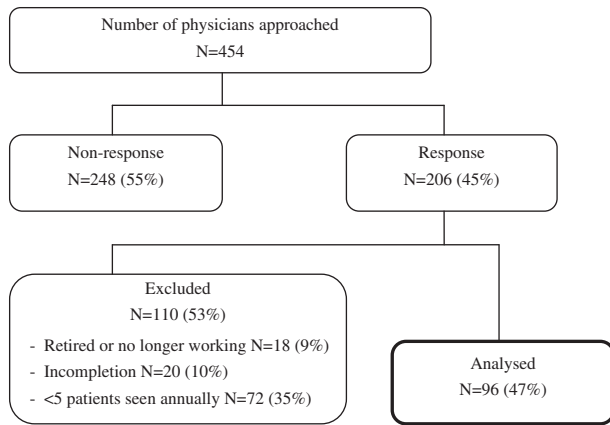


Figure 1. Response and selection of the study participants.

## Results

### Participants

Two hundred and six of the 454 physicians (45%) responded. Surgeons were significantly less likely to respond (29%) than other physicians (50%). Of the 206 replies received, 18 questionnaires (9%) were returned unopened because of retirement or having left the hospital. Twenty respondents (10%) were excluded because of incompleteness of the questionnaire. Another 72 respondents were excluded (54%) because they had seen fewer than five patients during the previous year who were being treated for cancer and were within the reproductive age group. Significantly more responding gynecologists were excluded (74%) than any other physicians (31%) (Figure 1).

The resulting population ( $N = 96$ , 47%) included 28 (29%) gynecologists, 22 (23%) medical oncologists, 19 (20%) surgeons, 16 (17%) radiotherapists and 11 (12%) hematologists. The population's mean number of years of practice was  $13.3 \pm 7.8$  years. Radiotherapists (mean =  $17.1 \pm 9.5$  years) had spent significantly more years in their current position than hematologists (mean  $7.9 \pm 5.0$  years). Seventy percent of the study population was male. There were slight, but not significant, differences between each discipline's number of patients (women younger than 45 years in need of *gonadotoxic therapy*) seen annually.

### Practice patterns of fertility preservation among physicians

Fifty-nine (62%) physicians took action to protect ovarian function before or during gonadotoxic therapy. The most common action was to refer patients to a fertility specialist (46%). Ovarian transposition was offered significantly more often by gynecologists (25%) and radiotherapists (25%) than by the other disciplines (4%). No significant differences were found between the disciplines in the other fertility preservation options.

The most important reasons not to offer fertility preservation options were factors concerning the disease, such as a poor prognosis or a need for immediate therapy (62%). A significantly larger percentage of the oncologists (27%) than other disciplines (5%) reported that they were influenced by FP-bound factors, such as the costs and availability of FP and

knowledge about the options. No significant differences were found between the disciplines in the other options.

### Physicians' attitudes towards fertility preservation

If the possible fertility preservation options were standardized (i.e. structured in a protocol or guideline available to all physicians), almost half of the physicians (43%) would offer all of their patients options for fertility preservation.

Almost all physicians (96%) considered quality of life after gonadotoxic therapy to be important and the majority of the physicians (59%) considered infertility after a malignancy to be important (score six or higher on a 7-point Likert scale). Providing information about infertility and the options regarding fertility preservation were considered to be important by 81% of the physicians (score six or higher on a 7-point Likert scale).

## Discussion

To our knowledge, only six previous studies have assessed oncologists' practice and attitudes regarding treatment-related infertility and regarding fertility preservation options in female cancer patients of reproductive age undergoing gonadotoxic therapy [5–11].

Our study results show that while eight out of 10 physicians considered it important to discuss infertility after gonadotoxic treatment with patients, only six out of 10 took action to preserve fertility. The most important reason not to offer fertility preservation options were poor prognosis or need for immediate start of therapy. If the options were standardized, still less than half of the physicians would offer them to *all* of their patients. They may not be of importance to all of their patients, but since they cannot judge whether it is of importance to a patient in front of them, they feel the moral duty to inform patients about possibilities for FP.

Care should be taken when comparing the findings of this study to those of the previous studies, because there were various sample and measurement differences. Our study results may be specific for female patients of reproductive age and not comparable to physicians' practice and attitudes in fertility preservation in male patients [14,15], children [16] or adolescents [17]. Despite these differences, some similarities in the results are worth mentioning. In line with our finding that 62% of the physicians took action to protect ovarian function before or during gonadotoxic therapy, Forman showed that 82% referred patients, but did so *rarely* [6].

Physicians' intention to discuss gonadotoxic therapy's impact on fertility in our study (81%) is slightly less prevalent than physicians' discussion of the treatment's impact on fertility in Forman's survey in the USA (95%) [6]; but more prevalent than physicians' discussion of fertility issues with their (younger) patients in Anderson's study in the UK (63%) [16] and in Quinn's study in the USA (47%) [11].

The finding that less than half of the physicians would offer FP to their patients if the options were standardized is notable given that 81% of the physicians indicate it to be important. The response rate of our survey was 45%, notably higher than in other studies (varying from 15% to 40%) [6,8–11], except for Arafa, who reported a response rate of 57% among Saudi Arabic oncologists [7].



Some limitations of this survey have to be mentioned. First, the response rate of 45% is rather low, although this is higher than that of many other studies conducted in similar professional bodies. A low response makes the introduction of self-selection bias plausible. Physicians who were more interested in the subjects of (in)fertility and fertility preservation options were possibly more likely to discuss fertility issues with their patients and consequently might have been more likely to participate in this study. This may indicate that our study findings, i.e., that 81% of the physicians considered fertility preservation to be important to discuss with their patients and that 62% of the physicians took action to protect ovarian function before or during gonadotoxic therapy, are rather an overestimation than an underestimation of the current situation in the Netherlands. Second, the study population consisted of physicians working within the most populated Western region of the Netherlands. Outside this region, physicians may view fertility preservation differently due to differences in patient populations and availability of fertility preservation options. Many other factors such as race, ethnicity, religion, sex and family situation of the physician were not surveyed in this study, but may have significant influence on the decisions made.

In conclusion, and considering these limitations, our results show that most physicians who responded to our survey considered infertility to be a major issue to be discussed with their patients and most intended to take action to protect ovarian function before or during gonadotoxic therapy. However, there is room for improvement in the way that knowledge is disseminated to patients.

Guidelines for patient education on the side effects of cancer treatment and on fertility preservation options should be established, and standardized into protocols that can be used throughout different cancer treatment centers. In addition, information resources for patients should be more widely distributed. Printed brochures on the effect of cancer treatment on fertility as well as fertility preservation options, both established and experimental, should be available for all oncologists to hand out to their patients. Contact addresses for referral should be listed on a national website on fertility preservation. Ultimately, good counseling and adequate action to preserve fertility will add to the future quality of life of female cancer patients of reproductive age.

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### Declaration of interest

None to declare.

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#### ► Current knowledge on the subject

- Little is known about oncologists' practice and attitudes regarding treatment-related infertility and fertility preservation.
- Quality of life is influenced by better survival after cancer treatment and possible negative side-effects on fertility after cancer treatment.

#### ► What this study adds

- Infertility is a major issue to be discussed with cancer patients in relation to their cancer treatment.
- Physicians are willing to discuss fertility preservation options, but are not taking action to facilitate a dialogue with their patients.