

# Public fertility preservation programme for cancer patients in Hong Kong

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## ABSTRACT

**Introduction:** Fertility preservation (FP) offers cancer patients the opportunity to have biological children after completing treatment. This study was performed to review the experience and changes in service demand since the implementation of a public FP programme for cancer patients in Hong Kong.

**Methods:** This retrospective study included men and women who attended an assisted reproduction unit for public FP services before cancer treatment from August 2020 to February 2023. Their medical records were reviewed and the results were compared with findings from our previous study to evaluate trends in service demand.

**Results:** During the study period, there were 48 consultations for female FP, compared with 72 women who presented for FP from 2010 to 2020 prior to establishment of the public FP programme. The median time from referral to consultation was 3 days (interquartile range [IQR]=2-5). Eighteen women (37.5%) underwent 19 cycles of ovarian stimulation for oocyte or embryo cryopreservation. Thirty women (62.5%) received gonadotropin-releasing hormone agonists during cancer treatment. There were 58 consultations for male FP during the study period, compared with 265 men who presented for sperm cryopreservation from 2005 to 2020. The

median time from referral to consultation was 4 days (IQR=2-7). Fifty-five men (94.8%) attempted sperm cryopreservation, and 49 (84.5%) successfully preserved sperm.

**Conclusion:** Since the establishment of a public FP programme for cancer patients, there has been an increase in the demand for FP services at our centre. Regular review of FP services is warranted to assess changes in demand and identify areas for improvement.

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### New knowledge added by this study

- Since the establishment of a public fertility preservation (FP) programme, there has been an increase in the number of patients seeking FP services at our centre.
- Reproductive-age men seeking FP were more likely than reproductive-age women to undergo gamete cryopreservation.
- Only 62.5% of women received gonadotropin-releasing hormone agonists during cancer treatment; the reasons for not receiving the agonists were not recorded.

### Implications for clinical practice or policy

- The cost of FP may be a barrier to patients considering this option.
- Public funding for medications and gamete storage can support reproductive-age patients in pursuing FP before cancer treatment.
- Further research is needed to improve FP, especially for reproductive-age women.

## Introduction

Many individuals are diagnosed with cancer during childhood, adolescence, and young adulthood. Worldwide, there were approximately 1 335 100 new cancer cases among adolescents and young adults in 2019<sup>1</sup>; the incidence rate was 44.99 per 100 000 people.<sup>1</sup> In 2020, the incidence rate for cancer among

Hong Kong children and adolescents (aged 0-19 years) was 160 cases per 1 000 000 people.<sup>2</sup> There were 177 newly diagnosed cancer cases in this age-group (92 in male patients and 85 in female patients).<sup>2</sup> The survival rates for childhood and adolescent cancers are encouraging. In a retrospective cohort study from a research hospital in the United States,<sup>3</sup> the

## 香港癌症患者公共生育力保存計劃

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**引言：**生育力保存服務為癌症患者提供了在完成治療後生育孩子的機會。本研究旨在回顧香港癌症患者公共生育力保存服務實施以來的經驗和服務需求變化。

**方法：**這項回顧性研究納入了2020年8月至2023年2月期間在癌症治療前就生育力保存服務到一所輔助生殖中心就診的患者。我們比較此次研究結果與先前的研究結果，以評估服務需求的趨勢。

**結果：**在研究期間，48位女性接受了生育力保存諮詢，而在公共生育力保存計劃建立之前，在2010年至2020年期間有72位女性接受相關諮詢。從轉介到諮詢的中位數時間為3天（四分三位數=2-5）。18位女性（37.5%）接受了19個週期的卵巢刺激以保存卵子或胚胎。30位女性（62.5%）在癌症治療期間接受了促性腺激素釋放激素激動劑。研究期間，有58位男性接受了生育力保存諮詢。而在2005年至2020年期間，有265位男性進行了精子冷凍保存。從轉介到諮詢的中位數時間為4天（四分三位數=2-7）。55位男性（94.8%）嘗試冷凍保存精子，49位男性（84.5%）成功保存精子。

**結論：**自從為癌症患者建立公共計劃以來，本中心對生育力保存服務的需求不斷增加。有必要恆常檢視這項服務，以評估需求變化及找出需要改善的地方。

5-year overall survival rate exceeded 83%. Similarly, in Hong Kong, the 5-year survival rate among women diagnosed with breast cancer, the most common cancer in reproductive-age women, was 84% between 2010 and 2017.<sup>2</sup>

Chemotherapy or pelvic radiotherapy may affect fertility, either temporarily or permanently. Considering advances in cancer treatment and improved post-treatment survival rates, fertility should be discussed at the time of cancer diagnosis, especially for younger patients who have not yet completed their families. International guidelines regarding fertility preservation (FP) recommend that clinicians inform cancer patients about the potential effects of cancer and its treatment on reproductive function, as well as FP options.<sup>4,5</sup> In a semi-structured phone interview study of female cancer survivors who were diagnosed with invasive cervical cancer, breast cancer, Hodgkin lymphoma, or non-Hodgkin lymphoma at age  $\leq 40$  years, participants were interviewed an average of 10 years after diagnosis.<sup>6</sup> Those who had wanted children at the time of diagnosis but were unable to conceive subsequently reported distress related to their interrupted fertility.<sup>6</sup> Additionally, patients who do not receive accurate and timely information regarding FP are at risk for psychological distress.<sup>7</sup> In our recently published cross-sectional questionnaire study of reproductive-age women in Hong Kong who had been diagnosed with breast cancer,<sup>8</sup> only

44% of those women were aware of FP; however, 46% of the women felt that fertility concerns affected their cancer treatment decisions.<sup>8</sup>

The most common FP options include sperm cryopreservation for men and embryo or oocyte cryopreservation for women. Other options for women include pharmacological ovarian protection using gonadotropin-releasing hormone (GnRH) agonists, ovarian tissue cryopreservation, and ovarian transposition. In Hong Kong, FP was previously self-funded and only available through private services. Sperm cryopreservation costs approximately HK\$4400 to HK\$6600 for 2 years, whereas oocyte and embryo cryopreservation costs are approximately HK\$15000 to HK\$20000.<sup>9</sup> Our centre launched the first public FP programme for cancer patients in Hong Kong, beginning in August 2020. Here, we review the two-and-a-half-year experience of providing public FP services to cancer patients in Hong Kong.

## Methods

This retrospective study included men and women who attended the Centre of Assisted Reproduction and Embryology at The University of Hong Kong–Queen Mary Hospital for FP services before cancer treatment, from the establishment of our public FP programme in August 2020 until the end of February 2023.

### Criteria for public fertility preservation services

During the study period, we provided public FP for cancer patients  $< 35$  years old, expressed a desire for future fertility, had a survival rate exceeding 50% after cancer treatment, had no living children, and had not undergone prior chemotherapy or pelvic radiotherapy. In women, an antral follicle count of  $> 7$  on pelvic ultrasound was required. These criteria were adapted from The Edinburgh Selection Criteria for ovarian tissue cryopreservation.<sup>10</sup>

There was no minimum age requirement for FP. Male adolescents could undergo sperm freezing if they were able to provide sperm samples for cryopreservation. For patients aged  $< 18$  years, we included their parents in discussions prior to proceeding with FP treatment.

During the study period, the public FP programme offered up to 40 cycles of sperm freezing and 20 cycles of oocyte/embryo freezing per year.

### Referral process

Patients diagnosed with cancer who were expected to undergo gonadotoxic treatments were referred to our FP service by surgeons, oncologists, paediatricians, haematologists, private practitioners, and cancer support groups. Clinicians completed a

referral letter, which can be downloaded from our centre's website.<sup>11</sup> Patients or their doctors can also contact us via email. Additionally, a chat group was established between Hong Kong Children's Hospital and our centre to facilitate rapid referrals.

After we received a referral, the patient was scheduled for an appointment in the public FP clinic within 1 week. Our centre maintained a flexible clinic schedule, which allowed urgent cases to be accommodated within the existing clinic framework, 5 days per week.

### Fertility preservation counselling

The details of our FP programme were previously published.<sup>12</sup> Information sheets and videos about the FP services offered by our centre were readily accessible to the general population and patients through our website<sup>13</sup> and YouTube channel.<sup>14</sup> Patients were encouraged to review these materials before attending the public FP clinic. For men, sperm banking was arranged on the same day as counselling. For women, the options of oocyte and embryo preservation were discussed if feasible. Embryo preservation was only offered to women who were legally married. In Hong Kong, assisted reproductive technology is regulated by the Human Reproductive Technology Ordinance.<sup>15</sup> This ordinance limits the storage duration for frozen gametes in cancer patients to 10 years or until the patient reaches the age of 55 years, whichever is longer.<sup>15</sup> The storage duration for frozen embryos is limited to 10 years.<sup>15</sup> Cryopreserved gametes and embryos can only be used after a patient recovers from their illness and is legally married.<sup>15</sup> Posthumous use of cryopreserved gametes and embryos is prohibited.<sup>15</sup>

The use of GnRH agonists for pharmacological ovarian protection was discussed either after cryopreservation or if cryopreservation was not feasible. Such agonists were usually administered monthly or every 3 months during chemotherapy.

The characteristics of men who underwent sperm cryopreservation and women who underwent ovarian stimulation for oocyte or embryo cryopreservation were prospectively entered into our database. Medical records (both in paper and electronic formats), including data from the assisted reproductive technology database at our centre and the Hospital Authority's electronic clinical management system, were retrieved and reviewed. These records encompassed demographic data, cancer type, cancer treatment, FP method chosen, ovarian stimulation cycle characteristics, semen analysis, reproductive outcomes, and follow-up information, if available.

All women who attended our centre for FP were asked to return to our late-effects clinic for gonadal function monitoring after the completion of cancer treatment. All men were asked to undergo

semen analysis when they wished to conceive after the completion of cancer treatment.

### Statistical analysis

Data were analysed using SPSS (Windows version 26; IBM Corp, Armonk [NY], United States) and are presented as median (interquartile range [IQR]) or as number (percentage). P value was calculated by Chi squared test.

## Results

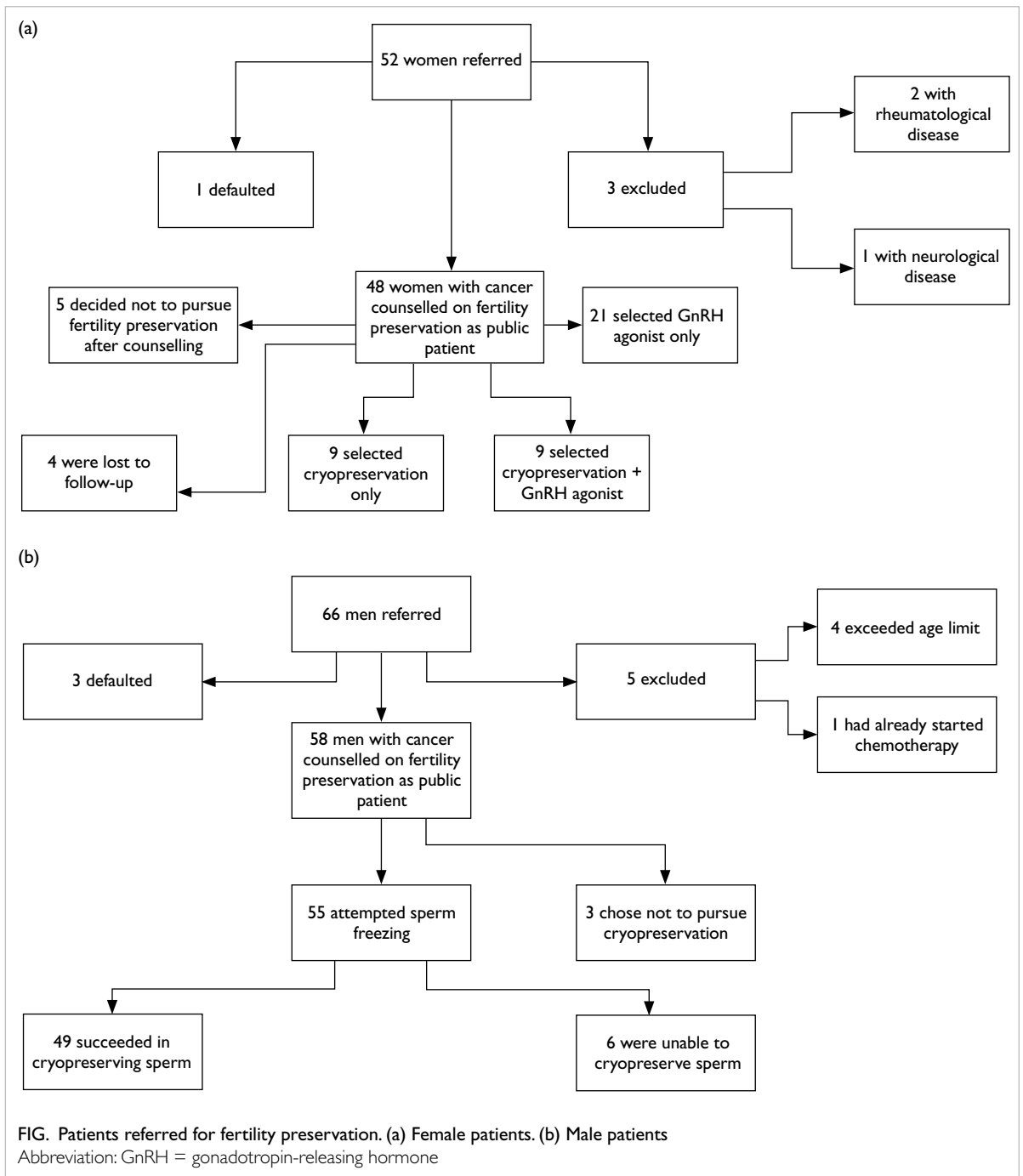
### Women

Fifty-two women were referred to our public FP clinic between August 2020 and February 2023. Three women were excluded from the analysis because they had non-malignant conditions, including rheumatological disease (systemic lupus erythematosus) and neurological disease (multiple sclerosis). Additionally, one woman missed her clinic appointment. Therefore, the final analysis included 48 women (Fig a). The median age of these women was 30 years (IQR=25-33). The cancer outcomes of these women are shown in Table 1. Regarding marital status, 36 women (75.0%) were single, 11 (22.9%) were married, and one (2.1%) was divorced. All were nulliparous, except for one married woman (2.1%) with a livebirth was ineligible for publicly funded FP due to the programme's criteria. She then selected GnRH agonist treatment after counselling. The median time from referral to consultation was 3 days (IQR=2-5).

Eighteen women underwent 19 cycles of ovarian stimulation for oocyte or embryo cryopreservation (Table 2). One woman underwent an additional self-financed stimulation cycle because she only achieved two frozen oocytes in the first cycle. She achieved two additional frozen oocytes in the second attempt. Thirteen women cryopreserved oocytes, whereas five women cryopreserved embryos (three at the cleavage stage and two at the blastocyst stage). The median time between consultation and ovarian stimulation was 5 days (IQR=2-12) [Table 2]. All women with breast cancer received letrozole co-treatment during ovarian stimulation.

One woman developed moderate ovarian hyperstimulation syndrome requiring hospital admission. Oocyte retrieval was uneventful, and 45 oocytes were retrieved. However, 3 days after oocyte retrieval, she was admitted with abdominal distension, shortness of breath, and vomiting. She was diagnosed with moderate ovarian hyperstimulation syndrome, which resolved with conservative management.

There was no significant age difference between women who proceeded with oocyte/embryo cryopreservation and those who did not. The median age of women who proceeded with oocyte/



embryo cryopreservation was 28 years (IQR=24.0-32.8), whereas the median age of women who did not proceed with oocyte/embryo cryopreservation was 31 years (IQR=26.8-33.0) [Table 3].

Among patients with breast and gynaecological cancers, six of 10 (60.0%) and six of 13 (46.2%) underwent oocyte/embryo cryopreservation, respectively, compared with five of 19 (26.3%) women with haematological cancers and one of six (16.7%) women with other solid tumours (Table 3).

Among the 48 women who attended the clinic,

nine (18.8%) proceeded with oocyte or embryo cryopreservation alone, nine (18.8%) underwent cryopreservation followed by the use of GnRH agonists, 21 (43.8%) received GnRH agonists alone, five (10.4%) decided against FP after counselling, and four (8.3%) were lost to follow-up. Those who chose GnRH agonists received this treatment from their primary oncology team.

At the end of February 2023, among the 48 women, 22 exhibited disease remission, 21 were continuing treatment, four were deceased, and one

TABLE 1. Diagnoses and outcomes of cancer among women seeking fertility preservation (n=48)\*

		Remission (n=22)	Treatment (n=21)	Deceased (n=4)	Lost to follow-up (n=1)
Acute leukaemia	6	2	3	1	
Hodgkin lymphoma	3	2	1		
Non-Hodgkin lymphoma	8	5	2	1	
Others	2		2		
Breast cancer	10 (20.8%)	2	8		
Gynaecological cancer	13 (27.1%)				
Cervical cancer	1	1			
Endometrial cancer	1	1			
Ovarian cancer	11	7	3		1
Gastrointestinal cancer	2 (4.2%)	1		1	
Lung cancer	1 (2.1%)			1	
Central nervous system cancer	3 (6.3%)	1	2		

\* Data are shown as No. or No. (%)

had been lost to follow-up (Table 1). None of the women have returned to use their frozen oocytes or embryos, nor have any reported natural conception since their cancer diagnosis.

### Men

Sixty-six men were referred to our public FP clinic during the study period (Fig b). Five men were excluded: four had exceeded the age limit and one had already begun chemotherapy. Fertility preservation counselling at a private clinic was offered to those who were not eligible for the public FP service. One man, who exceeded the age limit, underwent self-funded sperm cryopreservation. Three men missed their clinic appointments. Therefore, the final analysis included 58 men (Fig b). The median age of the men was 26 years (IQR=18.3-32.8). The cancer outcomes of these men are shown in Table 4. Regarding marital status, 51 men (87.9%) were single and seven men (12.1%) were married. One man (1.7%) had a child but was unmarried. The remaining 57 men (98.3%) had no offspring. The median time from referral to consultation was 4 days (IQR=2-7).

Among the 58 men who attended the clinic, 55 attempted sperm freezing and three chose not to undergo cryopreservation after counselling. Six men were unable to cryopreserve sperm (Fig b). One, aged 14 years, was unable to provide a semen sample; four men submitted semen samples containing no sperm. One man had previously attempted sperm cryopreservation at a private hospital, but no sperm were found in his ejaculate. He subsequently underwent testicular sperm extraction at our hospital; no sperm were retrieved. The ages of the men with no sperm in their semen ranged from 15 to 34 years.

TABLE 2. Cycle characteristics of women who underwent ovarian stimulation (n=19)\*

Age of women, y	31 (26-33)
Waiting time after consultation, d	5 (2-12)
Antral follicle count	17 (10-21)
Duration of ovarian stimulation, d	12 (10-13)
Serum oestradiol level on day of trigger injection, pmol/L	5585 (3242-10154)
FSH dosage, IU	3375 (2850-3900)
Ovarian stimulation protocol (n=19)	
Antagonist	5 (26.3%)
Antagonist plus letrozole	8 (42.1%)
Progesterin-primed ovarian stimulation	6 (31.6%)
No. of oocytes retrieved	15 (6-19)
No. of oocytes or embryos cryopreserved	8 (5-14)

Abbreviations: FSH = follicle-stimulating hormone; IU = international units

\* Data are shown as No. (%) or median (interquartile range)

The median number of vials of cryopreserved sperm was 5 (IQR=5-5) and the median sperm concentration was 18.8 million/mL (IQR=4.3-52.8).

At the end of February 2023, among the 58 men, 29 exhibited disease remission, 18 were continuing treatment, six were deceased, and five had been lost to follow-up (Table 4). None of the men have returned to use their frozen sperm.

As of this writing, six men and four woman who attended the FP clinic have died.

## Discussion

This is the first review of a public FP programme for cancer patients in Hong Kong. Our study showed

that among the 48 women who attended during the study period, 37.5% (n=18) underwent oocyte/embryo cryopreservation and 62.5% (n=30) chose GnRH agonists for FP. In contrast, among the 58 men who attended for FP before cancer treatment, >90% attempted sperm cryopreservation.

We previously published a review of our self-funded FP service from 2010 to 2020.<sup>12</sup> During that period, 72 women attended consultations for

FP, and 20 of them underwent 22 cycles of ovarian stimulation for oocyte or embryo cryopreservation.<sup>12</sup> Additionally, from 1995 to 2020, 265 men underwent sperm cryopreservation.<sup>12</sup> Over the years, there were increases in the numbers of men and women seeking FP; the increase was more prominent among women.

For comparison, we selected the period from 2018 to 2020 (ie, the 2.5 years immediately preceding the launch of the public FP programme). During that period, 19 women were referred for self-funded FP prior to cancer treatment, and 10 (52.6%) underwent oocyte or embryo cryopreservation. Fifty-eight men were referred for FP and underwent sperm cryopreservation. In the years prior to the launch of the publicly funded FP programme, we had already begun networking with various specialties, which likely contributed to the gradual increase in awareness and demand for FP services.

### Public fertility preservation programme

A successful FP programme requires good networking, flexibility, and a patient-friendly clinic environment. During the establishment of the public FP programme, we have networked with other specialties to enhance collaboration. Our centre aimed to simplify logistics so that consultations could be arranged as quickly as possible, allowing FP counselling and procedures to be completed within the short window of opportunity before cancer treatment. In our public FP clinic, the median waiting times from referral to consultation were 3 days for

TABLE 3. Characteristics of women with or without oocyte/embryo cryopreservation (n=48)\*

	No cryopreservation (n=30)	Cryopreservation (n=18)	Total	P value
<b>Cancer diagnosis</b>				
Breast cancer	4 (40.0%)	6 (60.0%)	10	0.203
Haematological cancer	14 (73.7%)	5 (26.3%)	19	
Gynaecological cancer	7 (53.8%)	6 (46.2%)	13	
Other solid tumours	5 (83.3%)	1 (16.7%)	6	
Age of women, y	31 (26.8-33.0)	28 (24.0-32.8)		0.233
<b>Parity</b>				
Nulliparous	29	18		0.434
Primiparous	1	0		
Multiparous	0	0		

\* Data are shown as No., No. (%) or median (interquartile range), unless otherwise specified

TABLE 4. Diagnoses and outcomes of cancer in men seeking fertility preservation (n=58)\*

		Remission (n=29)	Treatment (n=18)	Deceased (n=6)	Lost to follow-up (n=5)
Haematological cancers	20 (34.5%)				
Acute leukaemia	6		3	3	
Hodgkin lymphoma	8	7	1		
Non-Hodgkin lymphoma	6	2	2	1	1
Testicular cancer	12 (20.7%)	8	2		2
Mediastinal germ cell tumour	3 (5.2%)	2			1
Extragenital germ cell tumour	1 (1.7%)	1			
Central nervous system cancer	5 (8.6%)	5			
Oro/nasopharyngeal carcinoma	3 (5.2%)				
Nasopharyngeal cancer	2		2		
Carcinoma of the hard palate	1			1	
Sarcoma	8 (13.8%)				
Osteosarcoma	3	1	2		
Other sarcoma	5	2	3		
Carcinoma of the liver	2 (3.4%)		2		
Gastrointestinal cancer	4 (6.9%)	1	1	1	1

\* Data are shown as No. or No. (%)

women and 4 days for men. Among women who chose oocyte or embryo cryopreservation, the median time from consultation to the start of ovarian stimulation was 5 days (IQR=2-12). In our previous study, the time from consultation to oocyte retrieval was 17 days (IQR=13-30).<sup>12</sup> Notably, our previous study did not investigate the waiting time from referral to consultation; therefore, direct comparisons cannot be performed. Compared with our previous study regarding FP for cancer patients at our centre,<sup>12</sup> the proportion of women who ultimately underwent oocyte or embryo cryopreservation increased from 28% to 38% in the public FP programme. However, further monitoring is needed to determine whether this difference represents a true upward trend due to increased awareness and easier access to the service. Additionally, patient characteristics and cancer types may vary across time periods.

For reproductive-age women with cancer, the receipt of specialised counselling regarding fertility issues, followed by FP, has been linked to less regret and improved quality of life among survivors.<sup>16</sup> Providing our patients with accessible FP counselling and affordable treatments is an essential aspect of comprehensive oncology care. A clinical practice guideline from the American Society of Clinical Oncology indicates that FP should be initiated as early as possible in the treatment process to allow for the widest range of options.<sup>17</sup> Referral to FP services enables patients to receive counselling from reproductive medicine specialists, empowering them to make informed decisions about fertility treatment.

At our FP clinic, patients were able to consult reproductive medicine specialists who discussed the potential effects of gonadotoxic cancer treatments on future fertility and described FP options. Local regulations concerning gamete storage and assisted reproduction were also explained. Patients were informed that they must be legally married to use frozen gametes in the future, and that gametes cannot be used posthumously.

### Gonadotropin-releasing hormone agonists

In our cohort, only 62.5% of women received GnRH agonists during cancer treatment; the reasons for not receiving GnRH agonists were not recorded. Gonadotropin-releasing hormone agonists are usually administered monthly or every 3 months during cancer treatment, although their effectiveness depends on the type of cancer treatment. Some studies of breast cancer patients have shown that GnRH agonists can reduce the risk of premature ovarian insufficiency, but the fertility benefit remains uncertain.<sup>18-20</sup> Most studies have focused on outcomes such as the maintenance or resumption of menstruation, prevention of treatment-related premature ovarian failure, and

ovulation. In a Cochrane review<sup>20</sup> which discussed randomised controlled trials that examined the effect of GnRH analogues for chemotherapy-induced ovarian failure in premenopausal women, 12 randomised controlled trials were included. Eleven studies reported rates of menstruation recovery or maintenance, four studies measured treatment-related premature ovarian failure, and seven studies reported the rates of pregnancy.<sup>20</sup> However, there are limited data regarding live birth rates.<sup>20</sup> A meta-analysis of randomised studies concerning ovarian suppression using GnRH agonists during chemotherapy in breast cancer patients found that temporary ovarian suppression with a GnRH agonist in young breast cancer patients was associated with a reduced risk of chemotherapy-induced premature ovarian insufficiency; it also appeared to increase the pregnancy rate without negatively influencing prognosis.<sup>21</sup> Thus far, the benefit of GnRH agonists in other malignancies is unclear. A long-term analysis of young female lymphoma patients showed that GnRH agonists were not effective in preventing chemotherapy-induced premature ovarian insufficiency and did not improve future pregnancy rates.<sup>22</sup> According to the European Society of Human Reproduction and Embryology guideline on female FP,<sup>4</sup> GnRH agonists should be offered as an option for protecting ovarian function in premenopausal breast cancer patients undergoing chemotherapy; importantly, limited evidence exists regarding their protective effects on ovarian reserve and potential future pregnancies.<sup>4</sup> In malignancies other than breast cancer, GnRH agonists should not be routinely offered as an option for protecting ovarian function protection and FP without discussing the uncertainty of their benefit.<sup>4</sup> Gonadotropin-releasing hormone agonists during chemotherapy should not be considered as a substitute for established FP techniques, such as cryopreservation. They can be offered in addition to cryopreservation or when such techniques are not feasible.<sup>4</sup> Despite the use of GnRH agonists, patients may experience premature ovarian insufficiency. Gonadotropin-releasing hormone agonists are currently provided as a self-financed option; women are often referred back to their oncology team, who prescribes and administers these agonists after FP counselling. The proportion of patients who underwent oocyte/embryo cryopreservation was higher among those with gynaecological or breast cancers than among those with haematological malignancies. This difference is likely due to the nature of their diseases and the urgency of initiating cancer treatment.

### Oocyte or embryo cryopreservation

For women who chose to proceed with ovarian stimulation for oocyte or embryo cryopreservation, oocytes were retrieved during a stimulated cycle.

Recombinant follicle-stimulating hormone could be initiated on any day of the menstrual cycle for ovarian stimulation (ie, 'random-start'), using either a GnRH antagonist or progestin-primed protocol. This random-start approach allowed ovarian stimulation without substantial delays and did not affect the number or quality of retrieved oocytes.<sup>4</sup> For women with hormone-sensitive cancers (eg, breast cancer), letrozole was routinely used during ovarian stimulation. The concomitant use of letrozole reduced circulating oestrogen levels and did not impair the efficacy of ovarian stimulation.<sup>23</sup> A systematic review and meta-analysis regarding the safety of hormonal stimulation in young women with breast cancer before starting cancer treatment, as well as survivors who underwent assisted reproduction after cancer treatment, showed no increased risk of breast cancer recurrence in women who underwent ovarian stimulation with concomitant letrozole treatment.<sup>24</sup> Despite using the 'random-start' approach, one cycle of ovarian stimulation required approximately 2 weeks.

### Limitations

This study had some limitations. It was a retrospective, single-centre study conducted over a short period of time; thus, it may not reflect situations in other regions. Due to resource constraints, we only included cancer patients who had not begun cancer treatment. Patients who did not meet the criteria for the public FP programme but still wished to pursue FP were referred to private clinics or other private centres upon receipt of their referral and therefore were excluded from this review. Patients who had already begun cancer treatment were also excluded from the public FP service. However, they could still be referred to our centre after stabilisation to assess fertility and explore self-funded FP options before undergoing more toxic chemotherapy, non-fertility-sparing radiotherapy, or surgeries. At the time of writing, our centre has not yet offered ovarian or testicular tissue cryopreservation. A 2018 survey of several Asian countries (eg, Australia, China, and India) revealed that ovarian tissue cryopreservation was available for prepubertal girls and postpubertal women who were unable to delay the initiation of chemotherapy.<sup>25</sup> Testicular tissue cryopreservation also was provided to prepubertal boys in Australia, China, India, Indonesia, Japan, and Taiwan.<sup>25</sup> A recently published pilot study from Hong Kong demonstrated the feasibility of ovarian tissue cryopreservation and transplantation using xenografts in nude mice<sup>26</sup>; ovarian tissue cryopreservation has recently become available in Hong Kong.

The patients included in this study were counselled for FP, and many are still undergoing cancer treatment and monitoring; none have

returned to use the stored material. They were advised to return after cancer treatment for follow-up regarding their gonadal function. Patient satisfaction should also be evaluated. However, at the time of cryopreservation—typically close to the time of cancer diagnosis—patients may feel overwhelmed by the diagnosis and planned cancer treatments. Thus, patient satisfaction may be more accurately evaluated when the cancer is controlled or in remission.

### Future outlook

Despite the presence of the public FP programme, patients were required to pay for the medications used in ovarian stimulation, as well as the fees involved in oocyte handling, freezing, and storage of frozen gametes or embryos; these costs were considerably reduced compared with expenses in private clinics. Cost remains a major barrier to accessing FP services. Although a public healthcare system has been established in Hong Kong, cancer patients are often financially overwhelmed due to the loss of income after a cancer diagnosis, along with additional expenditures for various self-funded investigations or treatments. We recently performed a survey of the knowledge, attitudes, and intentions regarding FP among breast cancer patients; most participants thought that FP should be subsidised by the government or provided at no cost.<sup>8</sup>

### Conclusion

Since the establishment of a public FP programme for cancer patients, there has been an increase in the number of patients seeking FP services. More than 90% of men attempted sperm cryopreservation, whereas 37.5% of women underwent oocyte/embryo cryopreservation and 62.5% of women received GnRH agonists during cancer treatment. With further promotion, changes in funding policies, and a more accessible FP programme, the demand for FP services is expected to increase. Fertility preservation services should be regularly reviewed to assess changes in demand and identify areas for improvement.

### Author contributions

Concept or design: JKY Ko, EHY Ng.

Acquisition of data: DTY Chan.

Analysis or interpretation of data: DTY Chan, JKY Ko, EHY Ng.

Drafting of the manuscript: DTY Chan.

Critical revision of the manuscript for important intellectual content: All authors.

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.



## Conflicts of interest

All authors have disclosed no conflicts of interest.

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## Ethics approval

The study protocol was approved by the Institutional Review Board of The University of Hong Kong/Hospital Authority Hong Kong West Cluster, Hong Kong (Ref No.: UW 23-334). The requirement for informed consent was waived by the Board due to the retrospective nature of the research.

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