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## Fertility information needs and concerns post-treatment contribute to lowered quality of life among young adult female cancer survivors

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Addressing fertility is a key aspect of oncology care for young adult female cancer survivors (YAFCS) who receive gonadotoxic treatment. Fertility preservation (FP) may help to mitigate infertility risks (e.g., egg or embryo freezing), but most women do not preserve their fertility before treatment [1,2]. After treatment, lowered ovarian reserve leads to a shortened reproductive time window. For survivors hoping to have children in the future but are not yet ready to start family-building, FP after treatment may be appropriate to mitigate the risks of premature ovarian failure [3,4]. Reproductive health counseling is often missing or inadequate in post-treatment survivorship care [5,6], and lack of information, misconceptions, anxiety, and distress about fertility are common among this population [7]. Understanding the ways in which fertility and family-building concerns impact broader quality of life (QOL) domains is important to address this critical issue in young adult survivorship.

Reproductive concerns associated with cancer treatment are multidimensional, including difficulties with body image and sexuality; worries about dating, disclosure, and rejection from a (future) partner; difficulty relating to peers; concerns about womanhood and motherhood; feelings of inadequacy; and fears about being unable to fulfill important life goals [8–11]. The perception of impaired fertility alone is related to anxiety and depressive symptoms, fear, anticipated devastation, difficulties with self-esteem and identity, and lowered QOL [12,13]. After treatment, many YAFCS are uncertain about their infertility risks, reproductive viability, and family-building options [14,15]. Unmet information needs contribute to distress about unknown or potential fertility problems [16]. Notably, fertility distress may persist despite explicit reassurance from physicians discounting gonadotoxic treatment effects [17]. Distress may increase in survivorship as patients begin to focus on future plans and expectations in the same timeline as their peers, or as the implications of fertility problems and limited reproductive options are more fully realized in the midst of

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family-building pursuits [18,19]. Alternatively, YAFCS may minimize concerns or try to avoid thoughts about fertility and future family-building in an effort to manage distress and focus on normality [19–21]. Empirical examination of how fertility concerns relate to more general aspects of adjustment and well-being in post-treatment survivorship has been limited.

We previously reported on the fertility information needs and reproductive concerns of YAFCS after treatment and their uncertainty and distress when prompted to consider decisions about post-treatment FP (when applicable) and future family-building [22]. This study was unique in focusing on post-treatment fertility decisions in reference to plans for future family-building. Building on those findings, this secondary analysis aimed to evaluate the effects of unmet fertility information needs, reproductive concerns, and distress about fertility decisions on general QOL. Understanding the ways in which these issues may impact QOL in survivorship may inform the development of clinical and supportive care services to adequately address the range of survivors' needs.

## Methods

Participants were premenopausal females with a prior cancer diagnosis, 18–35 years old, who completed gonadotoxic treatment (i.e., systemic chemotherapy, pelvic radiotherapy, and/or pelvic surgery affecting reproductive function) 1 year prior, and were disease free. The Memorial Sloan Kettering (MSK) Institutional Review Board approved the study.

## Design

This is a secondary analysis of a cross-sectional, anonymous online survey [22]. Participants were recruited via social media outlets of MSK and cancer survivor advocacy groups (e.g., The Samfund and Stupid Cancer). Screener items confirmed eligibility as defined above. Standard questions assessed sociodemographic and medical information.

## Measures

Five items measured unmet fertility information needs. Participants responded (yes/no) to questions (“*Do you have as much information as you would like*”) regarding: risk of infertility, risk of early menopause, options to evaluate and preserve fertility, and information on alternative family-building. Sum scores were calculated (yes=0, no=1; range 0–5) such that higher scores indicated greater unmet information needs (Cronbach's  $\alpha=.81$ ).

The Reproductive Concerns after Cancer Scale (RCACS; 18 items) measured six domains: fertility potential, becoming pregnant, personal health, child's health, partner disclosure, and acceptance [23]. Participants answered on a 5-point Likert scale from “*strongly disagree*” to “*strongly agree*.” Mean total scores ranged from 18 to 90. Higher scores indicated higher levels of reproductive concern (Cronbach's  $\alpha=.83$ ).

Fertility decisional conflict was assessed using the Decisional Conflict Scale (DCS; low health literacy version) [24]. Four domains of personal uncertainty in making a fertility decisions were included: feeling uninformed, unclear about values, unsupported in decision-making, and uncertainty in which option to choose. Participants responded yes/no/unsure to

indicate their feelings about fertility decisions. Total scores ranged from 0 to 100 with higher scores indicating greater decisional conflict. Two items were excluded due to concern about participant burden and based on face validity. The final eight items demonstrated good internal reliability (Cronbach's  $\alpha=.84$ ).

The Quality of Life Scale–Cancer Survivor (QOL-SC) measured different aspects of adjustment and well-being in long-term cancer survivorship [25]. Due to concern about participant burden, five items were selected based on face validity. Participants rated (0–10) their general QOL (“*extremely poor*” to “*excellent*”), level of happiness (“*none at all*” to “*a great deal*”), life satisfaction (“*not at all*” to “*completely*”), the degree to which they felt in control of the things in their life (“*not at all*” to “*completely*”), and illness- or treatment-related changes in self-concept (“*not at all*” to “*extremely*”). Higher scores indicated better QOL. Based on inter-item correlation indices and reliability diagnostics, the self-concept item was excluded and a mean QOL score was derived from the remaining items, with good internal reliability (Cronbach's  $\alpha=.89$ ).

## Analyses

Pearson's correlations, t-tests, and ANOVAs evaluated bivariate relations among sociodemographic and clinical characteristics and QOL. Analyses excluded participants who did not want future children. Three linear regression models evaluated the effects of unmet fertility information needs, reproductive concerns, and fertility decisional conflict on QOL, controlling for age, years since treatment, employment status, income, relationship status, and nulliparity. The reproductive concerns model excluded infertile participants because RCACS items are based on unknown fertility potential. The fertility decisional conflict model did not include infertile participants or those who had previously undergone FP because the DCS measured distress about future FP and family-building. Exploratory analyses included analysis of covariance (ANCOVA) to evaluate differences between participants who reported higher vs. lower levels of QOL based on a median split, controlling for covariates found to be significant in primary analyses. This was done to better characterize the subgroup of participants with lower QOL.

## Results

Of the 714 respondents that accessed the survey, 359 (50%) met eligibility criteria and 346 completed the survey (97% of eligible respondents). Descriptives of the full sample have been previously published.<sup>22</sup> Participants averaged 29.9 years old ( $SD=4.1$ ), were primarily White (81%), married/partnered (60%), and 4.9 years post-treatment ( $SD=7.5$ ). Lymphoma (23%) and breast cancer (20%) were the most common cancer diagnoses. Eighty-two percent of participants did not have children at diagnosis and 70% indicated they *definitely* or *likely* wanted (more) children in the future; only 8% said they *definitely did not* want future children. Sixty women (17%) had undergone FP before or after treatment. At the time of completing the survey, 106 (31%) participants reported they were unable to get pregnant or carry a pregnancy due to treatment effects. Table 1 presents sociodemographic/medical characteristics.

On a ten point scale, participants on average reported levels of QOL of 7.3 (SD=1.9). In bivariate analyses, lower QOL related to being unemployed ( $t[281]=-3.49$ ,  $p=.001$ ; mean difference of .98) and lower household income (<50k vs. 50k;  $t[266]=-3.14$ ,  $p=.002$ ; mean difference of .74). Being unemployed with a household income of less than \$50,000 resulted in a mean QOL score that was 1.85 points lower than when survivors were employed with an income greater than \$50,000 (QOL scores:  $M=5.7$ ,  $SD=2.3$  compared to  $M=7.6$ ,  $SD=1.8$ ; Bonferroni test of mean difference,  $p<.001$ ). Item-level analysis indicated that participants struggled most with feeling in control ( $M=6.3$ ,  $SD=2.5$ ; Median=7.0): 32% scored 5 on a 0–10 scale, indicating a feeling of lacking control over their lives. Item-level ratings of general QOL ( $M=7.6$ ,  $SD=2.0$ ; Median=9.0), happiness ( $M=7.7$ ,  $SD=2.1$ ; Median=9.0), and life satisfaction ( $M=7.5$ ,  $SD=2.1$ ; Median=9.0) were higher. QOL scores did not vary by fertility status ( $t[272]=.743$ ,  $p=.46$ ), history of FP ( $t[273]=.53$ ,  $p=.55$ ), or desire for future children ( $F[2, 316]=.07$ ,  $p=.93$ ).

Primary regression analyses evaluated relations among fertility variables and QOL, controlling for age, years since treatment, employment status, income, relationship status, and nulliparity (Table 2). In separate models, greater unmet fertility information needs ( $\beta=-.22$ ,  $p=.001$ ) and, among fertile women, greater reproductive concerns ( $\beta=-.27$ ,  $p<.001$ ) related to lower QOL. Among fertile women without prior FP, greater conflict about post-treatment fertility decisions also related to lower QOL scores ( $\beta=-.21$ ,  $p=.01$ ). Consistent with bivariate analysis, younger age, being unemployed, and having lower income related to worse QOL across all models; no other covariates were significantly related.

### Exploratory Analyses

We evaluated differences between women reporting higher vs. lower levels of QOL, to identify potential risk factors for QOL deficits due to fertility-related problems. Three ANCOVA models were specified to compare QOL groups based on a median split across fertility variables, controlling for covariates found to be significant in primary analyses (i.e., age, employment, and income). Group differences suggested that women classified into the lower QOL group, compared to those in the higher QOL group, had significantly greater unmet information needs ( $F[1,225]=9.02$ ,  $p=.003$ ) and, among fertile women, greater reproductive concerns ( $F[1,170]=16.77$ ,  $p<.001$ ). Across reproductive topics, women in the lower QOL group, compared to women in the higher QOL group, reported higher levels of concern about having fertility problems and becoming pregnant, partner disclosure, and greater difficulty accepting fertility problems; both groups reported worries about personal health and the health of a future child (e.g., passing down a genetic risk for cancer). Among fertile women with no prior FP, classification into the lower QOL group was associated with higher levels of decision conflict about post-treatment fertility decisions compared to the higher QOL group ( $F[1, 145]=6.02$ ,  $p=.02$ ), representing a significant mean difference of 11 points ( $SE=4.26$ ,  $p=.02$ ).

Within the lower QOL group, 57–71% reported unmet information needs across all fertility topics, compared to 43–55% in the higher QOL group (chi-square tests for equality of proportions,  $p$ 's<.05). Areas of greatest reproductive concern in the lower QOL group included not being able to have children (79%), fears about future children's cancer risk

(62%), concern about (potential) partner's disappointment (61%), stress about getting pregnant (53%), and concerns about childbearing and cancer recurrence (47%). Overall, fewer women in the higher QOL group endorsed concerns and, when they did, their level of concern tended to be lower. Only 10% of the lower QOL group felt informed about their options for FP, compared to 25% in the higher QOL group. Within the lower QOL group, 87% wanted more guidance or advice and 60% wanted more emotional support when making a decision about FP and future family-building; whereas within the higher QOL group, a comparable proportion wanted more advice/guidance (74%;  $\chi^2=4.5$ ,  $p=.10$ ), but fewer wished for more emotional support (21%;  $\chi^2=23.9$ ,  $p<.001$ ).

## Conclusions

The psychosocial burden of fertility problems in cancer survivorship is well established [7]. We add to this literature by demonstrating the negative QOL implications of reproductive concerns and unmet informational needs when making fertility decisions about future family-building. Unmet decision support needs were also associated with lower QOL, suggesting key targets for intervention for post-treatment survivorship care. To our knowledge, this study and our prior findings [22] are the first to focus on YAFCS' decision-making about FP post-treatment and future family-building. The ways in which fertility experiences relate to QOL domains after cancer may have important implications for building targeted resources for young adult survivors and improving follow-up fertility counseling after treatment.

Importantly, although participants reported relatively high levels of QOL overall, the subgroup that reported lower QOL scores indicated significantly higher unmet needs and concerns about fertility issues. It may be that for certain YAFCS subgroups, fertility-related difficulties have more global effects on well-being and adjustment post-treatment. Forty-five percent of those within the lower QOL group reported that they wanted to have a child within the next three years, yet unmet information needs and concerns about fertility potential and likelihood for childbearing success were common. Most felt like they needed more advice and support to pursue family-building. It may be that the combination of unmet fertility care needs with impending family-building intentions led to greater distress and perceptions of worse QOL overall. Limited work has characterized how YAFCS' fertility concerns change over time or how other factors such as family-building intentions or partner-level factors may impact level of concern. Findings suggest there may be subgroups of YAFCS at risk for having negative fertility-related experiences lead to more global indices of distress.

Findings also suggested that survivors who are unemployed and with lower income may be at increased risk for QOL deficits. Those who are struggling financially and are under- or unemployed, and feeling a loss of control in their lives due to cancer, may have greater difficulty managing reproductive concerns, seeking fertility care, and making decisions that are in line with their family-building goals. Young adult cancer survivors report worse financial outcomes compared to non-cancer peers, including greater long-term medical expenses and debt [26]. Family-building after cancer poses significant cost if assisted reproductive technology or adoption is needed. Little is known about how financial

considerations impact survivors' expectations for family-building and decision-making about fertility-related care after treatment. Given the importance many YAFCS place on achieving motherhood [8,27], understanding the ways in which family-building decisions incorporate financial cost estimates is critical. It may be particularly important for those with employment- or income-related stress to receive early counseling about family-building options and strategies for financial planning. In order to develop resources and better counsel survivors, research is needed to determine how fertility and QOL experiences interact with financial concerns and subsequent family-building intentions and planning.

A challenge in survivorship care is helping young survivors cope with their reproductive concerns and think about future family-building preemptively. Adolescent-aged survivors sometimes report feeling too young to think about family-building and would rather prioritize normality to avoid potential distress [17]. Developmentally appropriate support services are needed, before and after treatment, to ensure YAFCS have the opportunity to make informed, values-based fertility decisions. Early planning and referral may be particularly important for those who are at risk for heightened fertility distress or QOL deficits or for those who may benefit from financial planning to prepare for future costs of assistive reproductive technologies or adoption. Pre-treatment fertility counseling leads to lower levels of post-treatment regret and better QOL [8,28], suggesting post-treatment counseling may be similarly beneficial.

Limitations include the cross-sectional design, which precludes any inferences about causality. We were unable to verify self-reported data with medical records about prior cancer treatment or post-treatment fertility status. Details of specific therapeutic exposures were unknown, and it was thus assumed that any chemotherapy exposure could pose some degree of fertility risk. We partnered with young adult cancer advocacy groups to recruit participants, which may not accurately represent all young adult survivors. Additionally, although we selected QOL items from a validated measure, these were secondary analyses and study procedures should be replicated with a larger sample using a more comprehensive QOL assessment.

This study highlights how unaddressed fertility information needs, concerns, and decisional conflict post-treatment may negatively impact QOL among YAFCS who want future children. Irrespective of FP history, family-building after cancer often involves difficult decisions surrounding the use of reproductive medicine, adoption or foster care, or choosing a life without children. Family-building decisions must be made amidst the lingering and long-term effects of cancer, which may include physical, psychosocial, and financial concerns. Follow-up fertility counseling post-treatment needs to be incorporated into survivorship care programs. Evidence-based support resources should be developed to guide providers and facilitate patients' understanding of their options and steps to prepare for future family-building, if desired.

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**Table 1**

Descriptive characteristics of 314 young adult female cancer survivors treated with gonadotoxic therapy

<b>Sociodemographic</b>		
<b>Age (years), M=29.7, SD=4.1</b>		
<b>Age at diagnosis (years), M=23.5, SD=7.3</b>		
	<b>n</b>	<b>%</b>
White	253	81
Relationship status		
Married/partnered	189	60
Single	125	40
Non-Hispanic/Latina	24	8
Completed college or higher	221	70
Nulliparous	236	75
<b>Clinical Information</b>		
<b>Cancer type (most common)</b>		
Lymphoma	74	24
Breast	61	19
Leukemia	38	12
Colorectal	25	8
<b>Treatment Impacting Fertility</b>		
Surgery	27	9
Radiation	51	16
Chemotherapy	256	82
Bone marrow transplant	32	10
<b>Fertility-related</b>		
Been told infertile	104	33
Underwent FP	58	19

Multiple regression analysis to evaluate quality of life effects of unmet fertility information needs, reproductive concerns, and decisional conflict.

**Table 2**

Step	Models predicting quality of life (QOL) <sup>a</sup>	R <sup>2</sup>	B	SE	$\beta$	t	p
<b>MODEL 1: Unmet Fertility Information Needs (F[7,221]=5.13, p&lt;.001)</b>							
1	Constant	0.10	0.10	7.61	0.93	8.16	<.001
	Control variables						
	Age at survey		-0.08	0.03	-0.17	-2.50	0.013
	Years post-treatment		0.03	0.02	0.09	1.43	0.156
	Employment (0=unemployed)		0.91	0.32	0.19	2.82	0.005
	Income (0=less than \$50k)		0.72	0.27	0.18	2.64	0.009
	Relationship status (0=single)		0.20	0.29	0.05	0.71	0.480
	Nulliparity (0=no children)		0.18	0.32	0.04	0.55	0.584
2	<b>Unmet fertility information needs<sup>b</sup></b>	<b>0.14</b>	<b>0.04</b>	<b>0.22</b>	<b>0.07</b>	<b>3.30</b>	<b>0.001</b>
<b>MODEL 2: Reproductive Concerns (F[7,166]=3.84, p=.001)</b>							
1	Constant	0.07	0.07	10.3	1.20	8.61	<.001
	Control variables						
	Age at survey		-0.60	0.04	-0.13	-1.59	0.114
	Years post-treatment		0.30	0.03	0.09	1.22	0.224
	Employment (0=unemployed)		0.91	0.35	0.20	2.63	0.009
	Income (0=less than \$50k)		0.53	0.29	0.14	1.82	0.071
	Relationship status (0=single)		-0.11	0.31	-0.03	-0.36	0.717
	Nulliparity (0=no children)		0.01	0.33	0.00	0.02	0.986
2	<b>Reproductive Concerns<sup>b</sup></b>	<b>0.14</b>	<b>0.07</b>	<b>-0.74</b>	<b>0.21</b>	<b>-3.55</b>	<b>&lt;.001</b>
<b>MODEL 3: Decisional Conflict (F[7,141]=2.08, p&lt;.05)</b>							
1	Constant	0.05	0.05	8.85	1.18	7.52	<.001
	Control variables						
	Age at survey		-0.05	0.04	-0.10	-1.16	0.250

Models predicting quality of life (QOL) <sup>a</sup>	B	SE	$\beta$	t	p
Years post-treatment	0.04	0.03	0.10	1.27	0.205
Employment (0=unemployed)	0.65	0.38	0.14	1.71	0.090
Income (0=less than \$50k)	0.34	0.32	0.09	1.05	0.294
Relationship status (0=single)	-0.28	0.35	-0.08	-0.81	0.421
Nulliparity (0=no children)	0.34	0.35	0.09	0.97	0.333
<b>2 Decisional Conflict<sup>b</sup></b>	<b>-0.01</b>	<b>0.01</b>	<b>-0.21</b>	<b>-2.58</b>	<b>0.011</b>

SE, standard error

<sup>a</sup>Three multiple regression models were specified with quality of life as the dependent variable.

<sup>b</sup>Higher scores indicate greater unmet information needs, reproductive concerns, and decisional conflict ( $p < .05$ ). Controlling for key sociodemographic covariates, greater unmet fertility information needs (Model 1), greater reproductive concerns (Model 2), and greater decisional conflict about fertility and family-building (Model 3) contributed to lower quality of life.