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PHYSICIAN PERCEPTIONS AND PRACTICE PATTERNS REGARDING FERTILITY PRESERVATION IN HEMATOPOIETIC CELL TRANSPLANT RECIPIENTS

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Abstract

Physician practice variation may be a barrier to informing hematopoietic cell transplant (HCT) recipients about fertility preservation (FP) options. We surveyed HCT physicians in the United States to evaluate FP knowledge, practices, perceptions and barriers. Of the 1035 physicians invited, 185 completed a 29-item web-survey. Most respondents demonstrated knowledge of FP issues and discussed and felt comfortable discussing FP. However, only 55% referred patients to an infertility specialist. Most did not provide educational materials to patients and only 35% felt that available materials were relevant for HCT. Notable barriers to discussing FP included perception that patients were too ill to delay transplant (63%), patients were already infertile from prior therapy (92%) and time constraints (41%). Pediatric HCT physicians and physicians with access to an infertility specialist were more likely to discuss FP and to discuss FP even when prognosis was poor. On analyses that considered physician demographics, knowledge and perceptions as predictors of referral for FP, access to an infertility specialist and belief that patients were interested in FP were observed to be significant. We highlight variation in HCT physician perceptions and practices regarding FP. Physicians are generally interested in discussing fertility issues with their patients but lack educational materials.

Keywords

Hematopoietic cell transplantation; autologous; allogeneic; fertility preservation; infertility; pregnancy; practice patterns

INTRODUCTION

Hematopoietic cell transplantation (HCT) has been associated with relatively high rates of infertility in both men and women.[1-8] However, fertility preservation (FP) among HCT recipients presents several challenges and practice variation among transplant physicians may be a barrier. Provider negative perceptions of the importance of fertility and low rates of discussion or referrals for FP have been reported to be among the barriers to FP in cancer patients and likely apply to physicians caring for HCT recipients.[9-13] Additional physician factors include specialty, age, knowledge and attitudes toward FP, and comfort with the topic. In addition, several patient factors such as prognosis, insurance status, availability of resources, and cost of procedures may also influence physician perceptions. HCT may have to be pursued urgently as patients frequently have diseases that are at high risk for relapse and physicians may not consider FP as a priority or may not feel that a patient has time to delay transplant to pursue FP. Finally, physicians may be reluctant to discuss FP with patients who have poor prognosis. In a survey of United States (US) oncologists, Quinn et al

found that only 47% of respondents routinely referred cancer patients of childbearing age to a reproductive endocrinologist, a practice recommended in the 2006 American Society of Clinical Oncology (ASCO) guidelines for oncologists.[10] To better understand physician perceptions and practice patterns regarding fertility after HCT, we conducted a national survey of adult and pediatric HCT physicians in the US. This study fills the gap in knowledge about provider specific barriers to FP in HCT recipients.

METHODS

Survey Instrument

We adapted a questionnaire that has been previously validated and used to assess oncologists' perceptions and practice patterns regarding FP among cancer patients.[10, 14, 15] With permission and participation of the authors, the survey was modified to address similar issues among HCT physicians. The final instrument (Supplement) maintained the broad survey components and content areas that were established by extensive preliminary studies. These domains included: (1) FP knowledge; (2) practice behaviors regarding FP; (3) barriers to FP; (4) FP attitudes and perceptions; and (5) demographic and practice information.

The survey instrument was piloted among 14 physicians from 6 transplant centers who were not associated with the study to obtain feedback on clarity and interpretation of questions and to estimate the time required to complete the survey. The final survey instrument consisted of 29-items and took 5-10 minutes to complete. The responses were generally on a Likert scale indicating degree of agreement with a list of statements (strongly agree to strongly disagree). Respondents were asked to respond based on their experience with HCT recipients who could now or later get pregnant or father a child (patient age 0-45 years).

Survey Administration

The study was conducted under guidance of the Institutional Review Board of the National Marrow Donor Program. Transplant centers that participate in the Center for International Blood and Marrow Transplant Research (CIBMTR) observational research database provide a list of names and email addresses of transplant physicians who practiced in their facility. This included all US centers performing allogeneic and autologous HCT and the majority of centers performing autologous HCT only. We used this list to invite 1035 transplant physicians to participate in the survey. Identifying information on survey invitees (name and email address) was not available to the study team – this information was available to research staff from the CIBMTR who were not involved with the study and were responsible for sending survey invites, tracking responses and sending reminders to non-respondents. Hence, survey responses were anonymous to the study team and the respondents could not be identified in the final dataset available for analysis. No incentive was provided for participation. Survey invites were sent via email with a link to the survey website. Two subsequent followup email reminders were sent 4 weeks apart.

Statistical Analysis

We used center volume to classify transplant center size. One question each asked respondents to report the average annual number of autologous and allogeneic HCT at their

center (<20, 20-50, 51-100, 101-200 and >200). Based on the distribution of responses to both questions, we classified centers as small (≤50 autologous HCT and <20 allogeneic HCT/year), medium (did not meet criteria for small or large size centers), and large (>100 autologous or >50 allogeneic HCT/year).

For descriptive purposes, we combined “Strongly agree” and “Agree” responses and “Always” and “Often” responses into one category. Similarly, we grouped “Strongly disagree” and “Disagree” responses and “Rarely” and “Never” responses.

Physician demographic characteristics and survey responses were summarized using frequencies and proportions. Bivariate analyses were performed to assess the association of likelihood of referring patients to an infertility specialist with physician characteristics and FP knowledge and perceptions. This was based on response to the question “I refer patients who have questions about fertility to an infertility specialist or reproductive endocrinologist”. Physicians who responded “Always” or “Often” to this question were compared with physicians who responded “Sometimes”, “Rarely” or “Never”. Physician factors considered for this analysis included: gender, year of graduation from medical school, size of transplant center, availability of infertility specialist, and whether respondent had previously taken care of patients who reported pregnancy after HCT. In addition to physician factors, we considered responses to questions on ‘fertility preservation knowledge’ as predictive factors for referral to an infertility specialist (response of ‘Strongly agree” or “Agree” to 4 or 5/5 questions in this section). We also considered “Strongly agree” or “Agree” response to one question under “fertility preservation attitudes and perceptions’ section (“patients are interested in learning about the effects of transplant on their fertility”) as a predictive factor for referral. All analyses were conducted using SAS statistical software (version 9.2, SAS Institute, Cary, NC). All P values are two sided with a statistical significance level set at 0.05.

RESULTS

Respondent Demographics

The overall response rate for our survey was 18% (185/1035). Table 1 shows the characteristics of survey respondents. Half of respondents (50%) practiced at large centers (>100 autologous or >50 allogeneic HCT annually). Access to an infertility specialist within their own center was available to 58% of respondents while another 25% reported access to an infertility specialist at another institution in their community. Physicians with access to an infertility specialist were significantly more likely to be practicing at a large transplant center (60% vs. 8% of those without access, $P < 0.001$).

We did not collect demographic characteristics of survey non-respondents and hence could not compare them with that of respondents. However, we contrasted characteristics of our cohort with information available through the American Society for Blood and Marrow Transplantation BMT Physician Survey that was conducted in 2010 (personal communication with Robert Krawisz). This survey reported that 70% of US transplant physicians were male (vs. 63% in our study), 14% took care of pediatric patients (vs. 14% in

our study), and 38% had completed training in blood and marrow transplantation prior to 1990 (vs. 49% of our study respondents had graduated from medical school prior to 1990).

Survey Responses

Figure 1 summarizes survey responses. Figures 2 and 3 highlight reported practice behaviors and barriers to FP based on practice type and access to infertility specialist.

Fertility preservation knowledge—The vast majority of respondents recognized that HCT has been linked to infertility and demonstrated recognition of present standard-of-care options for FP. Responses did not vary by gender or by patient population treated. Physicians who had access to an infertility specialist were more likely to recognize that psychosocial fertility-related distress occurs among transplant recipients (93% with access vs. 69% with no access; P=0.01).

Fertility preservation practice behaviors—Most respondents discussed the impact of transplant on future fertility and felt comfortable discussing fertility issues, although only half of respondents discussed FP with patients whose prognosis was poor. Most did not consult an infertility specialist with questions about FP and only half referred their patients. Educational materials on FP were generally not provided and only 35% felt that available materials were relevant to HCT recipients. Importantly, 40% of transplant physicians were unaware of ASCO fertility guidelines,[1] and another 29% said they ‘rarely’ or ‘never’ used these guidelines.

No notable differences in practice behaviors were observed by physician gender; except that a higher proportion of women physicians discussed FP with patients whose prognosis was poor (66% vs. 43% male physicians, P=0.02). We noted differences in practice behaviors among respondents who cared for adult recipients only compared to those who cared for pediatric recipients. While 98% of pediatric transplant physicians discussed FP with their patients, only 85% of adult physicians did (P=0.02). Pediatric providers were far more likely to discuss FP even when prognosis was poor (77% vs. 38% for adult physicians, P<0.0001). The most striking differences were noted based on access to an infertility specialist. Transplant physicians with access to an infertility specialist were significantly more likely both to consult (32% vs. 0%, P<0.0001) and to refer (60% vs. 0%, P<0.0001) patients to an infertility specialist, felt more comfortable in discussing FP with their patients (84% vs. 31%, P<0.0001), and were more likely to discuss FP when prognosis was poor (53% vs. 15%, p = 0.001). Additionally, providers with access to infertility specialists were more likely to provide educational materials (29% vs. 0%, P<0.0001) and were aware of the ASCO fertility guidelines (85% vs. 36%, P=0.009).

Barriers to fertility preservation—Many transplant physicians felt that patients were too ill to delay transplant for pursuit of FP options but generally recognized that patients did wish to discuss this topic. The majority felt that their patients were already infertile due to prior treatment. Barriers to FP included lack of access to infertility specialist, time constraints affecting ability to discuss fertility issues, ability of patients to afford FP and insurance coverage for FP (Table 2).

We observed no differences in reported barriers by physician gender. However, when considering practice type, pediatric practitioners were less likely to feel that their patients were too ill to delay transplant for FP (47% vs. 70% for adult providers, P=0.02), were less likely to feel that their patients were not interested in discussing fertility issues (8% vs. 24%, P=0.04) and were less likely to report that time constraints affected their ability to discuss FP (10% vs. 26%, P=0.003). Once again, the greatest differences were observed by access to an infertility specialist. Those with access were less likely perceive that patients do not want to discuss fertility (14% vs. 69% without access, P< 0.0001), report that their patients were already infertile due to prior therapy (40% vs. 92%, P<0.0001), report that lack of infertility specialists was a barrier (5% vs. 77%, P<0.0001), and perceive time constraints limited their ability to discuss fertility issues (16% vs. 77%, P<0.0001).

Fertility preservation attitudes and perceptions—Transplant physicians recognize that patients are interested in learning about the impact of transplant on their fertility. A greater proportion of respondents felt that risks of infertility were higher among recipients of total body irradiation, myeloablative conditioning and allogeneic HCT. There were no notable differences by gender or by practice type. Physicians with access to an infertility specialist were more likely to perceive patients were interested in learning about fertility (88% vs. 23% with no access, P<0.0001).

Factors Predictive for Consultation or Referral to Infertility Specialist

Table 3 lists survey responses and characteristics of physicians who consulted or referred their patients to an infertility specialist. Physicians who reported that they “Rarely” or “Never” consulted or referred were more likely to report specific perceived barriers to FP (e.g., patients not interested, referral challenges and time constraints). Physician gender, practice type or center size was similar among respondents who did and did not consult or refer patients to infertility specialists. Physicians who graduated from medical school prior to 1990 were more likely to consult or refer. Finally, access to an infertility specialist was an important determinant of whether physicians consulted or referred their patients for FP.

We conducted bivariate analyses that considered physician characteristics, knowledge about fertility issues in HCT recipients, and their perception about whether HCT recipients were interested in learning about effects of transplant on fertility. Two factors were significantly associated with referral to infertility specialist – access to an infertility specialist (0 referrals among physicians with no access, P<0.001) and physicians belief that patients were interested in learning about the effects of transplant on fertility (OR 6.07, 95% CI: 1.25-25.60, P=0.02).

DISCUSSION

This is the first study to provide important information about the knowledge, attitudes, practices and referral patterns of adult and pediatric HCT physicians regarding FP among transplant recipients. Several important themes emerge from our analysis. First, most transplant physicians were knowledgeable and comfortable discussing fertility issues relevant to their patients. This is in contrast to general oncologists where discussion rates are lower.[10, 13] However, awareness and use of formal guidelines, educational materials, and

resources for both physicians and patients were lacking. These rates were similar to those found among general oncologists who treat adults but lower than those found among a survey of pediatric oncologists.[10, 16] A need for physician and patient resources specific for HCT recipients was identified, as many physicians felt that FP guidelines and materials for cancer patients were not relevant to HCT recipients.

We identified several physician reported barriers that hinder discussions with patients about FP. Many physicians felt that transplant usually has to be pursued urgently and delaying transplant to pursue FP may not be in the best interest of the patient and that pre-transplant therapies can cause infertility. This concern is valid for many patients who have high-risk diseases that require urgent HCT and even though FP is discussed, there may not be sufficient time to pursue FP or FP methods may prove to be ineffective. Other perceptions that may serve as barriers to discussing FP were identified, including inability to afford FP by patients, lack of insurance coverage for FP, lack of patient interest in discussing FP and lack of sufficient knowledge to discuss FP. Insufficient time to discuss fertility issues was noted as a barrier by some. Availability of HCT specific physician and patient educational resources may mitigate some of these barriers. In addition, models of care may be considered where discussion about FP could be conducted by another provider from the transplant center (e.g., mid-level providers or social workers).

An important determinant in discussing fertility with patients undergoing transplant is having access to an infertility specialist. Transplant physicians without access to these specialists were far more likely to underestimate the psychosocial impact of infertility and to believe that patients do not wish to discuss fertility. They were significantly less likely to consult and to refer to infertility specialists, and were even less aware of guidelines, educational materials, and resources available to assist them and their patients. Our findings behoove transplant physicians to reach out to and foster collaborative relationships with their colleagues who are experts in FP to facilitate appropriate and timely care of HCT recipients who are interested in FP. In addition, general adult and pediatric oncologists may not always discuss and pursue FP with their patients.[10, 13, 16] Education and outreach to oncologists would also facilitate appropriate and timely interventions for FP prior to a patient referral for HCT.

We also observed significant differences between adult treating and pediatric transplant physicians' knowledge, attitudes, and practices. Most notably, pediatric providers were more likely to discuss infertility with patients who had poor prognosis and were less likely to feel that their patients were too sick to discuss FP or that time constraints limited this conversation. However, practice type was not associated with likelihood of consultation or referral to infertility specialist.

In their survey of US oncologists, Quinn et al observed that referrals for FP were more likely among female physicians, physicians with favorable attitudes about FP, and physicians whose patients routinely asked about FP.[10] We also found that the likelihood of referral was higher among physicians who felt that their patients were interested in learning about fertility and FP. Physician characteristics such as gender, practice type, year of medical

school graduation or transplant center size were not found to be predictive of referral to infertility specialist in multivariate analyses.

Some limitations of our study have to be considered. The response rate to our survey was lower than what has been reported for email/web physician surveys not providing an incentive (typically 25-40%).[17, 18] Furthermore, physicians who elected to participate may be relatively more knowledgeable about survivorship and fertility issues, and thus this sample may not be representative of the transplant community and the barriers to FP may even be greater among transplant physicians in general. This bias may also explain the high proportion of respondents who felt comfortable discussing and actually discussed FP with their patients. On the same note, physicians might overestimate their frequency of discussing impact of HCT on fertility.[19] Also, our findings are specific to physicians practicing in the US and different medical, cultural and economical factors may influence FP practices for physicians who practice in other countries.

In conclusion, our study highlights the variation in practices and perceptions about FP among US adult and pediatric HCT physicians and identifies barriers to having physician-patient discussions about the impact of HCT on fertility. We also identify a need to develop educational materials and guidelines for physicians that may facilitate the discussion of FP with their patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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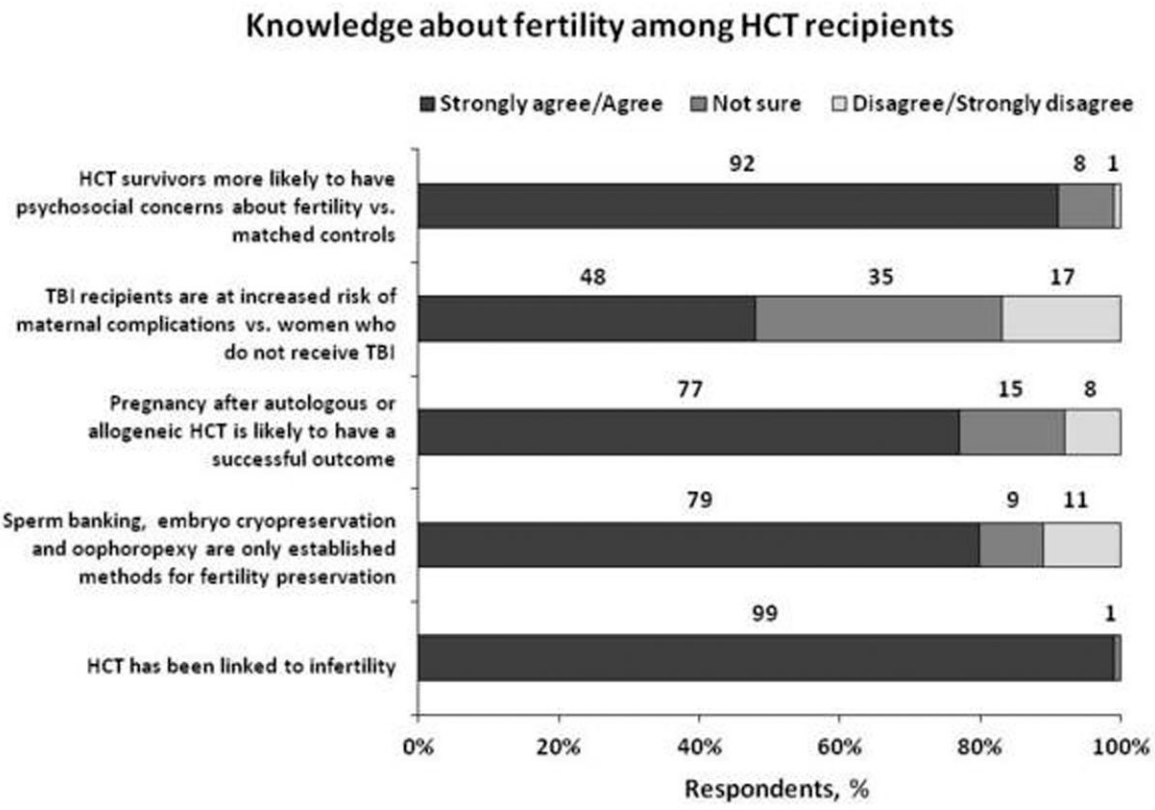
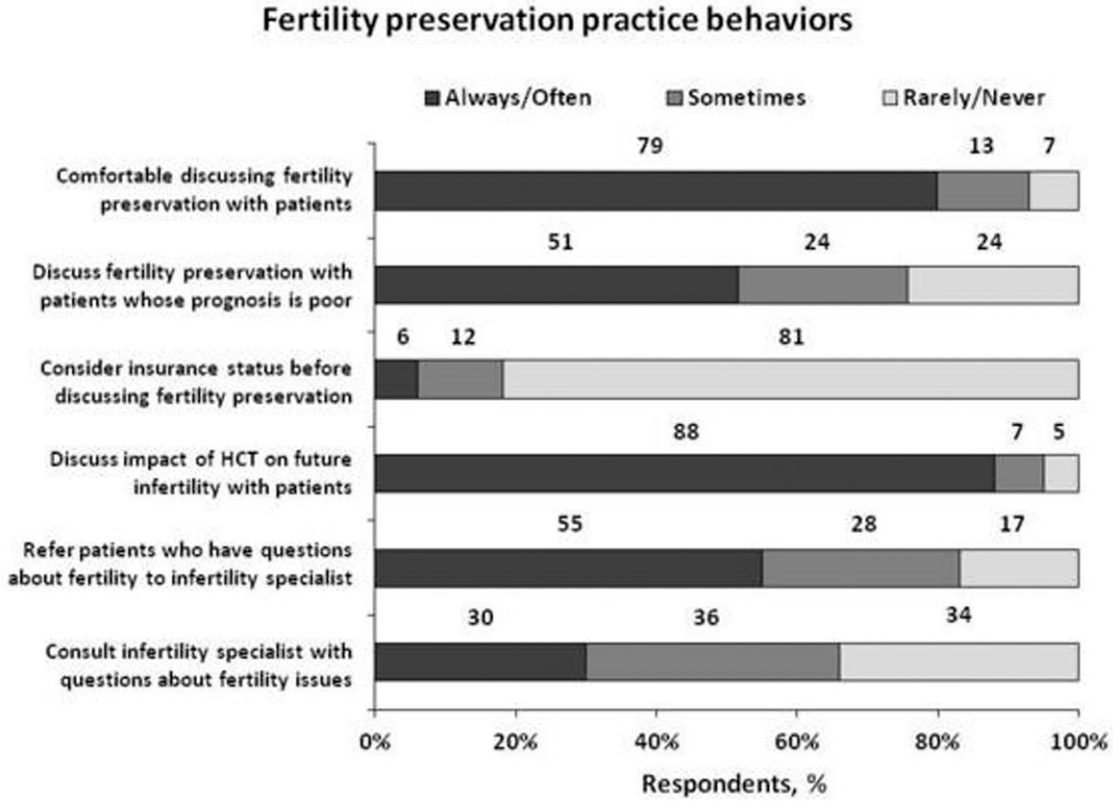
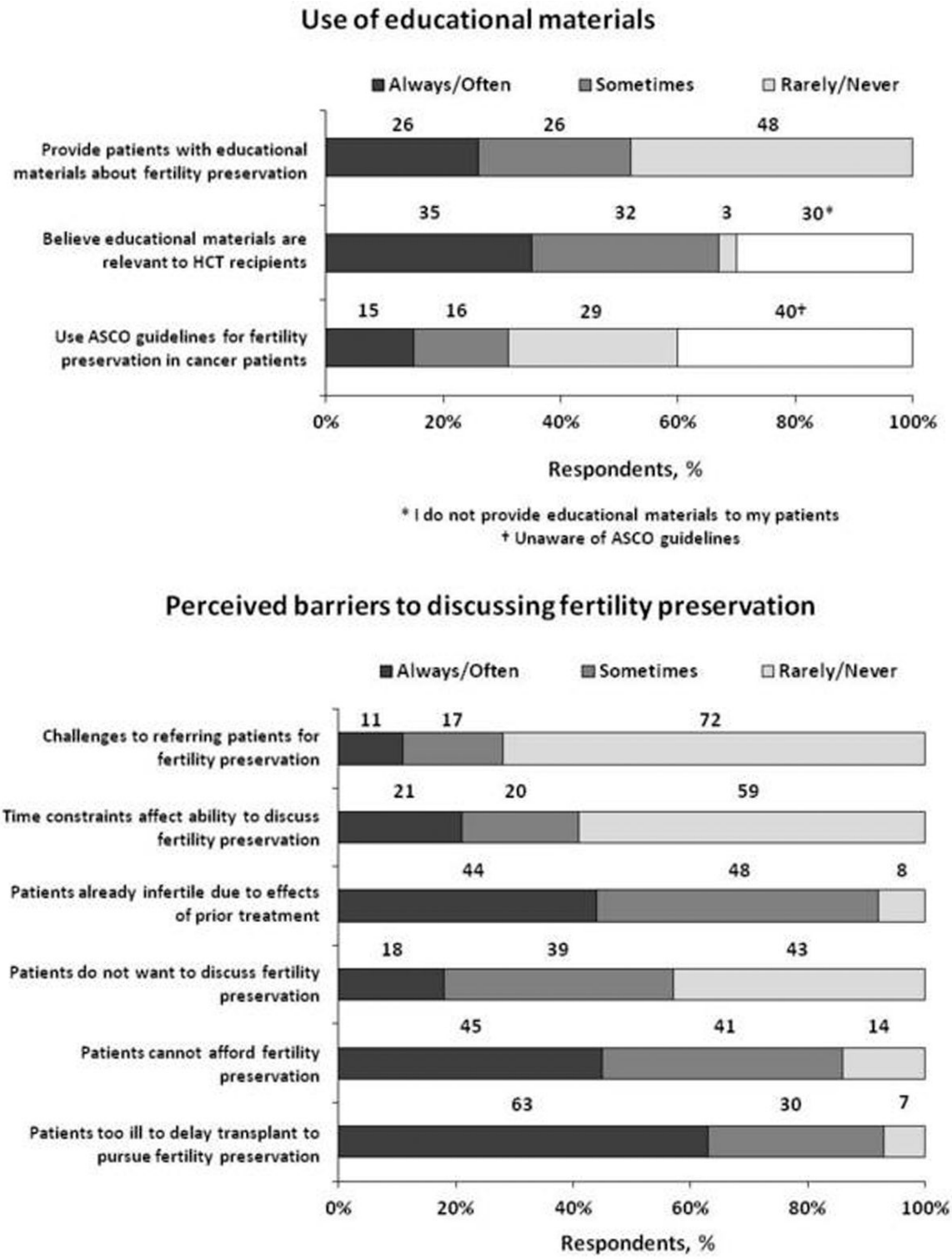






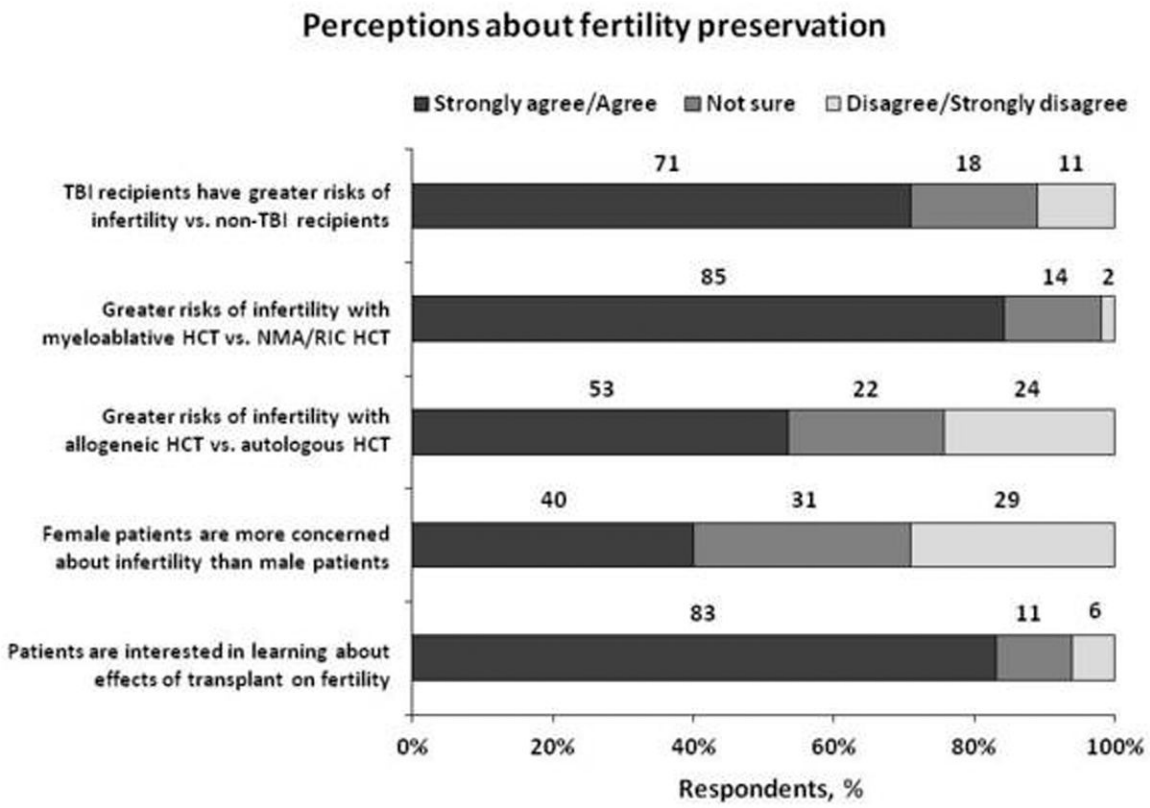
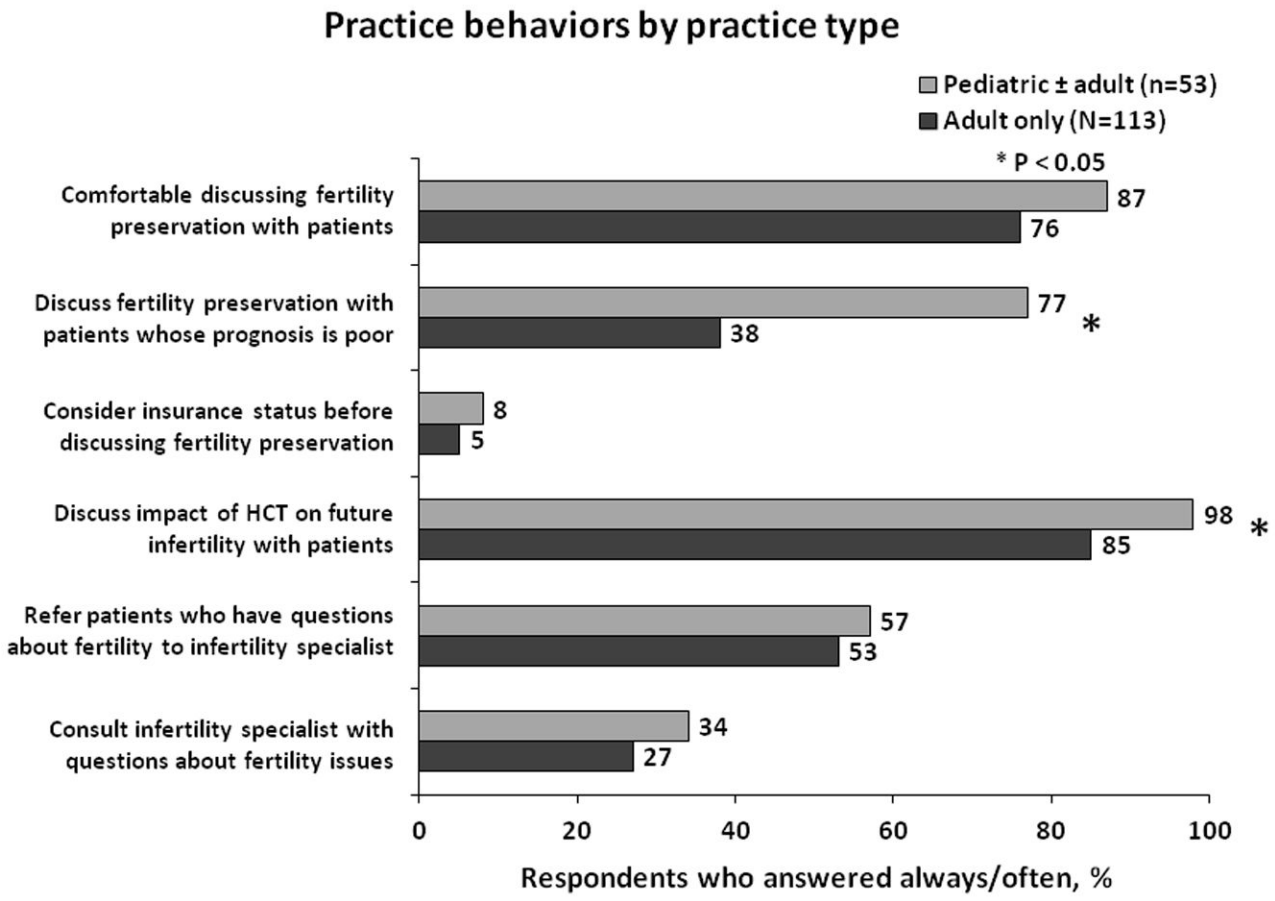


Figure 1.

Physician responses to survey on fertility preservation perceptions and practice behaviors showing: (a) knowledge about fertility among HCT recipients, (b) fertility preservation practice behaviors, (c) use of educational materials, (d) perceived barriers to discussing fertility preservation and (e) perceptions about fertility preservation



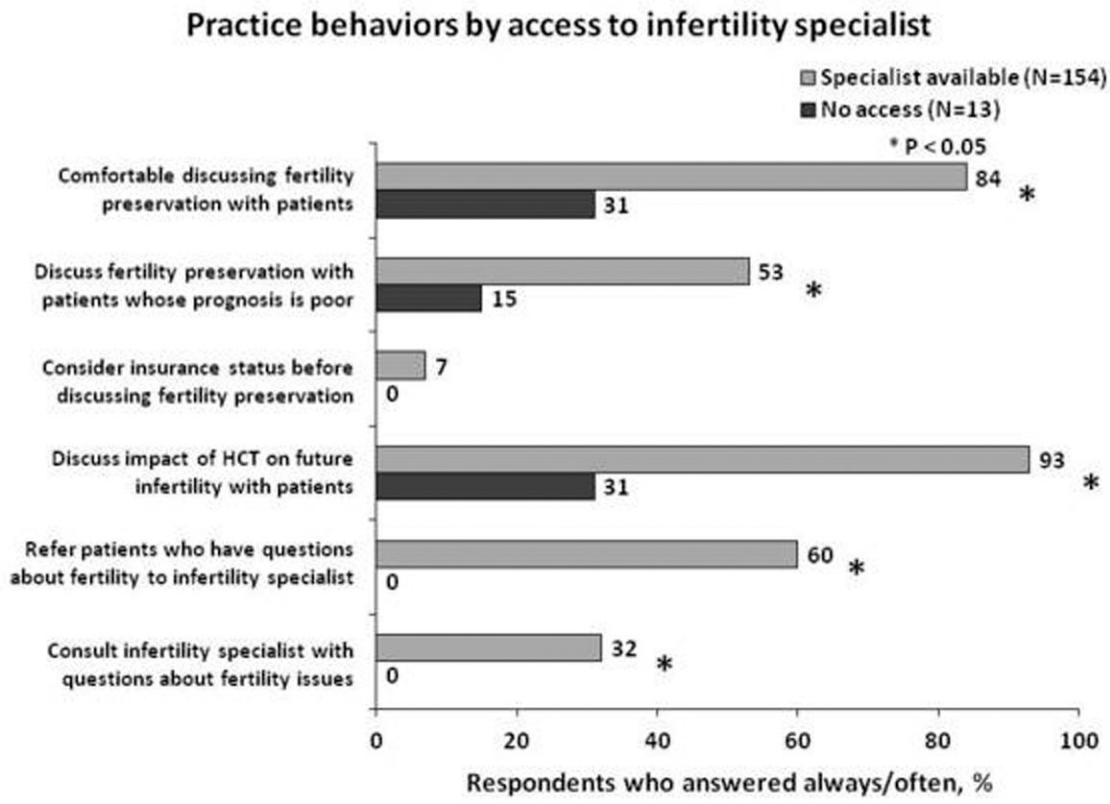
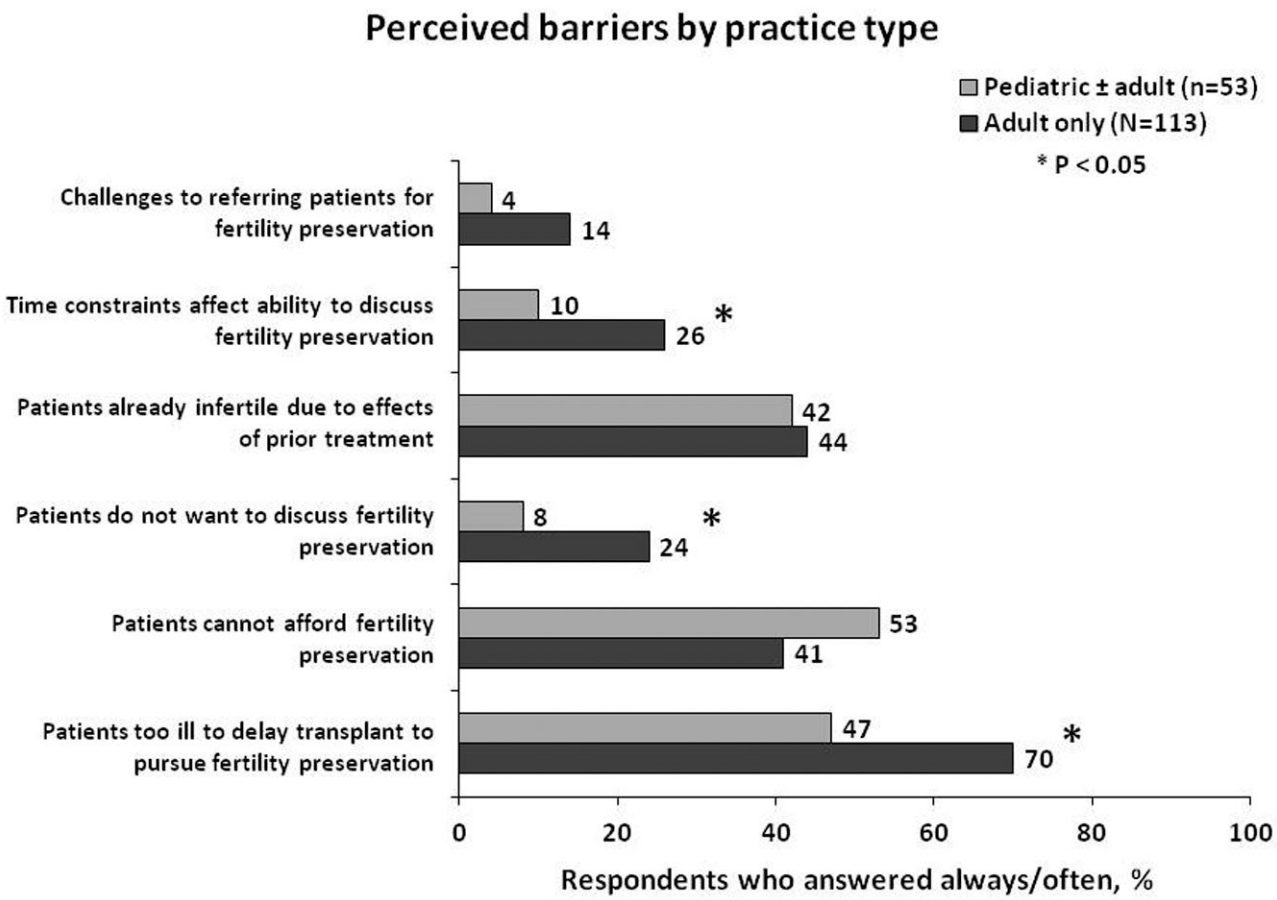


Figure 2.

Reported fertility preservation practice behaviors for HCT recipients by physician practice type (adult HCT only vs. pediatric ± adult HCT) and access to an infertility specialist at the same institution or within their community



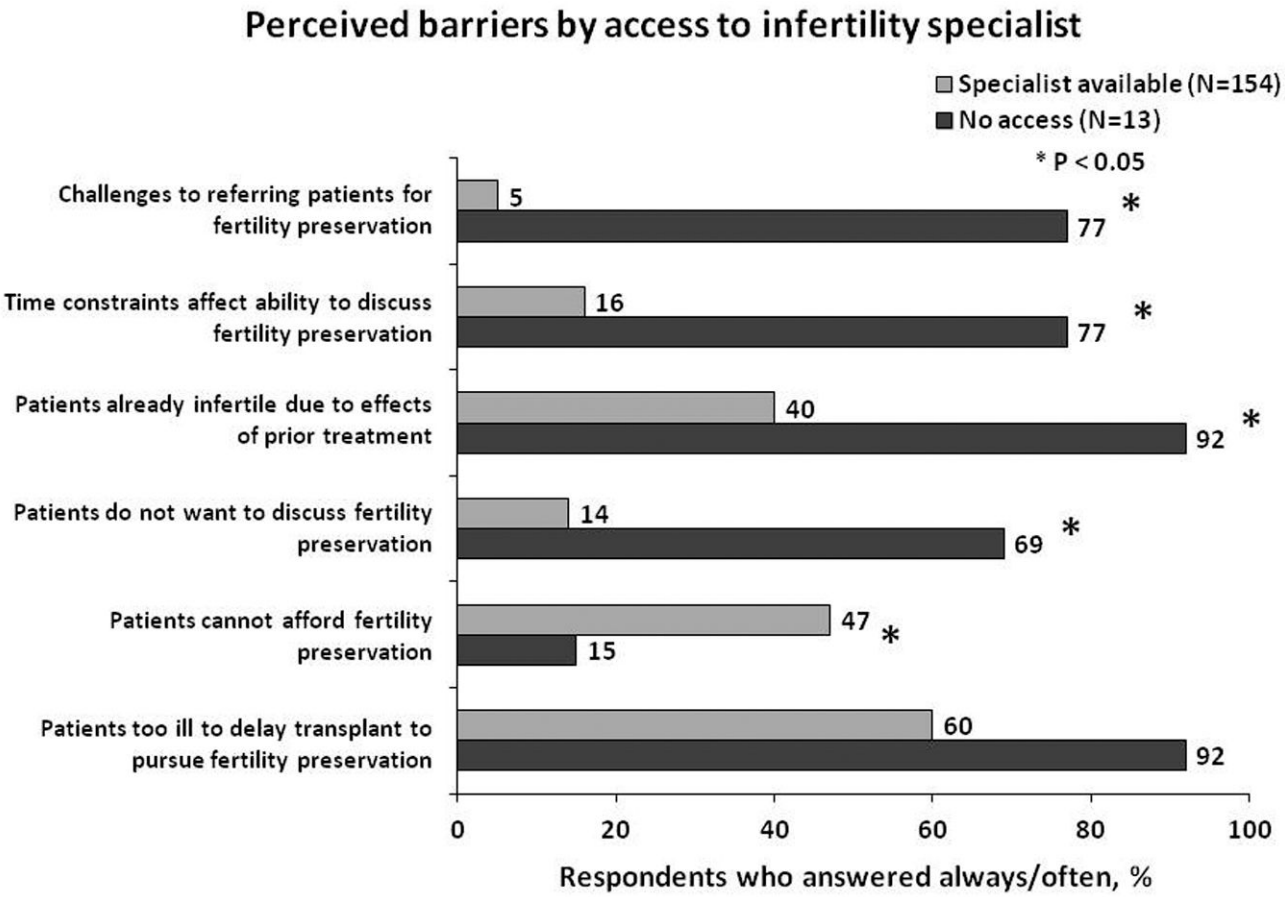


Figure 3.

Perceived barriers to discussing fertility preservation with HCT recipients by physician practice type (adult HCT only vs. pediatric ± adult HCT) and access to an infertility specialist at the same institution or within their community

Table 1

Demographic characteristics of physicians who responded to the survey

Characteristic	N (%)
Sample size	185
Race/ethnicity	
Hispanic or Latino	7 (4)
Not Hispanic or Latino	163 (88)
Declined	15 (8)
Race	
White	135 (73)
Asian	30 (16)
More than one race	2 (1)
Declined	18 (10)
Gender	
Male	116 (63)
Female	53 (29)
Declined	16 (9)
Year of medical school graduation	
1965-1969	3 (2)
1970-1979	33 (18)
1980-1989	54 (29)
1990-1999	56 (30)
2000-2004	16 (9)
Declined	23 (12)
Patient age treated	
Adult only	113 (61)
Pediatric only	36 (20)
Both adult and pediatric	17 (9)
Declined	19 (10)
Center size (based on self-reported transplant volume/year)	
Small	23 (12)
Medium	51 (28)
Large	93 (50)
Declined	18 (10)
Access to an infertility specialist or reproductive endocrinologist	
Yes, within respondents institution	107 (58)
Yes, in another institution in respondents community	47 (25)
No	13 (7)
Declined	18 (10)

Characteristic	N (%)
Median number of HCT recipients that respondent has cared for who reported getting pregnant or fathering a child (range)	3 (0-30)

Table 2

Primary perceived barriers to discussing fertility preservation with HCT recipients

Characteristic	Responses* (%)
My typical patient is too ill to delay treatment	102 (55%)
Insurance does not cover fertility preservation	64 (35%)
Patients cannot afford fertility preservation	61 (33%)
Time constraints limit fertility preservation discussion	50 (27%)
Do not have sufficient knowledge to discuss fertility preservation	30 (16%)
Do not have information to give to patients about fertility preservation	28 (15%)
Patients do not want to discuss fertility preservation	25 (14%)
There is no place/person to refer my patients	22 (12%)
No barriers	29 16%)

* Respondents could choose multiple responses

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Table 3

Fertility preservation barriers reported and characteristics of physicians who consulted or referred their patients to an infertility specialist

Characteristic	Consult infertility specialist, %†			P-value	Refer to infertility specialist, %†			P-value
	Always/often	Sometimes	Rarely/never		Always/often	Sometimes	Rarely/never	
N	54	64	62		98	50	31	
Barriers*								
Patients too ill to delay transplant	47	64	76	0.008	55	69	77	0.14
Patient cannot afford fertility preservation	45	48	43	0.64	48	43	37	0.39
Patients do not want to discuss fertility preservation	6	13	34	0.0003	13	12	45	0.0001
Patients already infertile	39	33	60	0.03	38	47	61	0.16
No place to refer patients	4	2	26	<0.0001	3	4	45	<0.0001
Time constraints	4	18	37	0.001	12	18	53	<0.0001
Insurance does not cover fertility preservation	55	40	38	0.03	45	45	37	0.09
Physician characteristics								
Gender				0.45				0.90
Male	73	63	71		70	66	70	
Female	27	37	29		30	34	30	
Year of medical school graduation				0.02				0.05
Prior to 1990	62	65	44		62	56	37	
1990 and later	38	35	56		38	44	63	
Practice type				0.59				0.53
Adult patients only	63	69	72		67	65	77	
Pediatric ± adult patients	37	31	28		33	35	23	
Center size				0.59				0.17
Small	8	14	18		12	9	28	

Characteristic	Consult infertility specialist, %†			P-value	Refer to infertility specialist, %†			P-value
	Always/often	Sometimes	Rarely/never		Always/often	Sometimes	Rarely/never	
Medium	33	28	32		30	30	31	
Large	59	58	50		58	61	41	
Access to infertility specialist				<0.0001				<0.0001
Yes, in my institution	80	64	52		69	70	41	
Yes, in another institution in my community	20	36	27		31	26	21	
No	0	0	21		0	4	38	

*"Always" or "Often" responses are shown

†Column percent; P-value compares "Always/often", "Sometimes" and "Rarely/never"