

5-2014

Cancer Diagnosis During Pregnancy: Evaluating the Challenges Faced by Oncologists

Shannon Kaye Mulligan

Follow this and additional works at: http://digitalcommons.library.tmc.edu/utgsbs_dissertations



Part of the [Obstetrics and Gynecology Commons](#), and the [Oncology Commons](#)

Recommended Citation

Mulligan, Shannon Kaye, "Cancer Diagnosis During Pregnancy: Evaluating the Challenges Faced by Oncologists" (2014). *UT GSBS Dissertations and Theses (Open Access)*. 458.

http://digitalcommons.library.tmc.edu/utgsbs_dissertations/458

This Thesis (MS) is brought to you for free and open access by the Graduate School of Biomedical Sciences at DigitalCommons@TMC. It has been accepted for inclusion in UT GSBS Dissertations and Theses (Open Access) by an authorized administrator of DigitalCommons@TMC. For more information, please contact laurel.sanders@library.tmc.edu.

CANCER DIAGNOSIS DURING PREGNANCY: EVALUATING THE CHALLENGES
FACED BY ONCOLOGISTS

by

Shannon Kaye Mulligan, BA, BS

APPROVED:

Syed S. Hashmi, MD, MPH, PhD
Supervisory Professor

Larissa Meyer, MD, MPH

Mildred Ramirez, MD

Myla Ashfaq, MS, CGC

Claire Singletary, MS, CGC

APPROVED:

Dean, The University of Texas
Graduate School of Biomedical Sciences at Houston

CANCER DIAGNOSIS DURING PREGNANCY: EVALUATING THE CHALLENGES
FACED BY ONCOLOGISTS

A
THESIS

Presented to the Faculty of
The University of Texas
Health Science Center at Houston
and
The University of Texas
MD Anderson Cancer Center
Graduate School of Biomedical Sciences
in Partial Fulfillment
of the Requirements
for the Degree of
MASTER OF SCIENCE

by

Shannon Kaye Mulligan, BA, BS
Houston, Texas

May, 2014

ACKNOWLEDGEMENTS

The success of any project depends largely on the encouragement, commitment, and hard work of many others apart from myself. I would like to express my gratitude for my advisor and acting thesis chair, Kate Wilson, MS, CGC for her support, help, and having an idea that I was excited to develop with her as my thesis project. Without her encouragement and guidance, this project would not have been possible. I would like to thank my committee, Dr. Syed Hashmi, Dr. Larissa Meyer, Dr. Mildred Ramirez, Claire Singletary, MS, CGC and Myla Ashfaq, MS, CGC; their direction, input, and support was vital for the development and success of the project, and I am grateful for their continued support. I would like to thank Dr. Syed Hashmi for coming on as the official chair of the project when it was needed, and for being invaluable in the data analysis process, particularly for suggesting how to approach my analysis so that it would be as comprehensive and thorough as possible.

I would like to thank those individuals whose input and willingness to contribute was instrumental in the development of this project: Dr. Angel Rodriguez for his input in the development of this project and involvement at the Methodist Hospital, and Amber Froehlich for being an invaluable resource in navigating the IRB there. I would like to thank those who helped me attend tumor boards at the Methodist Hospital, including Dr. Angel Rodriguez and Dr. Aparna Kamat, for their help and flexibility in coordinating my attendance. I would like to thank Dr. Andrea Milbourne for helping in my efforts to include The UT M. D. Anderson Cancer Center in this project, and Dr. Larissa Meyer for helping facilitate IRB submission there. I would additionally like to thank Leslie Dunnington, MS, CGC, for her help in distributing surveys at the Memorial Hermann Hospital System, and helping ensure I had maximized my sample size. I am exceedingly grateful for all of the nurse navigators and hospital support personnel, for their willingness to help me in coordinating attending different tumor boards at the Memorial Hermann Hospital System, including Karen Davin, Jessica Burgess, Angela Sisk, Krystie Fenton, Deidra Teoh, Lilian Sweeney, Monica Pearles, Jasmine Hicks, Sylvia Brown, Carol Lewis, Amy Deutsch, and Ami Gates.

Finally, I would like to thank the directors and supervisors of the UT GCP in their encouragement and support throughout my training, and my classmates for their motivation and friendship along this journey. And I want to thank my family and friends, especially my husband for his unconditional support while I've worked towards becoming a genetic counselor.

CANCER DIAGNOSIS DURING PREGNANCY: EVALUATING THE CHALLENGES FACED BY ONCOLOGISTS

Shannon Kaye Mulligan, BA, BS

Advisory Professors: Syed S. Hashmi, MD, MPH, PhD; Kate Wilson, MS, CGC

Cancer during pregnancy is occurring more often than in the past, and it is estimated that cancer is diagnosed in approximately 1/1000 pregnancies. A consensus exists that management of these patients should prioritize survival of the mother and minimize teratogenic effects to the fetus, and utilize a multidisciplinary approach, involving medical oncology, surgical oncology, radiation oncology, radiology, and a maternal fetal medicine specialist. In spite of this consensus, there is not a standardized approach for treating cancer in women diagnosed during pregnancy. Due to the relative infrequency of this situation in the oncologic setting, the aims of this study were to determine how comfortable oncologists are discussing pregnancy issues related to treatment, specifically termination and fetal risks, to determine what oncologists view as their primary responsibilities in the management of a woman diagnosed with cancer during pregnancy, and to identify the challenges oncologists face when treating a woman diagnosed with cancer during pregnancy. An 18 question survey was developed and distributed to oncologists at The Methodist Hospital and the Memorial Hermann Hospital system. The results from 53 completed anonymous surveys showed that oncologists who have treated at least one patient diagnosed with cancer during pregnancy are significantly more likely to be comfortable treating this patient population ($p < 0.01$). Thus, providing care to one patient within this population may be sufficient to establish a level of comfort in providing clinic care to a patient diagnosed with cancer during pregnancy. Providers appear to recognize that a multidisciplinary approach is needed when treating this patient population, though have differing opinions regarding whom of these providers has the highest practice responsibility to address pregnancy-related topics, including termination of pregnancy and risk of teratogenic effects. Additionally, many providers acknowledge that barriers exist which create added challenges when treating this patient population.

TABLE OF CONTENTS:

Background.....	1
Materials and Methods.....	3
Results.....	3
Discussion.....	10
Appendix.....	13
References.....	19
Vita.....	22

LIST OF ILLUSTRATIONS:

Figure 1. Reported comfort level in treating a patient diagnosed..... 8
during pregnancy based on experience with this patient population

LIST OF TABLES:

Table 1. Participant Demographics..... 4

Table 2. Responses to the question pertaining to comfort level in.....5
discussing the effects of treatment

Table 3. Responses to the question pertaining to comfort level in..... 6
discussing prognosis, pregnancy options, and future considerations

Table 4. Patient management and practice responsibility..... 7

Table 5. Barriers which create challenges in managing patients..... 8
diagnosed with cancer during pregnancy

Background

Cancer during pregnancy is occurring more often than in the past, as women are delaying childbearing until later in life. Cancer is diagnosed in approximately 1/1000 pregnancies, with the most common cancers seen during pregnancy being breast cancer, cervical cancer, Hodgkin and Non-Hodgkin lymphoma, leukemias, and melanoma (1). The National Comprehensive Cancer Network (NCCN) published guidelines for treatment of breast cancer during pregnancy in 2006 (2). For additional cancers, a consensus exists that management should prioritize survival of the mother while minimizing teratogenic effects to the fetus (3); it is further suggested that a multidisciplinary approach be used, involving medical, surgical, and radiation oncology, radiology, and a maternal fetal medicine specialist (MFM) (4). In spite of this consensus, there is not a standardized approach for treating cancer in patients diagnosed during pregnancy.

Breast cancer is the most common cancer diagnosed in women, and the most common diagnosis during pregnancy. It is estimated to occur in 1/1500-1/4000 pregnancies, and approximately 10% of breast cancer patients younger than age 40 are diagnosed during pregnancy or up to one year postpartum (5, 6, 7). Several factors delay diagnosis, including physiological changes in the breast during pregnancy, making the diagnosis of advanced stage disease a common occurrence (8, 9). Breast surgery is safe during pregnancy, but a general agreement exists to postpone radiation therapy and endocrine therapy until the postpartum period, as both have been associated with a high risk of fetal toxicity (6, 10, 11). The young age at which pregnant women are diagnosed with breast cancer puts them at an increased likelihood of carrying a *BRCA1* or *BRCA2* mutation. In these instances, genetic testing for hereditary breast and ovarian cancer syndrome should be considered (12).

Additional cancers more commonly seen in pregnancy include cervical cancer, hematologic malignancies, leukemias, and melanoma. These diagnoses occur during pregnancy at rates from 1/6000 to 1/100000, with lymphomas being the most common, and melanoma being the most likely malignancy to metastasize to the placenta and fetus (3, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22). Treatment approaches for each of these cancers during pregnancy should be individualized depending on disease staging, gestational age, and treatment options.

When faced with a cancer diagnosis during pregnancy, a multidisciplinary approach is recommended, which may include oncologic specialties, surgery, and high risk obstetrics (9). Cancer management is associated with potential teratogenic effects, including clinical use of

supportive agents, ionizing radiation exposure, and infection-related fever (23, 24). Risks of fetal structural defects as a result of chemotherapy administration are greatest in the first trimester, and radiation therapy should be delayed until after delivery. Given the limited data regarding single-agent exposures, broad comparisons cannot be made to the risks associated with combination therapies utilized during cancer treatment (24). Chemotherapy treatment is thought to pose fewer risks when administered in the second and third trimesters, though exposure during this time has been associated with transient neonatal disorders. While these tend to resolve, the greatest concern associated with second and third trimester exposures is harmful effects on fetal brain development (7).

While some information is available regarding potential approaches to cancer management during pregnancy, outcome information is largely based on small numbers of case series. Additionally, pregnant women are excluded from nearly all cancer trials and drug trials, further preventing the establishment of clinical evidence to guide recommendations (11). In current practice, oncologists rarely recommend termination of pregnancy, as the historical practice of termination of pregnancy secondary to cancer has not been associated with improved survival (11, 25, 26, 27). The diagnosis of an aggressive or advanced disease may be an exception, as immediate treatment is needed to avoid patient mortality (11, 28, 29). Consideration of whether to terminate pregnancy following a cancer diagnosis should be made in the context of disease, agents and drugs to be used, probability of achieving a cure, and patient desires (30).

As the incidence of cancer during pregnancy continues to rise, clinicians will increasingly face challenges in managing cancer during pregnancy, particularly in developing a treatment plan to maximize maternal benefits and minimize the risk of adverse pregnancy outcomes (23). Studies in the past have tried to characterize approaches towards cancer during pregnancy, but information remains limited. Additionally, information regarding the scope of practice of oncologists in caring for a pregnant patient is scarce. A European study aimed to evaluate provider opinions and knowledge surrounding the treatment possibilities for patients with cancer in pregnancy and found that providers are uncertain regarding the timing and approach towards treating cancer during pregnancy (31). In light of deficiencies in the amount of information surrounding this topic in the oncologic setting, the goal of the current study was to gain more insight into the perceived views of pregnancy management and challenges faced by oncologists when treating women diagnosed with cancer during pregnancy.

Materials and Methods

A four-page survey was designed with 18 questions on oncologists' opinions and perceptions in the treatment of cancer during pregnancy (Appendix 1). The first section of the survey assessed oncologists' comfort level and experience with pregnant patients. The second half of the survey inquired about the practice responsibilities and challenges of oncologists when treating pregnant patients. Demographics, practice type, and self-reported number of pregnant cancer patients seen were also examined. Human subject research approval was obtained for the Methodist Hospital, the Memorial Hermann Health System, and the University of Texas Health Science Center by the Institutional Review Board at each site. Both online and paper survey data were collected beginning in October 2013, and ending in March 2014. SurveyMonkey (<http://www.surveymonkey.com>) was utilized for email survey distribution and data collection. Additionally, surveys were distributed during tumor board meetings at the Houston Methodist Hospital system and the Memorial Hermann Health System. Participants were not required to answer all questions; therefore, some answers have missing values.

Statistical analysis software, Stata (v.13.0, College Station, TX), was used to perform standard descriptive analysis of categorical variables, including number of respondents and percentages across categories. Kruskal-Wallis tests were used to compare differences in comfort level by various predictor factors. Univariable and multivariable logistic regression analyses were used to identify significant associations between respondents' demographic information, reported comfort level, perceived practice responsibilities, and barriers identified which create challenges when treating this patient population. Statistical significance was assumed at confidence intervals that did not include the null value (1.0) or at a p-value <0.05.

Results

Demographic Information

A total of 62 surveys were submitted: 5 surveys (8.1%) were excluded because all questions regarding cancer during pregnancy were unanswered, with 4 (6.4%) excluded because the survey was completed by an individual ineligible to participate in the study based on practice area. This left a final sample size of 53 (85.5%) for analysis. Table 1 shows the demographic data of the respondents. Most were medical oncologists (55.8%), with the remaining respondents divided between radiation, surgical, and gynecologic oncology. Approximately 83% of respondents had treated at least one patient diagnosed with cancer during pregnancy during their career, with 17% having no experience with this patient population.

Table 1. Participant Demographics

Institution (n=53)	n	%
Methodist	20	37.7
UT Memorial Hermann Hospital (UTMHH)	33	62.3
Survey Format (n=53)	n	%
Online	24	45.3
Paper	29	54.7
Gender (n=53)	n	%
Male	32	60.4
Female	21	39.6
Residency Completed (year) (n=53)	n	%
<1985	12	22.6
1985-1994	11	20.8
1995-2005	15	28.3
>2005	15	28.3
Years of Experience (n=53)	n	%
0-5 years	16	30.2
6-10 years	7	13.2
11-15 years	7	13.2
16-20 years	2	3.8
>20 years	21	39.6
Practice Area (n=52)	n	%
Medical Oncology	29	55.8
Surgical Oncology	7	13.4
Radiation Oncology	8	15.4
Gynecologic Oncology	8	15.4
Subspecialty (n=53)	n	%
Breast	16	30.2
GI	4	7.5
Hematology	4	7.5
Endocrine	0	0.0
Other	4	7.5
Not Applicable	25	47.2
Practice Setting (n=53)	n	%
Academic Hospital	25	47.2
Private Practice	24	45.3
Community Hospital	6	11.3
Cancer Center	4	7.5
Total Number of Pregnant Patients Seen During Career Span (n=53)	n	%
None	9	17.0
1-5	29	54.7
>5	15	28.3

Oncologist Comfort Level

The comfort level of oncologists in treating patients diagnosed with cancer during pregnancy was assessed using a 5-point Likert scale. Approximately 60% of respondents stated they were comfortable/very comfortable in treating this patient population, with remaining respondents being divided between feeling uncertain and uncomfortable/very uncomfortable. Comfort level in discussing effects of treatment on pregnancy management and/or the fetus, and in discussing prognosis, pregnancy options, and future considerations for the patient (Table 2) were assessed. Overall, participants displayed consistency in their degree of comfort when discussing various pregnancy-related topics with patients in regards to cancer management. At least 50% of participants reported being comfortable/very comfortable in discussing pregnancy related topics, with the discussion of long-term risks to the child being the exception (40%). Participants were comfortable/very comfortable (52%) in the discussion of termination of pregnancy, with 17% feeling uncertain, and 30% feeling uncomfortable/very uncomfortable.

Table 2. Responses to the question pertaining to comfort level in discussing the effects of treatment

Answer Options	Very Uncomfortable (%)	Uncomfortable (%)	Uncertain (%)	Comfortable (%)	Very Comfortable (%)
Risks of Chemotherapy	9 (17.0)	5 (9.4)	6 (11.3)	19 (35.8)	14 (26.4)
Risk of Teratogenic Effects	7 (13.2)	7 (13.2)	6 (11.3)	19 (35.8)	14 (26.4)
Risks of Surgery	7 (13.2)	8 (15.1)	7 (13.2)	20 (37.7)	11 (20.8)
Risk of treatment-related Birth Defects	8 (15.1)	7 (13.2)	9 (17.0)	16 (30.2)	13 (24.5)
Risk of Delivery Complications	9 (17.0)	6 (11.3)	9 (17.0)	20(37.7)	9 (17.0)
Risks of Radiation Therapy	8 (15.1)	6 (11.3)	12 (22.6)	14 (26.4)	13 (24.5)
Long-term Risks to the child	8 (15.1)	7 (13.2)	16 (30.2)	11 (20.8)	11 (20.8)
Risk of Transient fetal conditions	7 (13.2)	7 (13.2)	18 (34.0)	9 (17.0)	12 (22.6)

Table 3. Responses to the question pertaining to comfort level in discussing prognosis, pregnancy options, and future considerations

Answer Options	Very Uncomfortable (%)	Uncomfortable (%)	Uncertain (%)	Comfortable (%)	Very Comfortable (%)
Prognosis and effect of pregnancy on prognosis	7 (13.2)	4 (7.5)	9 (17.0)	18 (34.0)	15 (28.3)
Timing of Delivery with respect to the treatment plan	7 (13.2)	7 (13.2)	8 (15.1)	19 (35.8)	12 (22.6)
Implications for Future Fertility	6 (11.3)	5 (9.4)	11 (20.8)	15 (28.3)	16 (30.2)
Risk of cancer Metastasis	8 (15.1)	5 (9.4)	10 (18.9)	17 (32.1)	13 (24.5)
Implications for Breast Feeding	5 (9.4)	6 (11.3)	13 (24.5)	16 (30.2)	13 (24.5)
Termination of pregnancy	7 (13.2)	9 (17.0)	9 (17.0)	16 (30.2)	12 (22.6)

Oncologist Practice Responsibilities

The practice responsibilities of oncologists in managing women diagnosed with cancer during pregnancy were examined. Participants were questioned on whom they believe should be involved in the care of a patient diagnosed with cancer during pregnancy. They were additionally asked who has the highest responsibility to discuss termination of pregnancy and teratogenic risks to the fetus with the patient, and to rank sources they would refer to for information pertaining to teratogenic effects of cancer treatments during pregnancy (Table 4). MFM's and medical oncologists ranked highly across all questioning. Genetic counselors and surgical oncologists were ranked as having low responsibility to discuss termination of pregnancy and teratogenic risks to the fetus. In examining sources of reference for information pertaining to teratogenic effects of cancer treatment, MFM's ranked highest, with Ob/Gyns and a search engine such as PubMed ranking lowest as sources of information participants would reference.

Table 4. Patient management and practice responsibility

	Health Care Provider	Responsibility Rank		
		High (%)	Mid (%)	Low (%)
Responsibility to discuss termination of pregnancy as a treatment option	Medical Oncologist n=44	30 (68.2)	10 (22.7)	4 (9.1)
	MFM n=40	27 (67.5)	11 (27.5)	2 (5.0)
	Ob/Gyn n=40	26 (65.0)	11 (27.5)	3 (7.5)
	Genetic Counselor n=35	5 (14.3)	13 (37.1)	17 (48.6)
	Surgical Oncologist n=35	1 (2.9)	23 (65.7)	11 (31.4)
	Other n=1	1 (100.0)	0 (0.0)	0 (0.0)
	Health Care Provider	Responsibility Rank		
		High (%)	Mid (%)	Low (%)
Responsibility to discuss the teratogenic risks to the fetus related to cancer treatment options	Medical Oncologist n=45	36 (80%)	7 (15.6)	2 (4.4)
	MFM n=40	23 (57.5)	12 (30.0)	5 (12.5)
	Ob/Gyn n=36	16 (44.4)	12 (33.3)	8 (22.2)
	Radiation Oncologist n=36	9 (25.0)	22 (61.1)	5 (13.9)
	Genetic Counselor n=36	6 (16.7)	10 (27.8)	20 (55.6)
	Surgical Oncologist n=35	4 (11.4)	8 (22.9)	23 (65.7)
	Other n=3	3 (100.0)	0 (0.0)	0 (0.0)
	Health Care Provider	Reference Rank		
		High (%)	Mid (%)	Low (%)
Sources of reference for information pertaining to teratogenic effects of cancer treatments during pregnancy	MFM n=42	31 (73.8)	11 (26.2)	0 (0.0)
	Oncologist Colleague n=45	28 (62.2)	9 (20.0)	8 (17.8)
	Genetic Counselor n=36	11 (30.5)	14 (38.9)	11 (30.5)
	Teratogen Helpline n=35	11 (31.4)	13 (37.1)	11 (31.4)
	Ob/Gyn n=32	8 (25.0)	17 (53.1)	7 (21.9)
	PubMed n=32	7 (21.9)	10 (31.2)	15 (46.9)

Challenges

Participants were lastly asked to identify barriers which they felt created challenges when treating a patient diagnosed with cancer during pregnancy (Table 5). Approximately 20% of participants wrote-in additional barriers which they felt create challenges (Appendix 2). Approximately 80% of all respondents felt that there was at least one barrier, with most reporting more than one barrier. Of these, 83% had experience treating at least one pregnant patient in their career. Of those reporting no barriers, only one respondent (16%) had no experience treating pregnant patients in their career. Those who felt there were other challenges were primarily comfortable in treating patients diagnosed during pregnancy.

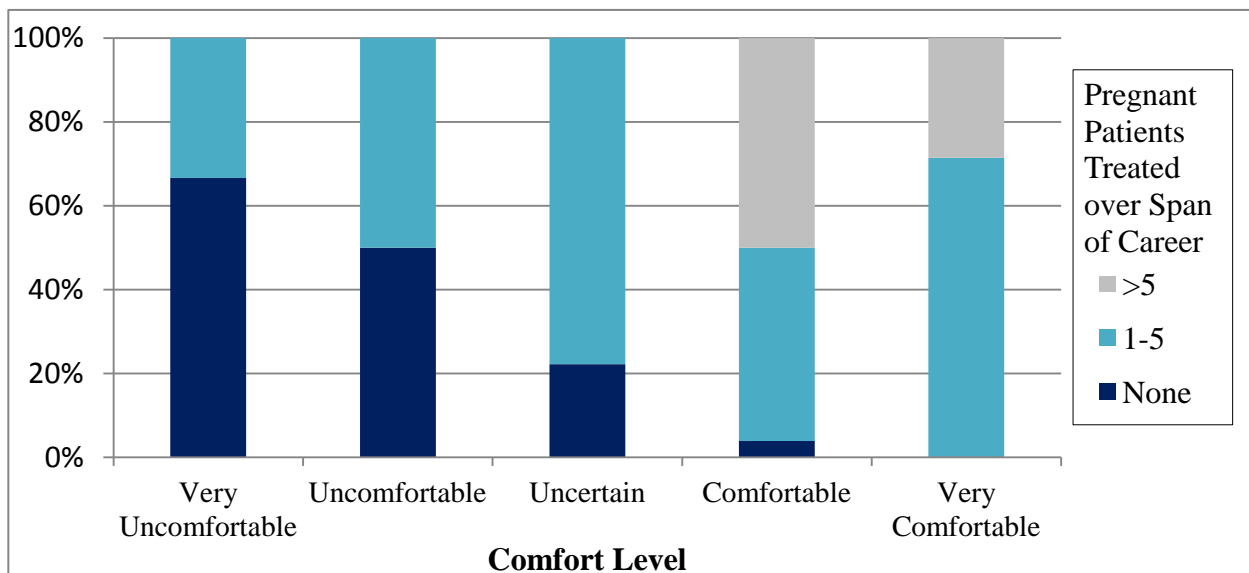
Table 5. Barriers which create challenges in managing patients diagnosed with cancer during pregnancy

Answer Options	Agree (%)	Disagree (%)
Lack of prevalence of this patient population creates barriers	34 (64.2)	19 (35.8)
Knowledge of safe treatment options creates barriers	31 (58.5)	22 (41.5)
Lack of standardization of care creates barriers	29 (54.7)	24 (45.3)
Amount of information available for reference creates barriers	28 (52.8)	25 (47.2)
There are no barriers	11 (20.8)	42 (79.2)
Other challenges create barriers	11 (20.8)	42 (79.2)

Statistically significant differences in comfort level were observed separately for gender, survey format, and institution; however, multivariable ordinal logistic regression analysis demonstrated that when controlling for experience with the patient population, the differences seen between institutions was found to be non-significant ($p=0.072$). Additionally, when controlling for the institution demographic, the differences seen between gender ($p=0.665$) and survey format ($p=0.230$) were found to be non-significant.

Associations between participant experience with patients diagnosed during pregnancy and comfort level in treating pregnant patients was assessed: participants who had treated at least one patient diagnosed during pregnancy were significantly more likely to feel comfortable when treating pregnant patients ($p<0.01$) (Figure 1).

Figure 1. Reported comfort level in treating a patient diagnosed during pregnancy based on experience with this patient population ($p<0.01$)



The comfort level of oncologists in discussing pregnancy-related topics associated with cancer treatment was also assessed. Pair-wise correlation analysis demonstrated that the topics assessed in Tables 2 and 3 were highly correlated with one another (at least 60%), with approximately 55% demonstrating greater than 80% correlation. Thus, if a participant was comfortable with one pregnancy-related topic, they were significantly more likely to be comfortable with all topics ($p < 0.001$). Overall, participants reported they are comfortable treating patients diagnosed with cancer during pregnancy and discussing pregnancy topics related to cancer treatment.

The oncologic sub-specialty of participants influenced comfort levels, with surgical and radiation oncologists significantly more likely to be uncomfortable with certain topics when compared to medical and gynecologic oncologists. These topics included discussing risks of surgery ($p < 0.01$), risks of chemotherapy ($p < 0.01$), risk of treatment-related birth defects ($p < 0.05$), risk of transient neonatal conditions ($p < 0.05$), risk of delivery complications ($p < 0.05$), risk of cancer metastasis ($p < 0.05$), termination of pregnancy ($p < 0.05$), timing of delivery with respect to the treatment plan ($p < 0.01$), and implications for breast feeding ($p < 0.05$). Participants who were uncomfortable discussing the following were significantly more likely to rank a genetic counselor as being a high reference for information pertaining to teratogenic effects of cancer treatments ($p < 0.05$): risks of surgery, risk of treatment-related birth defects, risk of transient neonatal conditions, long-term risks to the child, prognosis and the effect of pregnancy on prognosis, timing of delivery with respect to the treatment plan, risk of cancer metastasis, and implications for breast feeding. Oncologist colleagues and MFM's were consistently ranked highly for reference regarding teratogens; however this was not found to be statistically significant when compared with overall comfort in treating, or when examined for comfort level across all pregnancy-related discussion topics.

Participants who felt uncomfortable discussing pregnancy-related topics were significantly more likely to rank Ob/Gyns as having high responsibility to discuss termination of pregnancy ($p < 0.05$). However, participants who practice gynecologic oncology were significantly more likely to think an Ob/Gyn does not need to be involved in the care of a patient diagnosed with cancer during pregnancy ($p < 0.01$). Participants who felt uncomfortable discussing risks of teratogenic effects and risk of metastasis were significantly more likely to rank medical oncologists as having high responsibility to discuss teratogenic risks to the fetus ($p < 0.05$). Lastly, those who ranked genetic counselors as having high responsibility to discuss

teratogens were significantly more likely to be uncomfortable treating patients diagnosed with cancer during pregnancy ($p < 0.01$).

Those participants who that felt there were no barriers when treating this patient population were examined for comfort level when treating a patient diagnosed with cancer during pregnancy, but this was not found to be statistically significant ($p > 0.1$).

Discussion

The goal of this study was to identify the perceived views of pregnancy management and challenges faced by oncologists when treating women diagnosed with cancer during pregnancy. Few studies have specifically examined oncologist comfort level, though one demonstrated oncologist discomfort in utilization of psychosocial talk in comparison with nurses and physician assistants (32). To the best of current knowledge, this is the first study to assess the comfort level of oncologists in regards to cancer diagnosis during pregnancy. Given that 1/1000 pregnancies are diagnosed with cancer, it was thought oncologists would be uncomfortable discussing pregnancy recommendations. This study found the majority of participants had treated at least one patient diagnosed with cancer during pregnancy (83%), and participants with limited experience (1-5 patients) reported a greater level of comfort treating these patients compared to those with no experience (0 patients). Those who had treated more than 5 patients diagnosed with cancer during pregnancy were significantly more likely to feel comfortable when treating this patient population compared to those with less experience ($p < 0.01$). While the sample population was skewed due to the tertiary care environment of the institutions involved in this study, it appears that treating a few patients diagnosed with cancer during pregnancy may be sufficient for a provider to feel comfortable treating this patient population overall.

Comfort level in discussing termination of pregnancy was the only topic assessed that did not have a significant association with comfort level overall in treating this patient population ($p = 0.08$). Thus, provider comfort level in treating a patient diagnosed with cancer during pregnancy cannot be used as a predictor for comfort in discussing termination of pregnancy. Because participants tended to be less comfortable discussing termination of pregnancy, this may explain the high ranking of MFM's in regards to practice responsibility to discuss termination. However, many other factors influence comfort level in discussing termination aside from training and whether it traditionally falls within a provider's scope of practice. For instance, overall personal beliefs and feelings are likely to influence comfort level.

The findings of this study suggest medical oncologists and MFM's have a significant role in the management of this patient population. Genetic counselors were consistently ranked as having low responsibility to discuss pregnancy-related topics with patients. This study did not assess awareness of the practice competencies of genetic counselors, nor did it assess whether participants routinely work with a genetic counselor. Additionally, the distinction between different genetic counseling specialties was not taken into account. Participant responses may reflect that they feel a cancer genetic counselor has low responsibility to discuss these topics, but they may feel a prenatal genetic counselor has higher responsibility.

While the diagnosis of cancer during pregnancy more prevalent now than in the past, particularly as women continue to delay childbearing, barriers which create challenges when treating this patient population continue to exist. NCCN guidelines for the clinical management of women diagnosed with breast cancer during pregnancy were published in 2006 (2), but similar guidelines for additional cancers have not yet been established. Participants identified the lack of standardization of care as a barrier which creates challenges in the management of pregnant patients. Thus, the creation of guidelines for the treatment of other cancers during pregnancy may decrease the barriers perceived by providers, and potentially contribute to overall comfort when treating this patient population.

There were limitations to this study, first in the number of providers included in the study. Surveying a wider variety and larger number of providers may provide further insights to the clinical management of women diagnosed with cancer during pregnancy. The two institutions utilized in the study are in a tertiary care environment, with participants being more likely to have experience with pregnant patients than oncologists in the general setting. Therefore, it may be difficult to generalize the findings of this study across the field of oncology. Additionally, a large proportion of study participants subspecialize in the treatment of breast cancer, the only cancer for which standardized guidelines for treatment exist, creating a potential respondent bias.

In spite of limitations, the findings of this study provide a platform for future studies, which may include assessing provider knowledge and gathering opinions in regards to treatment approach, and in assessing the involvement of genetic counseling and genetic testing. Given the high ranking of MFM's in regards to practice responsibilities, the survey in this study could be administered to MFM's to assess whether trends in MFM comfort level reflect those demonstrated by oncologists. In addition, a study examining the knowledge of providers in

regards to the scope of practice of genetic counselors may provide additional insights regarding the importance of genetics when considering a cancer diagnosis during pregnancy.

In conclusion, the findings of this study suggest that experience with women diagnosed with cancer during pregnancy is directly related to comfort level in treating this patient population; providing care to a few pregnant patients may be sufficient to establish a level of comfort in an oncologist when treating pregnant patients. Oncologists recognize that a multidisciplinary approach is needed when treating this patient population, though have differing opinions regarding whom of these providers has the highest practice responsibility to address pregnancy-related topics. Additionally, comfort level and experience aside, oncologists acknowledge that barriers exist which create challenges when treating pregnant patients. Minimization of these barriers may contribute towards further increasing comfort level when treating a woman diagnosed with cancer during pregnancy.

Appendix

Appendix 1. Study Survey

Part I (Demographics)

1) What is your gender?

- Male
- Female

2) What year did you complete your primary residency?

_____ (year)

3) What year did you complete your fellowship and/or sub-specialty training?

Select all that apply:

- Fellowship: _____(year)
- Sub-specialty: _____ (year)
- Not Applicable

4) How many years have you been in practice?

Please choose one:

- 0-5 years
- 6-10 years
- 11-15 years
- 16-20 years
- >20 years

5) Which of the following best describes your area of practice?

Please choose one:

- Medical Oncology
- Surgical Oncology
- Radiation Oncology
- Gynecologic Oncology

6) Which of the following best describes your sub-specialty?

Please choose one:

- Breast
- GI
- Hematology
- Endocrine
- Other: _____
- Not Applicable

7) What is your primary practice setting?

Please select all that apply:

- Academic Hospital
- Private Practice
- Community Hospital
- Cancer Center
- Other: _____

8) On average, how many **new** patients in each setting below do you see each week?

Inpatient: _____ (number per week)

Outpatient: _____ (number per week)

Part II (comfort level/experience)

1) In the span of your career, how many patients have you treated who were undergoing **active treatment** for cancer during pregnancy?

Please choose one:

- None
- 1-5
- 6-10
- 11-15
- >15 Please specify approximately how many: _____

2) How comfortable do you feel treating a patient diagnosed with cancer during pregnancy?

- | | | | | |
|---------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Very
Uncomfortable (1) | Uncomfortable (2) | Uncertain (3) | Comfortable (4) | Very
Comfortable (5) |

3) How comfortable would you feel **discussing the following with a patient** diagnosed with any cancer during pregnancy? Please indicate your answer choice by marking the appropriate column below:

1= Very Uncomfortable; 2=Uncomfortable; 3=Uncertain; 4=Comfortable; 5=Very Comfortable

Discussing Effects of Treatment	1	2	3	4	5
Safety and fetal risks of surgery during pregnancy.					
Safety and fetal risks of radiation therapy administration during pregnancy.					
Safety and fetal risk of chemotherapy administration during pregnancy.					
Risk of teratogenic effects from cancer treatment during pregnancy.					
Risk of birth defects related to treatment.					
Risk of transient fetal conditions related to treatment.					
Long-term risk to the child following treatment during pregnancy.					
Risk of delivery complications related to cancer treatment.					

4) How comfortable would you feel **discussing the following with a patient** diagnosed with any cancer during pregnancy? Please indicate your answer choice by marking the appropriate column below:

1= Very Uncomfortable; 2=Uncomfortable; 3=Uncertain; 4=Comfortable; 5=Very Comfortable

Discussing Prognosis, Pregnancy Options, and Future Considerations	1	2	3	4	5
Prognosis and whether continuation of pregnancy affects the prognosis.					
Risk of cancer metastasis to the fetus and/or placenta.					
Discussing termination of pregnancy.					
How timing of delivery fits into the treatment plan.					
Implications for breast feeding.					
Implications for future fertility.					

Please respond to the remainder of the survey according to one of the following:

I do **not** have experience treating a patient diagnosed with cancer during pregnancy. The following reflects how I think I would approach this type of case.

OR

I **do** have experience treating a patient diagnosed with cancer during pregnancy. The following reflects how I approach this type of case.

Part III (practice responsibilities/challenges)

1) Do you **agree or disagree** with the following statements? Please indicate your answer choice by marking the appropriate column below.

	Agree	Disagree
Your management of a patient would change if she was pregnant at the time of diagnosis.		
It is one of your practice responsibilities to address pregnancy management with patients diagnosed with cancer during pregnancy.		
It is one of your practice responsibilities to make appropriate referrals for pregnancy management during cancer treatment.		
You know which specialists should be following your patient while she is being treated during pregnancy, and would feel comfortable making those referrals.		

2) Who do **you** think should be involved in the care of a patient diagnosed with cancer during pregnancy?

Please select all that apply:

- Medical Oncology
- Surgical Oncology
- Radiation Oncology
- OB/GYN
- MFM
- Genetic Counselor
- Other: _____
- Not sure

3) Please rank the following accordingly: Who do you feel has the primary responsibility of discussing termination of pregnancy as a treatment option with the patient?

1=highest responsibility; 6 = lowest responsibility

- _____ Medical Oncologist
- _____ Surgical Oncologist
- _____ OB/GYN
- _____ MFM
- _____ Genetic Counselor
- _____ Other: _____

4) Please rank the following accordingly: Who do you feel has the primary responsibility of discussing the teratogenic risks to the fetus related to cancer treatment options?

1=highest responsibility; 7 = lowest responsibility

- _____ Medical Oncologist
- _____ Surgical Oncologist
- _____ Radiation Oncologist
- _____ OB/GYN
- _____ MFM
- _____ Genetic Counselor
- _____ Other: _____

5) Please rank the following accordingly: Who/What would you refer to for information pertaining to teratogenic effects of cancer treatments during pregnancy, regardless of type of treatment?

1=refer to first; 2=refer to second; 3=refer to third, etc.

- _____ Oncologist Colleague
- _____ MFM
- _____ Ob/Gyn
- _____ Genetic Counselor
- _____ PubMed
- _____ Teratogen helpline/Teratogen information service
- _____ Other: _____

Appendix 2. Responses to part III, question 6 of the survey: Other barriers identified that create challenges when treating a patient diagnosed with cancer during pregnancy:

- Discussion of termination of pregnancy as an option
- No experience; refer to tertiary center
- Fear of litigation
- The obvious emotional component AND the stage of the patient, whether curable or whether already metastatic
- Pregnancy and cancer is a very difficult subject especially when radiation therapy had potentially devastating effects to a developing fetus. I also find people's religious views have a great barrier when decision making. Also the current political climate regarding abortion makes it difficult.
- A team effort is needed Although the above questions asked for a rank order--I believe the decision should be made with all team members mentioned above being involved Just the medical oncologist alone or MFM alone will not be able to make the right decision Each team member has a different expertise and different information to offer that can be utilized in decision making MFM and OBGYN and genetic counselor should be actively involved in decision making along with the various oncology colleagues The clinical pharmacist plays a very vital role here and needs to be involved in the decision making Reproductive Endocrinology can be another valuable team member to be involved here who can help address current as well as future issues,
- Historical reports about poor prognosis associated with pregnancy and cancer
- We routinely perform procedures with patients who are pregnant with and without cancer. We modify our procedures by using different medication for sedation to minimize radiation use, particularly in the first and second trimesters
- I think that the best data for management of breast cancer is out of MDACC in pregnancy; otherwise, data is scarce. However we do have the experience which is in fact well published.
- Concern for being sued if the fetus has any adverse effects.
- Rare.

References

1. Van Calsteren K, Heyns L, De Smet F, Van Eycken L, Gziri MM, Van Gemert W, Halaska M, Vergote I, Ottevanger N, Amant F. Cancer during pregnancy: an analysis of 215 patients emphasizing the obstetrical and the neonatal outcomes. *Journal of Clinical Oncology*, 28(4):683-689, 2010.
2. National Comprehensive Cancer Network: NCCN Clinical Guidelines in Oncology™. Breast Cancer, V.2.2012. Accessed at www.nccn.org/professionals/physician_gls/pdf/breast.pdf on February 27, 2013.
3. Morice P, Uzan C, Gouy S, Verschraegen C, Haie-Meder C. Gynaecological cancers in pregnancy. *The Lancet*, 379(9815):558-569, 2012.
4. Viswanathan S, Ramaswamy B. Pregnancy-associated Breast Cancer. *Clinical obstetrics and gynecology*, 54(4):546-555, 2011.
5. Janni W, Hepp P, Nestle-Kraeming C, Salmen J, Rack B, Genss E, Schindlbeck C, Friese K. Treatment of pregnancy-associated breast cancer. *Expert Opinion on Pharmacotherapy*, 10(14):2259–2267, 2009.
6. Azim Jr. HA, Gentilini O, Locatelli M, Ciriello E, Scarfone G, Peccatori FA. Managing pregnant women with cancer: personal considerations and a review of the literature. *ecancermedicalscience*, 5:204, 2011.
7. Amant F, Loibl S, Neven P, Van Calsteren K. Breast cancer in pregnancy. *The Lancet* 379(9815): 570-579, 2012.
8. Pentheroudakis G, Pavlidis N. Cancer and pregnancy: poena magna, not anymore *European Journal of Cancer*, 42(2): 126-140, 2006.
9. Guidroz JA, Scott-Conner CE, Weigel RJ. Management of pregnant women with breast cancer. *Journal of surgical oncology*, 103(4):337-340, 2011.
10. Ní Mhuireachtaigh R, O’Gorman DA. Anesthesia in pregnant patients for nonobstetric surgery. *Journal of Clinical Anesthesia*, 18(1):60-66, 2006.
11. Moran BJ, Yano H, Al Zahir N, Farquharson M. Conflicting priorities in surgical intervention for cancer in pregnancy. *The Lancet Oncology*, 8(6):536-544, 2007.
12. American College of Obstetricians and Gynecologists. Hereditary breast and ovarian cancer syndrome. ACOG Practice Bulletin No. 103. *Obstetrics and Gynecology*, 113(4):957, 2009.

13. Nguyen C, Montz FJ, Bristow RE. Management of stage I cervical cancer in pregnancy. *Obstetrical and Gynecological Survey*, 55(10):633-643, 2000.
14. Traen K, Svane D, Kryger-Baggesen N, Bertelsen K, Mogensen O. Stage Ib cervical cancer during pregnancy: planned delay in treatment--case report. *European Journal of Gynaecological Oncology*, 27(6):615-617, 2005.
15. Cohen JB, Blum KA. Evaluation and management of lymphoma and leukemia in pregnancy. *Clinical Obstetrics and Gynecology*, 54(4):556-566, 2011.
16. Muller AM, Ihorst G, Mertelsmann R, Engelhardt M. Epidemiology of non-Hodgkin's lymphoma (NHL): trends, geographic distribution, and etiology. *Annals of Hematology* 84(1):1-12, 2005.
17. Pereg D, Koren G, Lishner M. The treatment of Hodgkin's and non-Hodgkin's lymphoma in pregnancy. *Haematologica*, 92(9):1230-1237, 2007.
18. Brenner B, Avivi I, Lishner M. Haematological cancers in pregnancy. *The Lancet*, 379(9815): 580-587, 2012.
19. Lichtman M, Liesveld J. Acute myelogenous leukemia, in Collier B, Kipps TJ, Seligsohn U, Beutler E, Lichtman M (eds): *Williams Hematology* (ed 6). New York, NY, McGraw-Hill, pp 1047-1084, 2001.
20. Alexander A, Samlowski WE, Grossman D, Bruggers CS, Harris RM, Zone JJ, Noyes DR, Bowen GM, Leachman SA. Metastatic melanoma in pregnancy: risk of transplacental metastases in the infant. *Journal of Clinical Oncology*, 21(11):2179-2186, 2003.
21. Walker JW, Reinisch JF, Monforte HL: Maternal pulmonary adenocarcinoma metastatic to the fetus: First recorded case report and literature review. *Fetal & Pediatric Pathology*, 21(1):57-69, 2002.
22. Villani GM, Goldberg GL: Nongenital malignancies, in Cohen W (ed): *Cherry and Merkatz's Complications of Pregnancy*. Philadelphia, PA, Lippincott Williams and Wilkins, pp 624-627, 2000.
23. Shepard TH, Lemire RJ. *Catalog of teratogenic agents*. 12th ed. Baltimore: Johns Hopkins University Press, 2007.
24. Selig BP, Furr JR, Huey RW, Moran C, Alluri VN, Medders GR, Mumm CD, Hallford H, Mulvihill JJ. Cancer chemotherapeutic agents as human teratogens. *Birth Defects Research Part A: Clinical and Molecular Teratology*, 94(8): 626-650, 2012.

25. Bush H, McCredie JA: Carcinoma of the breast during pregnancy and lactation, in Allen HH, Nisker JA (eds): *Cancer in Pregnancy: Therapeutic Guidelines*. Mount Kisco, NY, Futura, 91-101, 1986.
26. Zemlickis D, Lishner M, Degendorfer P, Panzarella T, Burke B, Sutcliffe SB, Koren G. Maternal and fetal outcome after breast cancer in pregnancy. *American Journal of Obstetrics and Gynecology*, 166(3):781-787, 1992.
27. Berry, DL, Theriault RL, Holmes FA, Parisi VM, Booser DJ, Singletary SE, Buzdar AU, Hortobagyi GN. Management of breast cancer during pregnancy using a standardized protocol. *Journal of Clinical Oncology*, 17(3):855-855, 1999.
28. Koren G, Lishner M, Farine D. (eds): *Cancer in pregnancy: maternal and fetal risks*. Cambridge University Press, 1996.
29. Dildy III GA, Moise Jr KJ, Carpenter Jr RJ, Klima T. Maternal malignancy metastatic to the products of conception: a review. *Obstetrical & Gynecological Survey*, 44(7): 535–540, 1989.
30. Weisz B, Meirow D, Schiff E, Lishner M. Impact and treatment of cancer during pregnancy. *Expert review of anticancer therapy*, 4(5): 889-902, 2004.
31. Han SN, Kesic VI, Van Calsteren K, Petkovic S, Amant F. Cancer in pregnancy: a survey of current clinical practice. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, 167(1):18-23, 2013.
32. Morgan PA, de Oliveira JS, Alexander SC, Pollak KI, Jeffreys AS, Olsen MK, Arnold RM, Abernethy AP, Rodriguez KL, Tulsy JA. Comparing oncologist, nurse, and physician assistant attitudes toward discussions of negative emotions with patients. *The Journal of Physician Assistant Education*, 21(3): 13, 2010.

Shannon Kaye Mulligan was born in Dallas, Texas on September 18, 1987, the daughter of Virginia J. Mulligan and James A. Mulligan III. After completing her work at Bishop Lynch High School, Dallas, Texas in 2005, she entered Austin College in Sherman, Texas. She received the degree of Bachelor of Arts with a major in Mathematics and a minor in Chemistry from Austin College in May, 2009, graduating Cum Laude. At this point, she entered The University of Texas M. D. Anderson Cancer Center School of Health Professions in Houston, Texas. She received the degree Bachelor of Science with a major in Molecular Genetic Technology in August, 2010, graduating with honors. For the next two years, she worked as a certified medical technologist in the Molecular Diagnostics Laboratory at The University of Texas M. D. Anderson Cancer Center.

In August of 2012 she entered The University of Texas Graduate School of Biomedical Sciences at Houston.

Permanent address:

11705 Shoal Landing St.
Pearland, TX 77584