

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Barriers to care for women with low-grade endometrial cancer and morbid obesity: A qualitative study
AUTHORS	Cusimano, Maria; Simpson, Andrea; Han, Angela; Hayeems, Robin; Bernardini, Marcus; Robertson, Deborah; Kives, Sari; Satkunaratnam, Abheha; Baxter, Nancy; Ferguson, Sarah

VERSION 1 - REVIEW

REVIEWER	Brittany Davidson Duke University
REVIEW RETURNED	13-Nov-2018

GENERAL COMMENTS	<p>Love qualitative work being done to exam how we can better care for this growing patient population. This manuscript is written well.</p> <p>I have 2 comments:</p> <ol style="list-style-type: none">1. Line 60-61--standard of care for endometrial cancer. In the US, standard of care includes some form of lymph node assessment per NCCN guidelines. May want to mention this2. I would consider mentioning that in the Calle paper (Ref 1). The RR for death from cancer and obesity is highest for endometrial cancer (RR=6.25), higher than any other cancer reported in that study. Not only are women predisposed to this cancer because of their weight, but it appears they are also dying from this cancer because of their weight.
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REVIEWER	LaShaune Johnson Creighton University, USA
REVIEW RETURNED	24-Nov-2018

GENERAL COMMENTS	<p>This paper is clearly written, and adds nuance to a few critical conversations--research about weight stigma with patients who experience obesity, the (lack of) public awareness of gynecological cancers, and patient-provider communication. Table with representative quotes was useful for understanding themes. Explaining the coding plan and when/how you reached saturation was helpful. Explaining your previous experiences (and possible sources of bias) was the ethical thing to do here.</p>
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REVIEWER	W.H. van Harten Netherlands Cancer Institute, Amsterdam , The Netherlands University of Twente, Enschede, The Netherlands Rijnstate Hospital, Arnhem, The Netherlands
REVIEW RETURNED	03-Mar-2019

GENERAL COMMENTS	<p>This paper addresses the barriers to care for obese women diagnosed with low grade endometrial cancer, based on a survey that showed saturation after interviewing 15 women. As little research has been performed on the issue of obesity and actual experiences in oncological (surgical) treatment this is a relevant topic.</p> <p>A number of remarks can be made:</p> <ul style="list-style-type: none"> - first why selecting women with low grade endometrial cancer? This should be properly explained and the issue of generalization and relevance for a wider population should at least be discussed in the discussion. -the objective states a very broad objective " understanding experiences" whereas I would expect these to be specifically related to the issue of obesity, this gives room for " general experiences" to become mixed with specific, topic related experiences. The "finding" that there is little awareness nor on the significance of abnormal bleeding, is probably not specific for this group at all, or should be demonstrated to be so; in my view the questions/report should be much more focused on obesity and cancer in all regards. -that saturation was reached seems acceptable, however no underlying evidence is showed to proof this, nor a semi quantitative analysis of frequently mentioned issues or topics that seemed to have specific importance. - the results are presented in rather non-specific terms like: "subject to stigma", "streamlined care pathways" or " alack of effective weight loss interventions". The latter is a general problem so what is the specific issue related to treating patients with cancer? This should be expanded upon in the discussion. -I miss a part on further research, especially a qualitative in depth study (if adequately reported) should lead to a number of relevant issues in cinically relevant quantitative or psychosocial fields <p>Minor remarks:</p> <ul style="list-style-type: none"> -what is the relevance of mentioning the Da Vinci robots? l86 -is there a reference of more difficult conditions outside cancer centers?l66 -own research in l192 is confusing -participants would have wanted providers to have raised the issue of overweight and obesity earlier...what is specific for cancer patients? -"not all" in l219 is vague, rather state " nn of 15 stated that.." - the exact nature of the "struggles" indicated at in line 231 would be interesting -"multiple referrals" in l242, rather give impressions on how many futile attempts were reported. - issues like equipment and facilities for obese pts, could be reported -also on the abstract- more specifically -line 264 seems to contrast with many earlier remarks; that would merit further detail -I would skip the parts on general awareness also in the discussion
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	-why would you expect women to know about the link between overweight and cancer? that is also a general population issue, so what is specific?
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VERSION 1 – AUTHOR RESPONSE

RESPONSE TO REVIEWER COMMENTS

Reviewer 1, Comment #1: Line 60-61 – standard of care for endometrial cancer. In the US, standard of care includes some form of lymph node assessment per NCCN guidelines. May want to mention this.

Author Response: Thank you for this suggestion. We have amended the manuscript to indicate this and have added a reference to the NCCN guidelines.

Location of Modified Text:

- Introduction; Page 3; Line 63

Reviewer 1, Comment #2: I would consider mentioning that in the Calle paper (ref 1), the RR for death from cancer and obesity is highest for endometrial cancer (RR=6.25), higher than any other cancer reported in that study. Not only are women predisposed to this cancer because of their weight, but it appears they are also dying from this cancer because of their weight.

Author Response: Thank you for this recommendation. We have amended the manuscript to highlight this point.

Location of Modified Text:

- Introduction; Page 3; Lines 59-61

Reviewer 2, Comment #1: This paper is clearly written, and adds nuance to a few critical conversations – research about weight stigma with patients who experience obesity, the (lack of) public awareness of gynecological cancers, and patient-provider communication. Table with representative quotes was useful for understanding themes. Explaining the coding plan and when/how you reached saturation was helpful. Explaining your previous experiences

(and possible sources of bias) was the ethical thing to do here.

Author Response: Thank you for your comments. We appreciate your review of our work.

Location of Modified Text:

- N/A

Reviewer 3, Comment #1: Why selecting women with low grade endometrial cancer? This should be properly explained and the issue of generalization and relevance for a wider population should at least be discussed in the discussion.

Author Response: We emphasize that our research question and study design were intentionally focused specifically on women with low-grade endometrial cancer and obesity, and not on a broader cancer population with obesity.

Low-grade endometrial cancer is more strongly associated with obesity than any other malignancy. Nearly 65% of endometrial cancer patients have concurrent obesity at the time of diagnosis. As gynecologists, we see this patient population frequently, and have recognized that the presence of obesity can complicate the provision of standard surgical treatment. There is also a growing body of literature on weight stigma in healthcare, suggesting that patients with obesity may experience discrimination. Despite the association between obesity and endometrial cancer, we found no literature exploring barriers to health care or possible weight stigma in this patient population. We had a particular interest in understanding the experiences of this population in order to ultimately optimize their care, and focused our question and study design for this

reason. We have rewritten parts of the Introduction to clarify why we selected this patient population.

With respect to the issue of generalization, we have already stated in our Discussion that: "Our results may apply to other patient populations as well: the barriers described by participants may be relevant to all women with endometrial cancer and patients with other obesity-related diseases (line 367-369)." However, we emphasize that the goal of most qualitative work, including ours, is to provide a rich, contextualized understanding of a human experience through the intensive study of particular cases, and not to make inferences to populations that were not observed.

We therefore do not make additional generalizations beyond those already stated in the manuscript, as this would go beyond the scope of our study.

Location of Modified Text:

- Introduction; Pages 3-4, Lines 59-80

Reviewer 3, Comment #2: The objective states a very broad objective "understanding experiences" whereas I would expect these to be specifically related to the issue of obesity, this gives room for "general experiences" to become mixed with specific, topic related experiences.

Author Response: As stated in our response to Reviewer 3 Comment #1, the goal of this work was to provide a rich, contextualized understanding of the experiences of women with low-grade endometrial cancer and morbid obesity, from symptom onset to diagnosis to surgery. As a result, we were interested in both experiences related to the issue of obesity, and experiences related to the specific topic/disease; our objective was intentionally broad so that both could be captured. Indeed, some of the themes ultimately identified in our qualitative analysis were related to the issue of obesity (e.g. “Endometrial cancer patients with obesity are subject to stigma and poor provider communication”) and some were related to the disease (e.g. “Patients and providers lack knowledge on endometrial cancer”). We felt that elucidating both obesity- and disease-specific experiences would be critical to optimizing the care of these women.

Location of Modified Text:

- N/A

Reviewer 3, Comment #3: The “finding” that there is little awareness on the significance of abnormal bleeding, is probably not specific for this group at all, or should be demonstrated to be so; in my view the questions/report should be much more focused on obesity and cancer in all regards.

Author Response: We agree that our finding of a lack of awareness of the significance

of abnormal uterine bleeding is likely not specific to endometrial cancer patients with morbid obesity, and have already stated this in our Discussion: “Although we did not include patients with normal BMI, we suspect that this issue is irrespective of obesity (line 296-297).”

However, we feel this is a critical finding to report regardless. Demonstrating that our participants with morbid obesity did not recognize the significance of abnormal uterine bleeding, or that they were at increased risk of endometrial cancer, is important for healthcare providers to know. It suggests these patients were never counselled or warned about concerning symptoms, despite being a high-risk population. This finding emphasizes that providers must educate and screen these patients in order to facilitate the prevention or early detection of endometrial

cancer. We have amended our Discussion to better highlight this.

As explained in our response to Reviewer 3 Comment #1 and Comment #2, our research question and study design were intentionally focused on understanding the experiences of endometrial cancer patients with morbid obesity, and not on patients with other types of cancer or cancer in all regards. Thus, our findings around abnormal uterine bleeding indeed inform the care of the specific patient population that was of interest in this study. We have therefore not made changes to the manuscript in response to the latter part of this comment.

Location of Modified Text:

- Discussion; Page 13; Lines 294-296
- Discussion; Page 14; Lines 305-306, 311-313, 318-232

Reviewer 3, Comment #4: That saturation was reached seems acceptable, however no underlying evidence is showed to proof this, nor a semi quantitative analysis of frequently mentioned issues or topics that seemed to have specific importance.

Author Response: Because our study was qualitative (not quantitative) in design, we chose not to present numbers/percentages of individual comments, and focused instead on presenting major themes. However, we note that all 4 major themes were raised in almost every interview, and no interview discussed fewer than 3 major themes. We have added a column to Table 2 to show the exact proportion of interviews in which each theme was specifically mentioned. We feel that we have indeed provided a large amount of evidence in the form of direct quotations not only in the Results section, but also in Tables 2 and 3; these quotations encompass the full range of the 15 study participants. Finally, we emphasize that no new themes emerged after 11 interviews, but data collection and analysis was continued to 15 interviews to ensure that we had obtained a thorough data sample (lines 151-152).

Location of Modified Text:

- Table 2; Pages 23-26

Reviewer 3, Comment #5: The results are presented in rather non-specific terms like: “subject to stigma”, “streamlined care pathways” or “a lack of effective weight loss interventions”. The latter is a general problem so what is the specific issue related to treating patients with cancer? This should be expanded upon in the discussion.

Author Response: We offered several examples of what we mean by stigma in the Introduction (lines 69-73) and Results sections (lines 210-214, lines 215-218; lines 218-220; lines 220-224; lines 227-232). Streamlined care pathways refer to systems in which referrals are channeled directly to tertiary centers equipped to manage obesity (lines 351-356).

Finally, weight loss interventions are relevant to patients with endometrial cancer, because studies of survival outcomes in endometrial cancer patients have demonstrated that elevated BMI is associated with increased mortality even after curative hysterectomy. Thus, effective weight loss interventions could reduce morbidity and mortality in endometrial cancer survivors.

We have rephrased a paragraph in our Discussion to better highlight this.

Location of Modified Text:

- Discussion, Page 14-15, Lines 313-323
- Discussion, Page 15, Lines 324-326

Reviewer 3, Comment #6: I miss a part on further research, especially a qualitative in depth study (if adequately reported) should lead to a number of relevant issues in clinically relevant quantitative or psychosocial fields.

Author Response: Thank you for this comment. We had mentioned in our Discussion that: "Future research may evaluate perceived barriers to providing care to this population of patients

from the perspective of physicians (lines 371-372)." However, other questions did certainly arise from this work, and we have expanded on this paragraph in the Discussion.

Location of Modified Text:

- Discussion; Page 17, Lines 370-375

Reviewer 3, Comment #7: What is the relevance of mentioning the da Vinci robots? Line 86.

Author Response: The two sites from which we recruited patients have da Vinci robots. The relevance this is already mentioned (lines 88-93). Because the da Vinci surgical robot facilitates minimally invasive hysterectomy in patients with obesity, these centers receive many surgical referrals for women with morbid obesity, who were of interest in this study. This maximized

our ability to recruit patients from diverse backgrounds. We have edited this section in the Methods section to ensure that our rationale is clearer.

Location of Modified Text:

- Methods; Page 4-5; Lines 88-93

Reviewer 3, Comment #8: Is there a reference of more difficult conditions outside cancer centers? Line 66.

Author Response: There is significant regional variation with respect to cancer surgery in the province of Ontario (Citation: Urbach DR, Simunovic M, Schultz SE, editors. Cancer Surgery in Ontario: ICES Atlas. Toronto: Institute for Clinical Evaluative Sciences, 2008). However, we acknowledge that this may be a confusing sentence, and as such have removed it from the manuscript.

Location of Modified Text:

- Introduction; Page 3; Lines 66

Reviewer 3, Comment #9: Own research in Line 192 is confusing.

Author Response: We meant to indicate that participants learned of the association between obesity and endometrial cancer through online searches and independent reading, rather than from a physician directly. We have clarified this statement in the manuscript.

Location of Modified Text:

- Results; Page 9; Lines 196-198

Reviewer 3, Comment #9: Participants would have wanted providers to have raised the issue of overweight and obesity earlier. What is specific for cancer patients?

Author Response: Our participants did not indicate that they simply wanted to be informed of the general health risks of obesity earlier in life. Rather, as a result of their cancer diagnosis, they expressed a desire to have been counselled specifically on the association between obesity and malignancy earlier in life. This is what makes this issue specific to endometrial cancer patients, and we have edited the text to clarify this.

Location of Modified Text:

- Results; Page 9; Lines 204-205

Reviewer 3, Comment #10: "Not all" in line 219 is vague; rather state "nn of 15 stated that..."

Author Response: Thank you for this suggestion. We have made a change to the very next sentence, specifying that three patients had never felt stigmatized due to their weight.

Location of Modified Text:

- Results; Page 10; Line 226

Reviewer 3, Comment #11: The exact nature of the "struggles in obtaining an endometrial biopsy and/or imaging" indicated at in line 231 would be interesting.

Author Response: Patients described instances in which their physician struggled to obtain an endometrial biopsy in the office setting due to their body habitus. They were unable to perform a

speculum exam or obtain an adequate biopsy, and on many occasions had to bring patients to the operating room to perform a biopsy under general anaesthesia. Patients also experienced delay when imaging tests were not deemed possible or were considered inconclusive due to body habitus. We have added more detail on this in the manuscript. The representative

quotation included (lines 242-246) also highlights both issues.

Location of Modified Text:

- Results; Page 11; Lines 238-241

Reviewer 3, Comment #12: "Multiple referrals" are stated in line 242; rather give impressions on how many futile attempts were reported.

Author Response: This is already described in the manuscript at line 154, where patients saw a median of 2 specialists (range 2-4) before surgery was successfully arranged and performed.

To clarify this further, we have added this information to Table 1.

Location of Modified Text:

- Tables; Page 22; Table 1

Reviewer 3, Comment #13: Issues like equipment and facilities for obese patients, could be reported also on the abstract more specifically.

Author Response: Thank you for this comment. We have added a sentence to the abstract mentioning the specific clinical, administrative, financial, geographic, and facility- and equipment-related barriers to care for patients with morbid obesity.

Location of Modified Text:

- Abstract; Page 2; Line 39-40

Reviewer 3, Comment #14: Line 264 seems to contrast with many earlier remarks; that would merit further detail.

Author Response: Despite barriers and occasional negative interactions with healthcare providers or administrators, participants felt they had been well-cared for overall in that they believed their cancers

had ultimately been treated appropriately by an expert surgeon. This was what patients cared about the most, when reflecting back after surgery. We have clarified this in the text.

The representative quotation provided also alludes to the importance of this.

Location of Modified Text:

- Results; Page 12; Line 273-275

Reviewer 3, Comment #15: I would skip the parts on general awareness also in the discussion. Why would you expect women to know about the link between overweight and cancer? That is also a general population issue, so what is specific?

Author Response: We did not necessarily expect women in our study to know about the association between obesity and endometrial cancer, and in fact do cite other studies in our Discussion that confirm this is the case for women in the general population as well (lines 306-309). However, low-grade endometrial cancer is more strongly associated with obesity than any other malignancy in all epidemiologic studies on this topic. Women with morbid obesity are at high risk of developing endometrial cancer, and for this reason it is especially concerning that our participants had no knowledge of the impact of obesity prior to their cancer diagnosis.

If this patient population had been counselled on the association between obesity and endometrial cancer earlier in life, it could conceivably promote prevention or early detection

of endometrial cancer (lines 306, 311-313). Participants themselves endorsed wishing they had known about this earlier (lines 204-209). We hope our study provides additional evidence on the need for healthcare providers to counsel their patients about the association between obesity and endometrial cancer, and also reassure providers that while this is a sensitive discussion, it is one that many patients may actually want to have. We have rewritten parts of the Results and Discussion sections to clarify this.

Many participants commented on the link between obesity and endometrial cancer, and expressed various opinions on how this should be discussed by healthcare providers (lines 195-209). It was one of the most prominent themes raised by participants, and for this reason, we feel that we cannot leave it out of the study.

Location of Modified Text:

- Results; Page 9; Lines 204-205
- Discussion; Page 14; Lines 305-232

VERSION 2 – REVIEW

REVIEWER	W.H. van harten Netherlands cancer Institute
REVIEW RETURNED	30-Mar-2019

GENERAL COMMENTS	The authors have addressed most comments. I do however remain with the opinion that the general awareness issue and suggestions for endometrial cancer in overweight women is not well addressed. Overweight is carrying so many risks and needs so many lifestyle suggestions, that concluding that they were not aware of this risk of endometrial cancer and the related suggestions for the general female obese population, is not a surprising or specific finding nor combined with a very realistic advise on this point. I leave a final decision to the editor
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VERSION 2 – AUTHOR RESPONSE

Reviewer 3, Comment 1: The authors have addressed most comments. I do however

remain with the opinion that the general awareness issue and suggestions for endometrial cancer in overweight women is not well addressed. Overweight is carrying so many risks and needs so many lifestyle suggestions, that concluding that they were not aware of this risk of endometrial cancer and the related suggestions for the general female obese population, is not a surprising

or specific finding nor combined with a very realistic advise on this point. I leave a final decision to the editor.

Author Response: We have rewritten components of our discussion to provide specific recommendations on how the care and overall health of endometrial cancer patients with morbid obesity can be improved. Each of these recommendations stem directly from themes identified by our participants, and are corroborated by existing literature.

- Public education on endometrial cancer and its warning signs is needed, both through the use of widespread media campaigns and targeted counselling of high-risk populations by physicians. Education of women with morbid obesity may ultimately enable timely diagnosis and implementation of strategies for disease prevention.
- Primary prevention of endometrial cancer, using simple cost-effective strategies such as combined contraceptives and progestin-containing intrauterine devices should be considered routinely for women with morbid obesity, given the challenges associated with achieving sustainable weight loss.
- The postoperative period should be used as a window of opportunity to address the long-term health of endometrial cancer patients by initiating conversations about obesity, encouraging lifestyle changes, and offering referrals for bariatric surgery or professional supervision of weight loss. Endometrial cancer patients with concurrent morbid obesity are more likely to die of their cancer and also of comorbidities compared to leaner counterparts. Addressing obesity after curative treatment is therefore critical to optimizing the health of this population.

- Counselling on obesity must be delivered in a way that limits the stigmatization and healthcare avoidance described by our participants. We provide a number of suggestions on how communication with this patient population can be optimized.

Location of Modified Text:

- Discussion; Page 13-15; Lines 292-341
- Discussion; Page 17; Lines 371-377