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Title	**Variability in the quality of ultrasound reporting for uterine fibroids in Canada: results from a prospective cohort registry**
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Reviewer 1	Mr. Lee Treanor
Institution	Department of Medicine, University of Ottawa, Ottawa, Ont.
General comments (author response follows)	This is an interesting study which is applicable to help further understand the current reporting quality in the imaging of fibroids in Canada. A study such as this has not been conducted on a Canadian population. Lessons could be learned for future practice guidelines. I applaud the authors for their work. This is generally a well-written manuscript. Methods and background appear appropriate. There are some minor issues with presentation of results: 1. Page 9, line 33: "Baseline characteristics of women who had ultrasound only and MRI are shown in Table 1" a. Please fix wording to "…only ultrasound or MRI…" – done 2. Page 9, line 24: There were 80 women who had another imaging modality. What were these modalities? Were they excluded from your analysis? It is not specified. These were excluded from analysis. Other imaging modalities included Hysterosalpingography and computed topography 3. Page 10, line 40: "In other words, the odds of receiving a high quality ultrasound were 1.66 times greater if the same patient had imaging at 1 random study site as opposed to another." a. Please specify that it is the "…median odds of receiving…" Yes. This has been clarified Discussion well-written with applicable limitations. Would be interested to see why the authors think patients with MRI imaging reported lower menstrual bleeding scores. We also observed that patients undergoing MRI were more likely to have larger fibroids. These larger fibroids are more likely to be subserosal or intra-mural in location and less likely to contribute to heavy bleeding, rather more likely to result in bulk symptoms. This has been added to the discussion section.
Reviewer 2	Dr. Cathy Popadiuk
Institution	Department of Women's Health, Memorial University, Newfoundland and Labrador
General comments (author response follows)	The authors present their work resulting from the CAPTURE registry that prospectively follows a cohort of women with uterine fibroids from 19 study sites across Canada. The registry methods have been published in JMIR Res Protocol 2018;7:e10926 and the clinical trial is registered: ClinicalTrials.gov:NCT02580578. From the clinical trials site, the primary outcome measures included: 1. Uterine fibroid QOL37 score

	2. Ruta menorrhagia bleeding 15 Item questionnaire score 3. Participants with drug reactions. The duration for the score evaluations is 24 months and the estimated completion date is February 13, 2020 having started on July 31, 2015. This study is sponsored by Allergan which makes Fibristal used for the treatment of symptomatic fibroids. Recently concerns about severe liver toxicity associated with Fibristal have arisen and are being further investigated. Like many European countries, Canada has put out updated information (2019) to be cautious regarding Liver toxicity associated with this medication. It is very meritorious that in this clinical trial, the participants are being followed for drug reactions. Post-marketing surveillance can be challenging. It is also advantageous that the authors can share other data developed from the study registry. This study's two main objectives were: 1. Describe factors associated with the use of MRI to evaluate uterine fibroids 2. Evaluate the quality of, and variation in, US reporting within the Canadian Health-care system. 1. From the clinical trials website and supplementary listing, one can see the centers participating in the study from across the country, which included most provinces except Manitoba and PEI, and no territories. It is not clear why none of the Eastern provinces were included in this imaging study yet it is implied as having information from across the country. The groupings studied were: Western Ontario, Central Ontario, Eastern Ontario, Quebec, and Western Canada. There were two centers from Eastern Canada – complete list of participating centers in the appendix and now summarized in the results. The site in Nova Scotia and Newfoundland had few participants and therefore the random effect in the mixed model was unable to be estimated properly and would not permit a proper estimate of the median odds ratio. Although it is true that some provinces were not represented, overall we felt that the geographic distribution of the study closely represented that of the population density in Canada – with the majority of population in Ontario and Quebec (https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1710000901). Maritimes account of 5% of the Canadian population. 2. For the background, the authors outline that uterine fibroids are common and fibroid management is heavily influenced by imaging information. They thus wanted to evaluate imaging performed in Canada. They used a recent consensus guideline: The Morphological Uterus Sonographic Assessment guideline as their standard for comparison and created a quality rating based on 5 criteria that should be in the Ultrasound (US) reports: fibroid number, fibroid dimensions, uterine dimensions, fibroid type and fibroid location. They also summarized whether women had MRI, US or other tests but did not go into more detail about MRI evaluation, likely as there is no single standard for measurement and it did not appear to be the focus of the paper. It is also not clear why choice of imaging matters or how the imaging influences the decision making for fibroid

	management. As CMAJ is a journal applicable to all physicians and health care providers across the country, a bit more detail about fibroid management and how the various tests aid in treatment planning would add greatly to the background and perspective. Information added in the introduction: Fibroids can vary greatly in the size, shape, location and number between patients. This topographical information is needed to help guide treatment decisions and is particularly important for surgical planning. Although ultrasound is the mainstay for the diagnosis and monitoring of uterine fibroids, magnetic resonance imaging (MRI) can also be used.2. There are no clinical practice guidelines to help determine when an MRI should be ordered and many fibroid guidelines de-emphasize the role of MRI.3 The Society of Obstetricians and Gynaecologists of Canada Clinical Practice Guideline on the management of uterine fibroids advises that ultrasound imaging is the most widely used modality because of its availability, ease of use, and cost-effectiveness, but MRI is the most accurate modality as it provides information on the size, location, number, and perfusion of fibroids. The statistical analysis of this descriptive data and the US scoring measures was rigorous. Demographic and clinical variables were identified: age, BMI, parity and gravidity, family history of fibroids, previous procedural interventions, bulk symptoms, fibroid diameter, fibroid number, and QOL scores for symptoms (Uterine Fibroid symptom and Health related QOL, and Health Related QOL; and Aberdeen Menorrhagia severity scale for bleeding. In addition to continuous and parametric variables and their appropriate statistical analyses, unadjusted and adjusted logistic regression models were examined for associations between hypothesis-generating covariates and the outcome of having a high quality US. 3. In the results, it says the study included 1493 women from 19 practice sites in Canada. But again, the Atlantic provinces for some reason do not seem to have contributed to this imaging study. Why not? The total number of women from the 19 sites across Canada that had only US as the imaging modality was 1148. But were these women from the Ontario, Quebec and West Canada sites? Did Atlantic Canada sites not have any imaging for their participants and thus were excluded in the analysis? Table 1 has a nice summary of the demographics based on imaging modality and there are no Atlantic Canadians. 130 women were excluded from the analysis because they had their imaging more than 12 months from study start. The site in Nova Scotia and Newfoundland had few participants and therefore the random effect in the mixed model was unable to be estimated properly and would not permit a proper estimate of the median odds ratio. Patients who had MRI were found to have more numerous, and larger fibroids. The authors noted older patients were less likely to have an MRI based on an odds ratio per 5-year age increase 0.73 (95% CI 0.64-0.84); but in Table 1 the mean age for MRI was 40.24 and US 43.22 and similar results taking into account SDs.

	In the unadjusted analysis, older patients were more likely to have an MRI (OR per 5-year age increase 1.35, 95% CI1 0.19, 1.53). However, after adjusting for demographic and clinical characteristics, we saw that older patients were less likely to have an MRI (OR per 5-year age increase 0.74; 95% CI 0.64–0.85). As requested, both the unadjusted and adjusted results are now presented in the results. 4. As a reader, one would want to know when and why there would be a difference in imaging modality. If fibroids are larger and more numerous, is there a concern that requires MRI for better discrimination? Are these patients at greater risk of malignancy? Do the greater number and larger fibroids impact for treatment decision making otherwise? Often an MRI is requested by the radiologist for better discernment of features unclear on an US. More information on why the authors think MRIs are useful for fibroid management would be very helpful for the reader. Thank you for these comments, we have added these items to the discussion to allow the reader to understand why MRI may be beneficial in certain cases. The following has been added to the discussion section: Surgical planning for uterine preserving procedures may be particularly challenging with large and numerous fibroid. MRI, due to due to its better soft tissue contrast, larger field-of-view and multiplanar imaging capabilities, can be particularly helpful in such cases of surgical planning, as well as assessment of other differential diagnosis and potentially excluding malignancy. MRI also allows for the ease of characterization of numerous fibroids at once, which may be quite laborious with ultrasound. 5. Table 2 summarizes the quality of US reporting; the purpose of this paper. An adjusted linear mixed model including 1128 patients was used to examine the association of patient and institutional characteristics with receiving US that met all 5 high quality standards. Arguably, the most significant outcome of this paper was that patients from Central Ontario (the reference group) were more likely to have a high-quality report over those from Quebec. And patients from more populated cities (>=400,000 inhabitants) were more likely to receive a high-quality US report. But the modeling showed that the median OR across sites was 1.66. The inter-hospital variation was not explained by patient characteristics and only partially by region and city size. Ultimately, the most important result was that there was great variability in the quality of reporting among the 19 sites (if Atlantic sites were included). The figures, 1 and 2, give graphic representation of the distribution of US reports meeting each quality criterion and site-specific rates of high quality US per 100 USs respectively. The figures give a reasonable visual of the findings. For privacy reasons it appears that the 19 sites were not identified. Oddly, there were 19 dots on figure 2 but no mention of the East coast. It would be very helpful to the reader who lives outside Ontario, to outline which sites were grouped as central, western Ontario etc. It would also be helpful to identify which of the clinic and hospital sites were considered < and >= 400,000 population communities. These descriptors have been added to appendix 1. 6. For the interpretation, the authors state that their findings parallel previous studies that show MRI is a better imaging test for larger and more numerous

	fibroids. Again, for the general reader, why is this important for managing the fibroids? As well, do larger and more numerous fibroids cause worse symptoms? Intuitively one would think so, but does this information also impact on treatment: medical and or surgical? The authors note that "due to the cost differential between these imaging modalities, standardized algorithms that incorporate the cost-effectiveness of each modality would help to guide clinicians in their decision to order MRI." A comment about how the authors see cost differing between US and MRI would be helpful as depending on how human resource components and capital equipment is calculated would impact on these outcomes across the country. Furthermore, in many gynecologic practices, one doesn't order an MRI without direction to do so based on a preceding test such as US. Depending on regional practices this may differ, such as in Quebec where there is more opportunity for private clinic access. Added to the discussion: Surgical planning for uterine preserving procedures may be particularly challenging with large and numberous fibroid. MRI, due to due to its better soft tissue contrast, larger field-of-view and multiplanar imaging capabilities, can be particularly helpful in such cases of surgical planning, as well as assessment of other differential diagnosis and potentially excluding malignancy. MRI also allows for the ease of characterization of numerous fibroids at once, which may be quite laborious with ultrasound. Due to the cost differential between these imaging modalities, standardized algorithms that incorporate the cost-effectiveness of each modality would be helpful to guide clinicians in their decision to order MRI. We would suggest that after a high quality ultrasound assessment of fibroids, specific criteria are used to determine which patients would further benefit from an MRI. 7. The authors emphasize that there is great inter site variability for US reporting. "It is sobering that the odds of a Canadian woman with uterine fibroids receiving a high quality ultrasound were 1.66 times greater if the same patient had imaging at 1 random institution as opposed to another". Technically, the 19? sites in this study were not "random" but met the criteria to be included in this descriptive prospective study as participants. These sites may not be reflective of a more generalisable set of sites outside these centers. "Random" in this case refers to selecting a "random" patient within the study sample. We do feel that the variable selection of study sites (variable in location, size of city, academic vs community hospital) generally reflects the Canadian population and therefore these results are generalizable to the average patients with fibroids in Canada. 8. Very importantly, the authors state: ..much of the focus of international guidelines on uterine fibroids is on providing guidance on management rather than thorough evaluation of the condition. However, accurate diagnosis and assessment of uterine fibroids is essential to guide optimal selection of treatment strategies, particularly since fibroid characteristics are unique between patients." For the reader to get a better sense of the purpose of the imaging exercise, it is imperative to outline how the imaging then impacts on management. Our publicly funded health care system cannot fund tests strictly for the identification and characterization of individual patient's particular fibroids in and of itself without a downstream purpose such as management or reassurance that there is no cancer

	or other condition. Patients with other pelvic problems such as endometriosis were excluded from this fibroid study as per exclusion criteria. We have added the following explanation to the introduction: “Fibroids can vary greatly in the size, shape, location and number between patients. This topographical information is needed to help guide treatment decisions and is particularly important for surgical planning. The Society of Obstetricians and Gynaecologists of Canada Clinical Practice Guideline on the management of uterine fibroids advises that ultrasound imaging is the most widely used modality because of its availability, ease of use, and cost-effectiveness, but MRI is the most accurate modality as it provides information on the size, location, number, and perfusion of fibroids.” Furthermore, in the discussion section, we elaborate on the importance of accurate imaging prior to surgery – “Furthermore, if surgical management is chosen, accurate evaluation of fibroid topography will have implications for surgical planning (route, time, incision, etc) and patient counselling. Improper surgical planning may lead to suboptimal patient outcomes.” 9. And the authors showed that fibroid type (please list examples), number and location were more consistently reported than uterine and fibroid size. Arguably, measuring size in various dimensions requires more time and skill to identify maximum dimensions and complete measurements than counting and identification of simple anatomic. Fibroid type definition is provided in the methods: “Fibroid type – A report describing any of the following for the largest fibroid met the quality standard: submucosal (International Federation of Gynecology and Obstetrics type 0, 1, 2, unknown type), intramural, subserosal, cervical, pedunculated.” Agree with the later statement that measuring the size of the fibroid takes more time/skills but information is also necessary to guide treatment. 10. The authors very importantly outline the provincial and center variations as to who reports the scans, where they are performed and remuneration structures. Apparently larger cities in Ontario (reference site) have access to US technicians who can complete the scans and save images for the radiologist to review. Smaller centers and those in Quebec do not use technicians and the physician more likely has to do the scan herself. In some centers radiologists perform scans, in other places gynecologists. Remuneration is also important to consider. During the time of the data gathering for this study, Quebec had challenges with the provincial government for funding of US in private clinics and funding limitations impacted on scanning Added the following sentence to discussion - Renumeration for the physician reporting ultrasound may also influence this variability, but we were not able to capture this information through our study. Furthermore, larger volume centers may have access to ultrasound technicians who can complete the scans and save images for the radiologist to review. Smaller centers may not use technicians and the physician more likely has to do the scan themselves. There is also variability between gynecologists or radiologists reporting gynecologic ultrasound imaging reports.

	11. It is unfortunate that these variables could not be considered among the 19 sites. It does not seem unreasonable to be able to obtain the data as to whether techs did scans and who signed off on them (radiologist/gynecologist). The authors listed the lack of this information as a limitation of their study and important for future studies evaluating quality improvement initiatives. They also mentioned that the study did not review whether abdominal or transvaginal US was performed for the tests. This seems like a very significant factor not studied. In gynecology, unless there is a good reason for not having a transvaginal US, one would argue the standard for gynecologic imaging is transvag followed by abdominal US at one appointment. This deficiency suggests this study arose more as a post hoc analysis of the findings, rather than planning a primary outcome measure and indeed, this study was not among the 3 primary outcomes in the clinical trial outline. This was a posthoc analysis of the national fibroid database. Nonetheless the results highlight a significant gap in patient care- the quality of imaging for uterine fibroids. Unfortunately, given the retrospective nature of the database and that data collection has been completed, it is not possible for us to get the desired information. Although it would have been ideal to have this additional information, the results of the study must be interpreted in the context of the study design. We have outlined these limitations in the discussion. However, we feel that regardless of the mode of ultrasound or the person performing the ultrasound, the fact remains the same: the quality of ultrasound reporting is not uniform and has a lot left to be desired. Future studies and quality improvement initiatives can better evaluate these factor in an attempt to improve care. We discuss this in our conclusion: We propose that prompt evaluation of factors influencing imaging quality are necessary. Factors limiting quality of ultrasound reporting may include lack of knowledge, dissemination of imaging practice guidelines, limited training and time/resource restraints, as well as patient characteristics (i.e., elevated BMI). Identifying such limitations can focus areas of improvement. 12. In the conclusion the authors reference that if surgical management is chosen, accurate evaluation of fibroid topography will have implications for surgical planning. Putting this earlier in the paper would be helpful as would describing surgical options. The implications of accurate imaging for fibroids has been added to the introduction. In the discussion, we review surgical options (myomectomy vs. hysterectomy) and that these procedures may be performed by different approaches. In summary, this paper suggests that the Morphological Uterus Sonographic Asssessment (MUSA) consensus statement is not followed by most of the study sites participating in the CAPTURE study. This conclusion could have broader impact as an example of the potential lack of standardization in medical imaging. We have revised the conclusion to add the issue raised above: This study shows that MUSA guidelines for ultrasound evaluation of fibroids are not being consistently followed in many sites across Canada. This underscores the

	lack of standardization and variability in quality in uterine fibroid imaging in Canada.