

Accuracy of point-of-care intestinal ultrasound for Crohn's disease

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Abstract

Background: Point-of-care ultrasound (POCUS), performed by a gastroenterologist, provides safe and convenient imaging allowing for immediate clinical decision in Crohn's disease. The minimum training required to gain competency, its accuracy and clinical utility requires evaluation.

Methods: In this pilot study, Crohn's disease activity and extent were assessed using POCUS (performed by a single gastroenterologist following the completion of 200 supervised scans), magnetic resonance enterography (MRE) and ileo-colonoscopy. The presence of complications was assessed by POCUS and MRE. Accuracy of POCUS was analysed with respect to MRE and ileo-colonoscopy. Agreement between modalities was assessed using kappa coefficient.

Results: Forty-two patients had a POCUS paired with MRE. Thirty-eight patients had a POCUS paired with ileo-colonoscopy. When compared to MRE, POCUS was accurate in the assessment of disease activity (sensitivity 87.5%, specificity 61.1%, ROC 0.74), extent (sensitivity 77.8%, specificity 83.3%, ROC 0.81) and complications (sensitivity 85.7%, specificity 94.3%, ROC 0.90). Agreement between POCUS and MRE was moderate (kappa estimates 0.50, $P < 0.001$, 0.61, $P < 0.001$ and 0.76, $P < 0.001$) for disease activity, extent and complications, respectively. When compared to ileo-colonoscopy, POCUS was accurate in the assessment of disease activity (sensitivity 72%, specificity 86%, ROC 0.79) and extent (sensitivity 85.7%, specificity 86%, ROC 0.86). For POCUS and ileo-colonoscopy, kappa estimates were 0.55, $P < 0.001$ for disease activity and 0.62, $P < 0.001$ for disease extent.

Conclusion: POCUS performed by a gastroenterologist after completion of limited training is accurate for assessing Crohn's disease activity, extent and the presence of complications.

Keywords: intestinal ultrasound, GIUS, POCUS, Crohn's disease.

Introduction

Crohn's disease (CD) is a progressive, inflammatory disease occurring in genetically predisposed patients. The incidence of CD has been reported as high as 29.3 per 100,000 in Australia and is increasing worldwide.¹ The development of new drugs and therapeutic treatment strategies in the management of inflammatory bowel disease (IBD) have raised patient and clinician expectations. A 'treat to target' approach is an accepted strategy for IBD care, wherein objective measures of disease activity are sought and used to guide subsequent management.² Achievement of mucosal healing, assessed with colonoscopy, is

now the accepted target for treatment and is associated with reduced rates of clinical relapse, hospitalisation and surgery.³⁻⁸

The limitations of colonoscopy, including safety, access, cost and patient preference, have increased the importance of cross-sectional imaging for the regular monitoring of intestinal inflammation.^{9,10} Computed tomography (CT) and magnetic resonance enterography (MRE) are the most available current imaging modalities for the assessment of active disease but CT is associated with ionising radiation exposure and therefore inappropriate for repeated use,¹¹ while MRE is costly and access difficult. MRE is, however, widely considered the gold standard cross-sectional imaging modality for identifying active disease, particularly in the small bowel.¹² Taylor *et al.*, in a prospective

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doi: 10.1002/ajum.12218

study of patients with newly diagnosed Crohn's disease, compared the accuracy of MRE and small bowel ultrasound, when performed by specialist radiologists. Both MRE and ultrasound were found to have high diagnostic accuracy and were valid first-line investigations for disease assessment in the patients. The sensitivity and specificity of MRE was superior to ultrasound for small bowel, but not colonic disease.¹²

Gastrointestinal ultrasound (GIUS), performed by a gastroenterologist at the point-of-care (POCUS), is a cost-effective, non-invasive, radiation-free imaging method, which allows transmural assessment of the bowel wall and adjacent structures. POCUS can be used to in immediate clinical decision-making to optimise treatment.¹³

GIUS when performed by an experienced sonographer or gastroenterologist, in high volume centres, has been shown to have good sensitivity and specificity for the diagnosis of Crohn's disease and its complications including strictures, entero-enteric fistulae and abscesses.^{14–18} There is increasing acceptance internationally of POCUS as an accurate and valuable tool in the IBD imaging armamentarium^{19,20} and much recent interest from gastroenterologists performing GIUS at the bedside as an extension of their examination of patients with Crohn's disease. A growing body of evidence supports POCUS as a viable method of disease evaluation in IBD.^{13,21,22} A minimum training fulfilment of 150–200 supervised scans has been suggested²³, although there are few data supporting the competency achieved by such training. It remains to be determined whether POCUS, performed by a gastroenterologist with specific and defined training in intestinal ultrasound, but without training in general ultrasound, provides acceptable diagnostic accuracy and clinical utility¹⁹.

We hypothesised that POCUS, performed by a gastroenterologist with a minimum of 200 supervised scans in patients with Crohn's disease, provides accurate and clinically useful information about the activity and extent of Crohn's disease and about the presence or absence of intestinal complications including strictures, fistulas, abscesses or enter-enteric fistulae.

Methods

Ethics approval for this study was provided by the Quality and Risk Unit at our institution (approval QA 026/17). All ultrasound examinations were performed as part of routine clinical care. Given the retrospective nature of the study, patient consent was not required.

Patient selection and disease assessment

In this single specialist centre, retrospective pilot study, consecutive patients with a proven diagnosis of Crohn's disease who had a POCUS performed from February 2016 until October 2017 within three months of MRE, ileo-colonoscopy or both were included. Disease activity, disease extent and the presence of complications were assessed by POCUS and MRE. Complications, for the purposes of this study, were defined as strictures

(the presence of increased bowel wall thickness associated with fixed luminal narrowing) with pre-stenotic dilatation, enteric fistulas or the presence of a phlegmon or abscess. Only disease activity and extent were assessed using ileo-colonoscopy given the limitations of colonoscopy in the assessment of extra-mural complications. A single gastroenterologist performed all POCUS scans within three months of either MRE or ileo-colonoscopy without intervening change in medical therapy.

POCUS examination

A single gastroenterologist (EW) performed all scans included in this study. Immediately prior the gastroenterologist had performed 200 supervised scans in patients with IBD at a high volume intestinal ultrasound centre (Foothills Medical Centre, Calgary, Canada).

A standardised approach was used starting the examination from the left lower quadrant and examining the colon from the distal sigmoid to the caecum working proximally with examination of each colonic segment in turn. The terminal ileum was then evaluated, followed by systematic four-quadrant examination to include the remaining small bowel. All examinations were completed using a Supersonic Aixplorer machine utilising both a low frequency (4–9 MHz) curved probe and higher frequency (12–15 MHz) linear probe.

The presence of disease activity was defined as either 'active' or 'inactive'. Disease activity was deemed to be present if there was increased bowel wall thickness (>3 mm) with or without the presence of any additional established indicators of active inflammation: increased colour Doppler blood flow, loss of wall stratification, the presence of mesenteric inflammatory fat or the presence of lymph nodes.²⁴

The extent of disease was recorded for the purposes of this study as being 'limited', defined at ≤ 5 cm, or 'extensive', defined as > 5 cm in length. Where multiple segments of bowel were involved, this length is cumulative over the affected areas.

The presence or absence of complications as defined above was also recorded.

MRE

Eligible scan reports were reviewed. All scans were performed at a single centre experienced with performing MRE in patients with Crohn's disease. Disease was deemed to be active if there was bowel wall thickening with bowel wall enhancement, T2 wall hyper-signal or inflammatory change. The extent of disease was recorded for the purposes of this study as 'limited', defined at ≤ 5 cm, or 'extensive', defined as > 5 cm in length. The presence or absence of complications was also recorded.

Ileo-colonoscopy

Eligible ileo-colonoscopy reports were reviewed. Colonoscopy results were reviewed to determine both disease activity and extent. Active disease was defined as any ulceration seen at colonoscopy. As for POCUS examination, the extent of disease

was recorded for the purposes of this study as being 'limited', defined at ≤ 5 cm, or 'extensive', defined as > 5 cm in length.

Statistical analyses

Statistical analyses were performed using Stata 14.2 (StataCorp, College Station, TX). Summary data are reported as count (percentage). Contingency tables were constructed to compare pairs of the diagnostic modalities being examined in order to calculate sensitivity and specificity. These were then used to calculate the area under the receiver operating characteristic curves (AUROC). Cohen's kappa statistic was calculated, again comparing pairs of diagnostic modalities, to estimate inter-rater agreement.

Ethical approval

Ethics approval for this study was provided by the Quality and Risk Unit at St Vincent's Hospital Melbourne (approval QA 026/17).

Results

A total of 65 patients were included in this study. Demographic and treatment details of the patients included are shown in Table 1. Patients were divided into the POCUS and MRE analysis ($n = 42$) and the POCUS and ileo-colonoscopy analysis ($n = 38$) depending on the data available. Some patients were included in both analyses as POCUS, MRE and ileo-colonoscopy data were all available.

POCUS and MRE paired studies

Forty-two patients (50% males) had a POCUS paired with MRE (Table 2, Figure 1). Twenty-eight studies (67%) showed active disease on POCUS compared to 24 (57%) on MRE. When compared to MRE, POCUS was accurate in identifying active disease with a sensitivity 87.5%, specificity 61.1%, and AUROC 0.74.

Eighteen patients (43%) had active disease of > 5 cm on POCUS and 18 (43%) on MRE. POCUS identified extensive disease in comparison to MRE with a sensitivity of 77.8%, specificity of 83.3%, and AUROC 0.81.

Complications were identified in 8 (19%) on POCUS and 7 (17%) on MRE. POCUS identified complications in comparison with MRE with a sensitivity of 85.7%, specificity of 94.3% and AUROC 0.90.

Agreement between POCUS and MRE was moderate (kappa 0.50 (95% CI 0.24–0.76) $P < 0.001$, 0.61 (95% CI 0.37–0.85) $P < 0.001$ and 0.76 (95% CI 0.50–1.00) $P < 0.001$) for disease activity, extent and presence of complications, respectively.

POCUS and Ileo-colonoscopy paired studies

Thirty-eight patients (47% males) had a POCUS paired with ileo-colonoscopy (Table 3, Figure 2). Active disease was identified in 20 (53%) patients on POCUS compared to 25 (66%) on ileo-colonoscopy. When compared to ileo-colonoscopy,

Table 1: Patient demographics.

Demographics	POCUS and paired MRE, n (%)	POCUS and paired ileo-colonoscopy, n (%)
Total patients	42	38
Males	21 (50)	18 (47)
Active disease on POCUS	28 (67)	19 (50)
Drug treatment		
Steroids	10 (24)	10 (26)
5-ASA	4 (10)	6 (16)
Methotrexate	2 (5)	4 (11)
Thiopurine	17 (40)	11 (29)
Antibiotics	2 (5)	2 (5)
Anti-TNF	18 (43)	9 (24)
Vedolizumab	1 (2)	0 (0)

POCUS was accurate in the diagnosis of active disease with a sensitivity 72.0%, specificity 86.7%, and AUROC 0.79.

Ten (26%) patients had extensive disease on POCUS compared to 7 (18%) on ileo-colonoscopy. When compared to ileo-colonoscopy, POCUS identified extensive disease with a sensitivity of 85.7%, specificity of 86.2% and AUROC 0.86.

In our study, active disease was diagnosed more often at ileo-colonoscopy than at POCUS. Five patients had active disease seen at ileo-colonoscopy but not at POCUS. Of these, two had disease in the rectum, which cannot be viewed adequately using POCUS,¹⁶ one had very mild terminal ileum disease, one had mild right sided colitis, and one had mild recurrence at an ileo-caecal anastomosis. Significant ileal or colonic disease was not missed by POCUS.

Agreement between POCUS and ileo-colonoscopy was moderate (kappa 0.55 (95% CI 0.30–0.80) $P < 0.001$ for disease activity and 0.62 (95% CI 0.32–0.92) $P < 0.001$ for disease extent.

Discussion

The benefits of intestinal ultrasounds performed by the gastroenterologist delivering patient care are numerous, particularly the capacity for involving the patient in management decisions at the bedside and the ability to escalate clinical care immediately from the clinic.¹³ Physician-performed POCUS has been reported to strengthen rapport between doctors and patients in other chronic disease settings^{25,26} and allows acceptable diagnostic accuracy in the clinical context, without the need for formal radiology training or a full diagnostic knowledge and expertise in broader ultrasonography.²⁶ Data suggest

Table 2: POCUS and MRE paired examinations. Summary of results for disease assessment and accuracy.

Disease assessment: POCUS vs. MRE (n = 42)			
	POCUS	MRE	
Active disease n (%)	28 (67)	24 (57)	
Extensive disease n (%)	18 (43)	18 (43)	
Disease complication n (%)	8 (19)	7 (17)	

Accuracy: POCUS vs. MRE			
	Sensitivity (%)	Specificity (%)	AUROC
Disease activity	87.5	61.1	0.74
Disease extent	77.8	83.3	0.81
Disease complications	85.7	94.3	0.90

a high level of satisfaction with this test among patients in inflammatory bowel disease.²⁷

The learning curve for gastroenterologist-performed POCUS in IBD is not well established, despite increasing uptake by clinicians. We have not assessed different extents of supervised training, but chose a practical number of patients which was felt to be sufficiently large. POCUS, performed by a gastroenterologist with a minimum training of 200 supervised scans, is accurate for assessing clinically important disease parameters including Crohn's disease activity, extent and the presence of complications. Moderate agreement between POCUS and MRE, and between POCUS and ileo-colonoscopy, was demonstrated.

Our results reflect the established accuracy of intestinal ultrasound in the diagnosis of Crohn's disease. Recent meta-analyses report good to excellent sensitivity and specificity of ultrasound for diagnosis of Crohn's disease when compared to CT, barium study, MRE or endoscopy.^{28–30} The most recent meta-analysis, by Dong *et al.*,²⁸ reviewed 15 prospective studies in which ultrasound was used to evaluate active Crohn's disease. Overall sensitivity was 88.0% and specificity 97.0% for identifying active Crohn's disease with an AUROC of 0.94, indicating good diagnostic accuracy. In more than half of the 15 included studies, ultrasound was performed by experienced sonographers.

In the current study, POCUS demonstrated modest specificity (61.1%) when compared to MRE for the diagnosis of active disease. The ability for POCUS to provide bedside disease assessment, to triage severity, and allow for immediate clinical decision-making regarding further investigations or treatment, without the delays of MRE or ileo-colonoscopy is invaluable and outweighs this modest reduction in specificity. In this study, active disease was identified more frequently on POCUS when compared to MRE. This may relate to the criterion that any bowel wall thickening, even without other ultrasound features of inflammation, was interpreted as showing active

disease at POCUS but not on MRE, and also the likely superior sensitivity of POCUS for the diagnosis of low-grade inflammation when compared to MRE.

The significance of low-grade inflammation, often reflected by increased wall thickness in the absence of other radiological signs of inflammation, compared to complete normalisation of wall thickness and stratification (transmural healing) is controversial. Transmural healing is seen in only a minority (16%) of patients with Crohn's disease and only a proportion of patients with endoscopic mucosal healing. Whilst mild bowel wall thickness on imaging in the absence of any other features of active inflammation may hold prognostic importance,^{31–33} how accurately it reflects active Crohn's disease and future disease course is unknown and prospective studies are needed.

Strengths to this study include the use of a single gastroenterologist performing all included POCUS scans and the comparison of POCUS results to both MRE and ileo-colonoscopy. MRE scans included in this study were all performed using the same protocol at the same tertiary hospital by radiologists with extensive experience reading MRE in patients with Crohn's disease.

The major limitation of this study is the retrospective nature of the data. Larger, prospective studies are required to confirm these findings. This study used a simple definition for 'active' or 'inactive' disease and did not look at disease activity per bowel segment. A more sophisticated definition of disease activity at ultrasound, using a tool such as the simple ultrasonographic score for the assessment of Crohn's disease activity which has now been developed and validated,³⁴ may improve the sensitivity of POCUS for the identification of active disease. The use of an endoscopic score such as the Simple Endoscopic Score for Crohn's Disease (SES-CD)³⁵ would have provided more detailed information with regard to disease activity at endoscopy which would have allowed for a more sophisticated analysis of any correlation between endoscopic and ultrasound.

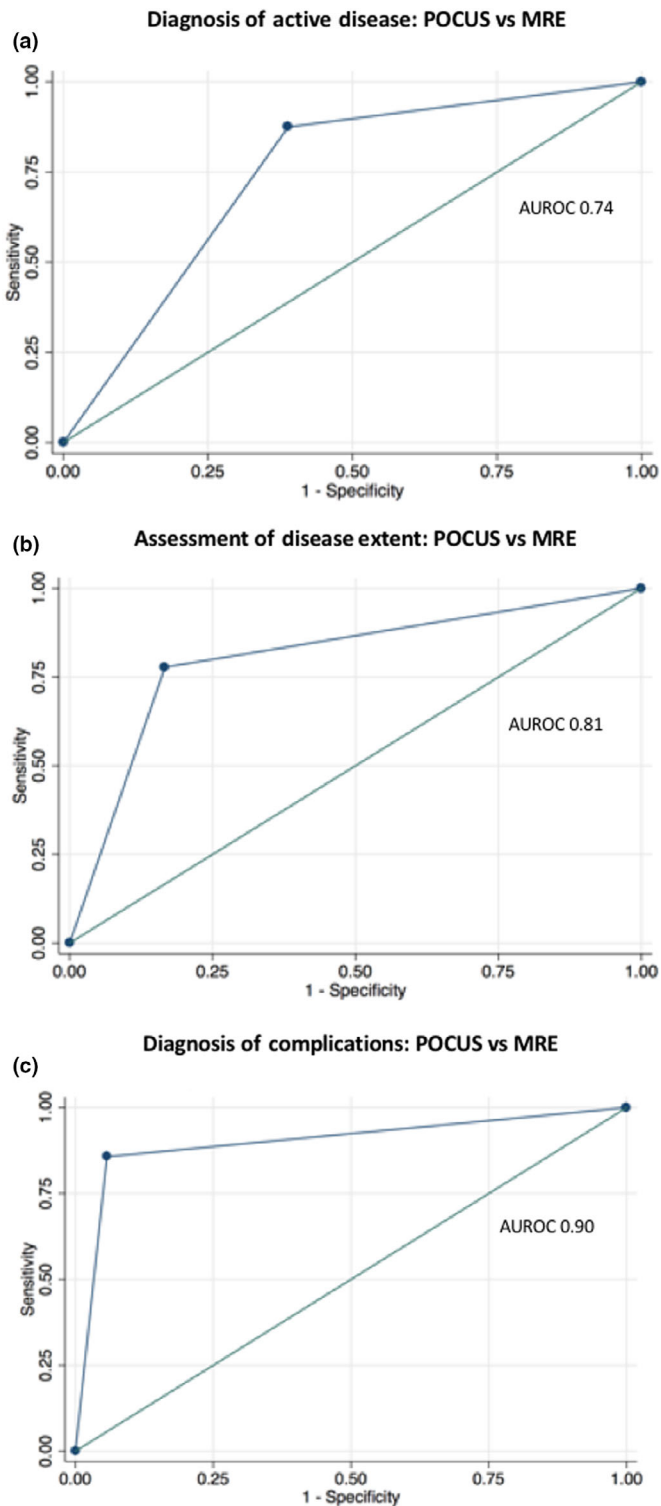


Figure 1: (a) Accuracy of POCUS compared to MRE in the diagnosis of active Crohn's disease. (b) Accuracy of POCUS compared to MRE in the assessment of Crohn's disease extent. (c) Accuracy of POCUS compared to MRE in the diagnosis of complications. [Colour figure can be viewed at wileyonlinelibrary.com]

Table 3: POCUS and ileo-colonoscopy paired examinations. Summary of results for disease assessment and accuracy.

Disease assessment: POCUS vs. Ileo-Colonoscopy (n = 38)		
	POCUS	Ileo-Colonoscopy
Active disease n (%)	20 (53)	25 (66)
Extensive disease n (%)	10 (26)	7 (18)

Accuracy: POCUS vs. Ileo-Colonoscopy			
	Sensitivity (%)	Specificity (%)	AUROC
Disease activity	72.0	86.7	0.79
Disease extent	85.7	86.2	0.86

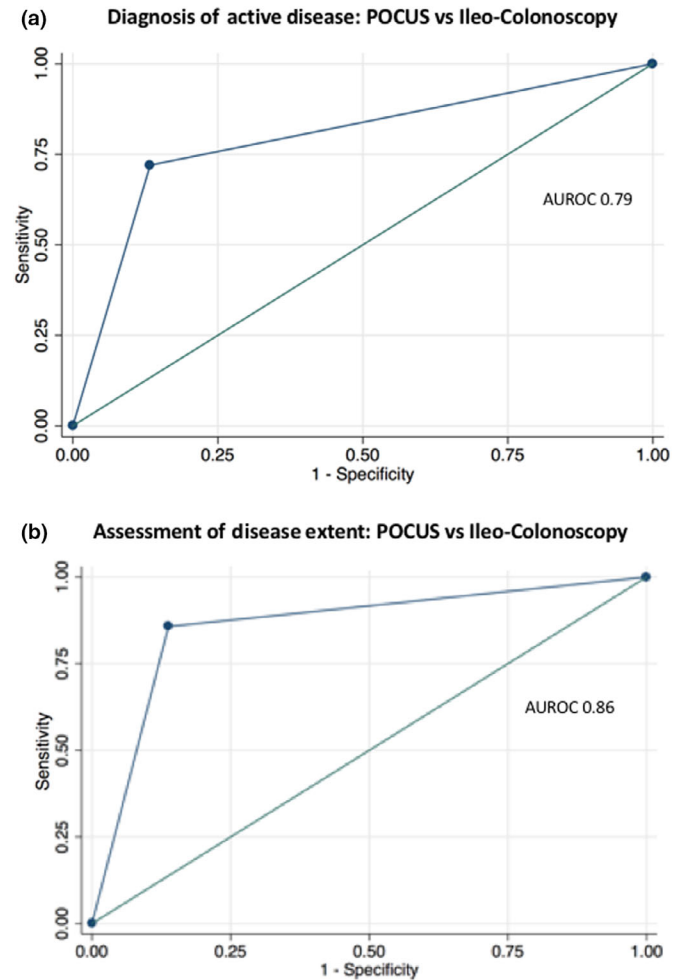


Figure 2: (a) Accuracy of POCUS compared to ileo-colonoscopy in the diagnosis of active Crohn's disease. (b) Accuracy of POCUS compared to MRE in the assessment of Crohn's disease extent. [Colour figure can be viewed at wileyonlinelibrary.com]

Different stages of ultrasound training and experience need to be evaluated. Although patients undergoing changes to medical therapy during the investigation period were excluded, it is possible that disease evolution or progress occurred during the time period between POCUS and ileo-colonoscopy or MRE. Same-day comparison of imaging modalities and ileo-colonoscopy would avoid such issues.

In summary, POCUS, performed by a gastroenterologist with limited training, is accurate, providing clinically useful information for the management of patients with Crohn's disease. Our data support gastroenterologist use of POCUS in the assessment and monitoring of these patients.

Acknowledgements

We wish to acknowledge AbbVie who provided the ultrasound equipment used for this study as part of an educational grant. No other specific funding for this project was received.

Conflict of Interest

The authors have no conflicts of interest to declare.

Funding

We gratefully acknowledge funding from AbbVie which allowed for the purchase of the ultrasound machine used in this study.

Disclosures

EK Wright has received research support from AbbVie and Ferring and has acted as a speaker at symposiums sponsored by AbbVie, Janssen and Pfizer; I Wang, D Wong, WR Connell and AJ Thompson have no disclosures; SJ Bell has received speakers fees from AbbVie, Janssen and Shire; KL Novak has received research support from AbbVie, acted as speaker for AbbVie, Janssen and Pfizer; MA Kamm has acted as an advisor to Abbott and Janssen, has received research support from AbbVie, and has acted as a speaker at symposiums sponsored by AbbVie and Janssen.

Declaration

The authorship listing of this manuscript conforms with the authorship policy. All authors have agreed to the content of this submitted manuscript.

Author Contribution

Emily Wright: Conceptualization (lead); Data curation (lead); Formal analysis (supporting); Investigation (lead); Methodology (lead); Project administration (lead); Writing-original draft (lead); Writing-review & editing (lead). **Ian Wang:** Data curation (lead); Formal analysis (supporting); Investigation (supporting). **Darren Wong:** Data curation (lead); Formal analysis (lead). **Sally Bell:** Supervision (supporting); Writing-review & editing (supporting). **William Connell:** Resources (supporting);

Supervision (lead); Writing-review & editing (supporting). **Alexander Thompson:** Supervision (lead); Writing-review & editing (lead). **Kerri Novak:** Conceptualization (supporting); Investigation (supporting); Methodology (supporting); Project administration (supporting); Supervision (lead); Writing-review & editing (supporting). **Michael A Kamm:** Supervision (lead); Writing-review & editing (lead).

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