

# Cervical Cancer Screening in Inflammatory Bowel Disease: Who Should Be Screening?

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## Abstract

**Background:** Immunosuppressed women with inflammatory bowel disease (IBD) are at elevated risk of cervical cancer yet have lower screening rates. The objective of this study was to assess the familiarity with cervical cancer screening recommendations, and the perceived responsibility for implementing screening among three physician groups involved in the clinical care of women with IBD: primary care physicians (PCP), gastroenterologists (GI) and gynecologists (GYN).

**Methods:** We anonymously surveyed a sample of 117 PCP, 52 GYN and 35 GI physicians affiliated with Saint Louis University, Saint Louis, MO, USA, from April 2018 to January 2019. The physicians completed a questionnaire addressing essential aspects of cervical cancer screening such as screening age, screening frequency, human papillomavirus (HPV) vaccination, comfort level in performing Papanicolaou (Pap) smears, perception of physician responsibility in terms of which physicians should perform Pap smears.

**Results:** A total of 2.6% of PCPs, 37% of GIs and 29% of GYNs reported familiarity with cervical cancer screening recommendations. In addition, PCP and GI had no definite opinions regarding which physicians should be in charge of cervical cancer screening and performing Pap smears. However, 94% of GYNs felt that they should be in charge of cervical cancer screening and performing Pap smears.

**Conclusions:** An apparent lack of familiarity exists among all three physician groups regarding cervical cancer screening recommendations in immunosuppressed patients with IBD. Similarly, there is no consensus regarding which specialty should be responsible for cervical cancer screening in this patient population.

**Keywords:** IBD; Cervical cancer screening; Immunosuppression

Manuscript submitted April 20, 2020, accepted May 14, 2020  
Published online October 8, 2020

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doi: <https://doi.org/10.14740/gr1287>

## Introduction

Inflammatory bowel disease (IBD) is characterized by chronic inflammation of the gastrointestinal tract and typically represents two distinct pathologies: ulcerative colitis and Crohn's disease. IBD is emerging as a global disease. In the United States alone, approximately 3.1 million people are estimated to have IBD [1]. Over the past several decades, the pathogenesis of IBD has continued to be better defined, and with increased knowledge of the disease, the number of new biological therapies has grown [2]. An increasing number of patients with IBD are anticipated to be chronically immunosuppressed and consequently vulnerable to opportunistic infections and intestinal and extra-intestinal cancers [3, 4].

Although cervical cancer rates in the United States are decreasing, the disease remains a major world health problem [5]. Decreasing rates of cervical cancer are attributed to the understanding that persistent human papillomavirus (HPV) is the most crucial factor contributing to disease development and progression [5]. Cervical cytology or Papanicolaou (Pap) smear is an inexpensive, effective, and widely available technique for cervical cancer screening that has been demonstrated to reduce cervical cancer incidence and mortality [6, 7]. In the past decade, many studies have investigated the association between cervical dysplasia and cervical cancer in patients with IBD. Having a diagnosis of IBD does not necessarily elevate the risk of cervical dysplasia. However, patients with IBD taking long-term immunosuppressant medications are at elevated risk of cervical dysplasia and malignancy [8-11]. Owing to an increased risk of progression of asymptomatic HPV infection to cervical dysplasia in immunosuppressed women [12]. In light of these findings, the American College of Obstetricians and Gynecologists (ACOG) [12], the American College of Gastroenterology [13] and a panel of health care professionals involved in cervical cancer research [14] have recommended an annual cervical cancer screening interval with Pap testing for chronically immunocompromised patients with IBD, instead of the more lenient screening interval of 3 to 5 years in the general population.

Despite these recommendations, several studies have revealed that women with IBD, as compared with otherwise healthy females, receive suboptimal screening for cervical cancer [6, 7, 15, 16]. Moreover, the broader picture indicates an overall disparity in adherence to preventive care guidelines

among patients with IBD [17, 18]. This discrepancy is thought to be because a large proportion of patients with IBD are diagnosed at a relatively young age [19], and tend to receive much of their medical care from a gastroenterologist, whereas they follow up with a primary care physician (PCP) less frequently for general health maintenance [20]. Simultaneously, both GIs and PCPs are often hesitant to assume the sole responsibility for providing preventative health care services to the IBD population [21-23], partly because of conflicting perceptions of responsibility [24].

In many health care systems, it is not clear whether the patient's PCP, GI, or gynecologist (GYN) should assume the primary responsibility of cervical cancer screening. Furthermore, no data are available assessing perceptions of the above health care providers regarding who should assume responsibility. This study's objective was to assess current thought processes and trends amongst PCP, GI, and GYN providers of who should be accountable for cervical cancer screening, provider familiarity with current recommendations, and how this familiarity translates to clinical practice.

## Materials and Methods

The study was conducted at Saint Louis University School of Medicine, St. Louis, MO, USA, from April 2018 to January 2019. It was approved by the Saint Louis University Institutional Review Board. The study design is a stratified random sampling of physicians. We anonymously surveyed 117 PCPs, 52 GYNs, and 35 GIs, using de-identified paper or electronic questionnaires. Participants included house staff and faculty physicians or affiliates of Saint Louis University, who completed the questionnaire on their own time. The study questionnaire was developed based on the American College of Gastroenterology's clinical guidelines on preventative care in IBD [13]. The questionnaire included eight questions that identified the study participant's knowledge of and comfort in caring for patients with IBD and managing cervical cancer screening (Table 1).

Data analysis was performed in IBM SPSS Statistics 24 software. Chi-square tests compared questionnaire data from PCP, GYN and GI providers. Odds ratios (OR) with 95% confidence intervals (CIs) were reported for categorical data. Independent sample *t*-tests were performed to compare means for continuous variables. Significance level was defined as  $\alpha$  less than or equal to 0.05.

## Results

For all study participants, the number and percentage of trainees and faculty for each specialty were as follows. PCP: house staff 101 (86%), faculty 16 (14%); obstetrics and gynecology: house staff 24 (46%), faculty 28 (54%); gastroenterology and hepatology: house-staff 13 (37%), faculty 22 (63%). The response rate for each specialty was 91%, 95%, and 88%, for PCPs, GIs, and GYNs, respectively.

### Comparison between PCPs and GIs

Almost half of the PCP and GI were not comfortable with performing Pap smears (PCPs 47%, GIs 57%). The difference in the number of patients with IBD seen by PCPs and GIs was significant: 97.5% of PCP encountered fewer than five IBD patients in their practice each month, as compared with 54% of GI physicians ( $P < 0.001$ ). Ninety-seven percent of PCPs and 63% of GIs were not familiar with the current cervical cancer screening recommendations ( $P < 0.001$ ). There was no significant difference between groups regarding awareness of the correct age to start cervical cancer screening and the age range to initiate HPV vaccination. However, 17.9% of PCPs chose the correct annual cervical cancer screening interval compared with 54% of GIs who opted for an annual screening interval ( $P < 0.001$ ). Notably, both PCP and GI providers had varying opinions as to which physician group should be in charge of screening and performing Pap smears. Fifty-two percent of PCPs thought that the PCP should be in charge of managing and keeping track of cervical cancer screening in patients with IBD. Compared with GIs, 40% indicated that the PCP should be in charge, and 45.7% indicated that the GYN should be in charge. However, both agreed that it is not practical for GI physicians to perform Pap smears in their clinics. These results are outlined in Table 2.

### Comparison between GYNs and GIs

One hundred percent of GYN responders were comfortable performing Pap smear as compared with only 43% of GI ( $P < 0.001$ ). Ninety-six percent of GYNs saw fewer than five patients with IBD each month, in contrast to 54% of GI ( $P < 0.001$ ). Self-reported knowledge of screening guidelines was low in both groups as 29% of GYNs and 37% of GIs were familiar with current screening recommendations ( $P = 0.42$ ). Regarding the correct age to initiate cervical cancer screening in patients with IBD, 71% of GYNs opted for age of 21 regardless of sexual activity as compared with 31% of GIs, and 15% of GYNs opted to start screening at time of sexual activity before age 21 as compared with 29% of GIs ( $P = 0.006$ ). Annual cervical cancer screening frequency was selected by 48% of GYNs and 54% of GIs ( $P = 0.004$ ). Ninety-four percent of GYNs indicated they should be in charge of cervical cancer screening and should perform Pap smears in patients with IBD ( $P < 0.001$ ). These results are outlined in Table 3.

### Comparison between PCPs and GYNs

Fifty-three percent of PCP providers were confident in their ability to perform Pap smears, whereas 100% of GYN providers were confident ( $P < 0.001$ ). There was no difference in the number of patients with IBD seen by PCP and GYN physicians: approximately 97% treated fewer than five patients with IBD per month. Approximately 29% of GYNs reported familiarity with cervical cancer screening guidelines in patients with IBD as compared to 2.67% of PCPs ( $P < 0.001$ ).

**Table 1.** Cervical Cancer Screening and Management in IBD Questionnaire

1. How comfortable are you performing Pap smears?
1) Comfortable
2) Not comfortable
2. How often do you take care of patients with IBD?
1) 0 to 5 patients every month
2) 6 to 10 patients every month
3) 10 to 15 patients every month
4) 15 or more patients every month
3. How familiar are you with the current recommendations for cervical cancer prevention and screening in patients with IBD?
1) Not familiar
2) Familiar
4. In general, based on your practice, when do you start screening for cervical cancer in female patients with IBD on immunosuppressive therapy using a Pap smear?
1) Not usually
2) At age 9 years irrespective of the time of sexual activity
3) At age 16 years irrespective of the time of sexual activity
4) At age 21 years irrespective of the time of sexual activity
5) At age 23 years irrespective of the time of sexual activity
6) At the time of sexual activity initiation but no later than age 9 years
7) At the time of sexual activity initiation but no later than age 16 years
8) At the time of sexual activity initiation but no later than age 21 years
9) At the time of sexual activity initiation but no later than age 23 years
5. In general, based on your practice, how often do you screen for cervical cancer in female patients with IBD on immunosuppressive therapy using a Pap smear?
1) Not usually
2) Every 1 year
3) Every 2 years
4) Every 3 years
5) Every 5 years
6. In general, based on your practice, what age group of patients with IBD do you routinely offer the HPV vaccination?
1) Not usually
2) Once the diagnosis of IBD is made (regardless of age)
3) 7 to 21 years old
4) 9 to 26 years old
5) 11 to 23 years old
7. In your opinion, in general, who should be in charge of managing (ordering, documenting, keeping track, and following up on results) cervical cancer screening and Pap smears for patients with IBD?
1) Primary care physician
2) Gynecologist
3) Gastroenterologist/IBD specialist
8. In your opinion, in general, who should be performing Pap smears for patients with IBD?
1) Primary care physician
2) Gynecologist
3) Gastroenterologist/IBD specialist

IBD: inflammatory bowel disease; Pap: Papanicolaou.

**Table 2.** Primary Care Physicians Versus Gastroenterologists

Questions	PCPs, n (%)	GIs, n (%)	$\chi^2$	P value
1. Comfort level			1.11	0.29
Comfortable	62 (53.0)	15 (42.9)		
Not comfortable	55 (47.0)	20 (57.1)		
2. Number of IBD patients seen monthly			47.42	< 0.001*
0 - 5	114 (97.4)	19 (54.3)		
6 - 10	3 (2.6)	9 (25.7)		
10 - 15	0 (0)	3 (8.6)		
15+	0 (0)	4 (11.4)		
3. Familiarity with guidelines			34.20	< 0.001*
Not familiar	114 (97.4)	22 (62.9)		
Familiar	3 (2.6)	13 (37.1)		
4. Timing of cervical cancer screening			12.23	0.09
Not usually	12 (10.3)	8 (22.9)		
Age 9, regardless SA	2 (1.7)	0 (0)		
Age 16, regardless SA	6 (5.1)	1 (2.9)		
Age 21, regardless SA	62 (53.0)	11 (31.4)		
Age 23, regardless SA	6 (5.1)	0 (0)		
At SA, no later than 9	0 (0)	0 (0)		
At SA, no later than 16	7 (6.0)	4 (11.4)		
At SA, no later than 21	18 (15.4)	10 (28.6)		
At SA, no later than 23	4 (3.4)	1 (2.9)		
5. Frequency of cervical cancer screening			26.16	< 0.001*
Not usually	27 (23.1)	11 (31.4)		
1 year	21 (17.9)	19 (54.3)		
2 years	10 (8.5)	2 (5.7)		
3 years	56 (47.9)	3 (8.6)		
5 years	3 (2.6)	0 (0)		
6. Who is offered HPV vaccine			4.05	0.40
Not usually	15 (12.8)	8 (22.9)		
Once diagnosed with IBD	10 (8.5)	4 (11.4)		
Age 7 - 21	11 (9.4)	2 (5.7)		
Age 9 - 26	67 (57.3)	15 (42.9)		
Age 11 - 23	14 (12.0)	6 (17.1)		
7. Who should be in charge			1.97	0.37
PCP	61 (52.1)	14 (40.0)		
GYN	46 (39.3)	16 (45.7)		
GI/IBD	10 (8.5)	5 (14.3)		
8. Who should be performing			4.35	0.11
PCP	56 (47.9)	11 (31.4)		
GYN	58 (49.6)	24 (68.6)		
GI/IBD	3 (2.3)	0 (0)		

IBD: inflammatory bowel disease; GI/IBD: gastroenterologist or IBD specialist; PCP: primary care physician; GYN: gynecologist; SA: sexual activity; HPV: human papillomavirus. \*P < 0.001.

**Table 3.** GYNs Versus GIs

Questions	GYN, n (%)	GI, n (%)	$\chi^2$	P value
1. Comfort level			38.58	< 0.001*
Comfortable	52 (100)	15 (42.9)		
Not comfortable	0 (0)	20 (57.1)		
2. Number of IBD patients seen monthly			22.94	< 0.001*
0 - 5	50 (96.2)	19 (54.3)		
6 - 10	2 (3.8)	9 (25.7)		
10 - 15	0 (0)	3 (8.6)		
15+	0 (0)	4 (11.4)		
3. Familiarity with guidelines			0.66	0.42
Not familiar	37 (71.2)	22 (62.9)		
Familiar	15 (28.8)	13 (37.1)		
4. Timing of cervical cancer screening			16.20	0.006*
Not usually	2 (3.8)	8 (22.9)		
Age 9, regardless SA	0 (0)	0 (0)		
Age 16, regardless SA	1 (1.9)	1 (2.9)		
Age 21, regardless SA	37 (71.2)	11 (31.4)		
Age 23, regardless SA	0 (0)	0 (0)		
At SA, no later than 9	0 (0)	0 (0)		
At SA, no later than 16	4 (7.7)	4 (11.4)		
At SA, no later than 21	8 (15.4)	10 (28.6)		
At SA, no later than 23	0 (0)	1 (2.9)		
5. Frequency of cervical cancer screening			13.46	0.004*
Not usually	7 (13.5)	11 (31.4)		
1 year	25 (48.1)	19 (54.3)		
2 years	0 (0)	2 (5.7)		
3 years	20 (38.5)	3 (8.6)		
5 years	0 (0)	0 (0)		
6. Who is offered HPV vaccine			14.30	0.006*
Not usually	4 (7.7)	8 (22.9)		
Once diagnosed with IBD	3 (5.8)	4 (11.4)		
Age 7 - 21	4 (7.7)	2 (5.7)		
Age 9 - 26	40 (76.9)	15 (42.9)		
Age 11 - 23	1 (1.9)	6 (17.1)		
7. Who should be in charge			27.02	< 0.001*
PCP	1 (1.9)	14 (40.0)		
GYN	49 (94.2)	16 (45.7)		
GI/IBD	2 (3.8)	5 (14.3)		
8. Who should be performing			10.20	0.001*
PCP	3 (5.8)	11 (31.4)		
GYN	49 (94.2)	24 (68.6)		
GI/IBD	0 (0)	0 (0)		

IBD: inflammatory bowel disease; GI/IBD: gastroenterologist or IBD specialist; PCP: primary care physician; GYN: gynecologist; SA: sexual activity; HPV: human papillomavirus. \*P < 0.01.

The two groups responded similarly, and no statistically significant difference was found in the starting age for cervical cancer screening: 53% of PCPs and 71% of GYNs opted to start screening at the age of 21 regardless of sexual activity status. However, 48% of GYNs elected to perform annual cervical cancer screening compared with only 18% of PCPs ( $P < 0.001$ ). PCPs had a mixed impression of which physician should be in charge of cervical cancer screening and Pap smears. Fifty-two percent of PCPs believed that the patient's PCP should perform screening, and 39% believed that GYNs should have this responsibility as compared with 94% of GYNs who felt that they should be responsible ( $P < 0.001$ ). Similarly, 50% of PCP felt that GYNs should perform Pap smears, as compared with 94% of GYN, who felt that they should perform Pap smears ( $P < 0.001$ ). These results are outlined in Table 4.

## Discussion

In our survey of Saint Louis University house staff and faculty, including GI, PCP, and GYN, we identified several aspects of cervical cancer screening trends in the care of patients with IBD. The study's focus was to gauge the respondents' comfort level in performing Pap smears, knowledge of cervical cancer screening guidelines (including age and frequency of screening), HPV vaccination, and the perception of who should be responsible for cervical cancer screening in patients with IBD. This is the first study to assess various obstacles in providing recommended cervical cancer screening in patients with IBD who are receiving immunosuppressive pharmacotherapy. As expected, most PCP and GYN providers (about 97%) encounter fewer than five patients with IBD in their clinics each month, thus indirectly contributing to the perception that many patients with IBD do not see PCPs or GYNs and are primarily managed by GIs, a finding consistent with those from published studies [13, 20]. Also, only 40% of GI and 50% of PCP reported feeling comfortable performing Pap smears.

More importantly, nearly 98% of PCPs and 70% of GYNs reported unfamiliarity with current recommendations of cervical cancer screening in patients with IBD. Surprisingly, 60% of GI physicians stated that they were not acquainted with these recommendations as well. This result was further reflected in the response to additional questions in which just 15% of PCPs, 15% of GYNs, and 28% of GIs answered correctly in electing to start screening at the age of onset of sexual activity but no later than age 21. Only 18% of PCPs chose to complete cervical cancer screening on an annual basis as compared with about 50% of GIs and GYNs. Crucially, ACOG recommends starting cervical cancer screening in people with HIV through Pap smears within 1 year of onset of sexual activity but no later than age 21 [25]. Although there are no societal recommendations for the starting age of cervical cancer screening in non-HIV immunosuppressed women, it is reasonable to generalize recommendations for HIV patients to this group as well [12]. As stated before, the screening interval for immunosuppressed patients with IBD should be every year [12, 13]. Our findings reveal knowledge gaps among all three physician groups and

provide an opportunity for improvement through educational initiatives.

In our study group, PCP and GI physicians were split approximately in half in their opinions of who should perform the responsibility of cervical cancer screening in the immunosuppressed IBD population: PCP or GYN. Interestingly, nearly 95% of GYN physicians were willing to take the complete ownership of cervical cancer screening in this patient population despite the high reported rate of unfamiliarity. All three physician groups overwhelmingly agreed that GIs should not perform Pap smears in their clinic. Based on our survey, GYN physicians are willing and able to take responsibility for cervical cancer screening in with patients with IBD. However, the predominant challenge is that most GYN (96.2%) see fewer than five patients with IBD each month. A unifying theme in our data set indicates two critical points, which may shed light on why women with IBD receive suboptimal cervical cancer screening: a lack of familiarity and a lack of ownership across specialties.

There are several hurdles to achieving optimal cervical cancer screening in patients with IBD, necessitating a multifaceted approach to the problem. Efforts should focus on several levels: patient, physician, and health care organization. Patient-level interventions could include adopting strategies to increase awareness about screening, providing reminder notifications to patients who are due for screening, and decreasing structural barriers to screening. Physician interventions should incorporate provider reminders to make screening recommendations and feedback to providers about their performance in attaining desired goals. These interventions have been supported by the Center for Disease Control (CDC) to boost cervical cancer screening in the community [26]. Organizational-level interventions that accomplish positive results include clear direction, functional infrastructure for quality improvement and leadership commitment, as elaborated upon recommendations by the US Department of Health and Human Services on cervical cancer screening [27]. Furthermore, based on our survey, physician education is a vital step in this process to facilitate familiarity with the recommendations, given that ~60% of GIs were not familiar with the recommendations, and 20-30% do not incorporate cervical cancer screening in their practice. Integrating specialties in a multidisciplinary clinic platform has been demonstrated to be beneficial in optimizing care of patients with complex medical conditions and is becoming more attractive in advanced IBD care [28, 29]. Although clinical outcomes have not yet been demonstrated in IBD care, the hope is this type of platform would provide a more inclusive environment in which all aspects of IBD care are met.

This study has several limitations. First, our sample size was relatively small and limited to faculty and trainees at one institution, limiting generalization of the results. Study participants also did not include family medicine providers and advanced practice providers who are likely to care for a large subset of patients with IBD. This group would probably have offered additional viewpoints in practice and perceptions. Also, of a total of 204 respondents, 138 (68%) of study participants were trainees, potentially resulting in a lack of knowledge among the study group that may have skewed the results. Finally, because our study was based on a survey questionnaire

**Table 4.** PCPs Versus GYNs

Questions	PCP, n (%)	GYN, n (%)	$\chi^2$	P value
1. Comfort level			36.24	< 0.001*
Comfortable	62 (53.0)	52 (100)		
Not comfortable	55 (47.0)	0 (0)		
2. Number of IBD patients seen monthly			0.21	0.65
0 - 5	114 (97.4)	50 (96.2)		
6 - 10	3 (2.6)	2 (3.8)		
10 - 15	0 (0)	0 (0)		
15+	0 (0)	0 (0)		
3. Familiarity with guidelines			26.13	< 0.001*
Not familiar	114 (97.4)	37 (71.2)		
Familiar	3 (2.6)	15 (28.8)		
4. Timing of cervical cancer screening			10.20	0.18
Not usually	12 (10.3)	2 (3.8)		
Age 9, regardless SA	2 (1.7)	0 (0)		
Age 16, regardless SA	6 (5.1)	1 (1.9)		
Age 21, regardless SA	62 (53.0)	37 (71.2)		
Age 23, regardless SA	6 (5.1)	0 (0)		
At SA, no later than 9	0 (0)	0 (0)		
At SA, no later than 16	7 (6.0)	4 (7.7)		
At SA, no later than 21	18 (15.4)	8 (15.4)		
At SA, no later than 23	4 (3.4)	0 (0)		
5. Frequency of cervical cancer screening			20.14	< 0.001*
Not usually	27 (23.1)	7 (13.5)		
1 year	21 (17.9)	25 (48.1)		
2 years	10 (8.5)	0 (0)		
3 years	56 (47.9)	20 (38.5)		
5 years	3 (2.6)	0 (0)		
6. Who is offered HPV vaccine			7.61	0.11
Not usually	15 (12.8)	4 (7.7)		
Once diagnosis with IBD	10 (8.5)	3 (5.8)		
Age 7 - 21	11 (9.4)	4 (7.7)		
Age 9 - 26	67 (57.3)	40 (76.9)		
Age 11 - 23	14 (12.0)	1 (1.9)		
7. Who should be in charge			45.17	< 0.001*
PCP	61 (52.1)	1 (1.9)		
GYN	46 (39.3)	49 (94.2)		
GI	10 (8.5)	2 (3.8)		
8. Who should be performing			30.94	< 0.001*
PCP	56 (47.9)	3 (5.8)		
GYN	58 (49.6)	49 (94.2)		
GI/IBD	3 (2.3)	0 (0)		

IBD: inflammatory bowel disease; GI/IBD: gastroenterologist or IBD specialist; PCP: primary care physician; GYN: gynecologist; SA: sexual activity; HPV: human papillomavirus. \*P < 0.001.

and not the analysis of actual clinical practice, there exists a component of self-serving bias inherent in this type of study design.

In conclusion, an increased risk of cervical dysplasia and malignancy in the immunosuppressed IBD population, along with sub-optimal cervical cancer screening efforts, represents substantial deficiencies in preventative care in patients with IBD. Our study examines the problem by understanding the perception of responsibility and knowledge of cervical cancer screening guidelines among the medical specialties involved in the clinical care of patients with IBD. Based on the study results, we propose a shared approach that requires GI providers to play a vital role in referring appropriate patients with IBD to GYN providers for cervical cancer screening. GYN physicians can then assume this responsibility, but GI physicians should manage adherence and progress at each follow-up visit. We propose clinical outcomes of this implemented strategy be measured with future quality improvement projects assessing this and other areas of IBD health maintenance. Furthermore, future guidelines that indicate which physician groups should be accountable for various aspects of cervical cancer screening in patients with IBD might produce desirable outcomes.

## Acknowledgments

None to declare.

## Financial Disclosure

None to declare.

## Conflict of Interest

None to declare.

## Informed Consent

Not applicable.

## Author Contributions

AC and FO contributed by writing the manuscript; ME and KP worked on data acquisition; KC helped with data analysis; KS and CP designed the study as well as provided critical revision of the manuscript; MBH contributed to study design and final approval of the manuscript.

## Data Availability

The authors declare that data supporting the findings of this study are available within the article.

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