



## RESEARCH ARTICLE

**REVISED** **A national cross-sectional survey of constipation in patients attending cancer centres in Ireland [version 2; peer review: 2 approved, 1 approved with reservations]**

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### Abstract

**Background:** The prevalence of constipation in patients with cancer is estimated at 50-90%. It is often associated with pain, anorexia, nausea and vomiting and impacts negatively on quality of life.

Despite its common occurrence, it is often poorly recognised and treated by healthcare professionals.

**Methods:** A national cross-sectional survey was conducted in Ireland to describe constipation prevalence and severity in patients attending cancer centres and to evaluate management efficacy. In-patients or patients attending day oncology wards in any of the country's eight designated cancer centres were eligible to participate. Participants were shown the Bristol Stool Chart and answered questions regarding stool appearance and sensation of incomplete defecation; they completed the Constipation Assessment Scale. Data on pain character and intensity, opioid use, and prescribed and over-the-counter laxative use were collected. Data were summarised using descriptive statistics. Significance of variations for continuous data were determined using t-tests. Conditional ordered logistic regression was undertaken to determine factors associated with constipation.

**Results:** The dataset comprised 491 patients. 24.8% had been reviewed by specialist palliative care; 14.5% by the anaesthetic pain team. In total, 42.2% of respondents were taking step 2 or step 3 opioids. Constipation prevalence was 67.6%; 19.4% of patients had Constipation Assessment Scale scores indicating severe constipation. A total of 46% of the respondents were not taking any laxatives. Of

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those who were taking laxatives, 54.8% reported constipation symptoms. While opioid use was strongly associated with participants reporting higher scores, this association was not seen in those patients receiving specialist palliative care.

**Conclusions:** Constipation remains a clinical problem in Irish cancer centres. Despite increased opioid use, patients receiving specialist palliative care were more likely to take laxatives and reported less constipation. Specialist palliative care practice should be studied in order to identify what are the transferable 'ingredients' of effective constipation management.

### Keywords

Constipation, neoplasms, guideline, palliative care, prevalence, cross-sectional studies

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**REVISED Amendments from Version 1**

The manuscript has been edited according to reviewer commentary to ensure consistency of terminology and to improve narrative order and flow. Additional detail (including reference to relevant literature) has been provided on the study context and impact on individual patient and societal levels. Greater explanatory detail on data collection has been provided including description of study instruments, time of data collection and acknowledgment of trade-offs that play an integral part of decision-making about what data to collect. The discussion of potential limitations associated with methods has been expanded. Clarification has been provided that this is the first national survey of constipation in patients attending cancer centres in Ireland, and greater detail has been provided on other international studies in order to provide greater understanding of comparability and generalisability.

**Any further responses from the reviewers can be found at the end of the article**

**Introduction**

Ireland has well-developed cancer and palliative care services and there is a growing focus on evidence-based practice and the development of learning healthcare systems<sup>1</sup>. National clinical guidelines have been published to support evidence-based practice and to improve the quality of care provided to patients. The management of cancer-related constipation has emerged as an area for improvement because it is a common condition that impacts negatively on quality of life, yet remains poorly recognised and treated<sup>2-4</sup>. Depending on methodology and population studied, its prevalence is estimated at 32–87%, with the highest incidence being reported in patients receiving opioids. This is significantly higher than the average prevalence of constipation in adults which has been estimated at 16%<sup>5</sup>. Constipation can be associated with pain, anorexia, nausea and vomiting. It can contribute to the development of haemorrhoids, anal fissures, urinary retention, bowel obstruction and delirium<sup>6,7</sup>. Accordingly, a national clinical guideline focused on constipation management for patients receiving palliative care was published in 2015<sup>8</sup>.

Although the literature contains reports of quality improvement initiatives focused on constipation management, efforts to improve quality have shown inconsistent results. Large scale initiatives are recognised to be challenging, and so effort has been focused on describing approaches that may be used to improve outcomes<sup>9,10</sup>. A key first step in quality improvement is convincing stakeholders that there is a problem relevant to them that needs to be addressed<sup>11</sup>. In Ireland, clinical experience suggested that the national guidelines were not being implemented outside of the hospice setting because clinicians failed to recognise the magnitude of the problem. There is a paucity of national data on constipation burden or management efficacy. Therefore, this study was carried out to establish the prevalence of constipation in patients attending cancer centres and to assess the efficacy of treatment. Little is known of the extent of constipation burden experienced by patients with cancer in Ireland. Reliable information on management efficacy is

lacking. The data will be of value as a source of comparative data given relative paucity of recent prevalence studies in cancer populations<sup>12-14</sup>. We hope to stimulate consideration of the factors associated with improved outcomes and re-double clinical practice efforts to reduce constipation burden.

**Methods****Ethics statement**

Ethical approval was obtained in each cancer centre (Beaumont Hospital Research Ethics Committee – Ref: 17/48; Galway University Hospitals: C.A. 1739; HSE South-Eastern Area Research Ethics Committee - approval date: 24.05.17; Mater Misericordiae University Hospital Research Ethics Committee Ref: 1/378/1913; St James’s Hospital /AMNCH Research Ethics Committee Ref: 2017-05 Chairman’s Action (10); St Vincent’s Ethics and Medical Research Committee - approval date 19.04.17; University College Cork Clinical Research Ethics Committee – Ref: ECM 4 (m) 09/05/17; University Hospital Limerick, Research Ethics Committee Ref: 062/17) and the lead University (University College Dublin Research Ethics Committee LS-E-17-105-O’Connor; 16.6.17). Written, signed informed consent was obtained via signature from each participant for data collection (survey and chart review) and publication of results.

**Study design and subjects**

A cross-sectional point prevalence study was carried out in the eight designated cancer centres in Ireland in 2017 (Beaumont Hospital, Galway University Hospital, University Hospital Waterford, Mater Misericordiae University Hospital, St James’s Hospital, St Vincent’s University Hospital, Cork University Hospital, University Hospital Limerick).

Pilot testing was initially carried out with a convenience sample of seven patients in one cancer centre. The pilot study provided a number of valuable logistical insights, such as providing an accurate estimation of time required to complete data collection, and how best to manage the distribution and storage of each of the three copies of the consent forms (patient, medical record and research team copies). Only minor changes to the data collection instrument were made, however. The term ‘medical chart’ was replaced with ‘medical record’ as the latter was better understood by participants and data collectors. Also, adopting the practice of Woolery *et al.*,<sup>15</sup> statements using lay terminology were used as clarifying descriptors for each Constipation Assessment Scale (CAS)<sup>16</sup> item for any participants who did not understand the original CAS item.

Subsequently, data collection was carried out on a single day in each centre. It had been intended to carry out the study in all centres on the same day but operational issues meant that data was collected in two hospitals one week later.

A wide range of clinicians (consultants, specialist registrars, clinical nurse specialists, Advanced Nurse Practitioners, Assistant Directors of Nursing and Nurse Tutors) acted as data collectors for the study. All data collectors completed mandatory pre-study training comprising an e-learning presentation

explaining how to follow the study protocol, carry out data collection and record data. A member of the research team was also present on the study day to oversee data collection and provide any additional support, as needed.

In-patients or patients attending day oncology wards were eligible to participate. Inclusion criteria were: (1) cancer diagnosis; (2) informed of diagnosis (3) aged  $\geq 18$  years; (4) English speaking. Exclusion criteria were: (1) surgery  $\leq 24$  hours prior to the study; (2) cognitive impairment or reduced level of consciousness; (3) patient deemed too unwell to participate by the clinician. The inclusion criteria and data collection methods were applied consistently across all study sites to reduce the potential for bias.

### Data collection

Data collectors first liaised with clinical nurse managers of each ward in order to identify eligible patients and then approached the potential participant. The data collector provided both verbal and written information on the study to the patient and answered any questions that were asked. Following this, patients were invited to take part in the study on that day. Although a ‘cooling off’ period of one hour was offered, patients could waive that if desired.

Demographic details were collected (gender and age) and the Constipation Assessment Scale (CAS)<sup>16</sup> completed. The Constipation Assessment Scale (CAS) is an 8-item self-report tool designed to measure bowel function in adults. It consists of a 3-point summated rating scale (0 = no problem; 1 = some problem; 2 = severe problem). Responses generate a constipation severity score where mild constipation is indicated by a score between 1–4; moderate between 5–9; and severe between 10–16. Evidence of reliability was supported by good internal consistency ( $r = 0.7–0.78$ ) and high test-retest coefficients ( $r = 0.98$ ) in the original validation study and in subsequent studies<sup>17,18</sup>. The CAS takes patients about 2 minutes to complete and is formatted at a reading level for 10–11 year olds. It is therefore associated with minimal participant burden.

Respondents were shown the Bristol Stool Chart<sup>19</sup> and asked “Can you look at this scale and thinking of the last time you had your bowels open, which picture best resembles what it looked like?”. The Bristol Stool Chart<sup>20</sup> is a visual equivalent to the Bristol Stool Form Scale<sup>21</sup>. The ordinal scale evaluates stool consistency and is a surrogate measure for gastrointestinal transit time. Loose or liquid stools occur when there is limited gastrointestinal water absorption and they are associated with rapid intestinal transit time; harder stools occur when there is slow intestinal transit time and excessive water absorption. Types 1 and 2 are abnormally hard stools, while Types 6 and 7 are abnormally loose stools. The scale is widely used in clinical practice and research. It has demonstrated substantial validity and reliability<sup>22</sup>. Concurrent validity as measured by comparison of classification with stool water was moderate (Spearman’s  $\rho = 0.491$ ,  $P < 0.001$ ).

Two questions were asked about medications: ‘Are you currently taking medication prescribed by your doctor to manage your

constipation?’ and ‘Are you currently taking medication that you purchased yourself to manage your constipation?’ Participants were not asked to provide the medication names; however, common laxatives that patients can purchase without a prescription in Ireland include bisacodyl, lactulose, senokot, dulcolax, fybogel, and milk of magnesia. Details on diagnosis, treatment and analgesics were extracted from chart review (see *Extended data* for a copy of the survey instrument<sup>23</sup>).

### Analysis

Data were summarised using descriptive statistics. Significance of variations for continuous data were determined using t-tests.

Two outcomes were examined: 1) the Constipation Assessment Scale (CAS); and 2) laxative use.

1) Conditional ordered logistic regression was undertaken to determine factors associated with constipation. A categorical variable based on CAS scores was the dependent variable: no constipation (CAS score=0); mild constipation (CAS score 1–6) or severe constipation (CAS score 7–16). The independent variables were:

- Age - categorised during data collection in accordance with requirements for ethical approval at study sites.
- Gender- collected as a binary variable at the time of data collection.
- Primary cancer site - grouped into nine categories according to site of origin
- Currently receiving chemotherapy - binary variable.
- Currently receiving radiotherapy - binary variable.
- Currently using opioids - binary variable (Step 2 [‘weak opioids’] or Step 3 [‘strong opioids’])
- Currently utilising specialist palliative care services – binary variable
- Laxative use - categorised into 4 groups capturing observed utilisation patterns: no use; using over-the-counter only; using prescription only; using a combination prescription and over-the-counter laxatives.

2) Random effects logistic regression was undertaken to examine factors associated with laxative use. The binary dependent variable was laxative use (yes if taking any type of laxative). The independent variables were:

- Age, gender, receiving chemotherapy, receiving radiotherapy, utilising specialist palliative care services and opioid use - these were handled in the same manner as described above
- Additionally, the CAS score total was included as a continuous variable.

Analyses were carried out using *Stata* 15<sup>24</sup>, and tests of statistical significance were at  $p \leq 0.05$ . In both models, odds ratios (OR) and 95% confidence intervals (CI) were estimated for each

independent variable. All cases with incomplete data for the CAS items were excluded from regression analysis. Number of missing cases are shown in all relevant tables (Table 3 and Table 4).

Reporting was provided according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) criteria<sup>25</sup> (see *Extended data* for a copy of the completed STROBE checklist<sup>23</sup>).

## Results

### Participants

In total, 491 patients were recruited (Table 1); 51.5% were female and 46.2% were aged  $\geq 65$  years. Haematological, breast and genitourinary cancers were the most common diagnoses. 44.6%

were attending Day Oncology or haematology services, with the remainder receiving inpatient care. The specialist palliative care team were providing care to 24.8%; 14.5% had input from the anaesthetic pain team. Pain was reported by 62.5% and Step 2 or 3 analgesics were being used by 42%. Patients who were receiving palliative care or pain team input were more likely to be taking 2 ('weak opioid') or step 3 ('strong opioid') analgesics than patients who were not receiving input ( $p < 0.001$ ).

### Prevalence

The prevalence of constipation among all participants was 67.6%, based on CAS criteria of a score of  $\geq 1$ . Only 8.3% of respondents reported no symptoms while 19.4% of respondents scored  $\geq 7$ , indicating severe constipation.

**Table 1. Participant characteristics.**

	Frequency	Percentage
<b>Gender:</b>		
Male	206	42.0
Female	253	51.5
Missing	32	6.5
<b>Age groups:</b>		
18-39	43	8.7
40-64	216	44.1
65-79	191	39.0
80+	36	7.3
Missing	5	1.0
<b>Cancer Site:</b>		
Haematological	117	23.8
Breast	77	15.7
Genitourinary	64	13
Lung	49	9.8
Lower Gastrointestinal	49	9.8
Upper Gastrointestinal	43	8.8
Neurological	9	1.8
Other/Multiple sites	63	12.8
Missing	20	4
<b>Anti-tumour treatment:</b>		
Receiving chemotherapy	351	71.5
Not receiving chemotherapy	123	25.0
Missing	17	3.5
Receiving radiotherapy	176	35.8
Not receiving radiotherapy	296	60.3
Missing	19	3.9
Had surgical intervention	241	49.1
Did not have surgical intervention	234	47.7
Missing	16	3.3

	Frequency	Percentage
<b>Laxative use:</b>		
None	226	46
Prescribed laxatives	158	32.2
Over-the-counter laxatives (self-medicating)	22	4.5
Both prescribed and over-the-counter laxatives	39	8.0
Missing/ not applicable (stoma)	46	9.3
<b>Specialist team involvement:</b>		
Specialist palliative care ('SPC') involved in care	122	24.9
SPC not involved in care	339	69.0
Missing	30	6.1
Specialist pain team ('Pain team') involved in care	71	14.5
Pain team not involved in care	371	75.6
Missing	49	10.0
<b>Site of recruitment:</b>		
Cancer centre 1	32	6.5
Cancer centre 2	50	10.2
Cancer centre 3	27	5.5
Cancer centre 4	64	13.0
Cancer centre 5	89	18.1
Cancer centre 6	91	18.5
Cancer centre 7	95	19.4
Cancer centre 8	43	8.8

### Symptom burden

Most commonly reported symptoms according to CAS ratings were reduced bowel movements (44.8%), change in the amount of gas passed rectally (44.8%) and abdominal distension or bloating (43.4%). The symptoms affecting patients most severely were reduced bowel movements (14.7%), abdominal distension or bloating (12%) and rectal fullness or pressure (11.4%). Further detail is provided in [Table 2](#).

Using the Bristol Stool Chart, 20.9% reported hard stools, 55.2% reported normal stools and 17.6% reported loose stools. A weak negative correlation ( $r = -0.1$ ), was observed for CAS scores and stool type, indicating that lower CAS scores were associated with looser stool.

### Management

Just under half (46%) were not taking laxatives. 32.2% were taking prescribed laxatives. Some patients were self-medicating by taking over-the-counter laxatives- 4.5% were taking over-the-counter laxatives alone, while a further 8.0% were taking both prescribed laxatives and supplementary over-the-counter laxatives. Despite taking laxatives, 54.8% of participants reported symptoms.

### Factors associated with constipation burden

Ordered logistic regression analysis was conducted to examine factors associated with constipation ([Table 3](#)). Female gender was associated with increased odds of reporting constipation burden (OR 1.975, 95% CI: 1.16-3.35;  $p = 0.012$ ). Those aged 80 and over were less likely to be constipated than those aged 18–39 (OR .285, 95% CI: .082-.995;  $p = 0.49$ ). Neither treatment with chemotherapy nor radiotherapy were associated with higher CAS scores. Unsurprisingly, opioid use was strongly associated with higher CAS scores (OR 2.19, 95% CI: 1.30-3.67;  $p = 0.003$ ). Importantly, no association between receiving SPC and increased constipation burden was noted (OR 1.33, 95% CI: 0.728 - 2.440;  $p = 0.35$ ). Patients who were constipated were more likely to be taking prescribed (OR 6.446, 95% CI: 3.43-12.15;  $p < .001$ ), over-the-counter laxatives (OR 3.171, 95% CI: 1.064-9.450;  $p = 0.04$ ), or a combination of both (OR 21.957, 95% CI: 8.001-60.254;  $p < 0.001$ ).

### Factors associated with laxative use

Although 39.8% experienced symptoms and were not taking laxatives, there was evidence that increased CAS scores were associated with increased odds of using laxatives (OR 1.510, 95% CI: 1.354-1.685;  $p < 0.001$ ). Being known to SPC



**Table 2.** Constipation Assessment Scale scores.

Item	No problem	Some problem	Severe problem	Missing data*
Abdominal distension or bloating	268 (54.6%)	154 (31.4%)	59 (12%)	10 (2%)
Change in the amount of gas passed rectally	254 (51.7%)	168 (34.2%)	52 (10.6%)	17 (3.4%)
Less frequent bowel movements	250 (51.0%)	148 (30.1%)	72 (14.7%)	21 (4.2%)
Oozing liquid stool	349 (71.1%)	86 (17.5%)	33 (6.7%)	23 (4.7%)
Rectal fullness or pressure	312 (63.5%)	103 (21.0%)	56 (11.4%)	20 (4.1%)
Rectal pain with bowel movement	343 (69.9%)	85 (17.3%)	42 (8.6%)	21 (4.3%)
Smaller stool size	288 (58.7%)	134 (27.3%)	40 (8.2%)	29 (6.0%)
Urge, but inability to pass stool	287 (58.5%)	131 (26.7%)	55 (11.2%)	18 (3.6%)

\*Missing data or not collected

**Table 3.** Ordered logistic regression examining factors associated with constipation burden.

Variable	Odds ratio	p-value	95% CI	
<b>Age category</b>				
<i>18-39</i>	REF			
<i>40-64</i>	.491	0.103	.209	1.155
<i>65-79</i>	.455	0.082	.187	1.103
<i>&gt;79</i>	<b>.285</b>	<b>0.049</b>	<b>.082</b>	<b>.995</b>
<b>Cancer site</b>				
<i>Upper gastrointestinal</i>	REF			
<i>Lower gastrointestinal</i>	.698	0.552	.213	2.286
<i>Genitourinary</i>	.430	0.130	.144	1.281
<i>Neurological</i>	.275	0.237	.032	2.338
<i>Haematological</i>	<b>.376</b>	<b>0.050</b>	<b>.141</b>	<b>1.00</b>
<i>Breast</i>	.456	0.147	.158	1.318
<i>Lung</i>	<b>.281</b>	<b>0.029</b>	<b>.089</b>	<b>.880</b>
<i>Other</i>	.387	0.110	.121	1.240
<i>Multiple</i>	.347	0.185	.072	1.65
<b>Gender</b>				
<i>Male</i>	REF			
<i>Female</i>	<b>1.975</b>	<b>0.012</b>	<b>1.164</b>	<b>3.351</b>
Receiving chemotherapy	.786	0.445	.424	1.457
Receiving radiotherapy	1.055	0.836	.636	1.751
Using opioids	<b>2.189</b>	<b>0.003</b>	<b>1.304</b>	<b>3.672</b>
Utilising specialist palliative care services	1.33	0.352	.728	2.440
<b>Using laxatives</b>				
<i>Nothing</i>	REF			
<i>Prescribed</i>	<b>6.446</b>	<b>&lt;0.001</b>	<b>3.430</b>	<b>12.114</b>
<i>Over-the-counter</i>	<b>3.171</b>	<b>0.038</b>	<b>1.064</b>	<b>9.450</b>
<i>Prescribed and over-the-counter</i>	<b>21.958</b>	<b>&lt;0.001</b>	<b>8.001</b>	<b>60.254</b>

**Table 4. Random effects logistic regression examining factors associated with laxative use.**

Variable	Odds ratio	p-value	95% CI	
<b>Age category</b>				
<b>18-39</b>	REF			
<b>40-64</b>	.935	0.895	.344	2.543
<b>65-79</b>	2.149	0.140	.779	5.932
<b>&gt;79</b>	1.098	0.899	.259	4.665
<b>Gender</b>				
<b>Male</b>	REF			
<b>Female</b>	.734	0.280	.418	1.287
<b>Receiving chemotherapy</b>	.759	0.426	.386	1.495
<b>Receiving radiotherapy</b>	.872	0.641	.489	1.552
<b>Utilising specialist palliative care services</b>	<b>2.953</b>	<b>0.002</b>	<b>1.476</b>	<b>5.905</b>
<b>Using opioids</b>	<b>1.824</b>	<b>0.042</b>	<b>1.022</b>	<b>3.257</b>
<b>CAS score</b>	<b>1.51</b>	<b>&lt;0.001</b>	<b>1.354</b>	<b>1.685</b>

services (OR 2.952, 95% CI:1.476-5.905;  $p=0.002$ ) and opioid use (OR 1.824, 95% CI: 1.022-3.256;  $p=0.042$ ) were also associated with increased odds of using laxatives.

## Discussion

It has been observed that although there is a significant body of literature that examines the pharmacology of constipation management and best clinical practice, that the focus on cancer is limited and largely focused on opioid-induced constipation<sup>26</sup>. This study represents the first national survey of constipation attending cancer centres in Ireland and to our knowledge, worldwide. Study findings are notable in that significant constipation symptom burden is evident. The finding that 67.7% of participants were constipated echoes findings of high prevalence in specialist palliative care settings and in patients receiving opioids in Europe and the United States,<sup>12-14</sup>. Symptom profile was similar to the original CAS validation study<sup>16</sup>. Chronic constipation in the general population is more commonly seen in women<sup>27</sup>, and this association was also found in our study population. Opioid use, also unsurprisingly, was found to be most strongly associated with constipation in our study participants.

It has been observed that in recent years, there has been an increasing trend in self-medication with over-the-counter medications. Medications that are commonly available in Ireland and Europe without prescription include simple analgesics,

vitamins and herbal remedies, cough remedies, anti-diarrhoeals and laxatives. Common over-the-counter laxatives in Ireland include bisacodyl, lactulose, senokot, dulcolax, fybogel, and milk of magnesia. Despite their availability, relatively little is known about use of non-prescription laxatives in Ireland. A survey that was conducted in Northern Ireland in 2005 found that 11.4% of participants reported regular stocking of over-the-counter laxatives<sup>28</sup>. Participants in this study demonstrate similar levels of use with 12.5% reporting use of non-prescription laxatives.

39.8% of participants were not taking laxatives despite symptoms, and 54.8% remained constipated despite taking laxatives. This points to a need not only to encourage appropriate laxative use but also to improve prescribing. Patients known to palliative care might be expected to be at higher risk of constipation due to opioid use and complex symptomatology. Importantly, an association between palliative care input and increased constipation burden was not observed. It is hypothesised that this is attributable to the fact that patients receiving palliative care benefitted from comprehensive symptom assessment and appropriate prescribing supported by guideline use. It points to the value of systematic constipation assessment in practice.

Different countries have taken different approaches to the development of constipation guidelines<sup>29</sup>. In Ireland, the only



national guideline on constipation is titled ‘Management of Constipation of Adult Patients Receiving Palliative Care’<sup>8</sup>. Acknowledging that misperceptions exist regarding the term ‘palliative care’<sup>30</sup>, and noting the high prevalence of constipation found in the broader cancer population studied, it is possible that the title acted as a barrier to uptake. Planning is key to successful guideline development<sup>31</sup>, and identification of scope a critical first step<sup>32</sup>. While it is possible to develop broad guidelines, considerable resources are required and influence decisions regarding scope. Given the lack of improvement seen to date, we suggest that a broader approach in future guidelines should be considered to reduce fragmentation of practice and build momentum in quality improvement.

Study limitations include the fact that patient experience outside cancer centres is not described. While the multi-site design adds to the robust nature of data collection, logistical challenges meant that the study was not carried out on a single day and centres demonstrated variability in recruitment. Data collection was conducted in 2017 and it would be informative if the study were repeated and comparative data obtained for analysis. Practical lessons learned from this study should benefit any planned national survey- for example, selection of data items for collection necessitated efforts to balance comprehensiveness of data collection against burden to study participants who were attending hospital for cancer treatment. The experience of completing the survey tool was that it was short and user-friendly, and this allows for the possibility of collecting a limited amount of additional data in future surveys. A further limitation of this study is that data on refusal rate was not collected. The study was conducted at a time of changing data protection laws in Ireland and gatekeeper concerns regarding the requirement for explicit consent for data processing resulted in restrictions on data collection being applied. Finally, given the disparity of a single agreed definition for constipation, a potential confounder is chronic constipation as defined by ROME Diagnostic Criteria<sup>33</sup>. Future studies should aim to characterise patients who have a pre-morbid diagnosis of chronic constipation.

## Conclusion

Cancer-related constipation remains inadequately recognised and treated in Ireland. The merits of symptom assessment and guideline application as evidenced by lower symptom burden associated with palliative care input are suggested. The confirmation of the high prevalence of constipation in the wider population, reaffirms the need to find more effective approaches to practice improvement across the cancer trajectory. Clinical guidelines are increasingly familiar part of clinical practice; they represent one option for improving the quality, safety and value of healthcare provision. This study highlights the need for further work to establish the efficacy of implementation of the management of constipation in Adult Patients Receiving Palliative Care guidelines. It provides a baseline against which progress can be tracked.

## Data availability

### Underlying data

Due to the nature of this research and the consent document, participants of this study were not asked to consent to the sharing of data beyond the research team and their collaborators. As a result, underlying data cannot be publicly provided. Researchers seeking to access the underlying dataset will need to apply directly to all University and Hospital Research Ethics Committees for approval. UCD Office of Research Ethics can be contacted at [research.ethics@ucd.ie](mailto:research.ethics@ucd.ie); the individual hospital research ethics committees can be contacted at [beaumontethics@rcsi.com](mailto:beaumontethics@rcsi.com); [colette.collins@hse.ie](mailto:colette.collins@hse.ie); [caroline.lamb2@hse.ie](mailto:caroline.lamb2@hse.ie); [soneill@mater.ie](mailto:soneill@mater.ie); [research@stjames.ie](mailto:research@stjames.ie); [svhgethics@ucd.ie](mailto:svhgethics@ucd.ie); [crec@ucc.ie](mailto:crec@ucc.ie); [joanne.oconnor@hse.ie](mailto:joanne.oconnor@hse.ie). Should approval be granted, the corresponding author is happy to facilitate access in circumstances where data are fully and irrevocably anonymised, where data are being accessed for the purposes of further research and where a data access agreement is signed that meets any and all requirements specified by the Lead University and Principal Investigator.

### Extended data

Open Science Framework: Ryan K. National cross-sectional study of constipation in patients attending cancer centres. <https://doi.org/10.17605/OSF.IO/ZXDSK><sup>23</sup>.

This project contains the following extended data:

- Strobe checklist Ryan National cross sectional study of constipation.pdf
- Survey Instruments Ryan National cross sectional study of constipation.pdf

Data are available under the terms of the [Creative Commons Zero “No rights reserved” data waiver](#) (CC0 1.0 Public domain dedication).

## Acknowledgements

We thank the patients and staff of the following hospitals for their participation and support of the study: Mater Misericordiae University Hospital, St Vincent’s University Hospital; Beaumont Hospital; St James’s University Hospital; Cork University Hospital; University Hospital Waterford; University Hospital Limerick; Galway University Hospital.

We would like to pay our respects to our co-author, Prof. Laserina O’Connor who died on 24th April 2022. Laserina was a dedicated clinician with a passion for improving the quality of care provided to patients. Her research was characterised by its attention to listening to the voice of the patient and by its support of healthcare professional development. We are grateful for the opportunity that we had to collaborate and learn from her.

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## Open Peer Review

Current Peer Review Status:   

### Version 2

Reviewer Report 19 October 2022

<https://doi.org/10.21956/hrbopenres.14824.r32934>

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#### Young D. Chang

Department of Supportive Care Medicine, Moffitt Cancer Center, Tampa, FL, USA

Thank you for inviting me to review your article. This is a national cross-sectional study with a direct survey among 491 patients attending multi-designated Irish cancer centers to assess prevalence, severity, and management efficacy of constipation in cancer patients. The study showed again high prevalence (67.6%) of constipation among cancer patients. Female and opioid use were associated with higher constipation related symptom burden, but not patients under the management of palliative care specialists although constipation is generally expected more common and serious with high complex symptom burden. Interestingly, higher symptom burden with high CAS scores, opioid use and palliative care specialists were associated with laxative use. It is suggesting that palliative care may be an efficient way of the management for complex cancer related symptoms.

My impression was that it was well written and also straightforward study design. I would just suggest some minor issues.

1. I know that you indicated what SPC stands for. But, in the sentence of "*being known to SPC services*" in result section. It would be better to add " Specialist palliative care (SPC) in the main manuscript to avoid confusion for readers.
2. I am curious what are the differences between 'prescribed' vs 'OTC' in terms of chosen agent, dosage etc. OR was much higher with prescribed + OTC than prescribed and OTC.

**Is the work clearly and accurately presented and does it cite the current literature?**

Yes

**Is the study design appropriate and is the work technically sound?**

Yes

**Are sufficient details of methods and analysis provided to allow replication by others?**

Yes

**If applicable, is the statistical analysis and its interpretation appropriate?**

Yes

**Are all the source data underlying the results available to ensure full reproducibility?**

Yes

**Are the conclusions drawn adequately supported by the results?**

Yes

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** Cancer related pain and fatigue

**I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.**

Reviewer Report 21 June 2022

<https://doi.org/10.21956/hrbopenres.14824.r32317>

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**Bridget Candy**

Marie Curie Palliative Care Research Department, Division of Psychiatry, University College London, London, UK

I am happy with the revisions made and have no new comments on the revised article version.

**Is the work clearly and accurately presented and does it cite the current literature?**

Yes

**Is the study design appropriate and is the work technically sound?**

Yes

**Are sufficient details of methods and analysis provided to allow replication by others?**

Yes

**If applicable, is the statistical analysis and its interpretation appropriate?**

Yes

**Are all the source data underlying the results available to ensure full reproducibility?**

Yes

**Are the conclusions drawn adequately supported by the results?**

Yes

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** I am a palliative care researcher who has undertaken research in the treatment of opioid induced constipation

**I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.**

Author Response 21 Jun 2022

**Karen Ryan**, University College Dublin, Dublin, Ireland

Many thanks for taking the time to review the latest version of the manuscript and for the helpful commentary that improved the paper. We are delighted that you are satisfied with the amendments.

**Competing Interests:** No competing interests were disclosed.

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## Version 1

Reviewer Report 10 December 2021

<https://doi.org/10.21956/hrbopenres.14496.r30749>

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**Rita Wickham**

Rush University College of Nursing, Chicago, IL, USA

This is a well-written, clinically useful paper that I will look forward to reading in its final, edited form. There are minor editorial issues in punctuation that an editor will easily fix. My suggestions for improving this research report center on the tools used and operational definitions, which affect results and discussion:

- The authors should include details of instruments. Demographic data includes more than age and gender and this is just a list. Need more information about the CAS and the Bristol Stool Chart (figure might be useful, given contention of under-assessment). For instance, the CAS is an easily understood patient-completed tool that evaluates eight potential manifestations of constipation rated on a 3-point scale (no problem, some problem, severe problem). It is scored ----- etc.. Psychometric data and info about use in other populations/translation would strengthen choice of tool (Doğan & Aktuğ (2017<sup>1</sup>), Woolery *et al.* (2006<sup>2</sup>), Dal Molin *et al.* (2012<sup>3</sup>)).

- Do the same for the Bristol Stool Chart (Amarenco G (2014<sup>4</sup>), Srinivas *et al.* (2019<sup>5</sup>)). These are just examples.
- You state you identified patients taking opioid analgesics step 2 & 3, but page 4 mentions only step 3. Which did you actually include? Although most clinicians may be familiar with the ladder concept, some may not be. It may be useful to include a brief modifier, i.e. step 2 (codeine-like) and step 3 (morphine-like).
- Another question I had was regarding what laxatives are OTC and which are prescription in Ireland. I don't know if these differ from my (and other) country.
- Table 1: Do you want to call them participants, patients, or patient participants? Consider different layout for this table, with columns for yes (n/percent), no (n /%), and missing. Would be easier to read.
- On page 5, report of CAS scores will make sense if information about the instrument is included in the earlier section.
- Page 7: include the actual correlation coefficient before the p value.
- I had a question about laxative use that you may or may not be able to address in the discussion section: do patients typically self-medicate with laxatives, or do health professionals recommend they start with OTC laxatives?
- The last sentence in the first paragraph of the Discussion is confusing. Consider more direct: The factors most commonly associated with constipation in this sample of cancer patients receiving palliative care were opioid use and female sex (has this been previously found?): And how about stressing enhanced systematic constipation assessment.

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**Is the work clearly and accurately presented and does it cite the current literature?**



Partly

**Is the study design appropriate and is the work technically sound?**

Yes

**Are sufficient details of methods and analysis provided to allow replication by others?**

No

**If applicable, is the statistical analysis and its interpretation appropriate?**

Yes

**Are all the source data underlying the results available to ensure full reproducibility?**

Yes

**Are the conclusions drawn adequately supported by the results?**

Yes

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** palliative care, symptom management

**I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.**

Reviewer Report 06 December 2021

<https://doi.org/10.21956/hrbopenres.14496.r30752>

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**Bridget Candy**

Marie Curie Palliative Care Research Department, Division of Psychiatry, University College London, London, UK

This national survey provides prevalence rate of constipation for people attending cancer centres in Ireland. It finds a high prevalence of constipation, and limited use of laxations. The authors recommend better prescribing supported by clinical guidelines.

To make the article suitable for publication I would recommend some tightening in the writing, there are some redundant words and lack of order/flow between sections. The authors interchange between palliative care and Palliative Care. The results presentation does not follow the order set out in methods, as in first prevalence and then severity and then management. If they follow this in the abstract, results and then in brief in the discussion it will make the paper

clearer.

- **Abstract and introduction:** It would be expected for the introduction to include what was said in the abstract background but to say it in more detail. For example, why are prevalence estimates so wide (50 to 90%). Also to set this in context what is the prevalence of constipation in the general population.
- **Method:**
  - They use fairly old data – you need to mention this in the discussion.
  - Helpful for readers to know more on the Bristol Stool Chart, as in number of items and what the items are.
  - I note there is limited/no data collection on opioid intake, cancer severity, and ethnicity/cultural difference. All these factors will effect constipation/how patient manages constipation.
- **Results:**
  - The authors need to give the reader some indication of how representative the 491 patients were of all such patients in Ireland. Also what about refusal rate?
  - Participant characteristics – you have not detailed whether prevalence differs between in and out-patients.
  - Table 1 – it is not that informative to give detail as stated on cancer centre recruitment. For instance, why is there a range of recruitment rates. Is it the case that the larger centres provided more participants?
- **Discussion:** Is this the first national survey in Ireland or even elsewhere – if so say so. They refer to your findings echoing other studies, it would be helpful if they could say whether these studies were in Ireland or elsewhere.
- **Conclusion:** Add Ireland to the first sentence.

**Is the work clearly and accurately presented and does it cite the current literature?**

Partly

**Is the study design appropriate and is the work technically sound?**

Yes

**Are sufficient details of methods and analysis provided to allow replication by others?**

Yes

**If applicable, is the statistical analysis and its interpretation appropriate?**

I cannot comment. A qualified statistician is required.

**Are all the source data underlying the results available to ensure full reproducibility?**

No source data required

**Are the conclusions drawn adequately supported by the results?**

Partly

**Competing Interests:** No competing interests were disclosed.**Reviewer Expertise:** I am a palliative care researcher who has undertaken research in the treatment of opioid induced constipation**I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.**

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## Comments on this article

**Version 1**

Author Response 12 Dec 2021

**Karen Ryan**, University College Dublin, Dublin, Ireland

Dear Drs Candy and Wickham,

Many thanks for your considered reviews and helpful commentary. We will revise the manuscript accordingly and look forward to providing an improved draft in the near future. We appreciate the time that has been given to providing peer review.

**Competing Interests:** Nil to declare