

'Constipation': One word, many meanings amongst persons with cancer: An observational study

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Abstract

Background: Constipation is common in people with advanced cancer and is associated with significant morbidity and health economic burden, but it is often sub-optimally managed. Despite international consensus diagnostic criteria for functional and opioid-induced constipation (Rome IV diagnostic criteria), the term 'constipation' means different things to different people, impacting assessment, diagnosis and management.

Aim: To investigate the association between persons with advanced cancer self-reporting of constipation, response to the Rome IV diagnostic criteria statements for opioid-induced constipation and differences according to personal demographics.

Design: Multicentre prospective observational study.

Setting/participants: Twenty-four community, hospice and hospital research sites in 10 European countries recruited 1200 adults with cancer taking opioids for cancer/cancer-treatment related pain.

Results: In response to the simple question 'Are you constipated?', 549 (45.5%) participants replied 'yes', 588 (49%) replied 'no' and 59 (5%) were 'unsure', but 713 (59.5%) participants met the Rome IV diagnostic criteria. Only 439 (61.5%) participants that met these criteria answered the simple question positively, whilst 230 (39%) answered negatively, although there was a statistically significant association between responses to the simple question and the criteria ($\chi^2(1, N=1136)=149.945, p=0.00001$). There were certain significant differences in self-reporting according to age and country of origin.

Conclusions: There is disparity between patients' self-reporting of constipation and the Rome IV diagnostic criteria. People with advanced cancer, especially those receiving opioid analgesics, need to be regularly assessed for constipation, but the use of a single question ('Are you constipated?') is inadequate.

Registry: European Study of Opioid Induced Constipation (E-StOIC), NCT05149833, <https://clinicaltrials.gov/study/NCT05149833>, 08/12/2021.

Keywords

Constipation, opioid-induced constipation, cancer pain, diagnosis, neoplasms

What is already known about the topic?

- Constipation in people with advanced cancer is associated with significant morbidity, impaired quality-of-life and health economic burden.
- Constipation is often inadequately managed in people with advanced cancer due to a combination of inadequate assessment, diagnosis, treatment and reassessment, and medication non-adherence.
- Rome Foundation international consensus diagnostic criteria have been developed for functional constipation and opioid-induced constipation, but the term 'constipation' means different things to different people.

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What this paper adds

- Opioid-induced constipation is common in people with advanced cancer receiving opioid analgesics, but there is a disparity between patients' self-report of constipation and the Rome IV diagnostic criteria.
- Patients' self-report differs according to age; younger (<65 years) participants were more likely to disregard the sensation of incomplete evacuation after defaecation.
- Patients' self-report differs according to country of origin; for example, Italian participants were more likely to disregard most of the Rome IV diagnostic clinical features.

Implications for practice, theory or policy

- The use of a single question ('Are you constipated?') is inadequate in identifying a significant proportion of patients with opioid-induced constipation in people with advanced cancer in Europe.
- Patients need to be asked about all of the features in the Rome IV diagnostic criteria.
- These implications are potentially generalisable to other types of constipation (i.e. functional constipation, secondary constipation), and other cohorts of patients (i.e. non-European patients, patients with non-malignant disease).

Introduction

Constipation is a common problem in patients with advanced cancer,¹ and is associated with significant morbidity (i.e. physical, psychological),^{2,3} impaired quality-of-life,^{2,4} and significant health economic burden (i.e. patient, health service).^{5,6} It may be due to a number of factors, including many drugs used for symptom control, and especially the opioid analgesics.¹ Other causes include functional constipation, and gastrointestinal diseases (e.g. diverticulosis, irritable bowel syndrome), neurological/psychiatric diseases (e.g. dementia, depression) and other systemic diseases (e.g. diabetes, hypothyroidism).¹ Research suggests that constipation is inadequately managed in this population of patients,⁷ and the reasons for this include non-diagnosis, inadequate assessment, inappropriate treatment, inadequate reassessment and non-adherence with prescribed laxative regimens (and often a mixture of factors).¹

Surprisingly, there is no universally accepted definition of constipation.⁸ In palliative care, it was defined as 'the passage of small, hard faeces infrequently and with difficulty',^{9,10} although it has been re-defined as 'the slow movement of faeces through the large intestine, resulting in infrequent bowel movements and the passage of dry, hard stools'.^{11,12} However, there are international consensus diagnostic criteria for functional constipation, opioid-induced constipation, and irritable bowel syndrome with predominant constipation (i.e. Rome Foundation diagnostic criteria).¹³

Importantly, the term 'constipation' means different things to different people, and there seems to be some cultural/regional differences in interpretation.¹⁴ For example, a survey of the Swedish population found that only 41% of females and 21% of males considered 'infrequent bowel movements' as indicative of constipation, whilst

only 44% of females and 43% of males considered 'hard stools' as indicative of constipation.¹⁵ Similarly, many South Koreans that self-reported having constipation disagreed with the statements relating to 'straining' (25.4% respondents), 'incomplete evacuation' (32.3% respondents), and/or 'anorectal obstruction' (38.4% respondents) within the Rome Foundation diagnostic criteria for functional constipation.¹⁶

The aim of this element of the European Study of Opioid-Induced Constipation (E-StOIC) was to investigate the association between persons with advanced cancer self-reporting of constipation (and especially self-reporting of not having constipation), and their response to the statements within the Rome IV diagnostic criteria for opioid-induced constipation (which are analogous to the Rome IV diagnostic criteria for functional constipation).¹³ Moreover, we sought to identify any differences in terms of patient demographics, that is, sex, age, country of residence.

Methods

Design

The study was a prospective observational study, which examined various aspects of opioid-induced constipation, including prevalence, diagnosis / assessment, clinical features/complications and management. The data on management of opioid-induced constipation have been separately published.¹⁷

Setting

The study was conducted at 24 research sites (see Acknowledgements) in 10 European countries (Denmark, Finland, France, Germany, Ireland, Italy, Netherlands,

Norway, Spain, United Kingdom). The research sites were either hospices, or hospitals with specialist palliative care services.

Population

The inclusion criteria were (a) age ≥ 18 years; (b) diagnosis of cancer; (c) diagnosis of cancer pain/cancer treatment-related pain; and (d) taking regular opioids for at least 1 week (i.e. opioid for mild-to-moderate pain, or opioid for moderate-to-severe pain). The exclusion criteria were (a) inability to provide informed consent; and (b) inability to complete study questionnaire (as result of cognitive impairment). The study questionnaire was provided in the 'local' language, and so participants needed to be proficient in the local language.

Sampling

Participants were recruited from inpatients and outpatients at the research sites. All patients that met the criteria for the study were eligible for entry into the study (i.e. convenience sampling, consecutive recruitment).

Recruitment

Potential participants were identified by the clinical team, and (with the person's permission) referred to the research team. They were given an information sheet about the study, and given the chance to ask the research team questions about the study. Informed written consent was obtained from participants prior to entry into the study.

Data collection

Data was collected on paper case report forms (in local language), and uploaded onto a central REDCap® database (in English). The study involved collection of demographic information, as well as assessment of Eastern Co-operative Oncology Group performance status (participant determined),¹⁸ and completion of Rome IV diagnostic criteria for opioid-induced constipation (see below).¹³ The official translations of the Rome IV diagnostic criteria were utilised as required in the study (with permission of the copyright holders, the Rome Foundation). In addition, patients were asked about their opinion about their bowel habit ('Are you constipated?'), and whether they agreed with the following definition of opioid-induced constipation: 'A change since initiating opioid therapy ("pain-killer") from baseline bowel habits that is characterised by any of the following: reduced bowel movement frequency; development or worsening of straining to pass bowel movements; a sense of incomplete rectal evacuation; harder stool consistency'.¹⁹ Participants also completed

the Bowel Function Index (to assess treatment response), and the Patient Assessment of Constipation Quality of Life questionnaire (to assess quality of life) – results not shown. In most cases, the researchers completed the questionnaire (with the patient answering the questions), but in some cases the participants completed the tools in the questionnaire themselves (with the researcher supporting the completion).

The Rome IV diagnostic criteria for opioid-induced constipation consists of six statements relating to constipation-related symptoms, and one 'exclusion' statement relating to the co-existence of diarrhoea in the absence of laxatives (Box 1).¹³ Patients were required to answer 'yes' or 'no' to each statement, and those that answer positively to ≥ 2 statements (and negatively to the exclusion statement) meet the Rome IV diagnostic criteria for opioid-induced constipation. It should be noted that the statements relate to 'new or worsening symptoms of con-

Box 1. Rome IV diagnostic criteria for opioid-induced constipation.¹³

Rome IV diagnostic criteria for opioid-induced constipation

1. New, or worsening, symptoms of constipation when initiating, changing, or increasing opioid therapy, that must include two or more of the following:
 - a) Straining during more than $\frac{1}{4}$ (25%) of defecations;
 - b) Lumpy or hard stools (Bristol Stool Form Scale 1–2) more than $\frac{1}{4}$ (25%) of defecations;
 - c) Sensation of incomplete evacuation more than $\frac{1}{4}$ (25%) of defecations;
 - d) Sensation of anorectal obstruction / blockage more than $\frac{1}{4}$ (25%) of defecations;
 - e) Manual manoeuvres to facilitate more than $\frac{1}{4}$ (25%) of defecations (e.g. digital evacuation, support of pelvic floor);
 - f) Fewer than three spontaneous bowel movements per week.
2. Loose stools are rarely present without the use of laxatives

stipation when initiating, changing, or increasing opioid therapy'. The Rome IV diagnostic criteria for opioid-induced constipation do not relate to a specific period of time.¹³

Data analysis

The sample size was pragmatic, and reflected the need to collect data from a large/heterogeneous cohort of patients. In terms of determining the prevalence of opioid-induced constipation, and assuming a similar prevalence to that suggested by an Expert Working Group of European Association of Palliative Care,²⁰ then a sample size of 1200 would provide a 95% confidence interval of $\pm 2.70\%$ for the estimate of the prevalence percentage.

Table 1. Characteristics of study participants.

Characteristic	All participants (<i>n</i> = 1200)	Participants with opioid-induced constipation ^a (<i>n</i> = 713)	Participants without opioid-induced constipation ^a (<i>n</i> = 487)
<i>Age</i>			
Median (range)	65 years (23–96 years)	64 years (23–94 years)	67 years (24–96 years)
<i>Gender</i>			
Female	611 (51%)	362	249
Male	589 (49%)	351	238
<i>Cancer primary location</i>			
Breast	137 (11.5%)	97	40
Endocrine	28 (2.5%)	14	14
Gastrointestinal	309 (25.5%)	158	151
Gynaecological	89 (7.5%)	45	44
Haematological	74 (6%)	39	35
Head & neck	60 (5%)	34	26
Lung	227 (19%)	144	83
Neurological	6 (0.5%)	4	2
Ophthalmic	1 (0%)	1	0
Skin	39 (3%)	29	10
Soft tissue & bone	40 (3.5%)	23	17
Unknown primary	21 (2%)	10	11
Urological & male genital	168 (14%)	114	54
No data	1 (0)	1	0
<i>Eastern Co-operative Oncology Group performance status (participant determined)</i>			
0	65 (5.5%)	40	25
1	357 (30%)	208	149
2	391 (32.5%)	242	149
3	332 (27.5%)	190	142
4	55 (4.5%)	33	22

^aBased on Rome IV diagnostic criteria.

It was decided in advance to replace patients that were recruited to the study but did not complete relevant sections of the questionnaire.

Descriptive statistics were primarily used to explain the data derived from study questionnaire (numbers, percentages; median, range). Standard statistical methods were used in the analysis. Chi-squared tests were used to assess the association between categorical data, with Yates continuity corrections employed as needed for nominal binary (2 × 2) categorical variables. An alpha 5% two-sided cut-off was used to determine a significant association between the two groups of patients.

Ethical issues

The study was sponsored by Trinity College Dublin, and received ethical approval in Ireland from the St. James's Hospital/Tallaght University Hospital Joint Research Ethics Committee (reference number – 0148) on 13th August 2021. The study received similar ethical approval in all other countries. The study was registered on CancerTrials.gov registry (reference number – NCT05149833). The study was conducted in accordance with the Declaration

of Helsinki, and the International Conference on Harmonisation guidance on Good Clinical Practice and conformed to the General Data Protection Regulations (GDPR; 2018); all data was treated as confidential. No ethical issues arose during the study.

Results of the study

One thousand, two hundred patients completed the study between 16th September 2021 and 28th November 2023, although 1204 patients were enrolled in the study: 4 participants were excluded, as they did not complete all necessary sections of the study questionnaire. The participant's characteristics are shown in Table 1. All of the countries recruited 120 patients, except for Ireland (*n* = 177), Denmark (*n* = 113) and Norway (*n* = 70).

In answer to the simple question 'Are you constipated?', 549 (45.5%) participants replied 'yes', 588 (49%) replied 'no', and 59 (5%) were 'unsure' (with missing data in four cases – 0.5%). However, 713 (59.5%) participants met the Rome IV diagnostic criteria, with only 439 (61.5%) participants that met these criteria answering the simple question positively (see Figure 1). Nevertheless, there was

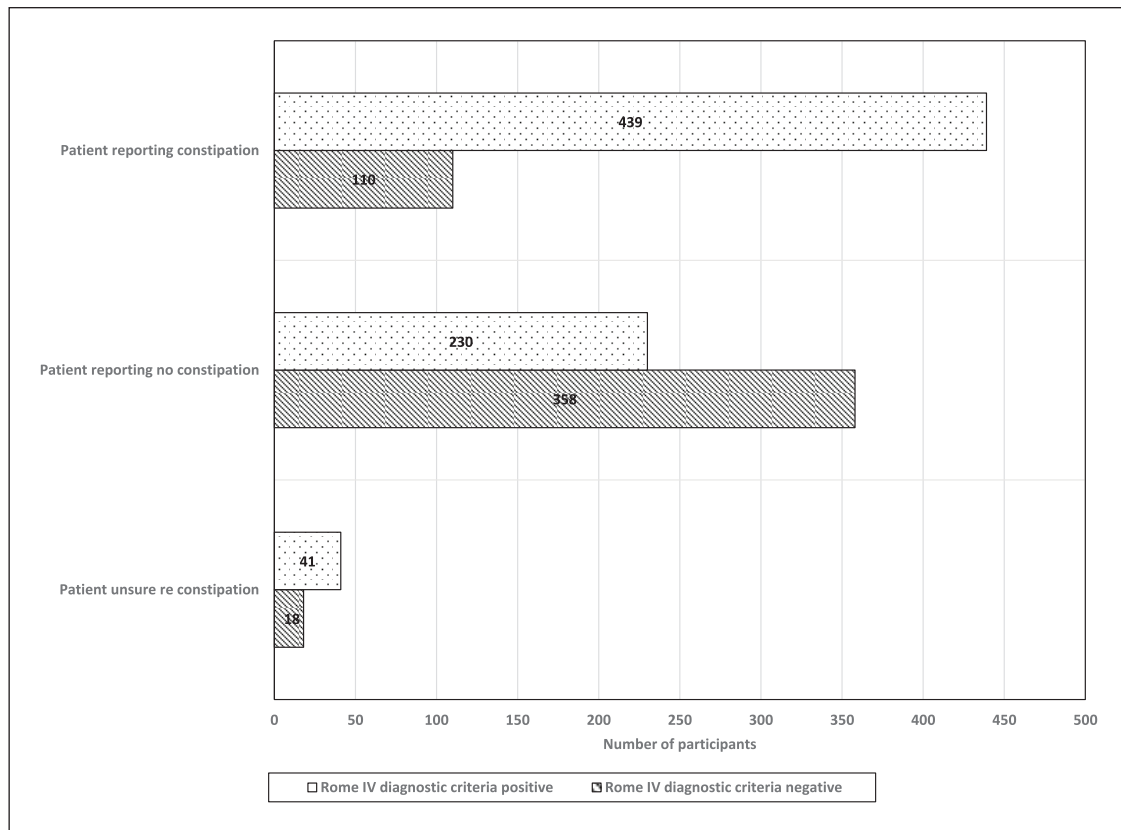


Figure 1. Patient opinion re constipation versus Rome IV diagnostic criteria for opioid-induced constipation.

a statistically significant association between the answer to the simple question and the response to Rome IV diagnostic criteria [χ^2 (1, $N = 1136$) = 149.945, $p = 0.00001$].

Many (58.5%) participants answering the simple question negatively acknowledged that they met one or more of the Rome IV diagnostic criteria individual statements, that is, one statement ($n = 114$), two statements ($n = 87$), three statements ($n = 71$), four statements ($n = 35$), five statements ($n = 34$) and all six statements met ($n = 3$). Thus, 230 (39%) participants answering the simple question negatively met the Rome IV diagnostic criteria (Figure 1). Table 2 shows the responses to the individual statements in participants answering the simple question negatively (and also positively).

In terms of participants answering the simple question negatively, there was no difference in response to any of the Rome IV diagnostic criteria individual statements in terms of sex (i.e. female, male). However, there were certain differences in terms of age (Table 3), and especially in terms of country of origin (Table 4). Thus, younger (≤ 65 years) patients that self-reported not having constipation were more likely to agree that they 'had the sensation of incomplete evacuation with more than 1/4 (25%) defecations' (Chi squared test: $p = 0.033$). In terms of country of origin, for example, Italian patients that self-reported not having constipation were more likely to

agree that they 'had to strain during more than 1/4 (25%) of defecations', whilst Irish patients that self-reported not having constipation were less likely to agree that they had 'lumpy or hard stools (BSFS type 1-2) for more than 1/4 (25%) of defecations' (Table 4).

Interestingly, 757 (63%) participants agreed with the Camilleri et al. definition of opioid-induced constipation, that is, agreed that there had been 'a change (*in various aspects of bowel function*) since initiating opioid therapy'.¹⁹ The latter group included 293 (50%) of the participants that answered the simple question negatively.

The data relating to the Bowel Function Index, the Patient Assessment of Constipation Quality of Life questionnaire and the management of opioid-induced constipation across Europe are reported elsewhere.¹⁷

What this study adds

The results of this study confirm that opioid-induced constipation is common in patients with advanced cancer receiving opioid analgesics, and that there is a disparity between patients' self-report of constipation and the Rome IV diagnostic criteria for opioid-induced constipation. Notably, this discrepancy relates not only to patients that self-reported not having constipation, but also to patients that self-reported having constipation

Table 2. Agreement with individual statements from Rome IV diagnostic criteria for opioid induced constipation in patients with and without self-reported constipation.

Statement from ROME IV diagnostic criteria for opioid induced constipation	Number of patients self-reporting 'constipation' agreeing with statement (<i>n</i> = 549)	Number of patients self-reporting 'no constipation' agreeing with statement (<i>n</i> = 588)
Had to strain during more than 1/4 (25%) of defecations	372 (67.8%)	184 (31.3%)
Had lumpy or hard stools (BSFS type 1–2) for more than 1/4 (25%) of defecations	303 (55.2%)	160 (27.2%)
Had the sensation of incomplete evacuation with more than 1/4 (25%) defecations	366 (66.7%)	222 (37.8%)
Had the sensation of anorectal obstruction/blockage with more than 1/4 (25%) defecations	262 (47.7%)	115 (19.6%)
Had to use manual manoeuvres to facilitate more than 1/4 (25%) defecations (e.g. digital evacuation, support of the pelvic floor)	91 (16.6%)	26 (4.4%)
Had fewer than three spontaneous bowel movements per week	291 (53%)	122 (20.7%)

Table 3. Agreement with individual statements from Rome IV diagnostic criteria for opioid induced constipation in patients without self-reported constipation (demographic data).

Statement from ROME IV diagnostic criteria for opioid induced constipation	Participants reporting no constipation (<i>n</i> = 588)	Female (<i>n</i> = 294)	Male (<i>n</i> = 294)	Statistics (female vs male)	≤65 years (<i>n</i> = 290)	>65 years (<i>n</i> = 297)	No data (<i>n</i> = 1)	Statistics (≤ 65 years vs >65 years)
Had to strain during more than 1/4 (25%) of defecations	184 (31.5%)	90 (30.5%)	94 (32%)	$\chi^2 = 0.057$ $p = 0.811$	102 (35.5%)	82 (27.5%)	0	$\chi^2 = 3.667$ $p = 0.056$
Had lumpy or hard stools (BSFS type 1–2) for more than 1/4 (25%) of defecations	160 (27%)	82 (28%)	78 (26.5%)	$\chi^2 = 0.077$ $p = 0.781$	84 (29%)	75 (25.5%)	1	$\chi^2 = 0.845$ $p = 0.358$
Had the sensation of incomplete evacuation with more than 1/4 (25%) defecations	222 (38%)	115 (39%)	107 (36.5%)	$\chi^2 = 0.394$ $p = 0.530$	122 (42%)	99 (33.5%)	1	$\chi^2 = 4.547$ $p = 0.033$
Had the sensation of anorectal obstruction / blockage with more than 1/4 (25%) defecations	115 (19.5%)	57 (19.5%)	58 (19.5%)	$\chi^2 = 0.000$ $p = 1.00$	64 (22%)	51 (17%)	0	$\chi^2 = 1.934$ $p = 0.164$
Had to use manual manoeuvres to facilitate more than 1/4 (25%) defecations	26 (4.5%)	16 (5.5%)	10 (3.5%)	$\chi^2 = 1.006$ $p = 0.316$	18 (6%)	8 (2.5%)	0	$\chi^2 = 3.489$ $p = 0.062$
Had fewer than three spontaneous bowel movements per week	122 (20.5%)	54 (18.5%)	68 (23%)	$\chi^2 = 1.748$ $p = 0.186$	54 (18.5%)	67 (22.5%)	1	$\chi^2 = 1.160$ $p = 0.281$

(9% total sample). Other researchers have reported similar findings.^{2,21,22}

Significant numbers of patients that self-reported not having constipation agreed that they met one or more of the Rome IV diagnostic criteria individual statements. Other studies have reported similar findings.^{2,16} This study identified some age-related differences, with younger (<65 years) participants more likely to disregard the sensation of incomplete evacuation after defaecation, and to

a lesser (not statistically significant) extent having to strain during defaecation. Moreover, this study identified numerous country-related differences, with Italian participants in particular more likely to disregard most of these clinical features. Of note, a systematic review of the literature suggested certain differences between Asian and 'Western' populations, and indeed between Asian populations, in terms of the pattern of responses to previous versions of the Rome Foundation diagnostic criteria for

Table 4. Agreement with individual statements from Rome IV diagnostic criteria for opioid induced constipation in patients without self-reported constipation (country data).

Statement from ROME IV diagnostic criteria for opioid induced constipation	Denmark (n = 78)	Finland (n = 35)	France (n = 32)	Germany (n = 61)	Ireland (n = 121)	Italy (n = 59)	Netherlands (n = 51)	Norway (n = 38)	Spain (n = 44)	United Kingdom (n = 69)	Statistics
Had to strain during more than 1/4 (25%) of defecations	23 (29.5%)	9 (25.5%)	4 (12.5%)	7 (11.5%)	52 (43%)	38 (64.5%)	11 (21.5%)	12 (31.5%)	9 (20.5%)	19 (27.5%)	$\chi^2 = 59.861$ $p \leq 0.001$
Had lumpy or hard stools (BSFS type 1–2) for more than 1/4 (25%) of defecations	25 (32%)	3 (8.5%)	2 (6%)	10 (16.5%)	54 (44.5%)	24 (40.5%)	6 (12%)	12 (31.5%)	7 (16%)	17 (24.5%)	$\chi^2 = 51.277$ $p \leq 0.001$
Had the sensation of incomplete evacuation with more than 1/4 (25%) defecations	29 (37%)	10 (28.5%)	7 (22%)	15 (24.5%)	56 (46.5%)	29 (49%)	19 (37.5%)	16 (42%)	11 (25%)	30 (43.5%)	$\chi^2 = 20.718$ $p = 0.014$
Had the sensation of anorectal obstruction/blockage with more than 1/4 (25%) defecations	16 (20.5%)	9 (25.5%)	5 (15.5%)	4 (6.5%)	32 (26.5%)	16 (27%)	5 (10%)	5 (13%)	8 (18%)	15 (21.5%)	$\chi^2 = 17.884$ $p = 0.037$
Had to use manual manoeuvres to facilitate more than 1/4 (25%) defecations	5 (6.5%)	2 (5.5%)	1 (3%)	1 (1.5%)	3 (2.5%)	6 (10%)	0 (0%)	2 (5.5%)	2 (4.5%)	4 (6%)	$\chi^2 = 10.539$ $p = 0.309$
Had fewer than three spontaneous bowel movements per week	20 (25.5%)	8 (23%)	3 (9.5%)	1 (1.5%)	19 (15.5%)	26 (44%)	6 (12%)	11 (29%)	6 (13.5%)	22 (32%)	$\chi^2 = 49.293$ $p \leq 0.001$

functional constipation / irritable bowel syndrome with predominant constipation.²³

All patients with advanced cancer, and especially those receiving opioid analgesics, need to be regularly assessed for constipation.¹ The 'gold standard' assessment of constipation involves a thorough clinical assessment by an experienced clinician. The latter involves not only taking a thorough history, but also performing an examination (abdominal, digital rectal), and undertaking relevant investigations wherever indicated.¹ One vital aspect of assessment is identification of the cause(s) of the constipation, since the optimal management of the constipation is dependent on the cause of the constipation.¹

Nevertheless, palliative care patients are usually only asked the single question ('Are you constipated?'), which has been shown to be an inadequate alternative to a thorough clinical assessment.² Moreover, the single question is much less sensitive/accurate than the Rome IV diagnostic criteria (in patients with opioid-induced constipation).² The 'issue' with the single question is the disparate meanings of the term within the general population, with some relating the term to frequency of defaecation, some to difficulty with defaecation and some to a combination of these things. Hence, the single question should not be used to assess/re-assess constipation in palliative care patients (or indeed other cohorts of patients).

The Multinational Association for Supportive Care in Cancer (MASCC) Palliative Care Study Group have suggested the following questions when assessing for constipation in clinical practice¹: (a) frequency of bowel movements?; (b) straining with bowel movements?; (c) consistency of stool (using Bristol Stool Chart)?; (d) sensation of incomplete evacuation?; (e) sensation of blockage in rectum/anus?; (f) current/previous use of laxatives?; (g) current/previous use of other measures; and (h) change in bowel function since starting opioid analgesia? (whenever appropriate).

The Rome IV diagnostic criteria for opioid-induced constipation have an accuracy of 81.9% in this population (as compared to a thorough clinical assessment by an experienced clinician). Further research is needed to improve this accuracy, and to determine potential differences in the diagnostic features of opioid-induced constipation versus functional constipation. Crucially, the Rome IV criteria are diagnostic tools, and are not assessment tools.

Strengths and limitations of the study

A potential limitation of this study is that the population was patients with advanced cancer receiving opioid analgesics (and so experiencing opioid-induced constipation, rather than functional constipation/secondary constipation from other causes). However, given the fact that the Rome IV diagnostic criteria for opioid-induced constipation are analogous to those for functional constipation, we feel that these results are generalisable to the wider

population of patients with advanced cancer in Europe (and probably other groups in Europe). It should be noted that there are no diagnostic criteria for secondary constipation from other causes. A strength of this study is the relatively large sample size, the fact that participants were 'real-world' patients (i.e. non-restrictive inclusion/exclusion criteria) and the fact that participants were recruited from 24 research sites in 10 different European countries.

Conclusion

The term 'constipation' means different things to different people, and the use of a single question ('Are you constipated?') is inadequate in terms of identifying a significant proportion of patients with opioid-induced constipation in European persons with cancer. Moreover, this undoubtedly applies to other types of constipation (i.e. functional constipation, secondary constipation), and other cohorts of patients (i.e. non-European patients, patients with non-malignant disease). It should be noted that there are a number of clinical tools to assess constipation in palliative care patients, including the Victoria Bowel Performance Scale (revised) and the Constipation Assessment Scale.

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Author contributions

AD conceived the study, and AD and NF developed the protocol. All the authors (AD, NF, JP and AT) were involved in the analysis and interpretation of the data. AD wrote the first draft of the manuscript, and all the other authors (NF, JP and AT) were involved in the revision of the manuscript. All the authors have approved the final version of the manuscript.

Declaration of conflicting interest

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: The study was an investigator-initiated study, with unrestricted research funding received from Kyowa Kirin International. AD has received personal fees for consultancy / educational activities from Kyowa Kirin International. None of the other authors have relevant conflicts of interest. The authors had full access to all of the data in this study and take complete responsibility for the integrity of the data and the accuracy of the data analysis.

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Research ethics and patient consent

The study received ethical approval in Ireland from the St. James's Hospital/Tallaght University Hospital Joint Research Ethics Committee (reference number – 0148) on 13th August 2021, and similar ethical approval in all other countries. All participants provided written informed consent.

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Data management and sharing

Requests for data sharing should be addressed to Professor Andrew Davies, Academic Department of Palliative Medicine, Our Lady's Hospice & Care Services, Harold's Cross, Dublin, D6W RY72, Ireland.

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