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Characteristics of the case mix, organisation and delivery in cancer palliative care: a challenge for good-quality research

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ABSTRACT

Objectives Palliative care (PC) services and patients differ across countries. Data on PC delivery paired with medical and self-reported data are seldom reported. Aims were to describe (1) PC organisation and services in participating centres and (2) characteristics of patients in PC programmes.

Methods This was an international prospective multicentre study with a single web-based survey on PC organisation, services and academics and patients' self-reported symptoms collected at baseline and monthly thereafter, with concurrent registrations of medical data by healthcare providers. Participants were patients ≥ 18 enrolled in a PC programme.

Results 30 centres in 12 countries participated; 24 hospitals, 4 hospices, 1 nursing home, 1 home-care service. 22 centres (73%) had PC in-house teams and inpatient and outpatient services. 20 centres (67%) had integral chemotherapy/radiotherapy services, and most (28/30) had access to general medical or oncology inpatient units. Physicians or nurses were present 24 hours/7 days in 50% and 60% of centres, respectively. 50 centres (50%) had professorships, and 12 centres (40%) had full-time/part-time research staff. Data were available on 1698 patients: 50% females; median age 66 (range 21–97); median Karnofsky score 70 (10–100); 1409 patients (83%) had metastatic/disseminated disease; tiredness and pain in the past 24 hours were most prominent. During follow-up, 1060 patients (62%) died; 450 (44%) < 3 months from inclusion and 701 (68%) within 6 months. ANOVA and χ^2 tests showed that

hospice/nursing home patients were significantly older, had poorer performance status and had shorter survival compared with hospital-patients ($p < 0.001$).

Conclusions There is a wide variation in PC services and patients across Europe. Detailed characterisation is the first step in improving PC services and research.

Trial registration number ClinicalTrials.gov Identifier: NCT01362816.

INTRODUCTION

The WHO definition of palliative care (PC) states that it should be available early in the disease trajectory and may be delivered alongside potentially curative treatments.¹ However, only 1 in 10 of those who need PC receive it.²

One reason for this may be that PC has often been misconstrued as end-of-life care³ and consequently referrals occur too late. A retrospective study showed that referrals took up to 16 months after being diagnosed with advanced cancer, with a median interval between the PC consultation and death of 1.4 months.⁴ However, there is now a persuasive argument that introducing PC early in patients with advanced disease has beneficial effects on physical symptoms, psychological distress, prognostication and survival.^{5–7}

Despite the positive development of palliative care units (PCUs) and PC specialist training for doctors and nurses,⁸ the integration of PC and oncology

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services varies widely. Furthermore, establishing PC as an academic field in its own right has progressed slowly.⁹ Recently, two large-scale European Commission funded projects, IMPACT (<http://www.impactpalliativecare.eu/>) and EURO IMPACT (<http://www.euro-impact.eu/>), have developed a set of recommendations for policymakers and decision-makers to help improve the quality of and access to PC in an ageing Europe,¹⁰ focusing on improving the quality of care at all levels and that specialist PC services should be available in all healthcare settings.

The first step in meeting these recommendations is to characterise PC services and their patients across multiple centres, settings and countries in Europe. To this end, the European Palliative Care Cancer Symptom study (EPCCS) was developed, supported by the European Association for Palliative Care (EAPC) Research Network (<http://www.eapcrn.org/>) and the European Palliative Care Research Centre (<http://www.ntnu.edu/prc/>).

We present here the main report from the EPCCS study, which describes the organisation and delivery of PC at specific centres across Europe. The key clinical characteristics of the patients at these centres are also described.

MATERIALS AND METHODS

Invitations to participate were distributed to EAPC-RN and PRC members and advertised at EAPC conferences.

The data collection consisted of three parts:

- Assessment of PC service: a single web survey on organisational and economic issues
- Registration of patients' medical data using a case report form completed by the healthcare providers (HCP-CRF) at each patient encounter
- Patients' self-reported data (patient-CRF) completed at each patient encounter.

All forms were forward-backward translated into the language of the participating centre.

Assessment of PC service

A one-time registration of institutional data was done using an English language web-based survey. This was completed in 2010 before any patients were included. The survey consisted of four parts covering (1) institution details; for example, type of hospital, size and catchment area, (2) description of the PC programme; for example, size, composition, types of PC services and anti-cancer treatment, (3) organisational issues and academic affiliations and (4) funding sources.

The healthcare provider-CRF

The HCP-CRF consisted of a brief set of medical and treatment-related variables, informed by the EAPC basic data set that was under development at the time,¹¹ a four-item version of the mini-mental state examination (MMSE),¹² using the suggested cut-off of

four (of maximum eight) to indicate possible cognitive failure,¹³ and the Karnofsky Performance Status Scale.¹⁴ A retrospective recording of date of death was performed in February 2014, ~6 months after inclusion of the last patients.

The patient CRF

The patient CRF consisted of key sociodemographic items: age, sex, education and living situation and questions about common cancer-related symptoms. This included two items from the Brief Pain Inventory (BPI)¹⁵ average and worst pain intensity during the past 24 hours, to be answered on a 0–10 numerical rating scale, two dichotomous questions on neuropathic pain (NP) symptoms (skin sensitivity/numbness) and breakthrough pain (BTP) adapted from Pain Detect¹⁶ and the Alberta Breakthrough Pain Assessment Tool,¹⁷ respectively. Depression was assessed by the two items on anhedonia and depressed mood from the Brief Patient Health Questionnaire-PHQ9,¹⁸ corresponding to the main items in the DSM-5 criteria for depression and assessing the frequency at which they have been bothersome during the past 2 weeks: 0='not at all', 1='several days', 2='more than half the days' and 3='nearly every day'. Furthermore, the revised version of the Edmonton Symptom Assessment System (ESAS-r)¹⁹ and the PC version of the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C15-PAL)²⁰ were used. The physical function scale of the QLQ-C15-PAL was scored from 1: 'not at all' to 4 'very much' transformed to a 0–100 scale.

PATIENTS AND SAMPLING

Eligible patients were: enrolled in the centre's PC programme: advanced, incurable cancer; age ≥ 18 years; written informed consent; eligible for at least one follow-up assessment after inclusion. Exclusion criteria were: patients being treated with curative intent; inability to comply with the study due to psychotic disorders, severe cognitive impairment or language problems; imminent death; or inability to come for follow-up due to medical, social or geographical reasons.

Ethical considerations

The study was performed according to the Declaration of Helsinki and was registered in the ClinicalTrials.gov database (No. NCT01362816). Ethical approval was obtained at each site.

Statistical analyses

Standard descriptive statistics, χ^2 tests and one-way ANOVAs were used to compare subgroups for the web survey and patient data as appropriate. Data from ESAS-r are presented as mean scores (SD) and categorised severity: 0–3=none/mild, 4–6=moderate and

7–10=severe. The significance level was set at $p < 0.05$. The ANOVA analyses were corrected for multiple comparisons using Bonferroni adjustments, with a resulting $p < 0.00625$. Dunnett's T3 or Tukey's post hoc tests were performed to test for differences in patient characteristics between centre categories. The ANOVAs were performed with the predefined four centre categories: cancer centres with PC beds, without PC beds, regional hospitals and hospices/nursing homes and also repeated using the following three categories: centres with PC beds, without PC beds and hospices/nursing homes. Survival was categorised in days < 30 , 30–89, 90–149, 150–179 with the latter category representing 6 months survival or longer. Sample size calculations were not performed as this was not a hypothesis-testing study. IBM SPSS Statistics V.20.0 for Windows (IBM Corporation, Armonk, New York, USA) were used for data analysis.

RESULTS

The web survey

Thirty-seven centres completed the web survey; the 30 centres that included patients presented were across 12 countries: Australia, Belgium, Canada, Denmark, Georgia, Germany, Italy, Norway, Portugal, Spain, Switzerland and the UK. The study ran from April 2011 through October 2013.

Table 1 shows characteristics of the participating centres, 27 European, 1 Australian, 2 Canadian. The majority, 24/30 (80%), were hospitals, in addition to four hospices, one nursing home and one PC home care service. Most centres (18/30, 60%) had rural and urban catchment areas; the remaining 40% covered urban areas.

Sixteen (67%) of the participating hospitals had designated inpatient PC beds, 28 (98%) had PC outpatient units and 25 (83%) had PC teams. A patient hotline for contact and questions was available in 19 (63%) centres. The annual number of PC patients treated ranged from 113 to 729, and 13 (43%) centres reported that patients with cancer constituted 90% or more of their PC patients.

State and/or community funding was predominant (26/30). Almost all centres (28/30) had easy access to general medicine or oncology inpatient units (26/30), as well as diagnostic facilities such as basic radiology (27/30), MRI (24/30), CT (24/30) and PET (16/30) scans. Twenty centres had chemotherapy and radiotherapy as part of their PC programmes, while one provided radiotherapy only. This was supplemented with other anti-cancer therapies such as targeted therapy, hormonal treatment and immunotherapy in 12 centres, while 9 centres did not provide any anti-cancer therapy. The average length of stay reported by the centres with inpatient PC beds varied from 7 to 73 days.

In all but three centres, the PC programme was led by a physician, two heads had a nursing background,

while one centre had a joint physician/nurse leadership. In 8 of the 30 centres, the lead practitioner had specialist PC training (seven physicians, one nurse). As per table 1, the number of physicians with specialist training and presence of physicians and nurses varied within the programmes. Physicians were physically available 24/7 in 17 of the 30 centres and on phone in 23/30 centres, while the corresponding numbers for nurses were 19/30 and 16/30 centres, respectively. Several other professions were also part of all PC programmes, most often social workers ($n=15$), psychologists and physiotherapists ($n=12$, both).

Professorships were present in 15 of the 30 PC programmes, varying from 0.2 to 3 full-time equivalents (table 1); 13 had a medical background. Academic positions, defined as research staff not doing clinical work, were present in 15 centres, varying from 0.3 to 8 full-time equivalents (senior researchers, PhD/master students). Two of the six centres in the hospice-nursing home category had part-time professorships.

Patient characteristics

Of the 1739 patient records, 41 were not included in the analyses, as the HCP ($n=31$) or patient CRFs ($n=9$) or both ($n=1$) were not completed at inclusion. Records with occasional missing values for single variables were retained, leaving a study sample of 1698 patients. Most patients, 46% ($n=778$), were included at hospital PC services, followed by general oncology departments (35%). Sixty-one per cent ($n=1017$) were outpatients.

The median age was 66 (range 21–97), and 50.2% were females (table 2). The mean MMSE score on the 0–5 scale was 4.5 (SD 0.9), with 29% having a score below 4, suggesting a degree of cognitive failure.¹⁸ The predominant diagnoses were gastrointestinal (31%), lung (20%) and breast cancer (17%). One or more comorbid conditions were reported in 60%, with heart disease being most common (28%; table 2). Eighty-three per cent had disseminated or metastatic disease, with bone (37%), liver (30%) and lung (30%) metastases being most frequent.

Anti-cancer therapy was received by 1015 patients (60%) at inclusion: chemotherapy ($n=707/42%$) and hormonal therapy ($n=172/10%$; table 2). Twenty-seven per cent of patients who died between 1 and 3 months after inclusion and 15% of those who died within 30 days from inclusion received chemotherapy at study entry. Fifty-nine per cent ($n=991$) were using opioids at baseline: this was sole analgesic therapy in 20% (198), combined with other analgesics in 793 (80%). Anti-depressants to treat depression were used by 16%.

A total of 1060 patients (62%) died during follow-up. Survival length for the 1035 patients with a verified date of death is categorised in table 2 and shows that 68% of these died within 6 months from inclusion.

Table 1 Centre characteristics*

Institution name	Country	Institution type†	Number of PC-beds	Professional background of head of PC programme	Physician specialists in the PC programme‡	Availability of physicians	Availability of nurses	Professors in the PC programme	Research staff in the PC programme§
Southern Adelaide Palliative Services, Adelaide, South Australia	AU	Cancer centre with inpatient PCU	15	Psycho-oncology nursing	PC spec: 2.5 Respiratory med: 0.6	24/7	24/7	Yes	Yes
University Hospital, Ghent	BE	Cancer centre with inpatient PCU	6	Anaesthesiol.	Anesth.: 0.8	Daytime/5	Daytime/5	Yes	–
Comprehensive Cancer Centre, Vratsa	BG	Cancer centre with inpatient PCU	15	Anaesthesiol.	Oncol.: 0.5 Anaesth.: 1 Surgery: 0.3 IntMed: 0.5	24/7	24/7	–	–
Cross Cancer Institute, Northern Alberta	CA	Cancer centre without inpatient PCU	–	PC specialist Oncology	Oncol: 5 GP: 13	24/7	24/7	Yes**	Yes
The Edmonton Zone Palliative Care Program, Alberta	CA	Cancer centre with inpatient PCU	22	PC specialist	GP: 13	24/7	24/7	Yes**	–
Cantonal Hospital, St. Gallen	CH	Cancer centre with inpatient PCU	26	Oncology Internal Med.	Oncol.: 2.7 IntMed.: 4.3	24/7	24/7	Yes	Yes
Kantonsspital Graubünden, Chur	CH	Regional hospital with inpatient PCU	8	PC specialist	IntMed: 1	Daytime/5	24/7	Yes	–
Rigshospitalet, Copenhagen	DK	Regional hospital	–	Oncology	Oncol.: 1 Anaesth.: 1	24/7	Daytime/5	Yes	Yes
Bispebjerg Hospital, Copenhagen	DK	Regional hospital with inpatient PCU	12	Oncology	Oncol: 1 Anaesth. 2	24/7	Daytime/5	–	Yes
Hospital Universitario Arnau de Vilanova, Lleida	ES	Regional hospital	–	GP	GP: 2	Daytime/5	Daytime/5	–	Yes
Clínica Universidad de Navarra, Pamplona	ES	Cancer centre without inpatient PCU	–	Radiation oncology	Oncol.: 1 GP: 1	Daytime/5	Daytime/5	–	–
Hospital Centro de Cuidados Laguna, Madrid	ES	Hosp-nursing-home	43	GP	GP: 6.4	24/7	24/7	–	Yes
Institut Catala D'Oncologia, Barcelona	ES	Cancer centre with inpatient PCU	18	Internal Med.	Oncol.: 1 Anaesth.: 0.5 IntMed.: 1 GP: 2 Geriatrician: 4	Daytime/5	24/7	–	Yes
Cancer Prevention Centre (CPC), Tbilisi	GE	Cancer centre with inpatient PCU	22	PC specialist Oncology	Oncol.: 3 Surgery 1 GP: 8	24/7	24/7	Yes	Yes
Fondazione IRCCS Istituto Nazionale dei Tumori, Milan	IT	Cancer centre with inpatient PCU	10	Neurology	Oncol.: 2 Anaesth.:1	Daytime/5	24/7	–	Yes

Continued

Table 1 Continued

Institution name	Country	Institution type†	Number of PC-beds	Professional background of head of PC programme	Physician specialists in the PC programme‡	Availability of physicians	Availability of nurses	Professors in the PC programme	Research staff in the PC programme§
Hospital of Piacenza, Piacenza	IT	Regional hospital with inpatient PCU	12	Oncology	Oncol.: 1 Anaesth.:1 IntMed.: 0.5 GP: 0.5	24/7	24/7	Yes	Yes
Hospice Villa Speranza, Rome	IT	Hosp-nursing-home	621	Oncology	Oncol.: 2.5 Surgery: 1 IntMed.: 2 GP: 1	24/7	Daytime/5	Yes	–
Istituti Clinici di Perfezionamento Hospital, Milan	IT	Regional hospital	–	Anaesthesiol.	Oncol.: 0.5 IntMed.: 0.5	Daytime/5	Daytime/7	–	–
U.O. Complessa Cure Palliative e Terapia del Dolore Istituti Clinici di Perfezionamento, Milan	IT	Cancer centre without inpatient PCU	–	Anaesthesiol./Oncology	Oncol.: 0.3 Surgery: 0.2 IntMed.: 0.5	Daytime/7	Daytime/5	–	–
University of L'Aquila, L'Aquila	IT	Regional hospital with inpatient PCU	4	Oncology/neurology+nursing	Oncol.: 3 Neuro: 0.3	24/7	24/7	Yes	–
Arcispedale Santa Maria Nuova Reggio Emilia	IT	Regional hospital	–	Oncology	Oncol.: 1	Daytime/5	Daytime/5	–	–
St. Olavs University Hospital, Trondheim	NO	Cancer centre with inpatient PCU	12	Oncology	Oncol: 2.5 GP: 1	24/7	24/7	Yes	Yes
Oslo University Hospital, Oslo	NO	Cancer centre with inpatient PCU	8	Oncology	Anesth. 3 IntMed.: 1 GP: 1 Gynaecol: 1	24/7	24/7	Yes	Yes
Haraldsplass Deaconess Hospital, Bergen	NO	Regional hospital with inpatient PCU	8	Anaesthesiol.	Anaesth. 2 IntMed.: 1 GP: 1	24/7	24/7	Yes	Yes
Øya Community Hospital, Trondheim	NO	Hosp-nursing-home§	8	GP	GP: 0.3	Daytime/5	24/7	–	–
Instituto Português de Oncologia de Lisboa Francisco Gentil, EPE, Lisbon	PT	Cancer centre without inpatient PCU	–	Internal Med.	IntMed.: 2	Daytime/5	Daytime/5	–	–
St Gemmas Hospice, Leeds	UK	Hosp-nursing-home	32	PC nurse specialist	–	Daytime/5	24/7	Yes	–
West Lothian Community Specialist Palliative Care Team, Edinburgh	UK	Hosp-nursing-home	–	PC specialist	–	24/7	Daytime/5	–	–
Nottingham University Hospitals, Nottingham	UK	Cancer centre with inpatient PCU	20	PC specialist	PC spec.: 4 Anaesth.: 0.1	Daytime/5	24/7	–	Yes
Marie Curie Cancer Care Glasgow Hospice, Glasgow	UK	Hosp-nursing-home	30	PC specialist	–	24/7	24/7	–	–

*Information in web survey based on data from 2010.

†Four categories: cancer centre with inpatient PCU (palliative care unit), cancer centre without inpatient PCU, Regional hospital, Hospice, nursing-home, hospice at home.

‡Numbers refer to full-time equivalents.

§Defined as persons doing research, not clinical work, including senior researchers, PhD candidates and Master students.

**Joint professorship.

AU, Australia; Anaesthesiol/anaesth., Anaesthesiology; BE, Belgium; BG, Bulgaria; CA, Canada; CH, Switzerland; DE, Denmark; ES, Spain; GE, Georgia; GP, General practitioner; Gynaecol, Gynaecologist; IntMed, Internal Medicine; IT, Italy; NO, Norway; Oncol, Oncology; PCU: Palliative care unit; PT, Portugal.

Table 2 Patient characteristics at inclusion

Variable	N=1698, n (%)	Missing, n
Gender		0
Female	852 (50.2)	
Male	846 (49.8)	
Education (years)		20
<10	544 (32)	
10–12	700 (42)	
>12	434 (26)	
Living situation		7
Alone	349 (21)	
With spouse/partner	737 (43)	
With spouse/partner and children	376 (22)	
With others (children or adults)	210 (13)	
In an institution	19 (1)	
Country		0
Australia, 1 site	35 (2)	
Belgium, 1 site	95 (6)	
Bulgaria, 1 site	28 (2)	
Canada, 2 sites	94 (6)	
Denmark, 2 sites	100 (6)	
Georgia, 1 site	19 (1)	
Italy, 7 sites	605 (35)	
Norway, 4 sites	235 (14)	
Portugal, 1 site	58 (3)	
Spain, 4 sites	233 (14)	
Switzerland, 2 sites	68 (4)	
UK, 4 sites	128 (7)	
Treatment setting		38
Inpatients	348 (21)	
Outpatients	1017 (61)	
Home care	295 (18)	
Comorbidity (numbers)		5
0	679 (40)	
1	638 (39)	
2	283 (16)	
3 or more	93 (5)	
Primary cancer diagnosis*		4
Digestive organs	520 (31)	
Respiratory organs†	343 (20)	
Breast cancer	284 (17)	
Male genital organs	126 (7)	
Gynaecological	99 (6)	
Urinary	75 (4)	
Head	58 (4)	
Leukaemia or lymphoma	44 (3)	
Malignant connective/soft-tissue tumours	40 (2)	
Skin cancer/malignant melanoma	36 (2)	
CNS tumours	24 (1)	
Secondary/ill-defined malignant tumours	24 (1)	
Malignant endocrine tumours	11 (1)	
Other‡	10 (1)	

Continued

Table 2 Continued

Variable	N=1698, n (%)	Missing, n
Disease status		8
Metastatic/disseminated	1414 (83)	
Local/locally advanced	276 (17)	
Survival, days from inclusion		663§
<30	151 (15)	
30–89	299 (29)	
90–149	184 (18)	
150–180	67 (6)	
>180	334 (32)	
Treatment with chemotherapy at inclusion		3
Yes	707 (42)	
No	998 (58)	
Treatment with chemotherapy by the survival group (days)		
<30	23 (15)	
30–89	80 (27)	
90–149	85 (46)	
150–180	26 (39)	
>180	162 (49)	
Treatment with opioids at inclusion		22
Yes	991 (59)	
No	685 (41)	

*Based on ICD-10 diagnoses from patient records.

†Including eight patients with laryngeal cancer.

‡Including malignant bone tumours (n=8), multiple primary cancers (n=2).

§Incl. 25 patients reported dead, but with no date registered.

Table 3 displays the patients' mean scores on physical functioning, pain and ESAS. Mean scores above 3.0 were found with tiredness (4.3 SD 3.0), drowsiness (3.1 SD 2.9) and well-being (3.6 SD 2.7), and for average and worst pain intensity past 24 hours (3.2 SD 2.7 and 4.0 SD 3.3). ESAS scores ≥ 7 , indicating severe symptom intensity, varied from 4% in nausea to 27% with tiredness, relative to 15% and 27% for average and worst pain intensity, respectively. Thirty-seven per cent confirmed episodes of BTP during the past 24 hours (**table 3**).

Table 4 displays selected medical and patient-reported variables grouped by four centre categories: cancer centres with (n=11) and without inpatient PCUs (n=4), regional hospitals (n=9) and hospices/nursing homes (n=6).

Overall, patients included from the hospice/nursing home category were significantly older, less likely to receive chemotherapy, had poorer physical performance and reported significantly more tiredness compared with patients in the other three centre categories (p values 0.03 to <0.001). Their survival time from inclusion was also significantly shorter (p<0.001; **table 4**). Five of the regional hospitals had PCUs with inpatient beds, and one could argue that it may be arbitrary to differentiate between cancer

Table 3 Patient self-report of symptoms and physical functioning

Variables	N=1698			N	%	N	%	N	%
	Mean	SD	Missing	0–3	0–3	4–6	4–6	7–10	7–10
Pain*	2.1	2.3	14	1246	(74)	308	(18)	141	(8)
Tiredness*	4.3	3.0	13	654	(41)	541	(32)	450	(27)
Nausea*	1.0	2.1	21	1471	(88)	138	(8)	68	(4)
Depression*	2.5	2.9	17	1144	(68)	318	(19)	219	(13)
Anxiety*	2.3	2.8	18	1183	(70)	315	(19)	192	(11)
Drowsiness*	3.1	2.9	31	994	(60)	396	(23)	277	(16)
Appetite*	3.0	3.2	23	1322	(78)	240	(14)	128	(8)
Well-being*	3.6	2.7	35	837	(50)	552	(33)	274	(17)
Shortness of breath*	1.8	2.5	14	1320	(78)	238	(14)	26	(8)
Pain intensity, average past 24 hours†	3.2	2.7	9	991	(59)	449	(26)	249	(15)
Pain intensity, worst, past 24 hours†	4.0	3.3	21	796	(47)	418	(25)	463	(27)
Physical functioning‡	64.3	29.2	14						
				N	%				
				yes	yes				
PHQ9 depression§	339	(20)	28						
Anhedonia	553	(32)	33						
Depressed mood	437	(26)	30						
Neuropathic pain¶	560	(34)	65						
Breakthrough pain last 24 hours**	608	(37)	44						

*ESAS-r: 0–10 scale, higher score implies higher symptom intensity/poorer well-being, 'right now'.¹⁹

†BPI: 0–10 scale, higher score implies higher pain intensity.¹⁵

‡QLQ-C15-PAL: 0–100 scale, higher score implies better functioning.²⁰

§PHQ9: 'yes' indicates a score of 2 or 3 on the 0–3 scale assessing the frequency at which people have been bothered by anhedonia (little interest or pleasure in doing things) and depressed mood during the past 2 weeks: 2='more than half the days' and 3='nearly every day'.¹⁸

¶'Does the skin in the painful area feel different from normal, more numb or more sensitive?': yes/no, adapted from PainDetect.¹⁶

**'Have you had flare-ups of breakthrough pain in the last 24 hours?': yes/no, adapted from the Alberta Breakthrough Pain Assessment Tool.¹⁷

centres and regional hospitals with inpatient PCUs. Thus, the analyses were repeated with three centre categories: hospitals with (n=16) and without PC beds (n=8) and hospices/nursing homes (n=6), yielding similar results (data not tabulated).

DISCUSSION

This is the first study to characterise PC services and patients across a wide range of centres and countries. There were differences and similarities in organisational issues, number of physician specialists, academic affiliations and research activities across the participating centres. Most centres had outpatient clinics, easy access to general medicine or oncology units, and 83% had in-house PC teams. Cancer was the predominant disease within the PC programmes, and one-third offered chemotherapy and radiotherapy as part of their programme. All centres reported that their PC teams were multidisciplinary, although the size and composition varied.

Overall, patient characteristics based on the HCP registrations correspond to findings from other studies in PC or advanced cancer regarding the most common diagnoses, about 60% receiving opioids,^{21–23} and a median age around 66 years,^{5, 24} albeit higher than some studies.^{25, 26} Mean scores on the self-reported

symptoms on the ESAS resembled previous reports, with tiredness being most pronounced.^{19, 21, 24} It is noteworthy, however, that the mean pain score on the ESAS was <3, with only 8% scoring in the upper range (≥ 7), whereas the mean pain scores on the average and worst pain items of the BPI exceeded 3, with 15% and 27% of patients reporting high pain intensity (≥ 7). This may indicate suboptimal pain treatment, still a persistent problem.²⁷ It does once again underline the necessity to use different time windows when assessing pain intensity. A prevalence of BTP of 37% is lower than the 50% reported in a review presenting pooled analyses of the BTP literature.²⁸ Without a more thorough assessment, it is difficult to ascertain if this reflects true BTP or end-of-dose failure of medication.

Patient characteristics differed when compared across our four predefined categories of participating centres (table 4), and the same differences remained significant when using a three-centre categorisation. The 233 patients within the hospice/nursing home services had a significantly shorter survival, reported significantly more tiredness, were more often receiving opioids and were less prone to get chemotherapy, compared to hospital patients. The fact that 42% of patients overall were receiving anti-cancer treatment on inclusion may in part be explained by the fact that

Table 4 Patient characteristics, grouped by centre types*

	Cancer centre with PCU† N=11 N (%)	Cancer centre without PCU† N=4 N (%)	Regional hospital N=9 N (%)	Hospice, nursing-home‡ N=6 N (%)	p Value
No. of patients	666–685 (97–100)	234–230 (98–100)	546–534 (98–100)	233–224 (96–100)	
Chemotherapy at inclusion	272 (39.8)	119 (50.9)	290 (53.1)	26 (11.3)	<0.001§
Using opioids	392 (58.2)	136 (58.4)	311 (57.3)	152 (67.3)	0.06§
Breakthrough pain¶	252 (37.8)	77 (33.5)	207 (38.8)	72 (32.0)	0.22§
PHQ9, depression**	136 (20)	45 (20)	104 (19)	54 (24)	0.53§
Survival (days)	Missing 237 n=448	Missing 119 n=115	Missing 278 n=268	Missing 29 n=204	<0.001§
<30	58 (12.9)	8 (7.0)	36 (13.4)	49 (24.0)	
30–89	132 (29.5)	27 (23.5)	63 (23.5)	77 (37.7)	
90–149	86 (19.2)	22 (19.1)	48 (17.9)	28 (13.7)	
150–180	31 (6.9)	13 (11.3)	15 (5.6)	8 (3.9)	
>180	141 (31.5)	45 (39.1)	106 (39.6)	42 (20.6)	
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	p Value††
Age (years)	63.7 (12.2)	64.8 (11.9)	65.6 (12.0)	73.1 (11.5)	<0.001
Karnofsky score	68.7 (15.5)	71.6 (13.2)	68.4 (17.0)	55.4 (15.1)	0.03
Average pain intensity‡‡	3.1 (2.6)	3.2 (2.7)	3.2 (2.9)	3.2 (2.7)	0.95
Worst pain intensity‡‡	3.9 (3.2)	4.3 (3.5)	3.7 (3.2)	4.0 (3.2)	0.84
Tiredness§§	4.0 (2.8)	4.5 (2.9)	4.5 (3.1)	5.0 (3.0)	<0.001
Drowsiness§§	3.3 (2.8)	2.8 (3.1)	2.8 (2.9)	3.3 (3.0)	0.01
Well-being§§	3.8 (2.5)	3.8 (2.8)	3.5 (2.8)	3.7 (2.8)	0.32
Physical functioning¶¶	66.7 (28.2)	72.1 (25.4)	67.8 (27.1)	44.3 (31.6)	<0.001

*Grouped according to information given on the web survey.

†PCU: palliative care unit with inpatient beds.

‡Including one hospice at home-service.

§ χ^2 tests for categorical variables.

¶‘Have you had flare-ups of breakthrough pain in the last 24 hours?’=yes, adapted from the ABPAT.¹⁷

**Presence of PHQ9 depression=yes, indicates a score of 2 or 3 on the 0–3 scale assessing the frequency at which people have been bothered by anhedonia (little interest or pleasure in doing things) and depressed mood during the past 2 weeks: 2=‘more than half the days’ and 3=‘nearly every day’.¹⁸

††One-way ANOVAs after correcting for multiple comparisons using Bonferroni adjustments.

‡‡BPI 0–10 scale, higher score implies higher pain intensity.¹⁵

§§ESAS-r: 0–10 scale, higher score implies higher symptom intensity/poorer well-being.¹⁹

¶¶QLQ-C15-PAL: 0–100 scale, higher score implies better functioning.²⁰

the majority (70%) were outpatients, which may reflect a healthier subset of PC patients. This is further substantiated with longer survival among those receiving chemotherapy (table 2), but may also indicate that integration between oncology and PC is slowly emerging, with more emphasis on symptom control.

Cancer centres with or without inpatient PCUs recruited >50% of the patients (table 4). Thus, it may be speculated that anti-cancer treatment was administered closer to the end of life in these centres than, for example, in smaller regional hospitals, as reported.²⁹ However, the use of anti-neoplastic therapy in an acute PCU was investigated²⁶ and it was concluded that this was limited to a small percentage of patients and was associated with characteristics such as younger age, female sex and cancer diagnoses, similar to findings in a Norwegian study.³⁰

The ongoing discussion about chemotherapy towards the end of life is important as intensive

treatment at this stage has been associated with poorer quality of life.^{6 31 32} In this study, 15% who died within 1 month after inclusion received chemotherapy, relative to 10% and 18% in other studies.^{30 33} These numbers still indicate a need for discussion and a potential for improvement. Even if conclusions about potential overtreatment cannot be drawn from this study, the percentages receiving chemotherapy seem relatively high. Although the numbers were small when split by centre categories, we found that the lowest proportion of patients getting chemotherapy during the last month was in the hospice/nursing home category (4%), as expected, second to patients from cancer centres with PCUs (14%; table 4). This may be because patients in the latter category were recruited from PCUs, rather than from general oncology units, implying that the principles of good PC with optimal symptom management were in the forefront, and probably that the prognostication accuracy was better.

An important issue arising from this study relates to the representativity of the patient sample. Recruitment of centres was based on self-selection, and most institutions were hospitals and provided anti-cancer treatment as part of their PC programmes. Furthermore, 50% of centres, also including hospices, had an academic affiliation in the form of professorships and/or personnel doing research. Most centres with academic affiliations or with stakeholders involved with international networks have an obligation to do research and probably also receive some funding to do so. This is in contrast to smaller community-based centres providing PC to groups of patients with other medical and sociodemographic characteristics. On the other hand, our results point to a tendency towards more academia in PC overall and a high level of competence, although university affiliations vary throughout Europe.⁸ Research is necessary to fulfil the obligation of improving the quality, competence and access to PC, as emphasised in the EU declaration on PC.¹⁰ Thus, efforts must be taken to optimise the generalisability of research findings. Routine data collections may be useful,³⁴ and the registration of non-participants in studies provides a more complete picture of PC patients.^{21 35} Another recommendation is related to the need for a standardised, uniform description of patient characteristics, a shortcoming that has been addressed for decades.^{36 37} Thus, a major strength of this study is the use of an early version of the recently published EAPC basic data set,¹¹ consisting of a minimum set of basic sociodemographic and medical variables, supplemented by patients' self-reported symptoms.

Further, it is noteworthy that most centres had easy access to general oncology and diagnostic facilities and that 35% of patients were recruited from general oncology units, even if treatment within a PC programme was an explicit inclusion criterion. This may be taken to indicate an integration between general oncology and PC, a frequently addressed issue^{3 38} since the Temel study in 2010,⁶ although a global consensus on what constitutes integration is lacking.³⁹ It should be remembered, however, that this study did not aim to explore the integration of oncology and PC per se.

It may be argued that our study is primarily a hospital-based study, as there were few other types of settings. As can be inferred from the results, there were many similarities between the hospital settings. However, since permission and access to patients for research purposes vary across and within centres, we did not specifically investigate potential differences between cancer centres and regional hospitals. To get valid results on this, a much more detailed characterisation of centres is necessary that was not feasible in a large-scale study like this.

Some limitations apply. First, comparing patient data across institutions is difficult, and it could be

argued that another categorisation of centres may have given different results. On the other hand, results were relatively similar when analyses were performed with four and three categories, respectively, and significant differences were found when comparing hospices/nursing homes with the other categories. It should also be remembered that the results are based on quantitative data and do not purport to evaluate the quality of care. The relatively high percentage of potential cognitive deficits (29%) may be attributed to the use of the 4-item MMSE version¹³ that lacks sufficient validation, although corresponding with other results.⁴⁰ Some centres performed a consecutive sampling, whereas others recruited a convenience sample due to shortage of staff. Ideally, identical procedures should have been followed everywhere, although a complete standardisation is difficult as collaborators may have restricted access to patients. However, with more than 1600 patients, we believe that the sampling strategy did not introduce a substantial bias, compared to other studies in PC or advanced cancer, although it cannot be ruled out that the frailest patients were not included.^{21 35}

The study's strengths are related to the participation from countries throughout Europe and beyond, representing a variety of settings that recruited more than 50 PC patients from general and specialised units, the large sample size, the use of well-known assessment tools and the simultaneous registration of patient and organisational data.

The findings from this study are helpful in informing our research agenda for future work. It is clear that heterogeneity exists, and therefore detailed characterisation in future work is imperative to facilitate comparison. We argue that there is a need to conduct prospective studies with consecutive sampling of patients who are well characterised with patient-reported outcome measures and objective ratings by HCPs that seek to further define the patient population and needs in advanced cancer. This is an important step as the increasing cancer incidence and the exponential increase in the elderly means that more PC services will be outside of specialised institutions and more likely to be in non-specialist settings, particularly primary care.

CONCLUSION

The wide variation in PC services and patients across Europe is essential as it enables a true picture of PC with implications for the development of services, research and funding. It is encouraging that the advocated approach of integrated oncology and PC is being realised in many centres. The high level of research activities provides grounds for optimism that PC, traditionally regarded as a having a paucity of evidence supporting practice, is attempting to change this by integrating research. We propose that future studies provide thorough descriptions of PC

organisation and case mix to increase the generalisability of PC research.

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Contributors All authors have recruited 50 patients or more to the study, registered data, stored these and been responsible for shipment of forms to the trial office. All authors have commented on the manuscript drafts, the final version and approved the submitted manuscript. All authors outside

Norway have assisted in the preparation of study forms and documents and been responsible for ethics approvals and study conduct at their sites. MJH, PS, BL, CB, SK, GJ and AC are responsible for the study initiation and protocol. SK and MJH have applied for and received funding.

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Data sharing statement Since this is a non-profit study with limited funding and no financial incentives to study collaborators (or patients), the database will be shared with the study responsible at each study site. Several manuscripts are forthcoming that represent no replications of the data presented in the manuscript submitted here to *BMJ Support Pall Care*, as this is the main publication from the EPCCS study. Therefore, other EPCCS publications were intended for publication after acceptance of this submitted publication. One paper was published as E-pub ahead of print, April 2016 (PMID:27061408). Further, all publications are subject to approval by the project management group to avoid conflicts and dual publications. As of now, data are shared with: Australia, D Currow: breathlessness, Belgium; K Pardon/L Deliens, depression + local integration, Norway: JH Loge/Hjermstad: pain and depression, Norway: Skeidsvoll: cachexia, Norway: Klepstad: Breakthrough pain, Spain: Noguera/Centeno: Hospital vs home care, Denmark: Sjøgren/Kurita: Cognitive function, Switzerland: Strasser/Hui: Integration.

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