

Original Article

Dying With Unrelieved Pain—Prescription of Opioids Is Not Enough



Åsa Klint, MD, Elisabeth Bondesson, BSc, Birgit H. Rasmussen, PhD, Carl Johan Fürst, PhD, and Maria E.C. Schelin, PhD

Institute for Palliative Care (Å.K., B.H.R., C.J.F., M.E.C.S.), Lund University and Region Skåne, Lund; Skåne University Hospital (Å.K.), Region Skåne, Lund; Department of Clinical Sciences Lund (E.B., C.J.F., M.E.C.S.), Faculty of Medicine, Lund University, Lund; Department of Pain Rehabilitation (E.B.), Skåne University Hospital, Lund; and Department for Health Sciences (B.H.R.), Faculty of Medicine, Lund University, Lund, Sweden

Abstract

Context. Fear of pain resonates with most people, in particular, in relation to dying. Despite this, there are still people dying with unrelieved pain.

Objectives. We quantified the risk, and investigated risk factors, for dying with unrelieved pain in a nationwide observational cohort study.

Methods. Using data from Swedish Register of Palliative Care, we analyzed 161,762 expected deaths during 2011–2015. The investigated risk factors included cause of death, place of death, absence of an end-of-life (EoL) conversation, and lack of contact with pain management expertise. Modified Poisson regression models were fitted to estimate risk ratios (RRs) and 95% confidence intervals (CIs) for dying with unrelieved pain.

Results. Unrelieved pain during the final week of life was reported for 25% of the patients with pain, despite prescription of opioids PRN in 97% of cases. Unrelieved pain was common both among patients dying of cancer and of nonmalignant chronic diseases. Statistically significant risk factors for unrelieved pain included hospital death (RR = 1.84, 95% CI 1.79–1.88) compared with dying in specialist palliative care, absence of an EoL conversation (RR = 1.42, 95% CI 1.38–1.45), and dying of cancer in the bones (RR = 1.13, 95% CI 1.08–1.18) or lung (RR = 1.10, 95% CI 1.06–1.13) compared with nonmalignant causes.

Conclusion. Despite almost complete prescription of opioids PRN for patients with pain, patients die with unrelieved pain. Health care providers, hospitals in particular, need to focus more on pain in dying patients. An EoL conversation is one achievable intervention. *J Pain Symptom Manage* 2019;58:784–791. © 2019 The Authors. Published by Elsevier Inc. on behalf of American Academy of Hospice and Palliative Medicine. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Key Words

Pain, pain relief, palliative, dying, cohort

Introduction

Fear of pain is often expressed by patients when discussing the last phase of life.¹ Fear of pain is also an immediate and common reaction among family members when their loved one's death is imminent, often expressed as “I don't want her to suffer.” In fact,

one fundamental aim of palliative care is pain relief irrespective of the nature of pain (physical, psychosocial, and/or spiritual).² Historically, palliative care was intended for patients with cancer, but it is now recognized as important also for patients with other life-threatening illnesses.³ In Sweden, as in many other Western societies, approximately 80% of deaths can be

Address correspondence to: Åsa Klint, MD, Palliativt Utvecklingscentrum, Medicon Village, Hus 404B, 22381 Lund, Sweden. E-mails: asa.klint@skane.se or asa_klint@hotmail.com

Accepted for publication: July 8, 2019.

classified as expected, as they are preceded by diseases such as disseminated cancer or other chronic illnesses without cure.⁴ According to the Swedish Health Care Act, palliative care should be provided to affected individuals, with highest priority to individuals approaching end of life (EoL).⁵ Still, there are people dying with unrelieved symptoms.⁴

The prevalence of pain in patients with cancer is estimated to be 35%–96%, depending on stage and type of cancer.^{6,7} Pain is less evident in chronic diseases other than cancer, yet research shows that it is a late symptom of diseases such as congestive heart failure, AIDS, and chronic obstructive pulmonary disease.^{7–9} The knowledge of pain management is vast, and a wide range of options for symptom relief are available. Studies indicate that pain relief could be accomplished in 45%–100% of patients with cancer^{10–12}; however, estimates of prevalence of pain and relief of pain in a dying population are scarce.

Relief of pain and other distressing symptoms is a fundamental part of attaining a “good death.”¹ Despite efficient methods for the assessment and treatment of pain, unrelieved pain is clinically perceived to be a common problem in dying patients. In this study, we quantify the risk of dying with unrelieved pain and investigate risk factors for this, with the overarching goal to identify areas for improvement.

Methods

Study Design and Population

Data from the Swedish Register of Palliative Care (SRPC) for 2011–2015 were used in this observational cohort study. A detailed description of this register is available in a publication by Lundström et al.¹³ In summary, the register has nationwide coverage, covering 53%–68% of all deaths in Sweden during the period investigated, 2011–2015. It includes data collected from all types of caregivers and more detailed data on deaths that were expected based on medical history. Data are collected using an EoL questionnaire completed after death by one or more members of the professional team (physician or nurse) engaged in the care of the dying patient. The questionnaire focuses on the last week of life and includes questions on whether the patient, as perceived by the team, experienced any symptoms, to what extent these were relieved, and whether external consultants were engaged to achieve symptom relief.

Cause of death information was obtained from the Swedish Cause of Death Register held by the Swedish National Board of Health and Welfare. Registration of cause of death is mandatory and is based on the International Classification of Diseases, 10th revision.¹⁴ The cause of death information, including underlying

cause of death and contributing causes, was linked to the SRPC using the national personal identification number assigned to all residents in Sweden.

The outcome of interest was *unrelieved pain during the final week in life*. In the SRPC, pain experienced by patients is classified into “completely,” “partly,” or “not at all” relieved. We combined the latter two categories into the category *unrelieved*, as less than 1% had “not at all” relieved pain, and this was contrasted to “completely” *relieved* pain.

Four risk factors for unrelieved pain were investigated: (I) cause of death; (II) place of death; (III) absence of an EoL conversation; and (IV) lack of contact with pain management expertise. These are outlined below, with additional details provided in [Appendix Table 1](#).

I. Cause of death was classified into six categories: noncancer and five groups of cancer. Four cancer groups were based on the most common metastatic sites (bone, brain, lung, and liver) but included also primary cancers of those sites. The classification was based on both underlying and contributing cause of death. The fifth group included patients with cancer in any other site as the underlying cause of death. Patients not meeting any of these criteria were classified as noncancer. This risk factor is investigated based on the assumption that cause of death is also the symptom-yielding condition during the final week of life.

II. Place of death was reported in seven categories, reclassified into three categories for this study: specialist palliative care, general in-hospital care (excluding inpatient specialist palliative care), and community-based care. This risk factor is investigated based on the assumption that place of death is also place of care during the final week of life.

III. An EoL conversation was reported to the SRPC as present if there was documentation in the medical record of a dialog with either the patient or a family member regarding the patient’s imminent death. We investigated the risk factor *absence of an EoL conversation*.

IV. The SRPC contains information on whether external expertise was consulted to relieve symptoms. The risk factor *lack of contact with pain management expertise* was present if no contact with the pain management or palliative unit was reported, as these two were considered equally skilled regarding management of EoL pain.

Information in the SRPC about diagnoses contributing to death was used to define a dichotomous variable: *multiple illnesses*, ≤ 2 vs. ≥ 3 diagnoses. Information about the symptoms pain, wheeziness, nausea, anxiety, respiratory distress, and confusion experienced during the final week of life was tallied in an attempt to summarize the dying experience.

The resulting variable, *number of symptoms*, was scored from 1 to 6, where 1 = one prevalent symptom and 6 = all six symptoms. A corresponding variable was created for *number of symptom-relieving prescriptions PRN*, ranging from 0 to 4.

Statistical Analyses

Descriptive data analysis was performed, including chi-squared test of equal distribution, to obtain the distribution of a number of factors by pain status (relieved vs. unrelieved) during the final week of life. Risk ratios (RRs) associated with each risk factor were estimated using modified Poisson regression within the framework of generalized linear models.¹⁵ All models are adjusted for age and sex. Additional confounding factors in each model are specified in Table 3. Complete case analysis was performed. To define a patient group in need of additional expert knowledge, the data set we used to evaluate *lack of contact with pain management expertise* was restricted to individuals in hospital or community-based care reported to have intense pain.

All data management and statistical analyses were performed using SAS Enterprise Guide v6.1 (SAS Institute, Cary, NC).

Ethical Considerations

Swedish law requires obtaining permission from an ethical review board before any research is initiated if it includes personal/individual data. However, when a person is deceased their data are no longer classified as “personal data” by the legal authorities in Sweden and are therefore no longer covered or protected by the Swedish ethical review board mandate. Nevertheless, we stored and handled the data in accordance with existing recommendations for research data.

Results

The SRPC data set contains information about the death of 281,051 people during the study period. Eighty four percent of these ($n = 236,527$) were reported as expected deaths as decided by the treating physician/nurse, based on the medical history. Table 1 gives a flow diagram of patients with an expected death. Pain was present during the last week of life in 68.4% of deaths. Despite opioids PRN prescribed to a vast majority (96.7%) of patients during the final week of life, 24.7% died with unrelieved pain. Because the aim of the study was to investigate pain relief, patients reported not to have had pain during the last week of life (26.5%) and patients for whom “unknown” was reported on this item (5.1%) were excluded. The excluded group was older than the

included patients and had a smaller proportion of deaths due to cancer (data not shown). Consequently, the subsequent results are based on information on 161,762 deaths.

Descriptive data are presented in Table 2. Some level of unrelieved pain was common among patients dying of cancer (26.4%), with prevalence varying between 21.7% and 29.8% for different cancer sites and also in patients dying of other causes (23.3%). Among patients dying in hospital, 37.1% had unrelieved pain, which is statistically significantly higher than for patients in specialist palliative care and community-based care (21.5% and 19.6%, respectively). Among patients with opioids prescribed PRN, 23.7% experienced unrelieved pain, whereas the corresponding number among those without opioids PRN was 52.9%. Regarding confounding factors, patients with unrelieved pain were, on average, two years younger than patients with relieved pain (79.5 vs. 81.5 years old; data not shown) and men had unrelieved pain to a larger extent than women. A dose-response relationship was seen between number of prevalent symptoms during the final week and proportion of patients with unrelieved pain. An inverse dose-response relation was found for number of symptom-relieving medicines prescribed PRN and unrelieved pain.

Table 3 presents the results of the regression analyses. The age- and sex-adjusted analyses showed an increased risk of unrelieved pain if dying of cancer in the bones (13%), in the lung (10%), and in the group with mixed primary cancers (“Other cancer”) (2%), compared with dying of a cause other than cancer. By contrast, patients dying of tumors in the brain or liver had a significantly lower risk of dying with some extent of unrelieved pain, compared with non-cancer deaths.

Place of death was a significant risk factor for unrelieved pain: dying in hospital was associated with 84% increased risk ($RR = 1.84$; 95% CI 1.79–1.88) of unrelieved pain, compared with dying at a specialist palliative care unit. By contrast, patients in community-based care compared with specialist palliative care had only a slightly increased risk of dying with unrelieved pain ($RR = 1.05$; 95% CI 1.02–1.08). This analysis was adjusted for cause of death, multiple illnesses, number of symptoms, age, and sex. Not having had an EoL conversation was associated with 42% increased risk ($RR = 1.42$; 95% CI 1.38–1.45) of unrelieved pain, adjusted for cause of death, contact with pain management expertise, place of death, multiple illnesses, age, and sex. Patients for whom pain management expertise had not been involved had 19% lower risk of unrelieved pain compared with those where pain expertise was contacted (analysis restricted to

Table 1
Flow Diagram of Occurrence of Pain During the Last Week of Life, Prescription of Opioids PRN, and Pain Outcome Among Expected Deaths Registered in the Swedish Register of Palliative Care (SRPC), 2011–2015

Pain		Opioids Prescribed PRN		Pain Outcome	
	<i>n</i> (%)		<i>n</i> (%)		<i>n</i> (%)
Yes	161,762 (68.4)	Yes	156,355 (96.7)	Unrelieved	36,995 (22.9)
		No	5092 (3.1)	Relieved	119,360 (73.8)
		Unknown	315 (0.2)	Unrelieved	2694 (1.7)
				Relieved	2398 (1.5)
No ^a	62,724 (26.5)			Unrelieved	189 (0.1)
Unknown ^a	12,041 (5.1)			Relieved	126 (<0.1)
Total	236,527 (100)		161,762 (100)		161,762 (100)

^aExcluded from further analyses.

patients with intense pain dying in hospital or community-based care, adjusted for cause of death, EoL conversation, place of death, multiple illnesses, number of symptoms, age, and sex).

Discussion

Pain during the final week of life was reported for 68% of patients. Almost one-quarter of these patients also died with some extent of unrelieved pain, despite nearly complete prescription of opioids PRN. We found that dying without pain being completely relieved is common, both among patients dying of cancer and of other chronic diseases. Primary cancer or metastases located to bone or lungs predicted unrelieved pain during the last week of life, compared with noncancer deaths, whereas cancer in the brain or liver did not. Compared with patients dying in specialist palliative care, the risk of dying with some extent of unrelieved pain was markedly higher for patients in hospitals, whereas, of note, dying in community-based care implied only slightly increased risk of unrelieved pain. Not having talked about the imminent death, in a so-called “EoL conversation,” was associated with increased risk of dying with unrelieved pain.

Opioids are considered to be the backbone of therapy for cancer pain¹⁰ and are also a common therapy of choice for pain in patients dying of other diseases. In addition to the individually selected and calibrated pain treatment, prescription of opioids PRN in 98% of cases has been an explicit goal in care for the dying in Sweden for almost a decade. The intention is good, and the goal is almost reached with opioid prescription PRN for 97% of patients with pain, an achievement that can be compared with 75% in UK hospitals.¹⁶ Yet our study shows that this is not enough, as almost 25% of these patients still die with unrelieved pain. When searching the literature, there are a vast number of studies presenting prevalence of pain, but few have looked into the subject *pain relief*,

and even fewer focus on the very EoL. Estimates of unrelieved pain at EoL vary from 10% to 54%,^{17–21} depending on the underlying disease and care setting.

Relief of pain is a complex concept, and complete pain relief may not be possible while maintaining clarity. Prevalence of chronic pain to a level that poses difficulties in daily life is estimated to be 10% in the general population,²² and this may therefore be a reasonable target level also in palliative care. Incidentally, 10%–15% dying with unrelieved pain is also the level achieved by the very best health care providers reporting to the SRPC. Given our results, it would seem that additional means to improve opioid use are needed, such as pain assessment, administration, and evaluation of effect, as well as other initiatives, both pharmacological and nonpharmacological.

One such initiative is preparing for imminent death by talking about it, and our results show that not having had one or several EoL conversations with the patient and/or next of kin significantly increases the risk of the patient dying with unrelieved pain. The concept of EoL conversation provides a common ground for all involved (patient, family, and health care staff) regarding the goal of care. There are studies showing benefits of having EoL discussions for the dying process, including reducing aggressive treatments near the end.^{23,24} Literature is sparse regarding the effect of an EoL conversation on pain outcome, but a Finnish study reports an odds ratio of 5.7 for dying with unrelieved pain when limited, compared with adequate, information was given about the forthcoming death.²⁵ Providing an EoL conversation was put forward as an area for improvement in an evaluation by the Swedish National Board of Health and Welfare in 2016.²⁶ In our material, at least one EoL conversation was documented for 80% of deaths, a high percentage, partly due to our inclusion of EoL conversations also with next of kin. The SRPC only records EoL conversations that are documented in the medical record, and consequently, there may have

Table 2
Descriptive Data (Counts and Row Percentages) by Pain Status Among Expected Deaths Recorded to Have Had Pain During the Last Week of Life (*n* = 161,762)

	Total	Pain Status During the Last week of Life		P-value
		Relieved <i>n</i> (%)	Unrelieved <i>n</i> (%)	
All expected deaths	161,762	121,884 (75.3)	39,878 (24.7)	
Age				
<50 years	2878	1892 (65.7)	986 (34.3)	<0.0001
50–69 years	23,678	16,724 (70.6)	6954 (29.4)	
70–89 years	93,893	70,586 (75.2)	23,307 (24.8)	
≥90 years	41,313	32,682 (79.1)	8631 (20.9)	
Sex				
Women	89,946	69,134 (76.9)	20,812 (23.1)	<0.0001
Men	71,816	52,750 (73.5)	19,066 (26.5)	
Cause of death				
Noncancer	94,537	72,465 (76.7)	22,072 (23.3)	<0.0001
Cancer	67,225	49,419 (73.5)	17,806 (26.4)	
Cancer in the bones	5643	3962 (70.2)	1681 (29.8)	
Cancer in the brain	3534	2768 (78.3)	766 (21.7)	
Cancer in the liver	6037	4602 (76.2)	1435 (23.8)	
Cancer in the lung	11,971	8543 (71.4)	3428 (28.6)	
Other cancer sites	40,040	29,544 (73.8)	10,496 (26.2)	
Place of death				
Specialist palliative care	33,882	26,603 (78.5)	7279 (21.5)	<0.0001
In-hospital care	42,982	27,043 (62.9)	15,939 (37.1)	
Community-based care	84,898	68,238 (80.4)	16,660 (19.6)	
End-of-life conversation				
Yes	128,353	98,935 (77.1)	29,418 (22.9)	<0.0001
No	21,919	15,445 (70.5)	6474 (29.5)	
Unknown	11,490	7504 (65.3)	3986 (34.7)	
Pain management consultant				
Yes	16,737	11,263 (67.3)	5474 (32.7)	<0.0001
No	139,899	107,487 (76.8)	32,412 (23.2)	
Unknown	5126	3134 (61.1)	1992 (38.9)	
Opioid prescription PRN				
Yes	156,355	119,360 (76.3)	36,995 (23.7)	<0.0001
No	5092	2398 (47.1)	2694 (52.9)	
Unknown	315	126 (40)	189 (60)	
Intense pain				
Yes	43,852	29,369 (67)	14,483 (33)	<0.0001
No	91,754	75,592 (82.4)	16,162 (17.6)	
Unknown	26,156	16,923 (64.7)	9233 (35.3)	
Multiple illnesses				
yes (≥3)	19,699	14,527 (73.7)	5172 (26.3)	<0.0001
No (≤2)	142,063	107,357 (75.6)	34,706 (24.4)	
Number of symptoms (anxiety, confusion, nausea, pain, respiratory distress, wheeziness)				
1	23,496	18,691 (79.5)	4805 (20.5)	<0.0001
2	51,145	40,226 (78.7)	10,919 (21.3)	
3	47,915	35,712 (74.5)	12,203 (25.5)	
4	28,289	19,985 (70.6)	8304 (29.4)	
5	9520	6355 (66.8)	3165 (33.2)	
6	1397	915 (65.5)	482 (34.5)	
Number of symptom-relieving prescriptions PRN (for anxiety, nausea, pain and wheeziness)				
0	3630	1689 (46.5)	1941 (53.5)	<0.0001
1	6071	3697 (60.9)	2374 (39.1)	
2	15,042	10,263 (68.2)	4779 (31.8)	
3	29,012	21,338 (73.5)	7674 (26.5)	
4	107,779	84,806 (78.7)	22,973 (21.3)	
Unknown	228	91 (39.9)	137 (60.1)	

Data Source: Swedish Register of Palliative Care (SRPC), 2011–2015.

been additional EoL conversations not recorded in the register. However, given the high number of recorded EoL conversations, we have no reason to believe this is an actual problem in our data.

Failure to identify the need for palliative care is a possible explanation for lack of an EoL conversation. However, anticipatory prescription of opioids is not standard practice in Sweden other than as part of

the list of essential drugs in care of the dying and thus, given the almost complete prescription of opioids PRN to the patients in our data, it seems that the patients with palliative care needs were in fact correctly identified. The reason for not having an EoL conversation is therefore unknown and may include both physician and patient/family factors. An EoL conversation can be perceived as a

Table 3
RRs With 95% CIs for Dying With Unrelieved Pain

Risk Factor	Crude RR (95% CI)	Adjusted RR (95% CI)
Model 1		
Cause of death (adjusted for age and sex)		
Non-cancer	1.0	1.0
Cancer in the bones ^a	1.28 (1.22–1.33)	1.13 (1.08–1.18)
Cancer in the brain ^a	0.93 (0.87–0.99)	0.79 (0.74–0.84)
Cancer in the lung ^a	1.23 (1.19–1.26)	1.10 (1.06–1.13)
Cancer in the liver ^a	1.02 (0.97–1.07)	0.91 (0.87–0.95)
Other cancer	1.12 (1.10–1.15)	1.02 (1.00–1.04)
Model 2		
Place of death (Adjusted for cause of death, multiple illnesses, number of symptoms, age, and sex)		
Specialist palliative care	1.0	1.0
In-hospital care	1.73 (1.69–1.77)	1.84 (1.79–1.88)
Community/other care	0.91 (0.89–0.94)	1.05 (1.02–1.08)
Model 3		
EoL conversation (Adjusted for cause of death, pain management team, place of death, multiple illnesses, age, and sex)		
Yes	1.0	1.0
No	1.29 (1.26–1.32)	1.42 (1.38–1.45)
Model 4		
Contact with pain management expertise ^b (Adjusted for: cause of death, EoL conversation, place of death, multiple illnesses, number of symptoms, age, sex)		
Yes	1.0	1.0
No	0.73 (0.70–0.76)	0.81 (0.78–0.85)

EoL = end of life; RR = risk ratio; CI = confidence interval.

Results from modified Poisson regression models 1–4, crude and adjusted for model-specific confounders.

^aIncludes both primary cancer and metastases.

^bRestricted to patients with intense pain cared for in hospital or a community setting ($n = 31,970$).

challenging task although it is not particularly time consuming or costly. However, it can achieve a value greater than pain relief per se, in giving the patient information that offers a chance to arrive at closure.

It is well known that pain is a common symptom among patients with cancer, but pain is present also among more than half of patients with chronic obstructive pulmonary disease, AIDS, heart disease, and renal disease.⁷ Also, unrecognized pain is more common in some noncancer populations, for example, in patients with dementia.²⁷ In a study by Brännström et al., patients with cancer were more likely to have opioids PRN than patients with heart disease.²⁸ Our study revealed that focus needs to be directed also toward pain relief in patients with other diseases, as they have pain that is unrelieved to almost the same extent as do patients with cancer. The difference in prevalence of unrelieved pain between patients with cancer vs. other diseases is statistically significant, yet may not be clinically relevant, as the proportion of affected people in either group is large. The difference in pain relief is greater between different cancer sites than between cancer and other chronic diseases; this could, however, also be due to differences in referral patterns.

The risk of dying with unrelieved pain is markedly higher if dying in hospital compared with specialist palliative care, but only slightly higher in community-based care. Despite an apparent difference in selection of patients to the different care settings, we find the small difference between community-based and specialist palliative care

striking, considering the difference in available resources. It is known that having uncontrolled symptoms is a common reason for hospital admission near EoL.²⁹ Our data contained no information regarding the reason for admission to the hospital where death eventually occurred; uncontrolled pain could therefore have been the reason for acute hospital admission, but this should not be an acceptable explanation for the low rate of pain relief, as hospitals have all resources available and should be best equipped to provide pain relief. It has been suggested that physicians' interest in symptoms is limited to using them as clues to give a correct diagnosis, whereafter the interest drastically declines.³⁰ Support from a palliative care team in hospitals has been identified as a way to improve the care, including symptom control.²⁹ Given the above reasoning, our results, showing a harmful effect regarding unrelieved pain after contact with the pain management expertise, are unexpected. The naïve causal interpretation is unlikely; more reasonable explanations for the finding are that the consultants were called on for patients with therapy-resistant pain and/or that they were called on too late.

Strengths and Limitations

The study is based on the population-based SRPC, which aims to collect data on all deaths in Sweden. The register is unique as it is not restricted to any specific care setting and comprises all causes of death. The validity of the register has been evaluated by Martinsson et al.³¹ who report difficulties with assessment of validity of symptoms and, in particular, symptom

relief, as information in the medical records was often lacking. In addition, systematic misclassification due to different interpretations of items in the EoL questionnaire depending on where the death occurred, that is, based on the experience of the staff, cannot be ruled out. Caregivers with a special interest in palliative care may also be more likely to report to the SRPC, and it is therefore probable that the coverage rate varies between different care settings. It is reasonable to assume that reporting caregivers, with a greater interest in palliative care, consequently provide better, or at least similar, quality of care than those not reporting to the register.

One limitation of our study is the rudimentary dichotomization of pain into relieved or unrelieved pain. The SRPC data contained three levels of pain relief: “completely,” “partly,” and “not at all” relieved. We acknowledge that the concept “partly” relieved is wide and also subjective. Thus, the extent and severity of unrelieved pain is uncertain. Furthermore, from a patient perspective, “partly” could mean a level of pain that is acceptable, but the extent of this more beneficial scenario is unknown. Fewer than 1% of observations reported “not at all,” which corresponds well to the comprehensive prescription of opioids PRN. Having “not at all” relief from pain could mean that pain was recognized late, not adequately treated, or actually beyond remedy. The measures taken to relieve pain, beyond opioids prescribed PRN, are not covered by the questionnaire. The question of pain relief, in a way, reflects the caregivers’ evaluation of their own efforts, indirectly implying a huge failure if reporting that they did not offer *any* relief of pain *at all* during the final week of life. In addition, we acknowledge that the care settings are unequally equipped in terms of training and attentiveness toward (relief of) symptoms. Another limitation is lack of further information regarding intensity of pain and earlier severe pain, which also would have yielded more in-depth insights into this research. Presence of severe pain earlier in the disease progression has been shown to reduce the chance of pain relief.³² Finally, we had no information on the potential confounding factor socioeconomic status.

The impact of unrelieved pain on quality of life in the dying population is a complex issue.³³ Future research is warranted to examine the proposed mechanisms behind unrelieved pain, for example, insufficient administration of opioids despite prescription and complex pain mechanisms where opioids are not enough. Such research should include pain assessment and evaluation of treatment, and also clinical intervention research to test, for example, more intensive pain assessment as a way to improved pain relief. In addition, the reason behind the counter-intuitive results regarding contact with pain management expertise needs to be investigated.

Conclusion

Our study shows areas that can be improved to provide more patients with a death free from pain. Currently, one in four patients with pain die with unrelieved pain despite opioids prescribed PRN, which should be regarded as a failure. Irrespective of where the patient is cared for when dying, pain relief should be provided. Our study shows room for improvement in hospitals in particular, which may benefit from better care structures and training. Specific focus should also be directed toward patients dying from nonmalignant diseases as they lack complete pain relief to a similar extent as patients with cancer. An EoL conversation is one feasible intervention that could reduce the number of patients dying with unrelieved pain, which ought to be available to most patients.

Disclosures and Acknowledgments

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sector. The Institute for Palliative care is supported by grants from the Kamprad Family Foundation and Mats Paulsson Foundation. The authors declare no competing interests.

References

1. Meier EA, Gallegos JV, Thomas LPM, Depp CA, Irwin SA, Jeste DV. Defining a good death (successful dying): literature review and a call for research and public dialogue. *Am J Geriatr Psychiatry* 2016;24:261–271.
2. WHO definition of palliative care [Internet]. WHO. Available from <http://www.who.int/cancer/palliative/definition/en/>. Accessed May 21, 2018.
3. Traue DC. Palliative care in non-malignant diseases. *J R Soc Med* 2005;98:503–506.
4. Årsrapport för svenska palliativregistret 2016 (Annual report of the SRPC 2016) [Internet]. Svenska Palliativregistret. Available from <http://media.palliativ.se/2017/03/Svenska-palliativregistret-%C3%85rsrapport-2017.pdf>. Accessed July 4, 2019.
5. Hälso- och sjukvårdslagen [Internet]. Available from https://www.riksdagen.se/sv/dokument-lagar/dokument/svensk-forfattningssamling/halso-och-sjukvardslag_sfs-2017-30. Accessed May 8, 2018.
6. van den Beuken-van Everdingen MHJ, Hochstenbach LMJ, Joosten EAJ, Tjan-Heijnen VCG, Janssen DJA. Update on prevalence of pain in patients with cancer: systematic review and meta-analysis. *J Pain Symptom Manage* 2016;51:1070–1090.e9.
7. Solano JP, Gomes B, Higginson IJ. A comparison of symptom prevalence in far advanced cancer, AIDS, heart disease, chronic obstructive pulmonary disease and renal disease. *J Pain Symptom Manage* 2006;31:58–69.
8. Blinderman CD, Homel P, Andrew Billings J, Tennstedt S, Portenoy RK. Symptom distress and quality of

life in patients with advanced chronic obstructive pulmonary disease. *J Pain Symptom Manage* 2009;38:115–123.

9. Nordgren L, Sörensen S. Symptoms experienced in the last six months of life in patients with end-stage heart failure. *Eur J Cardiovasc Nurs* 2003;2:213–217.

10. Ventafridda V, Tamburini M, Caraceni A, De Conno F, Naldi F. A validation study of the WHO method for cancer pain relief. *Cancer* 1987;59:850–856.

11. Zech DFJ, Grond S, Lynch J, Hertel D, Lehmann KA. Validation of World Health Organization Guidelines for cancer pain relief: a 10-year prospective study. *Pain* 1995;63:65–76.

12. Azevedo São Leão Ferreira K, Kimura M, Jacobsen Teixeira M. The WHO analgesic ladder for cancer pain control, twenty years of use. How much pain relief does one get from using it? *Support Care Cancer* 2006;14:1086–1093.

13. Lundström S, Axelsson B, Heedman P-A, Fransson G, Fürst CJ. Developing a national quality register in end-of-life care: the Swedish experience. *Palliat Med* 2012;26:313–321.

14. Swedish Cause of Death Register [Internet]. Available from <http://www.socialstyrelsen.se/register/dodsorsaksregistret>. Accessed January 25, 2019.

15. Zou G. A modified Poisson regression approach to prospective studies with binary data. *Am J Epidemiol* 2004;159:702–706.

16. End of life care audit-Dying in Hospital: National report for England 2016 [Internet]. London: Royal College of Physicians, 2016. Available from <https://www.rcplondon.ac.uk/projects/outputs/end-life-care-audit-dying-hospital-national-report-england-2016>. Accessed January 27, 2019.

17. Steindal SA, Bredal IS, Sørbye LW, Lerdal A. Pain control at the end of life: a comparative study of hospitalized cancer and noncancer patients. *Scand J Caring Sci* 2011;25:771–779.

18. Steindal SA, Bredal IS, Ranhoff AH, Sørbye LW, Lerdal A. The last three days of life: a comparison of pain management in the young old and the oldest old hospitalised patients using the Resident Assessment Instrument for Palliative Care. *Int J Old People Nurs* 2015;10:263–272.

19. Grond S, Zech D, Schug SA, Lynch J, Lehmann KA. Validation of World Health Organization guidelines for cancer pain relief during the last days and hours of life. *J Pain Symptom Manage* 1991;6:411–422.

20. Romem A, Tom SE, Beauchene M, Babington L, Scharf SM, Romem A. Pain management at the end of life: a comparative study of cancer, dementia, and chronic obstructive pulmonary disease patients. *Palliat Med* 2015;29:464–469.

21. Costantini M, Ripamonti C, Beccaro M, et al. Prevalence, distress, management, and relief of pain during the last 3

months of cancer patients' life. Results of an Italian mortality follow-back survey. *Ann Oncol* 2009;20:729–735.

22. Statens beredning för medicinsk utvärdering. Metoder för behandling av långvarig smärta en systematisk litteraturoversikt. V. 1. V. 1. [Internet]. Stockholm: Statens beredning för medicinsk utvärdering (SBU); 2006. Available from http://www.sbu.se/upload/Publikationer/Content0/1/smarta_fulltext.pdf. Accessed January 25, 2019.

23. Lundquist G, Rasmussen BH, Axelsson B. Information of imminent death or not: does it make a difference? *J Clin Oncol* 2011;29:3927–3931.

24. Wright AA, Zhang B, Ray A, et al. Associations between end-of-life discussions, patient mental health, medical care near death, and caregiver bereavement adjustment. *JAMA* 2008;300:1665–1673.

25. Miettinen TT, Tilvis RS, Karppi P, Arve S. Why is the pain relief of dying patients often unsuccessful? The relatives' perspectives. *Palliat Med* 1998;12:429–435.

26. National Guidelines – Performance Assessment 2016: End of life palliative care - Adherence to National Guidelines [Internet]. Stockholm: National Board of Health and Welfare, 2019. Report No.: 978-91-7555-466-2. Available from <http://www.socialstyrelsen.se/Lists/Artikelkatalog/Attachments/20993/2018-6-21.pdf>. Accessed January 25, 2019.

27. Van Den Noortgate NJ, Verhofstede R, Cohen J, Piers RD, Deliens L, Smets T. Prescription and deprescription of medication during the last 48 hours of life: multicenter study in 23 acute geriatric wards in Flanders, Belgium. *J Pain Symptom Manage* 2016;51:1020–1026.

28. Brännström M, Hägglund L, Fürst CJ, Boman K. Unequal care for dying patients in Sweden: a comparative registry study of deaths from heart disease and cancer. *Eur J Cardiovasc Nurs* 2012;11:454–459.

29. Cotogni P, Saini A, De Luca A. In-hospital palliative care: should we need to reconsider what role hospitals should have in patients with end-stage disease or advanced cancer? *J Clin Med* 2018;7:18.

30. von Gunten CF. Interventions to manage symptoms at the end of life. *J Palliat Med* 2005;8(Suppl 1):S88–S94.

31. Martinsson L, Heedman P-A, Lundström S, Axelsson B. Improved data validity in the Swedish register of palliative care. Nishimura W, editor. *PLOS One* 2017;12:e0186804.

32. Wang H-L, Kroenke K, Wu J, Tu W, Theobald D, Rawl SM. Predictors of cancer-related pain improvement over time. *Psychosom Med* 2012;74:642–647.

33. Caprio AJ, Hanson LC, Munn JC, et al. Pain, dyspnea, and the quality of dying in long-term care. *J Am Geriatr Soc* 2008;56:683–688.

Appendix

Appendix Table 1
Definition of the Investigated Risk Factors

Risk Factor	Definition Based on Data in the Swedish Register of Palliative Care and/or Cause of Death Register	
Cause of death	Cancer in the bones ^a	ICD-10 codes: C40–C41, C795
	Cancer in the brain ^a	ICD-10 codes: C71, C793
	Cancer in the lung ^a	ICD-10 codes: C34, C780
	Cancer in the liver ^a	ICD-10 codes: C22, C787
	Other cancer ^b	ICD-10 codes: C00–C21, C23–C33, C35–C39, C42–C70, C72–C77, C781–C786, C788–C792, C794, C796–C96
	Noncancer	All other
EoL conversation	Yes	EoL conversation with patient and/or next of kin
	No	No EoL conversation registered in the medical records. No EoL discussion with family/next of kin
Place of death	Specialist palliative care	Specialist palliative care ward. At home, with care provided by the specialist palliative care unit
	In hospital	Hospital ward (all wards except specialist palliative care)
	Community/other	All other (resident nursing home; private home with or without support from home care services, etc.)
Contact with the pain management team	Yes	Consultant from the palliative care unit or pain management unit
	No	None of the above or contact with other specialist/consultant from hospital, or spiritual or paramedical consultant

EoL = end of life; ICD = International Classification of Diseases.

^aUnderlying or contributing cause of death.

^bOnly underlying cause of death.