DYING WITH CANCER:
AN INTERNATIONAL PERSPECTIVE

WINNE KO

Doctoral dissertation

Thesis neergelegd ter verkrijging van de graad van
Doctor in de sociale gezondheidswetenschappen
Medisch-sociale wetenschappen

Department of Family Medicine and Chronic Care
Faculty of Medicine and Pharmacy
Vrije Universiteit Brussel

End-of-Life Care Research Group
Vrije Universiteit Brussel & Ghent University

Vrije
Universiteit
Brussel

VUB - UGent onderzoeksgroep
zorg rond het levenseinde

Chapter 1 General Introduction
1.1 Dying with cancer: concepts and definitions
1.2 Dying with cancer: how palliative care evolved
1.3 Dying with cancer: the public health context
1.4 Research challenges in Cancer Palliative Care addressed in this thesis
    (cross-country studies, palliative care in the last months of life, place of death & preferences and quality of life)
1.5 Research Questions
1.6 Methods and Data Collection
1.6.1 EURO SENTI-MELC study 2009-2011
1.6.2 International Place of Death (IPOD) (2008)
1.6.3 EOLIC 2007-2009

Part I Care provided to cancer patients in the final months of life
Chapter 2
Care provided and care setting transitions in the last three months of life of cancer patients: a nationwide monitoring study in four European countries BMC Cancer 2014. 14; 960.
Chapter 3
Final Transitions to place of death: patients and families wishes (submitted)

Part II Preferences of place of death of cancer patients according to GPs
Chapter 4
Awareness of General Practitioners concerning cancer patients' preferences for place of death: evidence from four European countries. Eur J Cancer 2013. 49(8): 1967-1974.
Chapter 5
Factors associated with preference met on place of death. J Pall Care 2014. 30(3): 141-150.

Part III Advanced lung cancer patients: place of death and quality of life
Chapter 6
Differences in place of death between lung cancer and COPD patients: A study in 14 countries using death certificate data. (submitted)
Chapter 7
Quality of Life of Advanced Lung Cancer Patients: a longitudinal study

Chapter 8- General discussion

8.1 Strengths and limitations of methodology
8.2 Summary of results
8.3 Interpretations of results
8.3.1 Care provided to cancer patients in the final months of life
8.3.2 Cancer patients’ preference for place of death according to GPs
8.3.3 Advanced lung cancer: place of death and quality of life
8.4 Implications: Practice, Policy and Research

Chapter 1
General Introduction

“I’m not afraid to die, I just don’t want to be there when it happens”
--- Woody Allen

Background

1.1 Dying with cancer: concepts and definitions

Death was used as a metaphor to compare with taxes in Benjamin Franklin's famous quote: "…in this world nothing can be said to be certain, except death and taxes…."[1] as both were thought to be inevitable. However, with scientific breakthroughs and improvements in social conditions (access to clean water and social welfare), longevity had been extended and the notion that death is certain is being increasingly challenged.[2,3] People believe that they should try everything possible to prolong their lives and an attitude of death-averse gradually developed in societies.

The death-denial discourse is particularly prominent in the case of cancer, where the metaphors of 'a war against cancer' and 'fighting' are often found in the mass media. As a result, as cancer progresses to the extent where the chances of curing is getting lower and the chances that a person would die goes higher, patients, families and sometimes even professional carers themselves, might find it hard to accept the reality.[4]At this stage, palliative care might be an alternative or complementary approach to help patients and their families.

Following are three definitions of palliative care.

Box 1: Definition of palliative care from the World Health Organisation (WHO)[5]

" Palliative care is an approach that improves the quality of life of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual."

Box 2: Definition of palliative care from the European Association of Palliative Care (EAPC), 2010[6]

" Palliative care is the active, total care of the patients whose disease is not responsive to curative treatment. Control of pain, of other symptoms, and of social, psychological and spiritual problems is paramount.

Palliative care is interdisciplinary in its approach and encompasses the patient, the family and the community in its scope. In a sense, palliative care is to offer the most basic concept of care – that of providing for the needs of the patient wherever he or she is cared for, either at home or in the hospital. Palliative care affirms life and regards dying as a normal process; it neither hastens nor postpones death. It sets out to preserve the best possible quality of life until death."

Box 3: Definition of palliative care from the Organisation of Economic and Co-operation Development (OECD), 2010[7]

"Palliative care describes the type of patient-centred and responsive care provided to patients with chronic or severe and life-threatening illnesses. In contrast with curative care often geared toward infectious or acute diseases, this approach is primarily focused on reducing pain and improving the quality of life through life prolonging treatments and therapies. Holistically incorporating the physiological and psychosocial needs of the patient, palliative care also seeks to involve the family and social networks of the patient"

The three definitions above show that palliative care is an approach of caring for patients who are no longer responsive to curative treatment and it encompasses a range of needs i.e. physical, psychosocial and spiritual. However, it is important to note that palliative care is not identical to terminal care, which might be used to characterise care provided to patients in their last few months, weeks and days of life. While the two terms are similar, palliative care can be integrated into a care plan from the point of diagnosis to ensure smooth transitions in later stages of illnesses and improve the overall quality of life of patients.

To facilitate understandings, throughout the thesis, the terms ‘terminal care’ and ‘end-of-life’ care will be used interchangeably, referring to the final months of life. On the other hand, palliative care is used as a term describing care potentially provided to patients from the point they receive a diagnosis of an advanced disease.

1.2 Dying with cancer: how palliative care evolved

Palliative care is generally understood as a multidisciplinary approach (physical, psychosocial, spiritual etc) in improving the quality of life of patients who had been diagnosed of a serious illness. Patients who are diagnosed with cancer often experience a lot of stress, such as choosing the appropriate medical treatment, facing an uncertain prognosis and the possibility of death. Along the disease trajectory, they might suffer from symptoms such as pain and fatigue, depression and deterioration of quality of life.[8-9] However, it is important to note that patients’ priorities might change. As the illness further progresses, patients might have to make difficult decisions about foregoing curative treatment and consider getting prepared about saying goodbye to their loved ones and complete unfinished businesses.[10-11] These show that there are many issues that care professionals (oncologists, GPs, nurses, psychologists, social worker, chaplains, therapists) have to tackle in a multi-disciplinary manner. The origin of this orientation of care could be traced back to the Middle Ages[12], but most would agree that its modern revival was marked by the establishment of the St. Christopher’s Hospice in London, the United Kingdom. The modern hospice movement[13] emerged in the 1960s led by Dame Cicely Saunders can be seen as a response to the failures of modern medicine in dealing with pain, psychosocial and spiritual issues related to death and dying. Historically palliative care was first developed among cancer patients and until today, cancer patients remain the largest disease group[14] receiving palliative care in many countries.

Figure 1 shows the disease trajectory of cancer, for most cancer patients, their physical functioning remain high even when the cancer is diagnosed as incurable. Physicians might consider patients reaching the end of the trajectory when there is a relatively sudden and evident decline in the patient's functioning. However, due to different individual trajectories of decline, the provision of palliative care should be need-based, while also taking into account the wishes of patients and families.

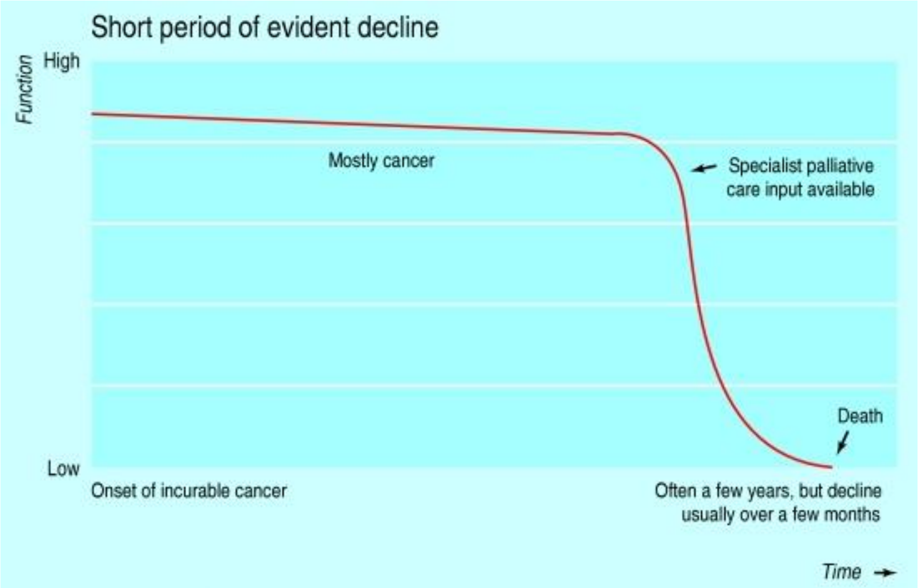


Figure 1: Disease trajectory of cancer[15]

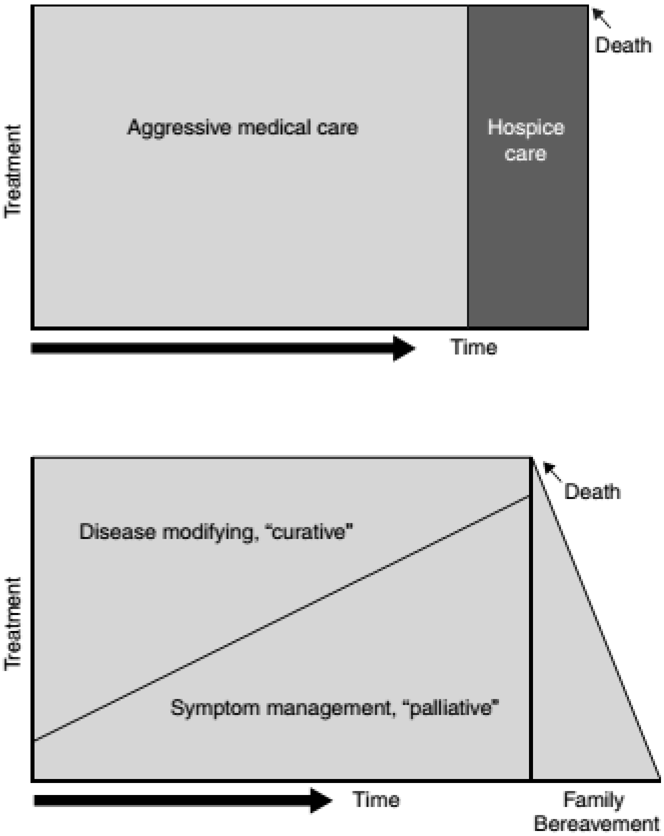


Figure 2: Appropriate care near the end of life[16]

In the past few decades, the concept of integrating palliative care into standard oncology care has been evolving.[17] Figure 2 shows the old and new concept of integrating palliative care into a life-limiting illness. The old concept dichotomises a disease trajectory into aggressive medical care and hospice (palliative) care stages, and physicians have to determine when to suspend the curative regime and make a shift to palliative care. On the other hand, the new concept believes that palliative care can be introduced to cancer patients concurrently with curative treatments. And as the disease progresses, the proportion of curative care will gradually decrease and the amount of palliative care increases. There is also growing evidence showing that palliative care and curative treatment of cancer could co-exist and could improve outcomes such as survival.[18]And the latest European Guide for Quality National Cancer Control programme[19]also included palliative care as part of the planning of cancer services.

Despite advocacy work by various organisations, the integration of palliative care into standard cancer care varied across Europe and many oncologists are not trained to adopt a holistic approach in their treatment of cancer patients.[20] Nonetheless, good integration is the key to ensure equal access to palliative care and cancer patients and their families could enjoy a better quality of life.

With the gradual expansion of services and depending on the country specific context, palliative care can be provided in a wide range of settings, including but not limited to: hospice, inpatient/out-patient/palliative care units in hospitals, nursing homes, home care teams and by family physicians/general practitioners (GPs).[20]

1.3 Dying with cancer: the public health context

“Public health refers to all organized measures (whether public or private) to prevent disease, promote health, and prolong life among the population as a whole. Its activities aim to provide conditions in which people can be healthy and focus on entire populations, not on individual patients or diseases. Thus, public health is concerned with the total system and not only the eradication of a particular disease.”[21]Applying a public health approach of palliative care means that ‘efforts organized by society to optimize the circumstances of the dying and all those involved through collective or social actions’.[22] Cancer is a disease that has been closely monitored, given the various cancer screening activities[23] and existence of national cancer registries.[24] Clear diagnosis and a relatively clear disease trajectory also facilitate the monitoring of disease progression. And historically palliative care has been developed within oncology settings since physicians could identify whether a cancer patient is entering the advanced stage of the illness. Therefore, cancer patients might be considered being a privileged group because of the nature of the disease. On the other hand, although more and more cancer patients are being cared for within communities in their final months of life, hospital care remain important for patients with complex needs, such as patients with haematological malignancies who require care from specialists. Understanding the needs of patients, families and ensuring the supply of qualified healthcare workforce would be a key part of public health policies in palliative care. Dying with cancer will continue to be a public health concern because of its scale, the changing demographics and the medicalisation of dying.

1.3.1 Growing burden of people affected by cancer

A recent study projected global cancer burden will nearly double by 2030, with 21.4 million cases and 13.2 million deaths.[21] This makes cancer continue to be a leading cause of death, together with cardiovascular diseases and respiratory diseases.[26] One important implication is that in spite of improving cancer diagnosis and treatment, the number of people being affected by cancer will inevitably increase. If we take into account the members surrounding the patient who might be affected by the disease, the number would be even greater. Demands for workforce with expertise in palliative care, numbers of institutions and allied health services, i.e. psychiatrists and social workers, would all go up. In view of this, how to expand palliative care to all those in need, including both cancer patients and their surrounding members, should be a top-priority among policy makers. Besides, cancer trajectory varies from person to person, and some people diagnosed of cancer might be able to live for years, with cancer as a chronic illness, caring and maintaining a good quality of life are crucial.

1.3.2 Changing demographics of the diseased[27]

Moreover, the ageing demographics throughout the developed world means that the population being first diagnosed of cancer would be quite different from a few decades ago when the model of palliative care was developed. For example, cancer patients are older with more co-morbidities, and the changing family structure implies fewer children are available as informal caregivers. Adapting to these changes would determine the success of maintaining the high quality of palliative care being provided to cancer patients. This is a challenging task especially in the current economic climate, but it also shows that apart from the knowledge that we already have about cancer palliative care, such as the prevalence of symptoms and barriers to physician-patient communications, there is still a vacuum of unknown to be filled.

1.3.3 Medicalisation of death and dying

Medicalisation of death and dying refers to the phenomenon that modern ‘medicine had totally overreached itself and was shaping up as a social institution intrinsically involved in social control’.[28] One example of this is the ‘hospitalization of dying’ where a bio-medical perspective is adopted in the care and treatment of dying and the majority of people died in hospitals. Early research in this area found that medical staff was not engaged with patients who were near death,[29] and the invasive care at the end of life[30] could be a painful death for both patients and families.

The epidemiological transition[31] that takes place in most of the developed world means that more and more people will die from non-communicable diseases (NCDs) such as cancer and chronic organ failure, and the number of premature and sudden deaths will reduce. And this will have implications on the increasing demand of palliative care services, especially for patients with cancer, a major NCD.

1.4 Research challenges in cancer palliative care addressed in this thesis

In this last section of the introduction, the core themes focused in this thesis will be further explained. In the literature of palliative care, many topics had been researched extensively in this field, ranging from various symptoms control[32-34] and psychological issues[35-37] to bereavement[38-40] and access to services[41-42].

Classic healthcare system research examines the input, process and output of the systems.[43] In this thesis, we wish to provide a general overview of the organisation of cancer palliative care in the countries studied, so the input/process/output framework is adopted to highlight the nature of the concepts we studied. Contexualising it in cancer palliative care, inputs/structure refers to resources that are poured into the healthcare systems, such as qualified healthcare professionals, institutions and facilities for provision of services. Process refers to the content of care from care professionals to patients and their families, i.e. communications about palliative care and transitions between care settings. Finally, output comprises of quality of care and quality of life of patients, and these components inform us whether improvements are needed for the input and process of our services.

Figure 3 is a schematic presentation by using the input-process-output framework to illustrate what we considered as challenges in cancer palliative care. The four themes are *cross-country studies, palliative care in the last months of life, place of death & preferences and quality of life.* Public health studies are in the structure/input box because they are cross-country studies, giving an overall picture about country-specific factors found in the studies. Studies on care settings transitions and communication belong to the process of care as they inform us about the content of care. Lastly, place of death, preferences and quality of life care are categorised as output because the results of these elements are related to the input and process of care and we wish to evaluate these outcomes.

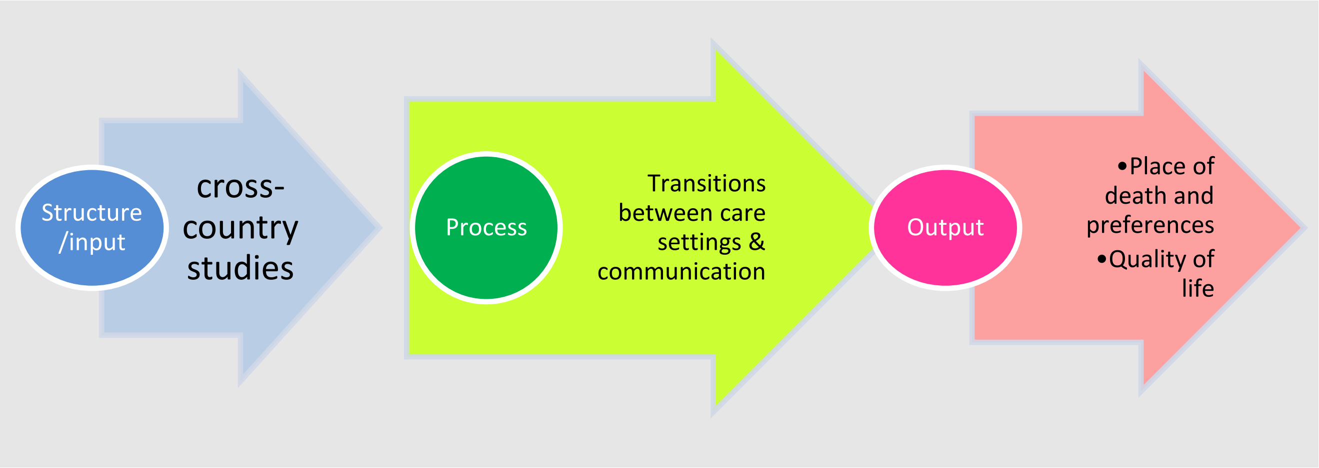


Figure 3: Schematic presentation of challenges identified in this thesis (adopted and modified from Albreht T et al 2014 and Busse and Wismar 2002)

1.4.1 Cross-country cancer palliative care

While there is an accumulating number of studies examining different healthcare practices across countries, this remains scare in the field of palliative care.[44] Healthcare is embedded within existing social, cultural and political institutions[28] and therefore, it is crucial to understand country-specific factors in planning efficient services. Countries globally organise their healthcare in various ways, reflecting historical development, cultural factors as well as preference of policy-makers and medical professionals. The different environment and its respective outcomes, such as satisfaction of health services users offer a natural laboratory for researchers to disentangle the different factors in operation. For instance, why do two countries with a similar cancer control programme result in different cancer incidence in lung cancer? This could be due to the varied effectiveness of tobacco control campaign, the perception of the harm of smoking in the two countries respectively. Furthermore, unlike some areas of medical research, i.e. drug invention, palliative care has a feature of caring for a very ill population,[45] and in order to understand the performances of the organising palliative care in a country, cross-country studies provide an opportunity to compare the pros and cons of different ways of organisation palliative care services.

As mentioned earlier, population-based data is indispensable for planning cancer palliative care on a nationwide basis. Yet currently, only a few studies in palliative care made use of population-based information,[46-47] and many existing studies focus on palliative care provided in specific settings, such as hospitals or nursing homes. Besides, using a standardised methodology across countries will facilitate interpretations and comparability of the results, thus representative data on a country-based level across countries would give insights about provision of palliative care. It is due to these reasons that the majority of the studies (5 out of 6) in this thesis are cross-country studies so that readers could compare the organisation of palliative care in the countries studied.

1.4.2 Care in the last months of life for cancer patients (care setting transitions and communication)

Frequent transitions between care settings in the last weeks or days of life are stressful for patients and their families and often do not improve the quality of care for terminally ill cancer patients.[48-49] Partly driven by costs concern[50], terminal hospitalisations might be considered as ‘inappropriate’ for cancer patients because it is believed that hospices or home care could potentially be superior to hospitals for caring dying cancer patients. Since cancer has a relatively identifiable dying and decline trajectory, physicians have the ability to make care plans for the final days or weeks including the foreseeable needs of transitions or hospitalisations. Nevertheless, little is known about the reasons behind these transitions and caring for someone until death is a burdensome task[51] and research showed that caregivers with a lower socioeconomic status might be at an even more disadvantaged position.[52] Therefore, knowing the purposes of transitions of care settings would allow palliative care practitioners to respect patients and families’ wishes by preventing unnecessary terminal transitions.

Communication between physicians, patients and families are vital because from the point of diagnosis, a lot of stressful decisions have to be made, such as types of treatment, goals of treatment (curative, life-prolonging, curative), places of care and death, options for palliative sedation, euthanasia or physician-assisted suicide. In addition, the culture of physician-patient relationship has been shifting from a paternalistic one (physicians making the important decisions) to a more co-operative (joint decisions between care professionals, patients and their caregivers after open discussions) manner. Existing literature highlighted the poor communications between physicians and patients or informal caregivers about care at the end-of-life[53-55], problems including physicians feeling their inability to do things for the patients, caregivers not feeling comfortable enough to ask questions and using euphemism in conversations among others. Good communication improves the quality of dying by providing patients and care givers with information and showing compassion from medical professionals.

This thesis will contribute to the existing literature by giving information on the prevalence of care setting transitions, where these transitions occur, the reasons of transitions and describing the care provided to advanced cancer patients in their final months of life.

1.4.3 Place of death & preferences

Place of death is regarded as one quality indicator of palliative care[56] and it is related to the overall quality of dying of patients.[57] It is known that patients preferred being cared for and dying at home.[58-60] Nonetheless, the majority of deaths still occurred in hospitals[61-62] in many countries. Achieving patients' preferences is becoming increasingly important in today's healthcare and in particular in palliative care, both because of a changing trend towards respecting patients' autonomous choices[63-64], and the belief that this is the final few things that healthcare professionals could do to honour one's death.

The observation that most cancer patients died at home could be due to a number of factors as outlined by a review[65], resources of home care (environmental factors), patients' preferences (individual factors) and types of tumour (illness-related factors). Besides, research has shown that patients' preferences could change along the disease trajectory and a preference indicated early in the trajectory might no longer be realistic as the disease progresses. Hence it is important that regular assessments are done with patients and families and to have an open discussion about the possible scenarios as the patient approaches death, so that informal caregivers could be well-prepared if dying at home is the patient's wish. Although there is a general move towards promoting home deaths in a few countries[62], such as the UK, Australia and Ireland, achieving a home death would require sufficient home care support, GPs or palliative care physicians closely involved in the case, as well as the availability of informal caregiver and the healthcare resources in the community.[66-69]

GPs are patients' first point of contact in many European healthcare systems,[70-71] and many of them have established long term relationships with their patients and continue providing care until the patient die. From this point of view, if GPs are equipped with better communication skills in end-of-life care and caring for dying cancer patients, a lot more among the population could benefit from palliative care. This will also create a more sustainable model through wider spread of generalist palliative care.[72]

Thus this thesis adds to the literature by giving answers to questions like how often do care professional know about the preferences of place of death of cancer patients? Does knowing the preference increase the likelihood of meeting the preference? And what is the role of GPs in achieving patients' home death wishes?

1.4.4 Quality of life

Quality of life (QoL) has become a frequent researched topic in cancer palliative care in recent years.[73-75] It is because for patients whose cancer is no longer curable with a limited life-expectancy, maintaining a good quality of life is a more realistic care goal and allows patients to enjoy their life to the fullest. Various definitions of QoL have been presented, such as "*the ability of patients to manage their lives as they evaluate it*",[76] "*the global evaluation of the good or satisfactory character of people's life*"[76], *"the totality of those goods, services, situations and state of affairs which are delineated as constituting the basic nature of human life which are articulated as being needed and wanted".*[76] Though with different emphases, the idea of QoL as a measurement tool is to inform healthcare professionals about the overall well-being of their patients and whether needs have been fulfilled.

Currently a number of questionnaires had been administered among cancer patients to measure the QoL, such as the QL-Index,[77]the Anamnestic Comparative Self-Assessment (ACSA),[78]the Functional Assessment of Cancer Therapy-General-7 (FACT-G7),[79]and the Functional Assessment of Chronic Illness Therapy-Palliative Care-14 (FACIT-PAL-14)[80] and so forth. One of the frequently used tools was the questionnaire developed by the European Organisation for Research and Treatment of Cancer (EORTC). Based on the original EORTC QLQ-C30 module, the Quality of Life group developed a shortened version (EORTC QLQ-C15-PAL) with only 15 items to generate an aggregate score of a cancer patient's QoL. This abbreviated version is meant to be applicable to a cancer palliative population that might be too frail to complete the full version.

In spite of scientific breakthroughs and better prevention strategies, 410,000 new cases of lung cancer were diagnosed in 2012.[81] Lung cancer is often associated with poor prognosis because symptoms are often presented at a later stage of the disease. For instance, 30-40% of non-small-cell lung cancer (NSCLC) were at stage IV at presentation.[82]And patients having NSCLC at stage IIIB and stage IV have an estimated 5-year survival of 7% and 2% respectively.[83] Therefore, for this group of patients, understanding their change in QoL as the disease progresses could provide guidance in setting treatment goals and addressing the unmet needs of patients.

This thesis attempts to add to the conventional wisdom about the changes of QoL of patients diagnosed with NSCLC and followed them until death, and secondly, to detect possible differences of changes in QoL between individuals and advanced lung cancer patients as a group.

1.5 Research Questions

Based on the background explained above, the following research questions have been formulated for the three parts of the thesis.

Part I: Care provided to cancer patients in the final months of life

1) What was the type of care and communication that cancer patients had in their last months of life?
2) What were the number of final transitions and the types of care settings transitions of cancer patients at the end of life, and how often were transitions to the place of death based on patients' or families' wishes?

Part II: Preferences of place of death of cancer patients according to GPs

3) How often are GPs aware of cancer patients' preferred place of death and what was the preferred place death as expressed to GPs?
4) How often are cancer patient preferences for place of death met, if known to GPs, and what are the factors associated with a preference to die at home?

Part III: Advanced lung cancer patients: place of death and quality of life of patients

5) What is the international pattern of place of death for lung cancer and COPD patients?
6) What is the quality of life of patients diagnosed with advanced lung cancer?

1.6 Methods and Data Collection

This thesis attempts to answer the above research questions through data analyses from three existing databases.

1.6.1 European Sentinel GP Networks Monitoring End-of-Life Care (EURO SENTI-MELC: 2009-2011)

Design

The European Sentinel GP Networks Monitoring End-of-Life Care (EURO SENTI-MELC) study continuously monitored end-of-life (EOL) care via the use of representative networks of GPs in 2009-2011 in four EU countries: 2009-2010 in Belgium, the Netherlands and Italy, and 2010-2011 in Spain. Data was collected nationwide, except in Spain, where only two regions (North: Castilla y León and East: Valencia) were included.

The study originated in 2004 in Belgium and 2005 in the Netherlands and adopted a mortality follow-back questionnaire design. The framework of the questionnaire had largely remained the same since then except minor changes to questions in each year's questionnaire.

Setting and participants

The GP networks represented from 0.8% (NL) to 4% (IT) of the population in the surveyed areas. Apart from Italy, networks in all countries are existing Sentinel GP networks involved in the surveillance of different health related topics.

The question, 'Was death sudden and totally unexpected?' (dichotomous answers: yes/no) was used to identify all non-sudden deaths. The rationale behind this question is that from a theoretical point of view, people who died suddenly, i.e. car accident (assuming the person does not already possess a life-threatening illness), would generally not fall within the population who has palliative care needs, and therefore, was less likely to be receiving any end of life care, as reported by their GPs. Nursing home deaths from the Netherlands were excluded bacause GPs discontinued their care after one's transition to a nursing home where care was taken over by specialist elderly care physicians.

Data collection procedure and content of the questionnaire

To minimise recall bias, physicians recorded deaths immediately after their patients died. Paper-based forms were administered in Belgium, the Netherlands and Castilla y León, whereas a web-based registration was adopted in Italy and an electronic registry in Valencia. Basic information of the patient (age, gender, underlying cause of death etc) was registered by the GPs. GPs also answered questions about the final three months of life of deceased patients. These questions were classified into three palliative care domains measuring: **medical care processes, communication processes and the circumstances of dying.**

1.6.2 International Place of Death (IPoD) (2008)

Study design

The second database used was from the International Place of Death (IPoD) study, which is a database of population level death certificate data. An open call was launched by the principal investigators (Dr. Joachim Cohen and Dr. Dirk Houttekier), and candidate partners negotiated a full year death certificate data with the respective authorities (i.e. national institute of statistics) for inclusion. The year 2008 was chosen as the reference year.

Exceptions were the USA (2007) and Spain (no data were recorded prior to 2010). Eventually, fourteen out of the 27 candidate countries obtained permissions for data use and their data were integrated into an international database.

Data collection and merging

The principal investigators pooled all data guaranteeing a uniform coding throughout the database. Death certification was executed in similar ways in the 14 countries: a physician or a certified person completes the part of the death certificate indicating cause of death (ICD-10 code was used), time and place of death, along with a limited range of demographic information (e.g. sex, education level, marital status, socio-demographic status) for the deceased. In some countries another part of the death certificate, containing more socio-demographic information of the deceased, is completed by a servant of the civil registration services. Additional information is then processed in the death certificate data by trained coders, following strict coding protocols with the necessary quality checks. The death certificate data was linked across a number of countries with similar population databases such as the Census Bureau in order to include more socio-demographic information about the descendants in the database. In all countries available statistics on health care supply (e.g. number of hospital beds and nursing home beds per 1000 inhabitants for inhabitants 65 or older) were linked to the health care area or region of residence within the database. In some countries (Czech Republic, Hungary, the Netherlands) the data protection measures precluded any information about the region of residence in combination with the other.

The outcome for our study was the place of death as recorded in the death certificate. The available categories of place of death were: hospital, home, nursing home, palliative care institution, or others). Figure 5 shows the countries included in our study.

Figure 5: Countries included in the IPOD study

1.6.3 End of Life Information and Communication (EOLIC) (2007-2009)

The last database utilised in this thesis is the EOLIC study, a longitudinal study examining the quality of life of patients diagnosed with advanced lung cancer. Data was collected from 2007 to 2009 by Prof. dr. Koen Pardon.

Study design

Patients who had been recently diagnosed with advanced lung cancer were contacted and interviewed with a standard questionnaire. Patients were included if they aged 18 or above, Dutch-speaking and both physically and psychologically fit to be interviewed. The interview was repeated every two months until the fourth interview and every four months until the sixth interview. When the patient died, the treating specialist and the GP were asked to fill in an after-death questionnaire.

Sample selection and inclusion criteria

Pulmonologists or oncologists of three university hospitals and 10 general hospitals recruited the patients. All hospitals had a multidisciplinary oncology program. The pulmonologists and oncologists were told to ask every consecutive patient with an initial diagnosis of stage IIIb or IV non-small-cell lung cancer (NSCLC) to participate in the study, over a period of one year. Both hospitalised patients and outpatients were eligible.

Ethics

The recruitment period lasted from February 2007 to February 2008. Patients gave written informed consent and were subsequently contacted by an interviewer to schedule an interview. After each interview, the patients were asked for their agreement to take part in another interview. The interview took place at the patient's home or in another setting where the patient felt comfortable. When the patient died, the pulmonologist or oncologist and the GP filled in an after-death questionnaire. In the case of the GP, who was previously informed of the patient's participation in the study, a letter was sent with an invitation to fill out the questionnaire. Communications with the specialist were through e-mail or phone.

Dissertation outline

This dissertation is organised into eight chapters, with the first chapter as a general introduction, including the concepts and challenges identified relevant to the thesis, research questions and methodologies used in the studies.

Chapter two to seven are six scientific articles in three parts, looking at palliative care in terms of 'Care provided to cancer patients in the final months of life', 'Cancer patients' preference for place of death' and 'Advanced lung cancer: Place of death and quality of life'.

Finally, chapter eight will be a general discussion of the research findings and the respective implications (practice, policy and research) for future cancer palliative care.

References

1. Franklin B 1789. http://en.wikipedia.org/wiki/Death_%26_Taxes (accessed 15th May 2014)
2. Broderick D. The Last Mortal Generation: How Science Will Alter Our Lives in the 21st Century. New Holland, 1999.
3. Rosofsky I. Nasty, Brutish, and Long: Adventures in Old Age and the World of Eldercare. Avery Trade, 2010.
4. Rousseau P. Death Denial. J Clin Oncol 2003; 21(9 Suppl): 52-53s.
5. WHO definition of palliative care. http://www.who.int/cancer/palliative/definition/en/ (accessed 10th May 2014)
6. EAPC definition of palliative care. http://www.eapcnet.eu/Corporate/AbouttheEAPC/Definitionandaims.aspx (accessed 10th May 2014)
7. OECD Health Policy Studies Value for Money in Health Spending. 2010. p.5
8. Janberidze E, Pereira SM, Hjermstad MJ, et al. Depressive symptoms in the last days of life of patients with cancer: a nationwide retrosepective mortality study. BMJ Support Palliat Care 2015. doi: 10.1136/bmjspcare-2014-000722. [Epub ahead of print]
9. Beernaert K, Deliens L, Vleminck A, et al. Is There a Need for Early Palliative Care in Patients in Patients With Life-Limiting Illnesses? Interview Study With Patients About Experienced Care Needs From Diagnosis Onward. Am J Hosp Palliat Care 2015. pii: 1049909115577352. [Epub ahead of print]
10. Miljkovic MD, Emuron D, Rhodes L, Abraham J, Miller K. “Allow Natural Death” versus “Do Not Resuscitate”: What Do Patients with Advanced Cancer Choose? J Palliat Med 2015. [Epub ahead of print]
11. Malhorta C, Farooqui MA, Kanesvaran R, Bilger M, Finkelstein E. Comparison of preferences for end-of-life care among patients with advanced cancer and their caregivers: A discrete choice experiment. Palliat Med 2015. pii: 0269216315578803. [Epub ahead of print]
12. (Eds) Clark D, Seymour J. Reflections on Palliative Care. Open University Press, 1999. p.66
13. (Eds) Clark D, Seymour J. Reflections on Palliative Care. Open University Press, 1999. p.69
14. Addington-Hall J and Hunt K. ‘Non-cancer patients as an under-served group’ in Cohen J and Deliens L (eds) *A Public Health Perspective on End of Life Care.* Oxford University Press, New York, 2012:151–167.
15. Murray SA. Illness trajectories and palliative care. BMJ 2005; 330(7498): 1007-1011.
16. Lynn J, Adamson DM. Living Well at the End of Life: Adapting Health Care to Serious Chronic Illness in Old Age. RAND Health, Washington, 2003.
17. Green JA, Jackson VA, Meier DE, Temel JS. Early integration of palliative care services with standard oncology care for patients with advanced cancer. CA Cancer J Clin 2013; 63(5): 349-363.
18. Temel JS, Greer JA, Muzikansky A et al. Early palliative care for patients with metastatic non-small-cell lung cancer. N Engl J Med 2010; 363(8): 733-742.
19. Albreht T, Borras J, Conroy F et al. European Guide for Quality National Cancer Control programme http://www.epaac.eu/images/WP_10/European_Guide_for_Quality_National_Cancer_Control_Programmes_EPAAC.pdf (accessed 20th May 2014)
20. Specialisation in Palliative Medicine for Physicians in Europe 2014. EAPC. 2014
21. Definition of Public Health, WHO.

http://www.who.int/trade/glossary/story076/en/ (accessed 13th Aug 2014)

22. (Eds) Cohen J and Deliens L. A Public Health Perspective on the End of Life Care. Oxford University Press. p.11.
23. von Karsa L, Anttila A, Ronco G et al. Cancer Screening in the European Union. Report on the implementation of the Council Recommendation on cancer screening. International Agency for Research on Cancer, Lyon. 2008
24. International Agency for Research on Cancer http://www-dep.iarc.fr/ (accessed 15th June 2014)
25. American Cancer Society. http://www.cancer.org/myacs/newengland/global-cancer-burden-to-double-by-2030 (accessed 8th Aug 2014)
26. Lozano R, Naghavi M, Foreman, Lim S, Shibuya K, Aboyans V, et al. The Lancet 2013. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. 380(9859): 2095-2128.
27. Lynn J. Living Long in Fragile Health: The New Demographics Shape End of Life Care. Hastings Center Report 2005; 35:6s, s14-s18.
28. McManus R. Death in a Global Age. Palgrave Macmillan, 2012, p.46
29. Glaser B and Strauss A. Time for Dying. Chicago, IL. Aldine, 1968.
30. Ellenshaw J, Ward C. Care of the dying patient: the last hours or days of life. BMJ 2003; 326.
31. McManus R. Death in a Global Age. Palgrave Macmillan p.48.
32. Ventafridda V, Ripamonti C, De Conno F, Tamburini M, Cassileth BR. Symptom prevalence and control during cancer patients' last day of life. J Pall Care 1990; 6(3): 7-11.
33. McCarthy EP, Philips RS, Zhong Z, Drews RE, Lynn J. Dying with cancer: patients' function, symptoms, and care preferences as death approaches. J Am Geriatr Soc 2000; 48(5 Suppl): S110-121.
34. Mercadante S, Fulfaro F, Casuccio A. The impact of home palliative care on symptoms in advanced cancer patients.Support Care Cancer 2000; 8(4): 307-310.
35. Vachon MLS, Kristjanson L, Higginson I. Psychosocial issues in palliative care: The patient, the family and the process and outcome of care. J Pain Symptom Manage 1995; 10(2): 142-150.
36. Mcillmurray MB, Thomas C, Francis B, Morris S, Soothhill K and Al-Hamad A. The psychosocial needs of cancer patients: findings from an observational study. Eur J Cancer Care(Engl) 2001; 10(4):261-269.
37. Teunissen SCCM, de Graeff A, Voest EE, de Haes JCJM. Are anxiety and depressed mood related to physical symptom burden? A study in hospitalized advanced cancer patients. Palliat Med 2007; 21(4): 341-346.
38. Goldstein J, Alter CL and Axelrod R. A psychoeducational bereavement-support group for families provided in an outpatient cancer center. J Cancer Educ 1996; 11(4): 233-237.
39. Grassi L. Bereavement in families with relatives dying of cancer. Curr Opin Support Palliat Care 2007; 1(1): 43-49.
40. Grbich C, Parker D, Maddocks I. The emotions and coping strategies of caregivers of family members with a terminal cancer. J Palliat Care 2001; 17(1): 30-36.
41. Grande G. 'Chapter 7: Access to palliative care' in Cohen J and Deliens L (ed), A Public Health Perspective on End of Life Care. London, Oxford University Press, 2013.
42. Zercan J, Stearns S, Hanson L. Access to Palliative Care and Hospice in Nursing Homes. JAMA 2000; 284(19): 2489-2494.
43. Busse, R., Wismar, M. (2002), 'Health target programmes and health care services – any

link? A conceptual and comparative study (part 1), in Health Policy, Issue 59, pp. 209–221.2

44. Corallo AN, Croxford R, Goodman DC, Bryan EL, Srivastava D, Stukel TA. A systematic review of medical practice variation in OECD countries, Health Policy, 2014; 114(1):5-14.
45. Dean RA, McClement SE. Palliative care research: methodological and ethical challenges. Int J Palliat Nurs 2002; 8(8): 376-380.
46. Addington-Hall, J. & McCarthy, M. Dying from cancer: results of a national population-based investigation. Palliat Med 9, 295–305 (1995).
47. Teno JM, Gozalo PL, Bynum JPW, et al. Change in End-of-Life Care for Medicare Beneficiaries. Site of Death, Place of Care, and Health Care Transitions in 2000, 2005, and 2009. JAMA 2013; 309(5): 470-477.
48. Burge FI, Lawson B, Critchley P and Maxwell D. Transitions in care during the end of life: changes experienced following enrolment in a comprehensive palliative care program. BMC Palliat Care 2005; 4:3.
49. Van den Block L, Deschepper R, Bilsen J, Van Casteren V, Deliens L. Transitions Between Care Settings at the End of Life in Belgium. JAMA 2007; 298(14): 1635-1639.
50. Luengo-Fernandez R, Leal J, Gray A and Sullivan R. Economic burden of cancer across the European Union: a population-based cost analysis. Lancet Oncol 2013; 14(12): 1165-1174.
51. Deejen JF, Taylor KL, Mangan P, Yabroff KR, Ingham JM. Care for the caregivers: a reviewer of self-report instruments developed to measure the burden, needs, and quality of life of informal caregivers. J Pain Symptom Manage 2003; 26(4): 922-953.
52. Lewis JM, DiGiacomo M, Currow DC, Davidson PM. Social capital in a lower socioeconomic palliative care population: a qualitative investigation of individual, community and civic networks and relations. BMC Palliat Care 2014; 13:30.
53. Morita T, Akechi T, Ikenaga M et al. Communication about the ending of anticancer treatment and transition to palliative care. Ann Oncol 2004; 15(10): 1551-1557.
54. Hagerty RG, Butow PN, Ellis PM et al. Communicating with realism and hope: incurable cancer patients’ views on the disclosure of prognosis. J Clin Oncol 2005. 23(6): 1278-1288.
55. Parker SM, Clayton JM, Hancock K et al. A Systematic Review of Prognostic/End-of-Life Communication with Adults in the Advanced Stages of a Life-Limiting Illness: Patient/Caregiver Preferences for the Content, Style, and Timing of Information. J Pain Symptom Manage 2007; 34(1): 81-93.
56. De Roo ML, Miccinesi G, Ontwuteaka-Philipsen BD, Van Den Noortgate N, Van den Block L, Bonacchi A, et al. Actual and preferred place of death of home-dwelling patients in four European countries: making sense of quality indicators. PLoS One 2014. 8;9(4):e93762.
57. Hales S, Chiu A, Husain A et al. The Quality of Dying and Death in Cancer and Its Relationship to Palliative Care and Place of death. J Pain Symptom Manage 2014. doi: 10.1016/j.jpainsymman.2013.12.240. [Epub ahead of print]
58. Gomes, B. and Higginson, I.J., ‘Home or hospital? Choices at the end of life’, J R Soc Med 2004;97(9): 413-414.
59. Higginson IJ, Sen-Gupta GJA. Place of Care in Advanced Cancer: A Qualitative Systematic Literature Review of Patient Preferences. J Pall Med 2000; 3(3): 287-300.
60. Gomes B, Higginson IJ, Calanzani N, et al. Preferences for place of death if faced with advanced cancer: a population survey in England, Flanders, Germany, Italy, the Netherlands, Portugal and Spain. Ann Oncol 2012; 23(8): 2006-2015.

61. Cohen J, Bilsen J, Addington-Hall J et al. Population-based study of dying in hospital in six European countries. Palliat Med 2008; 22(6): 702-710.
62. Gao W, Ho YK, Verne J, Glickman M, Higginson IJ and on behalf of the GUIDE_Care project. Changing Patterns in Place of Cancer Death in England: A Population-Based Study. PLoS Med 2013. 10: e1001410.
63. Stewart M. Towards a global definition of patient centred care. BMJ 2001; 322(7284): 444-445.
64. Epstein RM, Franks P, Fiscella K et al. Measuring patient-centered communication in patient-physician consultations: theoretical and practical issues. Soc Sci Med 2005; 61(7): 1516-1528.
65. Gomes B and Higginson I. Factors influencing death at home in terminally ill patients with cancer: systematic review. BMJ 2006; 332(7540): 515-521.
66. End of Life Care Strategy- Promoting high quality care for all adults at the end of life. Department of Health, UK, 2008.
67. Wye L, Lasseter G, Percival J, Duncan L, Simmonds B and Purdy S. What works in ‘real life’ to facilitate home deaths and fewer hospital admissions for those at end of life?: results from a realist evaluation of new palliative services in two English counties. BMC Palliat Care 2014; 13:37.
68. Tang ST, and Mccorkle R. Determinants of Congruence between the Preferred and Actual Place of Death for Terminally Ill Cancer Patients. J Palliat Care 2004; 19(4):230-237.
69. Decker SL, Higginson IJ. A tale of two cities: factors affecting place of cancer death in London and New York. Eur J Public Health 2007; 17(3): 285-290.
70. Van den Block L, Onwuteaka-Philipsen B, Meeussen K, et al. Nationwide continuous monitoring of end-of-life care via representative networks of general practitioners in Europe. BMC Fam Pract 2013,14:73.
71. Saltman RB and Figueras. Analyzing the evidence on European health care reforms. Health Affairs 1998; 17(2): 85-108.
72. Quill TE and Abernethy AP. Generalist plus Specialist Palliative Care – Creating a More Sustainable Model. N Engl J Med 2013; 368: 1173-1175.
73. Mei B and Mark L. A Systematic Review of Associations between Spiritual Well-Being and Quality of Life at the Scale and Factor Levels in Studies among Patients with Cancer. J Palliat Med 2014. doi:10.1089/jpm.2014.0189.
74. Rosenfeld B, Roth AJ, Gandhi S, Penson D. Differences in health-related quality of life of prostate cancer patients based on stage of cancer. Psychooncology 2004; 13(11): 800-807.
75. Pearce NJ, Sandon-Fisher R, Campbell HS. Measuring quality of life in cancer survivors: a methodological review of existing scales. Psychooncology 2008; 17(7): 629-640.
76. De Haws JCJM, van Knippenberg FCE. The quality of life of cancer patients: A review of the literature. Soc Sci Med 1985; 20(8): 809-817.
77. Spitzer WO, Dobson AJ, Hall J, Chesterman E, Levi J, Shepherd R. Measuring the quality of life of cancer patients: A concise QL-Index for use by physicians. J Chronic Dis 1981; 31(12): 585-97.
78. Bernheim JL, Theuns P, Mazaher M, Hofmans J, Filege H, Rose M. The Potential of Anamnestic Comparative Self-Assessment (ACSA) to Reduce Bias in the Measurement of Subjective Well-Being. Journal of Happiness Studies 2006; 7(2): 227-250.
79. Yanez B, Perman T, Lis CG, Beaumont JL, Cella D. The FACT-G7: a rapid version of the functional assessment of cancer therapy-general (FACT-G) for monitoring symptoms and concerns in oncology practice and research. Ann Oncol 2013; 24(4): 1073-8.
80. Zeng L, Bedard G, Cella D et al. Preliminary results of the generation of a shortened

quality-of-life assessment for patients with advanced cancer: the FACIT-Pal-14. J Palliat Med 2013; 16(5): 509-515.

81. Ferlay J, Steliarova-Foucher E, Lortet-Tieulent J et al. Cancer incidence and mortality patterns in Europe: Estimates for 40 countries in 2012. Eur J Cancer 2013; 49(6): 1374-1403.
82. Lu, C; Onn A, Vaporciyan AA et al. (2010). "78: Cancer of the Lung".Holland-Frei Cancer Medicine (8th ed.). People's Medical Publishing House.
83. Rami-Porta, R, Crowley JJ, Goldstraw P. The revised TNM staging system for lung cancer. Annals of Thoracic and Cardiovascular Surgery 2009; 15(1):4–9.

Part I Care provided to cancer patients in the final months of life

Chapter 2 **Care provided and care setting transitions in the last three months of life of cancer patients: a nationwide monitoring study in four European countries**

BMC Cancer 2014. 14; 960.

“Because I could not stop for Death, he kindly stopped for me” ---
Emily Dickinson

Title: Care provided and care setting transitions in the last three months of life of cancer patients: a nationwide monitoring study in four European countries

Winne Ko, MA[1], Luc Deliens, PhD[1,2], Guido Miccinesi, MD[4],Francesco Giusti, PhD[4], Sarah Moreels, MA[5], Gé A. Donker, MD, PhD[6],BregjeOwuteaka-Philipsen, PhD[3],Oscar Zurriaga, PhD[7,8], Aurora López-Maside**,** MD**[7],**Lieve Van den Block, PhD[1,9] on behalf of EURO IMPACT*

1End-of-Life Care Research Group, Vrije Universiteit Brussel (VUB), Brussels, Belgium and Ghent University
2Department of Medical Oncology, University Hospital Ghent, Ghent, Belgium
3EMGO Institute for Health and Care Research, Department of Public and Occupational Health, and Palliative Care Expertise Centre, VU University Medical Centre, Amsterdam, the Netherlands
4Clinical and Descriptive Epidemiology Unit, Cancer Prevention and Research Institute, ISPO,Florence, Italy
5Public Health and Surveillance, Scientific Institute of Public Health, Brussels, Belgium
6NIVEL, Netherlands Institute for Health Services Research, Utrecht, the Netherlands
7Public Health Directorate General, Health Department, Valencia, Spain
8Spanish Consortium for Research in Epidemiology and Public Health, CIBERESP, Spain
9Department of Family Medicine and Chronic Care, Vrije Universiteit Brussel (VUB), Brussels, Belgium

Disclosures and Acknowledgments
***Collaborators EURO IMPACT**
Van den Block Lieve, De Groote Zeger, Brearley Sarah, Caraceni Augusto, Cohen Joachim, Francke Anneke, Harding Richard, Higginson Irene, Kaasa Stein, Linden Karen, Miccinesi Guido, Onwuteaka-Philipsen Bregje, Pardon Koen, Pasman Roeline, Pautex Sophie, Payne Sheila, Deliens Luc

Acknowledgements
EURO IMPACT, **Euro**pean **I**ntersectorial and **M**ultidisciplinary **Pa**lliative **C**are Research **T**raining, is funded by the European Union Seventh Framework Programme (FP7/2007-2013, under grant agreement n° [264697]). EURO IMPACT aims to develop a multidisciplinary, multi-professional and inter-sectorial educational and research training framework for palliative care research in Europe. EURO IMPACT is coordinated by Prof Luc Deliens and Prof Lieve Van den Block of the End-of-Life Care Research Group, Ghent University &Vrije Universiteit Brussel, Brussels, Belgium. Other partners are: VU University Medical Center, EMGO Institute for health and care research, Amsterdam, the Netherlands; King's College London, Cicely Saunders Institute, London, Cicely Saunders International, London, and International Observatory on End-of-Life Care, Lancaster University, Lancaster, United Kingdom; Norwegian University of Science and Technology, and EAPC Research Network, Trondheim, Norway; Regional Palliative Care Network, IRCCS AOU San Martino-IST, Genoa, and Cancer Research and Prevention Institute, Florence, Italy; EUGMS European Union Geriatric Medicine Society, Geneva, Switzerland; Springer Science and Business Media, Houten, the Netherlands.

Abstract

(1) Background

This is an international study across four European countries (Belgium[BE], the Netherlands[NL], Italy[IT] and Spain[ES]) between 2009 and 2011, describing and comparing care and care setting transitions provided in the last three months of life of cancer patients, using representative GP networks.

(2) Methods

General practitioners (GPs) of representative networks in each country reported weekly all non-sudden cancer deaths (+18y) within their practice. GPs reported medical end-of-life care, communication and circumstances of dying on a standardised questionnaire. Multivariate logistic regressions (BE as a reference category) were conducted to compare countries.

(3) Results

Of 2,037 identified patients from four countries, four out of five lived at home or with family in their last year of life. Over 50% of patients had at least one transition in care settings in the last three months of life; one third of patients in BE, IT and ES had a last week hospital admission and died there. In the last week of life, a treatment goal was adopted for 80-95% of those having palliation/comfort as their treatment goal. Cross-country differences in end-of-life care provision included GPs in NL being more involved in palliative care (67%) than in other countries (35%-49%)(OR 1.9) and end-of-life topics less often discussed in IT or ES. Preference for place of death was less often expressed in IT and ES (32-34%) than in BE and NL (49-74%).Of all patients, 88-98%were estimated to have distress from at least one physical symptom in the final week of life.

(4) Conclusion

Although palliative care was the main treatment goal for most cancer patients at the end of life in all four countries, frequent late hospital admissions and the symptom burden experienced in the last week of life indicates that further integration of palliative care into oncology care is required in many countries.

Introduction

While survival rates for cancer have increased considerably, it is still one of the leading causes of death in many developed countries.[1-2] For people suffering from an advanced form of cancer, palliative care is recognised as the preferred form of care at the end of life (EOL). The World Health Organisation (WHO) defines palliative care as ‘an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual.’[3] Within the framework of palliative care, several topics are considered important,[4] such as the use of palliative care services, communication, advance care planning and the circumstances of dying. Palliative care has been developed differently in different countries in terms of processes, structures, policies and resources that support its delivery.[5-7] However, cross-country population-based studies aimed at describing these variations in actually delivered EOL care for people with cancer in Europe are scarce.[4,8-9] Existing studies are often restricted in the themes covered e.g. pain[10] or place of death[11] or in terms of the study population e.g. hospital or hospice settings.[12-13]

Comparative and nationwide EU studies measuring across different care settings and cancer types could inform us on organising palliative care for dying cancer patients. General practitioners (GPs) are highly accessible in Europe and they have a central coordinating role in patient care in most EU countries.[14] GPs can generally provide a good public health perspective on end-of-life care in their own country. In this study, we aim to use nationwide networks of GPs in four EU countries (Belgium [BE], the Netherlands [NL], Italy [IT] and Spain [ES]) to describe and compare the medical care process, patient-GP communication processes and the actual circumstances of dying of cancer patients in the four countries studied.

Methods

Design

Data were collected within the European Sentinel GP Networks Monitoring End-of-Life Care (EURO SENTI-MELC) study, which continuously monitored EOL care via the use of representative networks of GPs in 2009-2011 in four EU countries: 2009-2010 in Belgium, the Netherlands and Italy, and 2010-2011 in Spain. All countries were sampled nationwide except Spain, where two regions (North: Castilla y León and East: Valencia) were included.

Both the study protocol and an earlier wave of data (2008) comparing deceased cancer patients in Belgium and the Netherlands have been published.[4,15-16] Using a mortality follow-back questionnaire design, GPs reported all deaths in their practices (age≥18 yrs.) on the EOL care provided in the final months of life on standardised forms.

Palliative care in the four countries studied

Access to palliative care has been recognised as a right in all countries except NLalthough there it is covered by the national health insurance. In all four countries, some type of plan or national guideline for palliative care is available;[17] it is therefore understood that patients in these countries have access to palliative care. However, none of these countries recognise palliative care as a medical specialty and the model of palliative care provision varies. For example, GPs co-ordinate care in Italy and Spain in the primary care settings, while in Belgium the care is often shared in the context of a multidisciplinary team and in the Netherlands palliative care is provided mainly by the GPs in consultation with specialist teams.[7,17]

Setting and participants

In general the GP networks are representative of all GPs in the country in terms of age, gender and geographical distribution. Sentinel surveillance systems of GPs are used to provide information regarding the whole patient population in a country, particularly in countries where general practice is highly accessible. Percentages of the general population covered by the GP sentinel networks are 1.75% of the total Belgian population, 0.8% of the Dutch population, 2.2% in Valencia, 3.5% of the adult population in Castilla y Leon and 4% of the Italian population(per health district). For the specific purpose of our study we additionally analysed the representativity of the networks to cover all deaths in the country. These results were published earlier[16] showing that data collected from the GP networks had significant but small differences from available mortality statistics or death certificate studies in terms of age, gender and place of death.[16] In all countries GPs can identify deaths due to cancer and non-cancer and those dying at home as well as in institutional settings. GPs appear to underreport a limited number of deaths ie non-sudden hospital deaths and deaths of people under 65 years in Belgium, and possibly also sudden hospital deaths in all countries.[16] Apart from in Italy, the networks in all countries are existing Sentinel GP networks involved in the surveillance of different health related topics.[16] In 2009, the number of GPs participating in the study were 199 (1.8%) in Belgium, 59 (0.8%) in the Netherlands and 149 (4.3%) in Italy. In 2010, the figures were 189 (1.5%) in Belgium, 63 (0.8%) in the Netherlands, 94 (2.7%) in

Italy, and 173 in Spain (114 (3.4%) in Castilla and León, 59 (3%) in Valencia).

For this study, we included cancer patients only i.e. cancer as GP-reported 'underlying cause of death', and excluded those judged to have died 'suddenly and totally unexpectedly' by the GP. Nursing home deaths from the Netherlands were excluded since GPs discontinued their care after the transition to a nursing home where care is taken over by elderly care physicians.

Data Collection and measurements

To minimise recall bias, physicians recorded deaths immediately after the patient died. Paper-based forms were administered in Belgium, the Netherlands and Castilla y León, whereas a web-based registration was adopted in Italy and an electronic registry in Valencia. To ensure the quality of data collected, instructions on filling out the form were sent to GPs at the beginning of the year in all countries. Every GP is asked to fill in a weekly, standardised registration form, whether or not there was a deceased patient. Where a patient had died during that week, the GP filled in the questions concerning care and dying. Only if GPs registered weekly for26 weeks or more were their data included in the databases.

GPs answered questions about the final three months of life of deceased patients. These questions were derived from and developed in previous research.[4,16,18-19] A validated item, the MSAS-GDI, was included in the questionnaire.[21] Other items in the questionnaire had been pre-tested in the pilot studies with experts to increase validity and reliability. Further details can be found in the methodological paper published earlier.[16]

Questions were classified into three palliative care domains measuring**:**

- **Medical care processes(last three months and last week of life):**number of GP-patient contacts, transitions between care settings, use of specialist palliative care services, use of GP palliative care, costs and burden of informal caregivers as judged by the GP, treatment goals (cure, life-prolonging, palliative care in the final three months of life), terminal hospital admission(i.e. dying in the hospital) and timing of this admission
- **Communication processes:**
    1. Patient-GP conversations about primary diagnosis, incurability of illness, life expectation, possible medical complications, physical complaints, psychological problems, social problems, spiritual problems, options for palliative care, burden of treatments (options: *yes, no, not applicable*)
    2. EOL preferences for place of death and medical treatment as known to the GP

- **Circumstances of dying in the last week of life**

Physical and psychological symptom distress was measured using the Memorial Symptom Assessment Scale- Global Distress Index(MSAS-GDI).[21] GPs estimated:

1. Physical symptom distress: lack of appetite, lack of energy, pain, drowsiness, constipation, dry mouth, difficulty in breathing(dyspnoea) (GPs first indicated the presence of symptoms as *yes, no or unknown*; if yes, they indicated *not at all, a little bit, somewhat, quite a bit or very much*)
2. Psychological symptom distress: sadness, worry, irritation, nervousness (GPs first indicated the presence of symptoms as *yes, no or unknown*; if yes, they indicated *rarely occasionally, frequently, or almost constantly*)

Basic information about the patient (age, gender, type of malignancy, longest place of residence in the last year and place of death) was also registered by the GPs. Questions were first developed in Dutch and subsequently translated into French and English, and from English to Italian and Spanish through forward-backward procedures.[16]

Ethical approval

In Belgium the protocol of the study was approved by the Ethical Review Board of Brussels University Hospital of the Vrije Universiteit Brussel (2004). In Italy, ethics approval for data collection was obtained from the Local Ethical Committee ‘Comitato Etico della Azienda U.S.L. n. 9 di Grosseto’, Tuscany (2008). Ethical approval was not required for posthumous collection of anonymous patient data in the Netherlands[22-23] or Spain.[24-26] Patients and GPs remain anonymous to researchers and the institutes.

Statistical analysis

Descriptive statistics were employed to show the distribution of characteristics of the study population and Pearson’s chi-squared tests to detect cross-country differences ($p<.001$).

Further multivariate logistic regression analyses (with Belgium as the reference category) were performed to study the cross-country variations in EOL care controlling for differences in place of death, age and sex and, for the analyses regarding circumstances of dying, we additionally controlled for the number of GP contacts in the last week of life. Odds ratios (ORs) and 95% confidence interval (95% C.I.) were calculated. All analyses were completed with SPSS20.0 (IBM Corp, Armonk, NY)

Results

Characteristics of Patients

A total of 2,037 deceased cancer patients were identified from four countries(Table 1). Mean age was 73.1 years. Over 85% of cancer patients lived at home or with family in their last year of life. In Belgium and the Netherlands, 11% and 9% lived in a care home whereas the figure was 3% in Italy and 4% in Spain.

Home deaths were more common in the Netherlands (57.9%) and Spain (51.1%).Except for the Netherlands (17%), more than one third of cancer patients died in hospital in all countries (34%[BE], 38%[IT] and 35%[ES]).

Table 1: Characteristics of the Study Population: Non-sudden cancer deaths (*N*=2037)

Characteristics	Belgium (*N*=595)	The Netherlands (*N*=335)	Italy (*N*=830)	Spain (*N*=277)	*p*-value[b]
	N(%)	*N*(%)	*N*(%)	*N*(%)	
Age Group					.156
18-64	160(27.1)	90(26.9)	195(23.5)	59(21.3)	
65-74	131(22.2)	94(28.1)	210(25.3)	65(23.5)	
75-84	184(31.2)	103(30.7)	257(31.0)	97(35.0)	
85 or above	115(19.5)	48(14.3)	168(20.2)	56(20.2)	
Mean	72.5	71.9	73.6	74.2	
Gender					<.001
M	328(55.1)	177(53.2)	448(54.0)	186(67.6)	
F	267(44.9)	156(46.8)	382(46.0)	89(32.4)	
Types of malignancy					<.001
Lung	148(24.9)	80(25.0)	182(26.5)	53(19.8)	
Breast	51(8.6)	33(10.3)	57(8.3)	11(4.1)	
Colorectal	69(11.6)	38(11.9)	102(14.8)	49(18.3)	
Prostate	25(4.2)	23(7.2)	35(5.1)	29(10.8)	
Other	302(50.8)	146(45.6)	312(45.3)	126(47.0)	
Longest place of residence in the last year					<.001
Home or with family	516(87.2)	300(90.6)	799(96.5)	258(95.2)	
Care home	65(11.0)	30(9.1)	21(2.5)	10(3.7)	
Other	11(1.9)	1(0.3)	8(1.0)	3(1.1)	
Place of death					<.001
Home	196(33.2)	194(57.9)	377(45.5)	139(51.1)	
Nursing home/ Residential home for older people	71(12.0)	28(8.4)	41(5.0)	11(4.0)	
Hospital	198(33.5)	58(17.3)	312(37.7)	95(34.9)	
Palliative Care Unit/Hospice	122(20.6)	54(16.1)	94(11.4)	26(9.6)	
Elsewhere	4(0.7)	1(0.3)	4(0.5)	1(0.4)	

[a] Missing for agegroup: n=5, gender: n=4, Type of malignancy: n=166, Longest place of residence last year: n=15, Place of death: n= 11

[b] χ^2test on cross-country differences

Medical Care Processes at the End of Life

During the last three months of life, GPs had more than three contacts with patients in 23% (BE), 35% (ES), 42% (NL) and 58% (IT) of cases(Table 2).In all countries, more than half of cancer patients (between 52.6% and 69%) had at least one transition between care settings in their last three months of life. Specialist palliative care services were used in 37% of cases in NL, compared with 58%, 62% and 65% in ES, IT and BE respectively. GP palliative care was provided until death in 67% of cases in NL, compared with 49%, 44% and 35% in ES,BE and IT. Five percent of patients in Spain had difficulty in covering costs, differing from 20%, 38% and 43% in BE, NL and IT. From 31% in NL to 35%(BE), 42%(ES) and 78%(IT) of informal caregivers in the four countries were perceived to be overburdened.

In the last week of life, GPs had more than one contact with patients in two thirds of cases in all countries and 17% [NL] to 27%[ES] of patients were transferred to another setting. Terminal hospital admission was experienced by one in three patients in BE, IT and ES respectively, and by 17% in NL. These admissions occurred in the last week of life in one out of three cases except in ES where it was 48%. For all countries, palliative care was the main treatment aim for most patients in the last week of life (about 90% of patients in BE,NL and ES, and 80% in IT).

After controlling for differences in patient characteristics, variations in GP contacts in the last three months of life remained significant, as did the use of GP and specialist palliative care services.

Table 2: Characteristics of the medical care processes at the end of life

	Belgium(*N*=595)	The Netherlands(*N*=335)		Italy(*N*=830)		Spain(*N*=277)		*p*-value[a]
Characteristics	*N*(%)	*N*(%)	OR[b](95% C.I.)	*N*(%)	OR[b](95%C.I.)	*N*(%)	OR[b](95% C.I.)	
During the last three months of life:								
More than three GP-patient contacts[d]	137(23.0)	140(41.8)	**2.2(1.6-3.0)**	480(57.8)	**4.6(3.6-5.9)**	98(35.4)	**1.7(1.3-2.4)**	<.001
At least one transition to another care setting	407(69.0)	173(52.6)	0.8(0.6-1.2)	534(64.4)	0.9(0.7-1.3)	156(57.4)	0.7(0.5-1.1)	<.001
Specialist palliative care services initiated	370(65.1)	119(37.0)	**0.2(0.2-0.3)**	502(62.7)	1.2(0.9-1.6)	160(57.8)	1.0(0.7-1.4)	<.001
GP provided palliative care until death	262(44.0)	219(67.0)	**1.9(1.3-2.7)**	290(35.0)	**0.4(0.3-0.6)**	129(49.4)	0.8(0.5-1.2)	<.001
Difficult in covering care costs	92(20.3)	107(38.4)	**2.5(1.8-3.6)**	306(42.5)	**3.0(2.3-4.1)**	11(4.9)	**0.2(0.1-0.4)**	<.001
Informal caregivers feeling overburdened	183(34.9)	92(30.9)	0.7(0.5-1.00)	590(77.9)	**6.1(4.7-8.0)**	99(41.8)	1.1(0.8-1.6)	<.001
Palliation as important treatment goal (*v* curative/ prolonging life)	305(58.1)	223(76.4)	**2.2(1.6-3.1)**	418(60.9)	1.2(0.9-1.5)	138(63.3)	1.2(0.9-1.8)	<.001
During the last week of life:								
One or more GP-patient contacts	448(75.3)	286(85.4)	1.3(0.9-1.9)	625(75.3)	0.8(0.6-1.1)	178(64.3)	**0.4(0.3-0.6)**	<.001
At least one transition to another care setting	145(24.7)	56(16.8)	0.9(0.6-1.3)	159(19.5)	0.8(0.6-1.1)	71(27.4)	**1.5(1.1-2.3)**	0.002
Terminal hospital admission	198(33.5)	58(17.3)	**0.4(0.3-0.6)**	312(37.7)	1.2(1.0-1.5)[c]	95(34.9)	1.1(0.8-1.6)	<.001
Admission during last week(*v* before last week)[e]	70(35.7)	22(38.6)	1.2(0.6-2.2)	100(33.2)	1.0(0.6-1.4)	44(47.8)	**1.8(1.1-3.1)**	.084
Palliation as important treatment goal (*v* curative/ prolonging life)	522(91.9)	296(94.9)	1.4(0.8-2.6)	487(80.0)	**0.4(0.3-0.6)**	206(89.6)	0.9(0.5-1.5)	<.001

Abbreviations: GP, general practitioner; OR, odds ratio

Missing data:

During last 3 months of life: more than three GP-patient contacts: n=1%; at least one transition: n<1%; specialist palliative care initiated: n<4%; GPs' provision of pall care until death: n<3%; difficult in covering care costs: n<18%; informal caregivers feeling overburdened: n<11%

During last week of life: transferred at least once: n<3%; terminal hospital admission: n<1%; admission during last week: n<68%, palliation as important treatment goal during last week: n<16%

[a] χ^2test on cross-country differences

[b] Odd Ratios from multivariate logistic regression models. For these analyses, we compared end-of-life care between patients with cancer in the four countries, with Belgium as the reference category, and adjusted differences in place of death, age, gender and the types of malignancy. Odds ratios in bold are statistically significant at p<0.05

[c] Place of death not controlled for in multivariate analyses.

[d] median number of contacts during the last three months of life across countries was 3

[e] For patients who died in hospitals

Communication processes at the end of Life

In all countries, a large majority of GPs had discussed one or more topics (between 89% [IT] and 98%[NL]) (Table 3).Most GPs in NL (95%) discussed primary diagnosis with patients, compared with84%, 71% and 66% respectively in BE, ES and IT. Physical complaints were also frequently discussed (between 83% [IT] and 96% [NL]). Over half of patients had conversations with GPs on psychological problems (between 60%[IT] and 87%[NL]). One out of three patients talked about social problems with their GPs in IT(35%) and ES(34%), compared with57% and 70% in BE and NL respectively. ‘Spiritual problems’was the topic least often discussed in all countries, from about 15% in IT and ES to 32% in BE and slightly over half (54%) in NL. Except in IT(37%), over two-thirds of GPs in all countries had conversations on the options of palliative care (from 67%[ES] to 70%[BE] and 88%[NL]).

Other than in NL (74%), fewer than half of cancer patients expressed a preference for place of death (between 32%[IT] and 49%[BE]).Fewer than one-fifth of patients in ES(14%) and IT(18%) indicated at any time a preference about medical treatment, whereas the figures were 41% and 65% in BE and NL.

When other factors were controlled for, seven out of 10 of the aforementioned differences remained significant and topics such as the incurability of illness (more in NL, 5.0; less in IT &ES, 0.3)and options for palliative care (more in NL, 1.6; less in IT, 0.4) were less often discussed in IT and ES than in BE and the NL. The higher frequencies of discussions in NL on preference for place of death (OR 2.3, less in IT&ES, 0.4) and medical treatment(OR 2.4, less in IT 0.3 and ES 0.2) remained.

Circumstances of Dying in the last week of life

Suffering from physical symptoms was common among cancer patients, from 88% (IT), to 92% (BE &NL) and 99% (ES) of them experienced at least one symptom. Over 70% of the patients in all countries were in lack of energy, except in ES (57%). With NL being the exception (48%), 64%, 87% and 100% of patients in respectively BE, IT and ES were judged to be distressed from at least one psychological symptom. Respectively 66% [IT], 75%[BE], 79%[SP] and 87% [NL] of patients in all countries died in their preferred place of wish if known to the GP.

Results from multivariate analyses confirmed cross-country differences on symptoms included pain (more in IT [2.0] & ES [3.2]), dry mouth (more in IT [1.6]& ES[2.3]), feeling sad (more in IT [2.6]&ES[3.4]). Patients in NL were more likely (OR 1.8) and patients in IT (0.6) less likely, to die at one’s preferred location, compared to BE.

Table 3: Characteristics of Communication Processes at the End of Life

	Belgium(*N*=595)	The Netherlands(*N*=335)		Italy(*N*=830)		Spain(*N*=277)		*p*-value[a]
Characteristics	*N*(%)	*N*(%)	OR[†](95% C.I.)	*N*(%)	OR[b](95%C.I.)	*N*(%)	OR[b](95%C.I.)	
GP-patient conversations about:								
Primary Diagnosis	474(84.2)	303(95.0)	**3.1(1.8-5.4)**	505(66.4)	**0.3(0.3-0.5)**	157(70.7)	**0.4(0.3-0.6)**	<.001
Incurability of illness	416(74.4)	298(94.6)	**5.0(2.9-8.6)**	345(46.2)	**0.3(0.2-0.4)**	95(45.0)	**0.3(0.2-0.4)**	<.001
Life expectation	363(64.5)	282(89.5)	**4.1(2.7-6.2)**	277(37.0)	**0.3(0.2-0.4)**	56(27.1)	**0.2(0.1-0.3)**	<.001
Possible medical complications	393(70.1)	267(86.4)	**2.6(1.8-3.9)**	441(58.7)	**0.6(0.4-0.7)**	137(62.8)	**0.7(0.5-0.95)**	<.001
Physical complaints	514(90.7)	306(95.9)	**2.3(1.2-4.4)**	632(83.0)	**0.5(0.4-0.7)**	208(90.4)	0.9(0.5-1.6)	<.001
Psychological problems	416(74.3)	272(86.9)	**2.1(1.4-3.1)**	442(59.1)	**0.5(0.4-0.7)**	146(66.2)	**0.7(0.5-0.9)**	<.001
Social problems	284(56.5)	202(70.1)	**1.8(1.3-2.6)**	249(34.5)	**0.4(0.3-0.5)**	63(34.4)	**0.4(0.3-0.6)**	<.001
Spiritual problems	169(32.4)	156(54.4)	**2.1(1.5-2.9)**	104(14.4)	**0.3(0.3-0.5)**	27(14.7)	**0.3(0.2-0.5)**	<.001
Options for palliative care	389(70.0)	272(88.0)	**2.7(1.8-4.0)**	267(36.4)	**0.2(0.2-0.3)**	138(66.7)	0.8(0.5-1.1)	<.001
Burden of treatments	397(72.6)	244(81.6)	**1.6(1.1-2.3)**	367(50.0)	**0.4(0.3-0.5)**	136(68.3)	0.8(0.5-1.1)	<.001
Overall: One or more of these topics was discussed	447(94.1)	259(97.7)	2.2(0.9-5.4)	586(88.7)	**0.5(0.3-0.7)**	133(95.7)	1.2(0.5-2.9)	<.001
End-of-life preferences----Patient ever expressed a preference:								
For place of death	293(49.3)	245(73.8)	**2.3(1.7-3.1)**	267(32.2)	**0.4(0.3-0.5)**	85(34.0)	**0.4(0.3-0.6)**	<.001
About a medical treatment	225(40.5)	198(65.1)	**2.4(1.7-3.2)**	118(18.2)	**0.3(0.3-0.4)**	29(14.3)	**0.2(0.1-0.4)**	<.001

Missing data:

Prior to last month: Diagnosis, possible medical complication, psychosocial problems: n<10%; incurability of illness, life expectancy: n<11%; physical problems: n<8%, social problems; n<17%; spiritual problems, n<16%; options of palliative care, n<12%; burden of treatment: n<13%; one or more issues discussed: n<23%.

Preference for place of death: n<13%; preference about medical treatment: n<17%.

[a] χ^2test on cross-country differences

[b] Odds ratios from multivariate logistic regression models. For these analyses, we compared end-of-life care between patients with cancer in the four countries, with Belgium as the reference category, and adjusted differences in place of death, age, gender and the types of malignancy. Odds ratios in bold are statistically significant at p<0.05

Table 4: Circumstances of the Dying Process

	Belgium(*N*=595)	The Netherlands(*N*=335)		Italy(*N*=830)		Spain(*N*=277)		*p*-value[a]
Variable	*N*(%)	*N*(%)	OR[b](95% C.I.)	*N*(%)	OR[b](95% C.I.)	*N*(%)	OR[b](95% C.I.)	
Physical symptom distress in last week of life								
GP could make estimation[c]	520(87.4)	285(85.1)	**0.2(0.1-0.3)**	702(84.6)	**0.5(0.4-0.8)**	231(83.4)	0.8(0.5-1.3)	.355
Distress from at least one physical symptom	412(91.6)	215(91.9)	1.1(0.6-1.9)	571(88.4)	0.7(0.4-1.1)	134(98.5)	**5.8(1.4-24.8)**	.002
Lack of appetite	280(60.1)	120(49.6)	0.7(0.5-1.0)	299(47.8)	**0.6(0.4-0.8)**	67(49.6)	0.7(0.4-0.992)	.001
Lack of energy	344(72.0)	186(73.5)	1.1(0.8-1.7)	482(73.8)	1.0(0.8-1.3)	83(56.8)	**0.5(0.3-0.8)**	.001
Pain	93(23.7)	56(26.8)	1.4(0.9-2.2)	236(38.2)	**2.0(1.5-2.8)**	46(48.4)	**3.2(2.0-5.2)**	<.001
Feeling drowsy	142(32.9)	60(29.0)	1.0(0.7-1.5)	182(29.4)	0.9(0.7-1.2)	18(25.0)	0.6(0.3-1.1)	.438
Constipation	57(17.8)	22(13.8)	0.7(0.4-1.3)	158(27.7)	**1.7(1.2-2.4)**	26(32.1)	**2.1(1.2-3.8)**	<.001
Dry mouth	73(20.4)	44(22.6)	1.1(0.7-1.7)	177(30.9)	**1.6(1.1-2.2)**	34(39.5)	**2.3(1.3-3.8)**	<.001
Difficulty breathing	140(36.2)	58(32.8)	1.1(0.7-1.6)	243(40.6)	1.3(1.0-1.8)	40(60.6)	**2.5(1.4-4.4)**	<.001
Psychological symptom distress in last week of life								
GP could make estimation[c]	487(81.8)	258(77.0)	**0.2(0.1-0.3)**	649(78.2)	0.6(0.3-1.1)	208(75.1)	0.7(0.5-1.1)	0.096
Distress from at least one psychological symptom	241(63.9)	75(48.4)	**0.5(0.4-0.8)**	341(87.2)	**4.2(2.8-6.3)**	90(100)	Not estim.	<.001
Feeling sad	143(38.0)	42(25.1)	0.7(0.4-1.0)	247(58.9)	**2.6(1.9-3.6)**	57(67.1)	**3.4(2.0-5.8)**	<.001
Worrying	162(41.9)	50(29.9)	0.7(0.4-1.0)	164(41.7)	1.0(0.7-1.3)	54(63.5)	**2.2(1.3-3.7)**	<.001
Feeling irritable	87(25.9)	11(8.7)	**0.3(0.1-0.6)**	145(42.0)	**2.1(1.5-3.0)**	18(54.5)	**3.5(1.6-7.5)**	<.001
Feeling nervous	116(33.0)	16(11.8)	**0.3(0.2-0.5)**	146(42.6)	**1.6(1.2-2.3)**	22(46.8)	1.7(0.9-3.3)	<.001
Died at the place of wish[d]	**221(75.4)**	**214(87.3)**	**1.8(1.1-2.9)**	**176(65.9)**	**0.6(0.4-0.8)**	**67(78.8)**	**1.2(0.6-2.1)**	**<.001**

Missing data:

Physical symptoms were measured on five levels in the original questionnaire (not at all, a little bit, somewhat, quite a bit or very much), variables were later recoded into two categories: quite a bit and very much vs all others;

Missing values for physical symptoms Distress from at least one physical symptom: n<29%; Physical symptoms: lack of appetite: n<28%; lack of energy: n<26%; pain: n<17%; drowsy: n<19%; constipation: n<21%; dry mouth: n<22%; difficulty breathing: n<19%.

Psychological symptoms were measured on four levels in the original questionnaire (rarely, occasionally, frequently or almost constantly), variables were later recoded into two categories: frequently and almost constantly vs all others; Distress from at least one psychosocial symptom: n<51%; Psychosocial symptoms: feeling sad: n<49%, worry: n<50%, irritable: n<59%, nervous: n<57%.

Died at the preferred place of wish: information available for 44% of the patients

[a] χ^2test on cross-country differences

[b] From multivariate logistic regression models. For these analyses, we compared end-of-life care between patients with cancer in the four countries, with Belgium as the reference category, and adjusted differences in place of death, age, gender, types of malignancy and the number of GPs contact in the last week of life. Odds ratios in bold are statistically

significant at $p<0.05$

[c] For at least one symptom

[d] If the wish of the patient was known to the GP. For the death at the place of wish, we adjusted differences in the longest place of residence, number of GPs contact in the last week of life, age, sex and types of malignancy.

Discussion

Overall in all countries, four-fifths of cancer patients lived at home or with family in their last year of life. However, the study shows that transitions between care settings at the end of life are common in all countries i.e. more than half over the last three months of life and between 17-27% in the last week of life, and one third of patients (except in NL) died in hospital. There was also a substantial amount of cross-country variation in the provision of end-of-life care to cancer patients even though 80-95% had palliative care as an important treatment goal in their last week of life. While GPs were more strongly involved in palliative care in NL than in other countries, specialist palliative care services were used less often. End-of-life topics were less often discussed and preference for place of death was less often known by the GPs in IT and ES compared with BE and NL. More than 88% of all patients in all countries were estimated to have distress from at least one physical symptom in the final week of life and more than half of cancer patients from at least one psychological symptom.

Strengths and weaknesses

Strengths of the study include the administration of an analogous research design across countries and the weekly registration keeping recall bias limited, resulting in a robust four-country database of deaths, comparing actual end-of-life care practices. This information supplements the existing data from death certificates or cancer registries,[27] hence can serve as an important basis for organisational planning. However, some limitations should be noted. Selecting GPs as the source of information implies underestimation of certain types of care is possible. Nursing homes were excluded in the Netherlands, therefore elderly cancer patients might be underrepresented, although Dutch nursing homes are mainly occupied by people with neurodegenerative disorders.[28] Variations in medical practices exist across countries[29] and the quality of specialist palliative care services was not measured. Also, the questionnaire was kept short and further details on care provision were not available. Even though GPs could offer a macro view of the end-of-life care received by their patients, caregiver-reported outcomes might be more accurate for some items such as caregiver burden and patients' psychological symptoms in the last week of life. Currently these items were based on 'GPs' perception' after death, and therefore should be interpreted with caution as GPs might under/over-estimate the burden of care.

Common challenges in end-of-life care

One important common challenge concerns transitions between care settings,which were common during both the final three months (more than half in all countries) and the last week (between one in six and one in four cases)of life. A considerable number of patients (from a third to half) continued to be admitted to hospital in the last week of life and eventually died there. One third or more of informal caregivers of cancer patients were perceived as being overburdened (between 31% and 79%).

Transitions between care settings and terminal hospital admissions are incongruent with the wishes of most patients to die in familiar surroundings and may not only adversely affect the quality of care and the quality of dying of the patient[30-33] but also influence the quality of life of informal caregivers.[34-35] Although it is unclear from our study why these transitions took place, the results do show that all countries, though the Netherlands least, are struggling to meet most cancer patients' preferences for dying at home, often due to late hospital admissions. While most palliative care policies of EU countries advocate avoiding hospital death, these results call for the need to understand how this goal can be attained.

Cross-country differences in palliative care provision and end-of-life communication

Palliative care is organised differently in each of the four countries[7] and our results demonstrate large variations in the care delivered in the final three months. The Netherlands showed a lower percentage of specialist palliative care provision (one third vs. half or more in the other countries) and a stronger GP role in providing end-of-life care for cancer patients. In other countries, the role of specialist palliative care services in counselling regular caregivers is more pronounced in the final months of life. The emphasis on GPs being the primary palliative care providers in the Netherlands[36-37]–noticeably in education and policy – might be a possible explanation for this difference. Existing research showed that in some cases the involvement of specialist palliative care[38] might increase the proportions of home death, but this cannot be verified by our existing data. These differences might also be related to cultural, legal, societal and organisational variations in care.[39-41] Future studies need to shed light on the interplay between these factors to explain the variations we found.

GPs in the four countries engaged in conversations with their patients concerning prognosis, spiritual issues, palliative care and other end-of-life care issues to various degrees. This illustrates the huge variations in the topics discussed at the end of life in Europe corresponding with results found in previous studies in several other populations.[42-43] While in all countries physical complaints were frequently discussed, in some such as Belgium and the Netherlands incurability of illness and life expectation were also often discussed, which was not the case in Italy or Spain. Though standardisation in communication might not be feasible due to factors like cultural differences, it would be enlightening to find out how GPs in Belgium and the Netherlands approached patients in these difficult conversations,[4] for example whether communication guides could increase physician/patient communication.[44-45]

Furthermore, while all the four countries we studied affirm palliative care as a right for all patients, due to the differences in existing healthcare systems the content of care differs across the countries. Though the present study could not provide answers about the quality of care received by patients in these countries e.g. satisfaction of family, cost and benefit analyses, differences found in outcomes such as place of death and the number of contacts with patients in the last week of life might reflect the specifics of palliative care organisation, such as strong primary care in the Netherlands and the more frequent use of specialist palliative care in Belgium.

Circumstances of dying

Although the results concerning symptoms in the last week of life should be interpreted with caution considering that they were rated by GPs rated the symptoms in all countries GPs indicated that there is a high prevalence of symptom distress in the last week of life. This might reflect a common problem of symptom control in all countries. On the other hand, the proportions of missing values for physical and psychological symptoms were higher than other items in the questionnaire, which might reflect the limitation of using GPs in reporting them.Symptoms and distress levels reported by patients themselves are more accurate than those rated by proxies, including GPs, nurses or families. The present study did not include patients reported symptom burden (reporting could be burdensome at the end of life) and thus the results canonly be interpreted as what had been perceived by the caring GPs in the final months of life.

Implications for practice, policy and future research

The latest EAPC Atlas for Palliative Care[7] brings encouraging news to by illustrating recent changes such as the development of postgraduate courses in Belgian universities, the updated Dutch palliative care guidelines, the growth of palliative care support teams in Italy and a Spanish law (applicable in three regions) affirming citizens' rights to palliative care. Nevertheless, our results revealed that hospitalisations and transitions remain frequent. A lot of cancer patients also had a number of burdensome symptoms at the end of life according to their GPs, which suggests the need for the support of clinicians in assessing the distress of patients. Also, several country-differences became apparent such as in communications and types of palliative care delivery. National palliative care organisations may wish to consider adjusted policies or guidelines for GPs to improve their skills in end-of-life communications and countries could benefit from learning from each other to improve care.

Conclusion

Although palliative care was the main treatment goal for most cancer patients at the end of life in all four countries, frequent late hospital admissions and the symptom burden experienced in the last week of life indicates that further integration of palliative care into oncology care is required in many countries.

Abbreviations

GP-general practitioners, ORs-odd ratios, EOL-end-of-life, WHO-World Health Organisation,
BE-Belgium, NL-the Netherlands, IT-Italy, ES-Spain

References

1. U.S. Cancer Deaths Continue Long-Term Decline. http://www.cancer.gov/ncicancerbulletin/010813/page5 (accessed 10/6/2013)

2. Malvezzi M, Bertuccio P, Levi F, et al: European cancer mortality predictions for the year 2013. Ann Oncol2013,24:792-800.

3. WHO Definition of Palliative Care http://www.who.int/cancer/palliative/definition/en/ (accessed 10/6/2013)

4. Meeussen K, Van den Block L, Echteld MA, et al: End-of-Life Care and Circumstances of Death in Patients Dying As a Result of Cancer in Belgium and the Netherlands: A Retrospective Comparative Study. J Clin Oncol2011,29:4327-4334.

5. Smith AK, Thai JN, Bakitas MA, et al: The diverse landscape of palliative care clinics. J Palliat Med 2013,16:661-668.

6. Mazanec P, Daly BJ, Pitorak EF, et al: A New Model of Palliative Care for Oncology Patients with Advanced Disease. JHospPalliatNurs2009,11:324-331.

7. Centeno C, Lynch T, Donea O, et al: EAPC Atlas of Palliative Care in Europe 2013. Full edition. Milan: EAPC Press; 2013

8. Gao W, Ho YK, Verne J, Glickman M, Higginson IJ, GUIDE_Care project: Changing patterns in place of cancer death in England: a population-based study.PLoS Med 2013, 10:e1001410.

9. Gott M, Gardiner, Ingleton C, et al: What is the extent of potentially avoidable admissions amongst hospital inpatients with palliative care needs? BMC Palliat Care 2013,12:9.

10. Klepsted P, Fladvad T, Skorpen F, et al: Influence from genetic variability on opioid use for cancer pain: a European genetic association study of 2294 cancer pain patients. Pain 2011,152: 1139-1145.

11. Cohen J, Houttekier D, Onwuteaka-Philipsen B, et al: Which patients with cancer die at home? A study of sic European countries using death certificate data. J ClinOncol2010, 28:2267-2273.

12. Hall S, Davies A. An evaluation of the activity of a 7-day, nurse-led specialist palliative care service in an acute district general hospital.Int J PalliatNurs2013,19:148-150.

13. Maltoni M, Miccinesi G, Morino P, et al: Prospective observational Italian study on palliative sedation in two hospice settings: differences in casemixes and clinical care. Support Care Cancer 2012, 20:2829-2836.

14. Gérvas J, Pérez Fernández M, Starfield BH: Primary care, financing and gatekeeping in western Europe.FamPract1994,11:307-317.

15. Abarshi E, Echteld MA, Van den Block L, et al: Use of Palliative Care Services and General Practitioner Visits at the End of Life in The Netherlands and Belgium. J Pain Symptom Manage 2011,41:436-448.

16. Van den Block L, Onwuteaka-Philipsen B, Meeussen K, et al. Nationwide continuous monitoring of end-of-life care via representative networks of general practitioners in Europe. BMC FamPract 2013,14:73.

17. Evans N, Costantini M, Pasman HR, et al. End-of-Life Communication: A Retrospective Survey of Representative General Practitioner Networks in Four Countries. J Pain Symptom Manage 2014, 47:604-619.

18. Van den Block L, Deschepper R, Bilsen J, et al: Euthanasia and other end-of-life decisions: A mortality follow-back study in Belgium. BMC Public Health 2009,9:79.

19. Cartwright C, Onwuteaka-Philipsen BD, Williams G, et al: Physician discussions with terminally ill patients: A cross-national comparison.PalliatMed 2007,21: 295-303.

20. Hickman SE, Tilden VP, Tolle SW: Family reports of dying patients' distress: The adaptation of a research tool to assess global symptom distress in the last week of life. J Pain Symptom Manage 2001,22: 565-574.

21. Portenoy RK, Thaler HT, Kornblith AB et al: The Memorial Symptom Assessment Scale: an instrument for the evaluation of symptom prevalence, characteristics and distress.Eur J Cancer 1994,30A: 1326-1336.

22. Dutch Personal Data Protection Act (Unofficial English translation). http://www.dutchdpa.nl/Pages/en_wetten_wbp.aspx. (accessed 10/6/2013)

23. Wet bescherming persoonsgegevens. http://wetten.overheid.nl/BWBR0011468/geldigheidsdatum_24-10-2012. (accessed 10/6/2013)

24. Ley 41/2002, de 14 de noviembre, básica reguladora de la autonomía del paciente y de derechos y obligaciones en materia de información y documentación clínica. http://www.boe.es/buscar/doc.php?id=BOE-A-2002-22188. (accessed 10/6/2013)

25. Ley Orgánica 15/1999, de 13 de diciembre, de Protección de Datos de Carácter Personal. http://www.boe.es/buscar/doc.php?id=BOE-A-1999-23750. (accessed 10/6/2013)

26. Ley 14/1986, de 25 de abril, General de Sanidad. http://www.boe.es/buscar/doc.php?id=BOE-A-1986-10499. (accessed 10/6/2013)

27. (IOM) IoM: Describing Death in America: What We Need to Know. Washington DC, US. National Academy Press. 2003

28. Brandt HE, Deliens L, Ooms ME, van der Steen J, ven der Wal G, Ribbe MW. Symptoms, Signs, Problems, and Diseases of Terminally Ill Nursing Home Patients. A

Nationwide Observational Study in the Netherlands. Arch Intern Med 2005,165: 314-310.

29. Corallo AN, Croxford R, Goodman DC, Bryan EL, Srivastava D, Stukel TA. A systematic review of medical practice variation in OECD countries. Health Policy [Epub ahead of print] doi: 10.1016/j.healthpol.2013.08.002.

30. End-of-Life Hospital Care for Cancer Patients. Canadian Institute for Health Information. 2013

31. Smeenk FW, de Witte LP, van Haastregt JC, Schipper RM, Biezemans HP, Crebolder HF. Transmural care. A new approach in the care for terminal cancer patients: its effects on re-hospitalization and quality of life. Patient EducCounc1998,35: 189-199.

32. Improving End-of-life Care. NIH Consens State Sci Statements 21: 1-28m 2004

33. Meeussen K, Van den Block L, Bossuyt N et al: GPs' awareness of patients' preference for place of death. Br J Gen Pract2009,59:665-670.

34. Chen ML, Chu L, Chen HC: Impact of cancer patients' quality of life on that of spouse caregivers. Support Care Cancer 2004,12:469-475.

35. Wright AA, Keating NL, Balboni TA, Matulonis UA, Block SD, Prigerson HG. Place of death: correlations with quality of life of patients with cancer and predictors of bereaved caregivers' mental health. J ClinOncol2010,28:4457-4464.

36. Borgsteede SD, Deliens L, can der Wal G et al: Interdisciplinary cooperation of GPs in palliative care at home: a nationwide survey in The Netherlands.Scand J Prim Health Care 2007,25:226-231.

37. Groot MM, Vernooij-Dassen MJ, Crul BJ et al: General practitioners (GPs) and palliative care: perceived tasks and barriers in daily practice. Palliat Med 2005,19:111-118.

38. Houttekier D, Cohen J, Van den Block L, Bossuyt N, Deliens L. Involvement of Palliative Care Services Strongly Predicts Place of Death in Belgium. J Pall Care 2010; 13: 1461-1468.

39. Gysels M, Evans N, Meñaca A et al: Culture and End of Life Care: A Scoping Exercise in Seven European Countries. PLoS One 2012,7:e34188.

40. Jai J, Beavan J, Faull C: Challenges of mediated communication, disclosure and patient autonomy in cross-cultural cancer care. Br J Cancer 2011,105:918-924.

41. Searight HR, Gafford J: Cultural diversity at the end of life: issues and guidelines for family physicians. AmFam Physician 2005; 71:515-522.

42. Van der Heide A, Deliens L, Faisst K et al: End-of-life decision-making in six European countries: descriptive study. Lancet 2003,362:345-350.

43. Evans N, Costantini M, Pasman HR et al: End-of-Life Communication: A Retrospective Survey of Representative General Practitioner Networks in Four Countries. J Pain Symptom Manage 2013.[Epub ahead of print]doi: 10.1016/j.jpainsymman.2013.04.008.

44. You JJ, Fowler RA, Heyland DK. Just ask: discussing goals of care with patients in hospital with serious illness. CMAJ Jul 15, 2013

45. Balaban RB. A physician’s guide to talking about end-of-life care. J Gen Intern Med 2000,15: 195-200.

Chapter 3 **Final Transitions to place of death: patients and families wishes**

(submitted)

> "While you do not know life, how can you know about death? "
>
> --- Confucius

Title: Final Transitions to place of death: patients and families wishes

Authors: Ko W, MA[1], Miccinesi G,MD[2], Sarah Moreels, MA[3],
Donker GA, MD, PhD[4], Onwuteaka-Philipsen B, PhD[5], Alonso TV, MD, PhD[6],
Deliens L,PhD[1,7*], Van den Block L, PhD[1,8*]
on behalf of EURO IMPACT

1 End-of-Life Care Research Group, Vrije Universiteit Brussel (VUB) and Ghent University, Brussels, Belgium
2 Clinical and Descriptive Epidemiology Unit, Cancer Prevention and Research Institute, ISPO, Florence, Italy
3Public Health and Surveillance, Scientific Institute of Public Health, Brussels, Belgium
4 NIVEL, Netherlands Institute for Health Services Research, Utrecht, the Netherlands
5 EMGO Institute for Health and Care Research, Department of Public and Occupational Health, and Palliative Care Expertise Centre, VU University Medical Centre, Amsterdam, the Netherlands
6Public Health Directorate General, Health Department, Valencia, Spain
7 Department of Medical Oncology, Ghent University Hospital, Ghent, Belgium
8 Department of Family Medicine and Chronic Care, Vrije Universiteit Brussel (VUB), Brussels, Belgium

[*] contributed equally as last authors

Disclosures and Acknowledgments

*__Collaborators EURO IMPACT__

Van den Block Lieve, De Groote Zeger, Brearley Sarah, Caraceni Augusto, Cohen Joachim, Francke Anneke, Harding Richard, Higginson Irene, Kaasa Stein, Linden Karen, Miccinesi Guido, Onwuteaka-Philipsen Bregje, Pardon Koen, Pasman Roeline, Pautex Sophie, Payne Sheila, Deliens Luc

Acknowledgements

EURO IMPACT, **Euro**pean **I**ntersectorial and **M**ultidisciplinary **Pa**lliative **C**are Research **T**raining, is funded by the European Union Seventh Framework Programme (FP7/2007-2013, under grant agreement n° [264697]). EURO IMPACT aims to develop a multidisciplinary, multi-professional and inter-sectorial educational and research training framework for palliative care research in Europe. EURO IMPACT is coordinated by Prof Luc Deliens and Prof Lieve Van den Block of the End-of-Life Care Research Group, Ghent University &Vrije Universiteit Brussel, Brussels, Belgium. Other partners are: VU University Medical Center, EMGO Institute for health and care research, Amsterdam, the Netherlands; King’s College London, Cicely Saunders Institute, London, Cicely Saunders International, London, and International Observatory on End-of-Life Care, Lancaster University, Lancaster, United Kingdom; Norwegian University of Science and

Technology, and EAPC Research Network, Trondheim, Norway; Regional Palliative Care Network, IRCCS AOU San Martino-IST, Genoa, and Cancer Research and Prevention Institute, Florence, Italy; EUGMS European Union Geriatric Medicine Society, Geneva, Switzerland; Springer Science and Business Media, Houten, the Netherlands.

Abstract

Purpose

Transitions between care settings in the final months of life can sometimes be burdensome for patients and families. In most countries, there is little evidence on the frequency of different types of transitions and how often these transitions related to the wishes of patients and family. This is a four-country study (Belgium[BE], the Netherlands[NL], Italy[IT] and Spain[ES]) examining the prevalence, types and reasons of final transition between care settings of terminally ill cancer patients.

Methods

Data was collected from the EURO SENTI-MELC study over a two-year period 2009-2010 (except Spain from 2010-2011). General practitioners (GPs) within the representative sentinel networks registered weekly deaths of all patients in their practices on a standardised questionnaire. This includes patients' basic information, the number of transitions and wishes for the final transitions in the final months of life. All patients who died non-suddenly, aged 18 or above with cancer as an underlying cause of death were included in the analyses.

Results

A total of 2048 non-sudden cancer deaths were included from the four countries and 1276 (63%)patients had at least one transition between care settings in the final three months of life. 'Hospital death from home'(BE: 45%, NL: 25%, IT: 55% and ES: 47%) and 'home death from hospital' (BE: 16%, NL: 30%, IT: 17% and ES: 27%) were the two most frequent types of final transitions in the four countries. From 56% in the Netherlands, 62% in Belgium, 73% in Italy to 86% in Spain, GPs did not report a known wish from patients or families.

Conclusions

"Hospital deaths from home" is the most prevalent type of transition between care setting in three out of four countries studied. Wishes from patients or families were often not known by GPs for the main types of final transitions between care settings.

Keywords Advanced cancer, transitions, care settings, place of death, general practitioners, wishes

Introduction

Cancer is a life-threatening disease and in spite of progresses in its prevention and treatments, more than 8 million people died from it in 2012[1] and the numbers are estimated to rise.[2] Cancer care is costly, particularly in the year following diagnosis and the last year of life.[3,4,5] In Europe, cancer costs were at an estimation of €126 billion in 2009.[6]

Reducing unnecessary terminal hospitalisations can help curb the mounting healthcare costs[7] as well as improve the quality of end-of-life. Most people reside in their own homes in the last year of life[8] but the majority experienced at least one hospital transfer in the last months of life.[9-10] Comparative European data will inform us how different countries are performing on cancer end-of-life care and the possible room for improvements.

Transitions between care settings at the end-of-life can be burdensome[11-12] for patients and families and a recent study from the United States showed that about one-tenth of cognitively impaired nursing home patients had a transition in the last three days of life[13].These final transitions could be against a patient's wish to receive care at home until death.[14]Late hospice enrolment and hospital admissions are considered as indicators of poor end-of-life care.[15-17] Research in the United States found that 16% of cancer patients were admitted into hospitals in the last 7 days life[15] and 11-36% of cancer patients were enrolled in a hospice in the last 3 days before death.[7] While these transitions are needed under some circumstances, such as out of patients' and families' requests[18] or unmet care needs at home[19], little is known about to what extent, these transitions are according to patients or families' wishes.

The current study was conducted to examine the prevalence, types and wishes for final transitions between care settings of cancer patients in four European countries via representative general practitioners (GPs) networks.

The research questions of the study were:

1) How often were cancer patients transferred between care settings in the final three months of life?

2) What were the different types of final transitions to the place of death?

3) How often were patients' and families' wishes cited by GPs as reasons for the final transition?

Materials and Methods

Design

Data was gathered from the European Sentinel Network for Monitoring End-of-Life Care (EURO SENTI-MELC) study conducted in four European countries (Belgium [BE], the Netherlands [NL], Italy[IT]in 2009-2010 and Spain[ES] from 2010-2011). A retrospective mortality follow-back study design was adopted and representative general practitioners (GPs) networks were used for data collection. Except Italy, all three countries have established these networks for monitoring topics such as influenza and other acute or chronic conditions.[20]A new network in Italy was set up for this study. Further details for the study have been published.[20] These networks represented 0.8% (NL) to 4% (IT) of the patient population in the respective countries. Nursing home deaths in the Netherlands were excluded because GPs discontinue their care once a patient is transferred to a nursing home.

Data collection and measurements

GPs within the networks were asked to report all deaths of patients who are part of their practices weekly to minimise report biases. Basic information of the patient (age, gender, underlying disease, symptoms, longest place of residence in the last year and place of death) was registered by the GPs. They also reported the number of transitions and the respective reasons in the final three months of life. Questions were first developed in Dutch and subsequently translated into French and English, and from English to Italian and Spanish through forward-backward procedures.[20] The question *'Was death totally sudden and unexpected?'(yes/no)* was used to identify patients who potentially were able to benefit from end-of-life care.[21]Deceased patients aged 18 or above and with cancer as the underlying cause of death were included in the analyses. GPs registered "the **place of death** and **place(s) of residence** of the patient during the last 3 months (=90 days) before death" and "**for what reason(s) was the patient moved to the place where he/she died?**" For the first question, GPs filled in the place of death, and (maximum) three places of residence and the respective days of stay of the patient in the last three months of life. The pre-defined categories of place were *at home or living with family, care home/home for the elderly/nursing home, hospital, palliative care units/hospice and elsewhere*. GPs also gave responses to the question 'Only if the patient was moved one or more times during the final three months of life: for what reason(s) was the patient moved to the place where s/he died?' (More than one answer can be given). GPs could indicate if the move was the 'wish of the patient' or 'the wish of the patient's family or significant other(s)'.

Ethical approval

In Belgium the protocol of the study was approved by the Ethical Review Board of Brussels University Hospital (2004). In Italy, ethical approval for data collection was obtained from the Local Ethical Committee 'Comitato Etico della Azienda U.S.L. n. 9 di Grosseto', Tuscany (2008). Ethical approval was not required in the Netherlands or Spain due to the posthumous collection of anonymous patient data. Patients and GPs remain anonymous to researchers and the institutes.

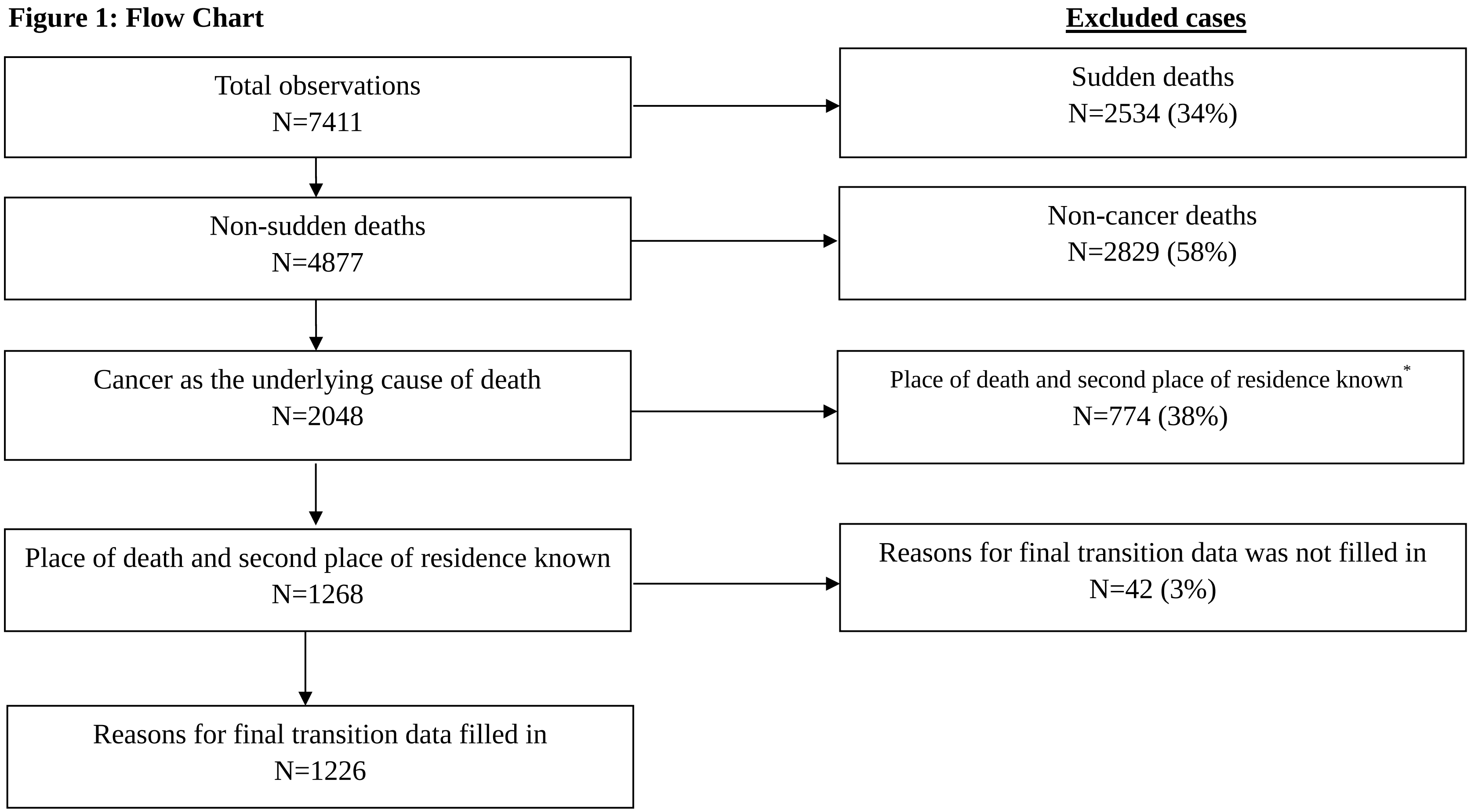
Statistical analysis

Descriptive statistics were used to describe the prevalence, types and reasons of transitions between care settings among deceased cancer patients. Pearson's chi-squared tests were used to identify cross-country differences ($p<.001$) on these items. All analyses were completed with SPSS22.0 (IBM Corp, Armonk, NY). For the analyses, we extracted the place of residence prior to death and the place of death to identify the types of final transition. For example, a patient was living at home and died in hospitals, it was labelled as a 'hospital death from home'. Only transitions between care settings that occurred 10% or more in at least one of the countries (that is among all types of transition between care settings, i.e. hospital deaths from home, only those occurred at least 10% for patients in once country was chosen) were included in the multinomial and multivariate logistic regressions.

Results

From the four countries over a two-year period, 7411 patients were included and 2048 non-sudden cancer deaths were identified (Figure 1). Among these, 1268 patients had their place of death and second place of residence known by their GPs and 1226 patients had their reasons for final transition recorded.

Figure 1: Flow Chart



*Place of death/second place of residence ‘not answered’, ‘unknown’ or ‘nursing home’ in the Netherlands

Characteristics of deceased cancer patients (N=2048)

More often patients were male (54-68%) and aged between 65-85 (56-60%) (Table 1).Lung, breast, colorectal and prostate were the four most common types of malignancy among the deceased cancer patients, with about one in four patients (except ES) died with lung cancer (24-27%). Sex and the type of malignancy differed between the four countries (p<0.001).

The distribution of place of death differed between the countries (p<0.001). Home deaths were 33% in Belgium, 46% in Italy, 51% in Spain and 58% in the Netherlands. From 17% (NL), 34% (BE), 35% (ES) to 38%(IT) of patients died in hospitals in the four countries. The proportions of palliative care unit (PCU)/hospice deaths were 10% (ES), 17% (NL), 34% (BE) and 38% (IT) respectively in the four countries. The numbers for a care home/ residential home for older people were 5-6%.Home/family (92-96%)and care home/residential home for older people (3-7%) were the two places where cancer patients resided in their last year of life. For the 2048 cancer patients who died non-suddenly, 53%(NL), 57%(ES) , 63%(IT) and 69% (BE) of patients had one or more transitions across the four countries.

Table 1: Characteristics of the sample (N=2048)

Characteristics/ Country		**Belgium (N= 595)**	**The Netherlands (N= 346)**	**Italy (N= 830)**	**Spain (N= 277)**	*p*-value
		N(%)	N(%)	N(%)	N(%)	
Sex	**Male**	328 (55)	185 (54)	448 (54)	186 (68)	*<0.001*
Age group	**18-64**	160 (27)	93 (27)	195 (24)	59 (21)	.234
	65-85	332 (56)	207 (60)	497 (60)	165 (60)	
	86 or above	98 (17)	46 (13)	138 (17)	53 (19)	
Type of malignancy	**Lung**	148 (25)	80 (24)	182 (27)	53 (20)	*<0.001*
	Breast	51 (9)	34 (10)	57 (8)	11 (4)	
	Colorectal	69 (12)	40 (12)	102 (15)	49 (18)	
	Prostate	25 (4)	24 (7)	35 (5)	29 (11)	
	Other	302 (51)	152 (46)	312 (45)	126 (47)	
Place of death	**Home**	196 (33)	194 (58)	377 (46)	139 (51)	*<0.001*
	Care home/ Residential home for older people	71 (12)	28 (8)	41 (5)	11 (4)	
	Hospital	201 (34)	58 (17)	312 (38)	96 (35)	
	PCU/Hospice	122 (21)	54 (16)	94 (11)	26 (10)	
	Elsewhere	0 (0)	1 (0)	4 (1)	0 (0)	
Longest place of residence last year	**Home/family**	516 (87)	309 (90)	799 (97)	258 (95)	*<0.001*
	Care home/ Residential home for older people	65 (11)	30 (9)	21 (3)	10 (4)	
	Other	11 (2)	1 (0)	8 (1)	3 (1)	
Patients with at least one transition		408 (69)	181 (53)	534 (64)	156 (57)	*<0.001*

missing: sex-N=4, age group-N=5, type of malignancy-N=167,place of death-N=25(nursing homes in the Netherlands-N=11), longest place of residence last year-N=17(nursing homes in the Netherlands-N=2), patients with at least one transition-N=17

Types of final transitions to place of death

The types of transitions to place of death are shown in Table 2 (N= 1226). There were twelve types of transitions found and four types were more prevalent (when occurred in more than 10% in at least one country; highlighted in grey). They were *hospital death from home, PCU/hospice death from home, PCU/hospice death from hospital* and *home death from hospital.* From 25% (NL), 45% (BE), 47% (ES) to 55% (IT) of cancer patients had a transition from home and died in hospitals.11% (IT), 12% (ES), 14% (BE)and16% (NL) of patients moved from home to PCU/hospice. On the other hand, 4% (ES), 6% (IT), 15% (BE) and18% (NL) of patients had a transfer from hospital to PCU/hospice. Finally, the proportions of patients which were transferred from hospital to home were 16% (BE), 17% (IT), 24%(ES) to 30% (NL). Multinomial logistic regressions showed cross-country differences between the three main types of final transition to place of death (with hospital death from home being the reference group because of the frequency) when controlling factors like age, sex and the type of malignancy.

Table 2: Types of final transitions to place of death among cancer patients (N=1226)[*]

Place of transition/Country	**Belgium (N=394)**	**The Netherlands (N=142)**	**Italy (N=530)**	**Spain (N=153)**	*p-value*[†]
	N(%)	N(%)	N(%)	N(%)	
Hospital death					
from home	176 (45)	36 (25)	289 (55)	72 (47)	ref
from care home	10 (3)	2 (1)	10 (2)	4 (3)	
from PC unit/hospice	1 (0)	0 (0)	2 (0)	0 (0)	
PCU/Hospice death					
from home	57 (14)	22 (16)	56 (11)	18 (12)	<0.05
from care home	5 (1)	2 (1)	2 (0)	0 (0)	
from hospital	58 (15)	25 (18)	31 (6)	6 (4)	<0.05
Home death					
from care home	1 (0)	4 (3)	11 (2)	7 (5)	
from hospital	62 (16)	42 (30)	91 (17)	37 (24)	p=0.748
from PC unit/hospice	4 (1)	1 (1)	4 (1)	4 (3)	
Care home death					
from care home	3 (1)	2 (1)	21 (4)	4 (3)	
from hospital	17 (4)	6 (4)	12 (2)	1 (1)	
from PC unit/hospice	0 (0)	0 (0)	1 (0)	0 (0)	

[*] Transitions to or from elsewhere excluded (n=7)

[†] p-value of cross-country difference with multinomial logistic regressions comparing the three main types of transitions between care settings
(hospital deaths from home as the reference category and controlling for Country, age, sex and types of malignancy at p<0.05

Wishes for final transition

Table 3 shows the prevalence of wishes for the final transitions of terminally ill cancer patients regardless of the direction of the move (N=1226). Cross-country differences were observed in terms of patients and families' wishes about the final transition (except family wishes and family wishes only)($p<0.001$).Among patients who experienced at least one transition in care settings in their final three months of life, from 56% in the Netherlands, 62% in Belgium, to 73% in Italy to 86% in Spain, no wishes from patients or families had been expressed regarding the transition. On the other hand, wishes about transition were indicated by5% (ES), 13% (IT), 27% (BE) and 28% (NL) of patients. Family wishes about transitions were expressed in 10% (ES), 18% (NL & IT) and 22% (BE) of the cases. From 5%in Spain, 9% in Italy, to 16% in Belgium and 26% in the Netherlands, only patients' own wishes were expressed about the transition. Finally, in 1% (ES), 4% (IT), 8% (NL) and 14% (BE) of patients, both wishes from patients and family were expressed concerning the final transition.

Table 3: Final transition and patients and/or families' wishes (N=1226)*

		Belgium (N= 394)	**The Netherlands (N= 142)**	**Italy (N= 530)**	**Spain (N= 153)**	*p*-value‡
		N(%)‖	N(%)‖	N(%)‖	N(%)‖	
No wish from patients or families		243 (62)	80 (56)	386 (73)	131 (86)	<0.001
Wishes from patients or families§	**Patients wishes+**	108 (27)	40 (28)	68 (13)	8 (5)	<0.001
	Family wishes+	87 (22)	25 (18)	97 (18)	15 (10)	0.002
	Patients wishes only	64 (16)	37 (26)	47 (9)	7 (5)	<0.001
	Family wishes only	33 (8)	12 (8)	76 (14)	14 (9)	0.019
	Both patients and family wishes	54 (14)	13 (8)	21 (4)	1 (1)	<0.001

*Transitions to or from elsewhere excluded (n=7)
+For the patients/ family wishes of final transitions, the category patient wishes was a sum of patients wishes only and patients and family wishes. Likewise, the category family wishes was a sum of family wishes only and patients and family wishes.
‡Binary logistic regression analyses on the cross-country differences on the wishes expressed on final transition, controlling for age, sex and types of malignancy at $p<0.001$.
§Multiple responses allowed.
‖Column percentages do not add up to 100 due to rounding off.

Wishes for transition per type of transition

A further analysis is presented in Table 4 on the wishes expressed for the four most frequent (>10% in one of the columns) types of transitions. Hospital death from home was the most prevalent type of transition (N=573). In 3% (ES), 8% (NL), 11%(IT), and 22% (BE) of patients, patients wishes was expressed for the transition. Family wishes were expressed from6% (NL),7% (ES), 15%(IT) to 18% (BE) of patients. Wishes expressed by both patients and families occurred in 1% (ES) to11% (BE) of patients.

Home death from hospitals (N=232) was the second main type of final transition. More than half of the patients in Belgium (N=37, 60%) had this transition with a wish from themselves. The figures were 48%, 19% and 11% in the Netherlands, Italy and Spain respectively. (p<0.001)About one-third patients (N=16, 26%) from Belgium and 14(NL)-18%(IT)in other countries were transferred from hospital to home with family wishes (p=0.009). Among 8% (IT)-23%(BE) of the transfers, patients and family wishes were both expressed.(p=0.057)

PCU/hospice death from home occurred for 153 patients. Patients wishes were expressed in 6%(ES), 7%(IT), 35%(BE) and 59%(NL) among the transitions (p<0.001). From 2% (IT), 6% (ES), to 18% (BE) and 36% (NL) in the four countries, the transfer took place with patient’s wishes (p=0.005).5% (IT) to 23% (NL) of patients were transferred with both patients and family wishes.

Lastly, 120 patients had a PCU/hospice death from hospitals. No significant cross-country differences were found with regard to the wishes expressed on the final transition. In 7% (IT) to 26% (BE) of patients, a wish from patients was indicated. Family wishes were expressed in 22% (ES) to 38% (IT) of the cases.

Table 4: Wishes and final transition, per type of transition (N=1078)*

Final transition/ Wishes[‡]	Hospital death from home (N=573)				PCU / hospice death from home (N=153)				PCU/ hospice death from hospital (N=120)				Home death from hospital (N=232)			
	BE (N=176)	NL (N=36)	IT (N=289)	ES (N=72)	BE (N=57)	NL (N=22)	IT (N=56)	ES (N=18)	BE (N=58)	NL (N=25)	IT (N=31)	ES (N=6)	BE (N=62)	NL (N=42)	IT (N=91)	ES (N=37)
	N(%)[§]				N(%)[§]				N(%)[§]				N(%)[§]			
Patients wishes	38 (22)	3 (8)	31 (11)	2 (3)	20 (35)	13 (59)	4 (7)	1 (6)	15 (26)	4 (16)	2 (7)	0 (0)	37 (60)	20 (48)	24 (26)	4 (11)
p-value[+]	0.004				p<0.001				0.248				p<0.001			
Family wishes	31 (18)	2 (6)	43 (15)	5 (7)	16 (28)	8 (36)	21 (38)	4 (22)	16 (28)	6 (24)	2 (7)	1 (17)	16 (26)	6 (14)	16 (18)	0 (0)
p-value[+]	0.143				0.160				0.245				0.377			
Patients wishes only	19 (11)	3 (8)	22 (8)	1 (1)	10 (18)	8 (36)	1 (2)	1 (6)	5 (9)	3 (12)	2 (7)	0 (0)	23 (37)	16 (38)	17 (19)	4 (11)
p-value[+]	0.754				0.005				0.777				0.015			
Family wishes only	12 (7)	2 (6)	34 (12)	4 (6)	6 (11)	3 (14)	18 (32)	4 (22)	6 (10)	5 (20)	2 (7)	1 (17)	2 (3)	2 (5)	9 (10)	0 (0)
p-value[+]	0.395				0.025				0.524				0.622			
Both patients and family wishes	19 (11)	0 (0)	9 (3)	1 (1)	10 (18)	5 (23)	3 (5)	0 (0)	10 (17)	1 (4)	0 (0)	0 (0)	14 (23)	4 (10)	7 (8)	0 (0)
p-value[+]	0.047				0.267				0.535				0.057			

*only transitions between care settings that occurred 10% or more in at least one of the countries in Table 2 were included here

[+] percentages are column percentages; binary logistic regressions on cross-country differences on reasons for transitions with respect to various final transitions (controlling for age, sex and types of malignancy)

[‡] Multiple responses allowed.

[§] Column percentages do not add up to 100 due to rounding off.

Discussion

Our results showed that in all four countries, more than half of the deceased cancer patients had at least one transition between care settings in their final three months of life. Four main types of transitions were identified in this population and the most prevalent types were from home to hospital and from hospital to home. Wishes from patients or families were only indicated for less than half of patients in most countries. From 25 to 55% of patients and families asked for a transition to a hospital from home in the final months of life. Among the wishes, countries differed on the prevalence of patient and family wishes.

Strengths and weaknesses

Family physicians in Europe have an important role of overall care for patients so they could provide valid data about terminal cancer care. Furthermore, the weekly reporting helps minimise recall biases. However, there are also a few limitations of the study. No information was collected on how GPs discussed the final transition or the patients/ families' attitudes about the quality of care associated with each place of care. The content of the care, i.e. interventions to prolong life was not available. And GPs' retrospective perception on the wishes could involve recall bias. Nevertheless, the participating GPs in the networks are also representative in terms of age, gender and geographical distribution of GPs in the four countries. In terms of representation at the patients' level, the non-sudden deaths in Belgium and the Netherlands were comparable to previous death certificate studies on end-of-life decisions. Data in Italy and Spain was compared with the total death rates in the country.[20]

Types of final transition to place of death

Many research studied the place of death of cancer patients[9,11,14], but few inform us where patients were staying prior to death. Our results showed that among patients who had at least one final transition, except in the Netherlands, almost half of them were residing at home and were transited to hospitals and died there. And for patients who died in PCU or hospices, they often resided at home or hospitals (to a lesser extent in Italy and Spain) prior to the final transfer. The proportions of home deaths from hospitals were highest in the Netherlands, followed by Spain, Italy and

Belgium. It seems that the four countries had a similar pattern on the final transition between care settings, patients moving from home to hospitals might reflect the care needs at the end of life, and patients leaving hospitals for home might be fulfilling a home death wish.

Final transitions

The number of transitions of terminally ill cancer patients varied across the four countries. The proportion of zero transitions was the highest in the Netherlands, followed by Spain, Italy and Belgium. While most patients had one transition, almost one in four patients had two transitions and one-tenth had three or more transitions. Studies[18,22] showed that care capacity of the setting, acute medical situations, respiratory problems and digestive problems were common reasons for cancer patients to be hospitalised. Therefore, some of the transitions might have been appropriate[19]to address the care needs of the patients and their families.

Wishes for final transitions

One interesting finding is the cross-national variations of wishes from patients or families on final transitions. Among patients experiencing a final transition in the final three months of life, the majority did not have a recorded wish from patients and/ or families. Nonetheless, it does not mean that patients or families did not have a wish, but that their GPs were not informed about the preference. The current literature emphasise the importance of communication at the end of life[23-24] and it might help understand results from our study.

Patient wishes were more frequently known by GPs in Belgium and the Netherlands while family wishes were more often known in Italy and Spain. These results are consistent with existing research showing that more patients were involved in end-of-life decisions in Belgium and the Netherlands (emphasis on patients' autonomy and early discussion of patient's end-of-life preferences),[25-27]whereas in southern Europe, families might play a more dominant role in decision-making.[28] The proportion of 'both patients and family wishes' is the lowest in Spain, followed by Italy, the Netherlands and highest in Belgium. A related thought might be the concept of shared decision-making in the four countries. Share decision-making had been said to be useful in end-of-life care communication where medical professionals, patients and families could give a voice in these decisions[29], but sometimes the two preferences might be in disagreements.[30] These results encourage practitioners in cancer end-of-life care to understand better the interaction between patients' autonomy, the role of families and healthcare professionals in decision-making.

Wishes and types of transitions

Another important observation is the types of final transitions between care settings requested by patients. From one tenth to almost two-thirds of patients in the four countries had a wish to be transferred from hospital to home and eventually died there, which is in accordance to the common view that patients wish to die at home.[31]However, except Spain, on average about one tenth of patients had a known wish to be transferred from home to hospital and died there. In addition, quite a few patients in Belgium and the Netherlands wished for a transfer from home/hospital to PCU/hospice in their final months of life. To understand these results fully, we would need to understand why these patients wished to be transferred to hospitals, for example, did patients and families know that someone was dying and the transfer would end up with a hospital death? Or was it because patients and families believe hospitals are places with the best type of care?

Conclusion

"Hospital deaths from home" is the most prevalent type of transition between care setting in three out of four countries studied. However, among the major types of final transition, wishes from patients or families were often not known by GPs for the final transitions between care settings. When wishes were known by GPs, only a minority involved patients or family wishes. Future research need to understand the reasons for patients and families' wishes for a hospital transfer.

Reference

1. Globocan 2012: Estimated Cancer Incidence, Mortality and Prevalence Worldwide in 2012. International Agency for Research on Cancer, World Health Organization. http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx (accessed 2nd June 2014)

2. Global Health: Advancing the Global Fight Against Cancer. American Cancer Society. http://www.cancer.org/aboutus/globalhealth/ (accessed 2nd June 2014)

3. Sullivan R, Peppercorn J, Sikora K, Zalcberg J, et al. Delivering affordable cancer care in high-income countries. Lancet Oncol 2011; 12(10): 88-109.

4. Yabroff KR, Warren JL and Brown ML. Costs of cancer care in the USA: a descriptive review. Nat ClinPractOncol 2011; 12(10): 933-980.

5. Riley GF and Lubitz JD. Long-term trends in Medicare payments in the last year of life. Health Serv Re 2010; 45(2): 565-576.

6. Luengo-Fernandez R, Leal J, Gray A and Sullivan R. Economic burden of cancer across the European Union: a population-based cost analysis. Lancet Oncol 2013; 14(12): 1165-1174.

7. Langton JM, Blanch B, Drew AN, Haas M, Ingham JM and Pearson SA. Retrospective studies of end-of-life resources utilizations and costs in cancer care using health administrative data: A systematic review. Palliat Med 2014 May 27. pii: 0269216314533813. [Epub ahead of print]

8. Perrels AJ, Fleming J, Zhao J, et al. Place of death and end-of-life transitions experienced by very old people with differing cognitive status: Retrospective analysis of a prospective population-based cohort aged 85 and over. Palliat Med 2014; 28(3): 220-233.

9. Van den Block L, Deschepper R, Bilsen J, Van Casteren V, Deliens L. Transitions Between Care Settings at the End of Life in Belgium. JAMA 2007; 298(14): 1635-1639.

10. Hinton J. Can home care maintain an acceptable quality of life for patients with terminal cancer and their relatives? Palliat Med 1994. 8(3): 183-196.

11. Teno JM, Gozalo PL, Bynum JPW, et al. Change in End-of-Life Care for Medicare Beneficiaries. Site of Death, Place of Care, and Health Care Transitions in 2000, 2005, and 2009.JAMA 2013; 309(5): 470-477.

12. Burge FI, Lawson B, Critchley P and Maxwell D. Transitions in care during the end of life: changes experienced following enrolment in a comprehensive palliative care program. BMC Palliat Care 2005; 4:3.

13. Gonzalo P, Teno JM, Mitchell SL, et al. End-of-Life Transitions among Nursing Home Residents with Cognitive Issues. N Engl J Med 2011; 365: 1212-1221.

14. Higginson IJ, Sen-Gupta GJA. Place of Care in Advanced Cancer: A Qualitative Systematic Literature Review of Patient Preferences. J Pall Med 2000; 3(3): 287-300.

15. Setoguchi S, Earle CC, Glynn R, et al. Comparison of prospective and retrospective indicators of the quality of end-of-life cancer care. J ClinOncol 2008; 26(35): 5671-5678.

16. De Roo ML, Leemans K, Claessen SJ, et al. Quality indicators for palliative care: update of a systematic review. J Pain Symptom Manage 2013; 46(4): 556-572.

17. Earle CC, Nevilles BA, Landrum MB, et al. Trends in the aggressiveness of cancer care near the end of life. J ClinOncol 2004; 22(2): 315-321.

18. Reyniers T, Houttekier D, Cohen J, Pasman HR, Deliens L. What justifies a hospital admission at the end of life? A focus group study on perspectives of family physicians and nurses. Palliat Med 2014. doi:10.1177/0269216314522317

19. Gott M. Avoidable for whom? Hospital use at the end of life. Palliat Med 2014; 28: 917.

20. Van den Block L, Onwuteaka-Philipsen B, Meeussen K, et al. Nationwide continuous monitoring of end-of-life care via representative networks of general practitioners in Europe. BMC FamPract 2013,14:73.

21. Murray S, Boyd K. Using the ‘surprise question’ can identify people with advanced heart failure and COPD who would benefit from a palliative care approach. Palliat Med 2011, 25(4): 382.

22. De Korte-Verhoef K, Pasman HR, Schweitzer BPM, et al. Reasons for hospitalisation at the end of life: differences between cancer and non cancer patients. Support Care Cancer 2014; 22(3): 645-652.

23. Tulsky JA. Beyond advance directives: importance of communication skills at the end of life. JAMA 2005; 294(3): 359-365.

24. Back AL, Anderson WG, Bunch L, Marr LA, Wallace JA, Yang HB and Arnold RM. Communication about cancer near the end of life. Cancer 2008; 113(7 Suppl): 1897-1910.

25. Ontwuteaka-Philipsen BD, van der Heide A, Koper D et al. Euthanasia and other end-of-life decisions in the Netherlands in 1990, 1995, and 2001. Lancet 2003; 362(9381): 393-399.

26. Donker GA, Slotman FG, Spreeuwenberg P, Francke AL. Palliative sedation in Dutch general practice from 2005 to 2011: a dynamic cohort study of trends and reasons. Br J Gen Pract 2013;DOI: 10.3399/bjgp13X673676.

27. van der Heide A, Deliens L, Faisst K, et al. End-of-life decision-making in six European countries: descriptive study. Lancet 2003; 362(9381): 345-350.

28. Gysels M, Evans N, Menaca A, et al. Culture and end of life care: a scoping exercise in seven European countries. PLoS One 2012; 7(4): e34188.

29. Charles C, Gafni A and Whelan T. Shared decision-making in the medical encounter: what does it mean? (Or it takes at least two to tango). SocSci Med 1997; 44(5): 681-692.

30. Hwang IC, Keam B, Kim YA and Yun YH; Factors Related to the Differential Preference for Cardiopulmonary Resuscitation Between Patients With Terminal Cancer and That of Their Respective Family Caregivers. Am J HospPalliat Care 2014. doi: 10.1177/1049909114546546

31. Gomes, B. and Higginson, I.J., ‘Home or hospital? Choices at the end of life’, J R Soc Med 2004;97(9): 413-414.

Part II Preferences of place of death of cancer patients according to GPs

Chapter 4 **Awareness of General Practitioners concerning cancer patients' preferences for place of death: evidence from four European countries**

Eur J Cancer 2013. 49(8): 1967-1974.

The secret of getting ahead is getting started
---Mark Twain

Title: Awareness of General Practitioners concerning cancer patients' preferences for place of death: evidence from four European countries

Winne Ko, MA[1], Monica Beccaro, MA[1], Guido Miccinesi, MD[2], Viviane Van Casteren, MD[3],Gé A. Donker, MD, PhD[4], Bregje Onwuteaka-Philipsen, PhD[5], María Teresa Miralles Espí, RN [6], Luc Deliens, PhD[5,7], Massimo Costantini, MD [1], Lieve Van den Block, PhD[7]on behalf of EURO IMPACT

1 Regional Palliative Care Network, IRCCS AOU San Martino - IST, Genoa, Italy
2Clinical and Descriptive Epidemiology Unit, Cancer Prevention and Research Institute, ISPO, Florence, Italy
3 Public Health and Surveillance, Scientific Institute of Public Health, Brussels, Belgium
4 NIVEL, Netherlands Institute for Health Services Research, Utrecht, the Netherlands
5 EMGO Institute for Health and Care Research, Department of Public and Occupational Health, and Palliative Care Expertise Centre, VU University Medical Centre, Amsterdam, the Netherlands
6 DireciónGral. de Investigación y SaludPublica., Conselleria de Sanitat. Generalitat C. Valenciana, Spain
7 End-of-Life Care Research Group (L.V.d.B., L.D.), Ghent University &Vrije Universiteit Brussel, Brussels, Belgium

Acknowledgements

On behalf of EURO IMPACT

Van den Block Lieve, Meeussen Koen, Brearley Sarah, Caraceni Augusto, Cohen Joachim, Costantini Massimo, FranckeAnneke, Harding Richard, Higginson Irene, Kaasa Stein, Linden Karen, Miccinesi Guido, Onwuteaka-Philipsen Bregje, Pardon Koen, PasmanRoeline, Pautex Sophie, Payne Sheila, Deliens Luc

Funding

EURO IMPACT, **Euro**pean **I**ntersectorial and **M**ultidisciplinary **Pa**lliative **C**are Research **T**raining, is funded by the European Union Seventh Framework Programme (FP7/2007-2013, under grant agreement n° [264697]). EURO IMPACT aims to develop a multidisciplinary, multi-professional and inter-sectorial educational and research training framework for palliative care research in Europe. EURO IMPACT is coordinated by Prof Luc Deliens and Prof Lieve Van den Block

of the End-of-Life Care Research Group, Ghent University &Vrije Universiteit Brussel, Brussels, Belgium. Other partners are: VU University Medical Center, EMGO Institute for health and care research, Amsterdam, the Netherlands; King’s College London, Cicely Saunders Institute, London, Cicely Saunders International, Londen, and International Observatory on End-of-Life Care, Lancaster University, Lancaster, United Kingdom; Norwegian University of Science and Technology, and EAPC Research Network, Trondheim, Norway; Regional Palliative Care Network, IRCCS AOU San Martino-IST, Genoa, and Cancer Research and Prevention Institute, Florence, Italy; EUGMS European Union Geriatric Medicine Society, Geneva, Switzerland; Springer Science and Business Media, Houten, the Netherlands.

Abstract

(1) Background

General practitioners (GPs) are at the first level of contact in many European healthcare systems and they supposedly have a role in supporting cancer patients in achieving their desired place of death. A four-country (Belgium, the Netherlands, Italy and Spain) study was carried out exploring current practices.

(2) Patients and Methods

EURO SENTI-MELC adopted a retrospective study design and data for this study were collected in 2010 through representative GPs networks in four countries. In the current study all non-sudden cancer deaths were included with weekly GP registrations.

(3) Results

The main study sample included 930 deceased cancer patients: preference for place of death was known by GPs for only 377. GP awareness on the preferred place of death varied across countries, 27 % in Italy, 36 % in Spain, 45 % in Belgium and 72 % in the Netherlands ($p<0.01$). The general level of preferences met was high, from 68 % (Italy) to 92 % (Spain).

(4) Conclusions

Despite the importance of being able to die in a preferred location, GPs were often unaware about patient preferences, especially in Italy and Spain. If GPs were informed, the preference was often met in all countries, indicating room for improvement in end of life care.

Keywords (maximum 6)

Place of death, general practitioners, sentinel network, preference met, advanced cancer patients, palliative care

Introduction

Cancer is a leading cause of death in Europe with standardised statistics demonstrating more than 169 deaths per 100,000 inhabitants annually died from malignancies.[1] Therefore, offering quality cancer care is crucial and palliative care is one element. Achieving patients' preference is a marker in assessing quality of care[2] and place of death deserves attention because it gives patients and their families a sense of control and thus improving the quality of death.[2] Meeting patients' preferences of place of death enhances the quality of cancer care in addition to other goals such as symptom control and spending time with family at the end of life.[3]

Existing literature shows that from 44% to 90% of individuals (both cancer patients and healthy population) worldwide desire to die at home [4-7] while these wishes often remain unfulfilled. Hospital deaths account for 35% to 65% cancer deaths in the UK and 45% in the Netherlands. [8-10] Information on how well this preference is met (congruence between actual and preferred place of death) is less known. One Italian survey reports an overall 67% of sampled patients died in their preferred place of death[11] whereas the proportion drops to just over 50% in an Irish study.[12] A recent study shows an increase of home deaths in Britain, from 18% in 2004 to 21% in 2010, the rise is more pronounced among cancer patients.[13] This might be related to the introduction of the End of Life Care Strategy in 2008,[14] which includes place of death as a quality indicator, demonstrating the potential benefits of integrating palliative care into public health.[15]

This study uses GPs as proxies for information. Though precise statistics on GPs' coverage are not available, previous studies highlight their role in improving palliative care services.[10,16-17] Abarshi shows that four-fifths of patients had their preference met when Dutch GPs knew them[10] while Meeussenet al. show that only 46% of Belgian GPs knew the preferred place of death of their cancer patients,[17] indicating room for improvements.

An international study on preference met with regard to GPs' involvement in end of life care for cancer patients would add to the knowledge on improving GP-patient communications.

---

[1] Details on standardised cancer mortality rate (per 100,000 inhabitants) in the four countries studied in 2009: Belgium 144.6 (2008), Netherlands 186.7, Italy 166.5,Spain 157.7.
(https://www.wiv-isp.be/Pages/EN-Home.aspx) (last accessed 7th Nov 2012)
(http://epp.eurostat.ec.europa.eu/portal/page/portal/statistics/search_database) (last accessed 6th Nov 2012)

The study aims of this article are:

1) to report GPs' awareness of preferred place of death of a sample of deceased cancer patients in four European countries(Belgium, the Netherlands, Italy and Spain)

2) to estimate the distribution of actual and preferred place of death from a sample of deceased cancer patients in the four countries and

3) to describe preference met in the sampled cancer patients

Methods

The EURO-SENTI MELC Study

The European Sentinel Network of the General Practitioners (GPs) to Monitor End-of-Life Care (EURO SENTI-MELC) is a large scale epidemiological descriptive study conducted in four European countries in 2009-2010 based on continuous full-year registration of all patients who died in the participating GP sentinel networks.The study started in Belgium in 2004 and expanded to the Netherlands in 2005 and has continued since then.

Observational unit

General practices are the observational units. The GP network covers 1.8% and 0.8% of the Belgian and Dutch national patient populations respectively.[18-19] The Spanish Sentinel Network has existed for more than 15 years[20] and engaged in end-of-life care study since 2010, representing 3.8% of the patient population in Castilla and León(northwest) and 3% in Valencia(east). Italian data are available from 2009 with a new GP network constituted for this study.[21] Data were collected from nine out of 146 health districts and cover about 4% of the patient population.

Study Population

All deceased aged 18 or above who were part of a GP's practice were included. Since this study examines the care delivered at the end of life (i.e. those theoretically receiving palliative care as their GPs identified them as terminally ill), all deaths occurred 'suddenly and totally unexpectedly' were excluded.[18]

Retrospective data collection

GPs reported place of death and circumstances of end-of-life care of deceased cancer patients weekly on a standardised questionnaire. They first identified the 'place of death of patient', and secondly indicated, 'Were you informed (verbally or in writing) of the patient's preference regarding place of death?': where the answer is **YES**, the GP would be asked **where did this patient prefer to die**. For both questions, five options were given, ***at***

home or living with family, in a care home(Belgium and Italy)/elderly home(Netherlands and Spain), in hospital, palliative care unit/hospice or elsewhere(namely). Dutch nursing home deaths were excluded since these patients were cared for by nursing home physicians once transferred.[22] Further information on the selection procedures of GPs Sentinel Networks in Belgium and the Netherlands has been published.[18,23]

Ethical approval

The protocol of the study was approved by the Ethical Review Board of Brussels University Hospital of the Vrije Universiteit Brussel and the local ethical committee in Grosseto, Italy. No specific ethical approvals were needed in the Netherlands or Spain because of the retrospective anonymous data collection.

Analyses

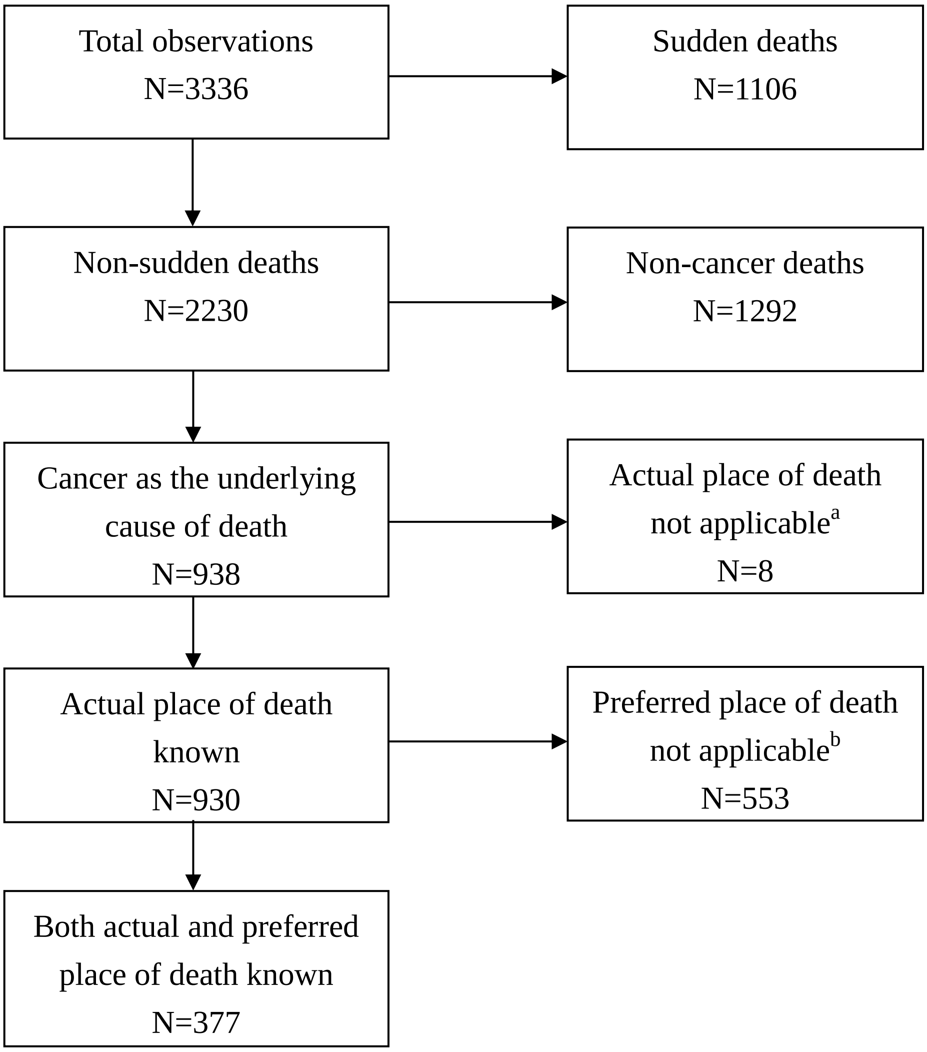
This is a cross-sectional study. Heterogeneity tests were conducted on cross-country differences (controlling for the types of malignancy) and *p*-values are shown. Numbers and proportions are reported on the variables: age, gender, cause of death and place of death. Analyses were completed using PASW Statistics 18, Release Version 18.0.0 (SPSS, Inc., 2009, Chicago, IL). The variable **preference met** was constructed based on information of actual and preferred place of death and a multivariate analysis (adjusting for age, gender and types of malignancy) was done to assess cross-country differences. Binomial proportion confidence intervals were estimated for preference met with MedCalc, Release Version 12.2.1. (MedCalc Software, 2012, Mariakerke, Belgium) Patients whose preferred place of death was unknown were excluded in this part of the analysis.

Results

Selection of sample (Figure 1)

A total of 3,336 deaths were reported from the four countries with 938 ‘non-sudden’ cancer deaths. Preference met on place of death was analysed for 377 patients whose ‘preferred’ and ‘actual’ place of death were known.

Figure 1: Overview of the obtained study sample



[a] nursing home deaths from the Netherlands

[b] preferred place of death not known by GPs or being nursing home in the Netherlands

Patient Characteristics

There was no difference between cancer patients in terms of age but more male patients were included. (Table 1).One fourth of patients aged between 18-64(except in Italy), 60% of patients aged between 65-85; the very old (aged 85 or above) comprised another 15%. Forty percent of cancer patients had malignancies other than the four main sites (lung, breast, colorectal and prostate).

Table 1: Cancer Patients' Characteristics (N=930)

	Belgium (N=292) N (%)	The Netherlands (N=181) N (%)	Italy (N=308) N (%)	Spain (N=149) N (%)	*p*-value[a]
Gender[b]					
Male	154(53)	106(59)	157(51)	98(66)	
Female	138(47)	73(41)	151(49)	51(34)	0.013
Age at death, years[c]					
18-64	71 (25)	47(26)	67(22)	35(24)	
65-85	171(59)	108(60)	185(60)	88(59)	
86 or above	47(16)	26(14)	56(18)	26(17)	0.912
Types of Malignancy[d]					
Lung	72(25)	46 (28)	74(28)	32(22)	
Breast	29(9.9)	8 (4.8)	16(6.1)	6(4.1)	
Colorectal	36(12)	28 (17)	37(14)	32(22)	
Prostate	15(5.1)	13 (7.8)	8(3.1)	13(9.0)	
Others[e]	140(48)	75(45)	127(49)	62(43)	0.024

[a] chi-square test used

[b] not answered:2 in the Netherlands

[c] missing: 3 in Belgium

[d] not answered: 15 in the Netherlands, 46 in Italy and 4 in Spain

[e] for others, the site of tumour is noted qualitatively and beyond the four main categories

NOTE: percentages may not add up to 100 due to round off

Actual Place of Death

Home was the most common place of death among 930 patients in all countries (Table 2). More than half of Dutch (61%) and Spanish (53%) died at home while only 35 % of Belgian and 45 % of Italian patients did so. Except in the Netherlands, more than one third of patients died in hospitals in all countries. Care home or hospice deaths were higher in the Netherlands and Belgium (23-31% in total)than in the other two countries (13-17% in total).

Table 2: Actual place of death of Cancer Patients (N=930)

	Belgium (N=292) N (%)	The Netherlands (N=181) N (%)	Italy (N=308) N (%)	Spain (N=149) N (%)	*p*-value[a]
ACTUAL PLACE OF DEATH					
Home	102 (35)	110 (61)	137 (45)	78 (53)	
Care home[a]	33 (11)	14 (7.7)	17 (5.5)	8 (5.4)	
Hospital	98 (34)	30 (17)	118 (38)	49 (33)	
Palliative care unit / Hospice	57 (20)	27 (15)	36 (12)	12 (8.2)	
TOTAL[b]	290 (100)	181(100)	308 (100)	147 (100)	<0.01

[a] Care home in Netherlands and Spain is residential home for elderly

[b] Not answered: 2 in Belgium and 1 in Spain; 1 indicated as elsewhere in Spain

[c] test for heterogeneity used, controlling for the five categories of malignancies (lung, breast, colorectal, prostate and others)

NOTE: percentages may not add up to 100 due to round off

GP awareness of preferred place of death

Cross-national differences were observed on GPs' awareness of their patients' preferred place of death (41 % in the four countries together, Table 3). Dutch physicians were the most informed (72%) and Italians the least (27%). When asked about the informants about preferred place of death, Belgian and Dutch GPs were mainly informed by patients (63 and 72%) whereas family members were the informants (53% and 54%) in Italy and Spain. Furthermore, one in five GPs in Belgium and the Netherlands were informed by both the patient and a family member compared to 6% in Italy and 13% in Spain.

There was a high percentage of 'unknown' preferences, hinting a lack of GPs' awareness. Only 389 (42%) of patients' preferences on place of death were documented. For known preferences, most were for dying at home, marked by the strong preference in Italy and Spain, wherenearly9 out of 10 cancer patients preferred home deaths. Almost 70% of cancer patients in Belgium and the Netherlands had the same preference. 20% of Belgian patients opted for a care home/palliative care unit and a palliative care unit was the second most (12%) preferred place of death in the Netherlands. There was no prominent second preferred place of death in Italy and Spain.

Table 3: GPs' awareness and preferred place of death of cancer patients

Characteristics	Belgium N(%)	Netherlands N(%)	Italy N(%)	Spain N(%)	*p*-value[f]
Whether GPs are informed about patients' preferred place of death[a] (N=930)	(N=292)	(N=181)	(N=308)	(N=149)	
Informed	130 (45)	129 (72)	83(27)	47 (36)	
Not informed	162 (56)	50(28)	225 (73)	84 (64)	<0.01
GPs informed by [b,c] (N=389)	(N=130)	(N=129)	(N=83)	(N=47)	
Patient himself/herself only	80 (63)	91(72)	33(40)	15 (32)	<0.01
A family member only	22 (17)	8(6.3)	45(54)	25 (53)	<0.01
Both	26 (20)	26(21)	5(6.0)	6(13)	0.057
Others	--(--)	1(0.0)	--(--)	1(2.1)	0.202
Preferred place of death of patients[d] (N=389)	(N=130)	(N=129)	(N=83)	(N=47)	
Home	92 (71)	100 (78)	73 (90)	35 (90)	
Care home[e]	14 (11)	12 (9.4)	1 (1.2)	2 (5.1)	
Hospital	6(4.7)	1 (0.8)	5 (6.2)	1 (2.6)	
Palliative care unit / Hospice	17 (13)	15 (12)	2 (2.5)	1 (2.6)	<0.01

[a] not answered: 2 in Belgium and 18 in Spain

[b] multiple answers possible

[c] Not specified: 2 in Belgium and 3 in the Netherlands

[d] Not applicable: 1 in Belgium, 1 in the Netherlands, 2 in Italy and 7 in Spain; 1 Spanish GP reported 'elsewhere' for preferred place of death

[e] Care home in Netherlands and Spain is residential home for elderly

[f] Test for heterogeneity used, controlling for the five categories of malignancies (lung, breast, colorectal, prostate and others)NOTE: percentages may not add up to 100 due to round off

Preference met between actual and preferred place of death (Table 4)

Spain and the Netherlands had the highest level of overall preference met (92% and 91% respectively), followed by Belgium (81%) and Italy(68%). Results from a multivariate analysis ($p<0.05$) confirmed this: Netherlands (OR: 5.7 [2.43-13.54]) and Spain (OR: 5.7[1.56-20.55]), with Italy as reference category (not shown in table).

One third of Italian patients (N=23, 32%) preferring home deaths died in hospitals.

Reviewing deaths in palliative care units (PCU) or hospices, Dutch patients (N=14, 93%) had a higher proportion of preference met than Belgian patients (N=13, 77%). There was complete preference met for Italian and Spanish patients in care home and PCU/Hospice, though the number was small.

Comparison of actual place of death with regard to GP awareness of preferences

We also found group differences when patients were dichotomised by GPs' awareness of the preference were found except in Italy (Table 5). In all countries, between40% to53% patients died in hospitals when their preferred place of death was unknown. Home deaths decreased substantially when GPs did not know the preferred place of death, reductions ranged from 11% in Italy to 42% in the Netherlands.

Table 4: Preference met of place of death for deceased cancer patients in four European countries (N=377)

Preferred place of death	**Actual Place of death**				Total	Preference met N(%; 95% CI)[c]
	Home N(%)	Care home[a] N(%)	Hospital N(%)	PCU[b] /Hospice N(%)	N(%)	
Belgium(N=129)						
Home	74(80)	1 (1.1)	6 (6.5)	11(12)	92(100)	105/129 (81% ; 73.6-87.7)
Care Home	--(--)	14(100)	--(--)	--(--)	14(100)	
Hospital	--(--)	--(--)	4(67)	2(33)	6(100)	
PCU / Hospice	--(--)	--(--)	4(24)	13(77)	17(100)	
The Netherlands (N=128)						
Home	92(92)	--(--)	3(3.0)	5(5.0)	100(100)	117/128(91%; 85.1-95.6)
Care Home[a]	2(15)	10(77)	--(--)	--(--)	12(100)	
Hospital	--(--)	--(--)	1(100)	--(--)	1(100)	
PCU / Hospice	--(--)	--(--)	1(6.7)	14(93)	15(100)	
Italy(N=81)						
Home	47(64)	1(1.4)	23(32)	2(2.7)	73(100)	55/81(68%; 56.6-77.8)
Care home	--(--)	1 (100)	--(--)	--(--)	1(100)	
Hospital	--(--)	--(--)	5(100)	--(--)	5(100)	
PCU / Hospice	--(--)	--(--)	--(--)	2(100)	2(100)	
Spain(N=39)						
Home	32(91)	--(--)	3(8.6)	--(--)	35(100)	36/39(92%; 79.1-98.4)
Care home[a]	--(--)	2(100)	--(--)	--(--)	2(100)	
Hospital	--(--)	--(--)	1(100)	--(--)	1(100)	
PCU / Hospice	--(--)	--(--)	--(--)	1(100)	1(100)	

[a] Care home in Netherlands and Spain is residential home for elderly

[b] PCU refers to Palliative Care Unit

[c] Binomial proportion confidence interval estimated

NOTE: percentages may not add up to 100 due to round off

Table 5: Actual place of death of cancer patients whose preferred place of death is known (N=377) versus unknown (N=553) by GPs

	Belgium		The Netherlands		Italy		Spain	
	Known (N=130) %	Unknown (N=162)[b] %	Known (N=129) %	Unknown (N=52) %	Known (N=83) %	Unknown (N=225) %	Known (N=47) %	Unknown (N=102)[b] %
Home	58	17	73	31	57	40	81	43
Care home[a]	12	11	7.8	7.7	4.8	5.8	8.5	4.0
Hospital	11	53	3.9	48	34	40	8.5	45
Palliative care unit / Hospice	20	19	16	14	4.8	14	2.1	11
p-value[c]	$p<0.01$		$p<0.01$		$p=0.01$		$p<0.01$	

[a] Care home in Netherlands and Spain is residential home for elderly

[b] Not answered: 2 in Belgium and 1 in Spain, 1 Spanish patient died elsewhere

[c] Test for heterogeneity used, controlling for the five categories of malignancies (lung, breast, colorectal, prostate and others)

NOTE: percentages may not add up to 100 due to round off

Discussions

This is the first cross-European study to measure preference met on place of death for cancer patients from a general practice population. For actual place of death, home deaths varied from one-third in Belgium to over 60% in the Netherlands. 70% to 90% of GPs reported home as the preferred location of their cancer patients. The proportion of preference met was high (over 80%), except in Italy. Both results are supported by existing literature.[6,10-11,17]

One finding is the large cross-country difference in GPs' awareness. Only one third of Italian and Spanish GPs knew the preferred place of death of cancer patients compared to more than two-thirds of Dutch GPs. There were more hospital deaths and fewer home deaths when GPs lacked the information. The differences amounted to over 40% in Belgium and the Netherlands, and more than 35% for Spain. Understanding the causes of these variations is vital for effective interventions. Possible explanations for GPs not knowing the preference include sudden deterioration of a patient's physical state[24-26] and patients remaining silent on their preference due to worries about burdening caregivers.[9] Unequal access to healthcare resources also implies patients from a lower socioeconomic class would die in hospitals.[9,27-28] Data from the World Health Organisation (WHO) and others demonstrate a slightly higher overall cancer mortality rate (with lung, breast, prostate and colorectal combined) in the Netherlands (16 %) than in Belgium(13 %), Italy(12 %) and Spain(13 %), and larger cross-country mortality differences on specific cancer types, e.g. lung(5.7% IT to 7.6%NL), breast(1.7%ES to 2.3%BE), colorectal(3.2%IT to 3.8% NL) and prostate(1.3%IT to 1.9%NL).[29-30] However, these differences in cancer death burden do not seem large enough to explain the observed differences in GPs' awareness of patient preferences and the multivariate analyses controlling for different frequencies in cancer type confirms this. Hence, differences might be more related to GP training and culture than to cancer death burden.

Training effective communications in these sensitive issues may enhance a favourable outcome as discussing end-of-life care is perceived as challenging.[31] For instance, the proportion of Dutch GPs' awareness of preferred place of death increased from 54% in 2005/06 to 72% 2009/2010, the change could be due to increased discussions.[32] Moreover, evidence shows preferences are more stable than we assume,[33] encouraging healthcare professionals not only to elicit that preference regularly, but also consider the available social and healthcare support.

On the other hand, the different source of informant might be a sign of cultural differences. The response for both patient and family was around 20% in the Netherlands and Belgium, the figure was lower in Spain (13%) and Italy (6%). Spanish and Italian GPs often learned about the preference from family members, opening up a speculation about cultural differences in communicating end-of-life issues. [34-36]

However, the questionnaire only captured a categorical preference from proxies, and knowing the ‘strength’ of that preference could help delineate the weight of place of death in comparisons with other goals of care.[1] One should remember that some patients do not have a preference on place of death or regard it as unimportant.

Strengths and limitations

This is a European-wide study on preference met on place of death among cancer patients, using GPs as proxies. The same methodology was applied in four countries, allowing comparisons across territories. The choice of countries, Belgium, the Netherlands, Italy and Spain reflects the diversity of healthcare systems and cultures. Furthermore, efforts have been made to achieve the best representativeness possible and GPs reported weekly to minimise recall bias.

Nevertheless there are limitations with employing GPs as proxies. The reported preference was based on GPs’ own observation which could be affected by their concept of ‘good death’. One possible bias is that the sampled patients maintained more contact with their GPs and thus making their preference better known than patients who had less contact with GPs.

Another weakness is that GPs did not know all the details and preferences of their patients. For instance, Dutch GPs were not the primary care providers for nursing home residents,[22] and many Italian GPs were not informed about a preferred place of death.

Though GP practice is highly accessible in the countries surveyed, we risked excluding patients outside the practice who might be socially deprived and could benefit from the care. These all imply further caution in interpreting the results.

Last but not least, the prompt question of ‘non-sudden death’ was used as a criterion in identifying the theoretical sample of palliative care group which means preferences of palliative care patients who died suddenly were unavoidably omitted.

Conclusion

It has been repeatedly reported that patients wish to die at home.[4-7] The article describes the current situation and explores conditions related to the preferred place of death in four European countries. Except in the Netherlands, the majority of GPs surveyed were not aware of the preferred place of death of patients and where this was the case, patients usually died in hospitals. Nonetheless, by offering training to GPs on end-of-life care communication, better arrangements can be made to enable people dying in their chosen location.

Achieving the desired place of death is a component of quality supportive care for our cancer patients but has also be shown to be contingent upon many other conditions such as family support and physical status in the final days. Further qualitative research would increase our understanding of the complexities of achieving the preference as well as the genuine preference of patients.

Reference

1. Crump, RT, Llewellyn-Thomas, HA. The importance of measuring strength-of-preference scores for health care options in preference-sensitive care, J of Clin Epidemiol 2012; 65(8):887-896.

2. Tang ST and Chen CH. Place of death and end-of-life care. In Cohen J and Deliens L, editors.*A Public Health Perspective on End of Life Care.*New York: Oxford University Press; 2012: p.21-34.

3. Steinhauser, KE, Christakis, NA, Clipp, EC, McNeilly, M, McIntyre, L and Tulsky, JA, Factor Considered Important at the End of Life by Patients, Family, Physicians, and Other Care Providers. Journal of American Medical Association 2000. 284(19): 2476-2482.

4. Fukui S, Yoshiuchi K, Fujita J et al. Japanese People's Preference for Place of End-of-Life Care and Death: A Population-Based Nationwide Survey. J Pain Symptom Manage. 2011; 42(6): 882-892.

5. Gomes B, Higginson IJ, Calanzani N et al.Preferences for place of death if faced with advanced cancer: a population survey in England, Flanders, Germany, Italy, the Netherlands, Portugal and Spain. Annals of Oncology 2012.Published on February 16, 2012.doi: 10.1093/annonc/mdr602

6. Townsend J, Frank AO, Fermont D at al. Terminal cancer care and patients' preference for place of death: a prospective study. BMJ 1990; 301(6749): 415-417.

7. Tang ST. When Death Is Imminent: Where Terminally Ill Patients With Cancer Prefer to Die and Why, Cancer Nurs 2003; 26(3): 245-251.

8. Gomes B, and Higginson IJ.Home or hospital?Choices at the end of life. J R Soc Med. 2004; 97(9): 413-414.

9.Thomas C, Morris S and Gatrell A. *Place of Death in the Morecambe Bay Area: Patterns and preferences for place of final care and death among terminally ill cancer patients and their carers.* Lancaster, United Kingdom: Lancaster University 2003.

10. Abarshi E, Onwuteaka-Philipsen B, Donker G. General practitioner awareness of preferred place of death and correlates of dying in a preferred place: a nationwide mortality follow-back study in the Netherlands. J PainSymptom Manage. 2009; 38(4): 568-577.

11. Beccaro M, Costantini M, Rossi PG et al. Actual and preferred place of death of cancer patients. Results from the Italian survey of the dying of cancer (ISDOC). J Epidemiol Community Health 2006; 60(5): 412-416.

12. Tierman E, Connor MO, Kearney OM and O'Siorain L. A Prospective Study of Preferred Versus Actual Place of Death Among Patients Referred to a Palliative Care Home-care Service. The Ir Med J. 2002; 95(8): 232-235.

13. Gomes B, Calanzani N, Higginson IJ. Reversal of the British trends in place of death: Time series analysis 2004-2010. Palliat Med. 2012; 26(2): 102-107.

14. End of Life Care Strategy-promoting high quality care for all adults at the end of life. Department of Health, United Kingdom 2008

15. Gomez-Bastiste X, Porta-Sales J, Pascual A, et al. Catalonia WHO Palliative Care Demonstration Project at 15 years (2005). J PainSymptom Manage. 2007; 33(5): 584-590.

16. Mitchell GK. How well do general practitioners deliver palliative care? A systematic review.Palliat Med. 2002; 16(6): 457-464.

17. Meeussen K, Van den Block L, Bossuyt N et al. GPs' awareness of patients' preference for place of death. Br J Gen Pract. 2009; 59(566): 665-670.

18. Van den Block L, Van Casteren V, Deschepper R et al. Nationwide monitoring of end-of-life care via the Sentinel Network of General Practitioners in Belgium: the research protocol of the SENTI-MELC study. BMC Palliative Care 2007; 6:6.

19. Meeussen L, Van den Block L, Echteld MA, Boffin N et al. End-of-life care and circumstances of death in patients dying as a result of cancer in Belgium and the Netherlands: a retrospective comparative study. J ClinOncol 2011; 29(32): 4327-4334.

20. Vega Alonso AT, ZurriageLlorens O, GalmesTruyols et al. Redescentinelasanitarias en Espana. Consenso para unaguia de principios y metodos.[Guide to the principles and methods of health sentinel network in Spain] (article in Spanish). Gac Sanit. 2006; Suppl 3: 52-60.

21. Deckers JGM, Paget WJ, Schellevis FG and Fleming DM. European primary care surveillance networks: their structure and operation. FamPract. 2006; 23(2): 151–158.

22. Hoek JF, Ribbe MW, Hertogh CM and van der Vleuten CP. The role of the specialist physician in nursing homes: the Netherlands' experience. Int J GeriatrPsychiatry 2003; 18(3): 244-249.

23. Donker GA. Continuous Morbidity Registration Dutch Sentinel General Practice Network 2010. Annual report. Utrecht, the Netherlands: NIVEL 2011.

24. Hinton J. Services given and help perceived during home care for terminal cancer. Palliat Med 1996; 10(2): 125-134.

25. Tang ST, Huang EW, Liu TW, Rau KM, Hung YN, Wu SC. Propensity for home death among Taiwanese cancer decedents, 2001-2006 determined by services received at end of life. J Pain Symptom Manage 2010; 40(4):566-574.

26. Schweitzer BP, Blankenstein N, Deliens L, van der Horse H. Out-of-hours palliative care provided by GP co-operatives: availability, content and effect of transferred information. BMC Palliat Care 2009; 28(8): 17.

27. Grande, GE, Addington-Hall, JM, Todd, CJ. Place of death and access to home care services: are certain patient groups at a disadvantage? SocSci Med 1998; 47(5):565-579.

28. Gatrell, AC, Harman, JC, Francis, BJ, ThomasC, MorrisSM, and McllllmurrayM.Place of death: analysis of cancer deaths in part of North West England. J Public Health Med 2003; 25(1): 53-58.

29. World Health Organisation European Detailed Mortality Database http://data.euro.who.int/dmdb/caparams.php(last accessed 18th Dec 2012)

30. La Vecchia C, Bosetti C, Lucchini F et al. Cancer mortality in Europe, 2000-2004, and an overview of trend since 1975. Ann Oncol 2010; 21(6): 1323-1360.

31. Slort W, Schweitzer BP, Blankenstein AH et al. Perceived barriers and facilitators for general practitioner-patient communication in palliative care: a systematic review. PalliatMed 2011; 25(6): 613-629.

32. Donker G, Abarshi E. Gewenste plaats van overlijden tijdig bespreken. Huisarts&Wetenschap 2010;53(5):247.

33. Higginson IJ, Hall S, Koffman J, Riley J and Gomes B: Time to get it right: are preferences for place of death more stable than we think? Palliat Med 2010, 24(3): 352-353.

34. Gysels M, Evans N, MeñacaA et al. Culture and end of life care: a scoping exercise in seven European countries. PLoSOne 2012; 7(4): e31488.

35. Van der Heide A, Deliens L, Faisst K et al. End-of-life decision-making in six European countries: descriptive study. Lancet 2003; 362(9381): 345-350.

36. Cherny NI. Controversies in Oncologist-Patient Communication: A Nuanced Approach to Autonomy, Culture, and Paternalism. Oncology(Williston Park) 2012; 26(1): 37-43,46.

Chapter 5 **Factors associated with fulfilling preferences for dying at home among cancer patients: the role of general practitioners**

J Pall Care 2014. 30(3): 141-150.

“Death ends a life, not a relationship”---

Mitch Albom, *Tuesdays with Morrie*

Title: Factors associated with fulfilling preferences for dying at home among cancer patients: the role of general practitioners

Winne Ko, MA[1], Guido Miccinesi, MD[2], Monica Beccaro, MA[3], Sarah Moreels, MA[4], Gé A. Donker, MD, PhD[5],BregjeOnwuteaka-Philipsen, PhD[6], Tomás V. Alonso, MD, PhD[7], Luc Deliens, PhD[1,6], Lieve Van den Block, PhD[1,8] on behalf of EURO IMPACT

1 End-of-Life Care Research Group, Vrije Universiteit Brussel(VUB), Brussels, Belgium and Ghent University
2Clinical and Descriptive Epidemiology Unit, Cancer Prevention and Research Institute, ISPO,Florence, Italy
3 Regional Palliative Care Network, IRCCS AOU San Martino - IST, Genoa, Italy
4 Public Health and Surveillance, Scientific Institute of Public Health, Brussels, Belgium
5 NIVEL, Netherlands Institute for Health Services Research, Utrecht, the Netherlands
6 EMGO Institute for Health and Care Research, Department of Public and Occupational Health, and Palliative Care Expertise Centre, VU University Medical Centre, Amsterdam, the Netherlands
7 Public Health Directorate General, Health Department, Valencia, Spain
8 Department of Family Medicine, Vrije Universiteit Brussel(VUB), Brussels, Belgium

Collaborators EURO IMPACT

Van den Block Lieve, De GrooteZeger, Brearley Sarah, Caraceni Augusto, Cohen Joachim, Costantini Massimo, FranckeAnneke, Harding Richard, Higginson Irene, Kaasa Stein, Linden Karen, Miccinesi Guido, Onwuteaka-Philipsen Bregje, Pardon Koen, PasmanRoeline, Pautex Sophie, Payne Sheila, Deliens Luc

Funding

EURO IMPACT, **Euro**pean **I**ntersectorial and **M**ultidisciplinary **Pa**lliative **C**are Research **T**raining, is funded by the European Union Seventh Framework Programme (FP7/2007-2013, under grant agreement n° [264697]). EURO IMPACT aims to develop a multidisciplinary, multi-professional and inter-sectorial educational and research training framework for palliative care research in Europe. EURO IMPACT is coordinated by Prof Luc Deliens and Prof Lieve Van den Block of the End-of-Life Care Research Group, Ghent University &Vrije Universiteit Brussel, Brussels, Belgium. Other partners are: VU University Medical Center, EMGO Institute for health and care research, Amsterdam, the Netherlands; King’s College London, Cicely Saunders Institute, London, Cicely Saunders International, London, and International Observatory on End-of-Life Care, Lancaster University, Lancaster, United Kingdom; Norwegian University of Science and Technology, and EAPC Research Network, Trondheim, Norway; Regional Palliative Care Network, IRCCS AOU San Martino-IST, Genoa, and Cancer Research and Prevention Institute, Florence, Italy; EUGMS European Union Geriatric Medicine Society, Geneva, Switzerland; Springer Science and Business Media, Houten, the Netherlands.

Abstract

Aim: The study aims to explore clinical and care-related factors associated with fulfilling cancer patients' preferences for home death across countries (Belgium[BE], the Netherlands[NL], Italy[IT] and Spain[ES]).

Methods: A mortality follow-back study was undertaken (2009-2011) via representative networks of general practitioners (GPs). This study included all patients aged 18+ who died from cancer and whose home death preference and place of death were known by the GP. Factors associated with meeting home death preference were tested using multivariable logistic regressions.

Results: Among 2,048 deceased patients, preferred and actual place of death was known in 42.6% of cases. Home death preference met ranged from 65.5%-90.9%. Country-specific factors included older age in BE, decision-making capacity and female in the NL. GPs' provision of palliative care was positively associated with meeting home death preference (ORs: BE: 9.9[95% C.I. 3.7-26.6], NL: 9.7 [2.4-39.9], IT: 2.6[1.2-5.5]) in all countries. (ORs of Spain not shown because a multivariate model was not performed)

Conclusion: Policies facilitating home deaths need to examine available resources for primary end-of-life care.

Introduction

Cancer continues to be a major leading cause of death in Europe with an estimated 1.75 million deaths in 2012.[1-2] During the advanced stage of the disease, multiple complex decisions often have to be made such as shifts in treatment aims and use of palliative care services. In this medical decision-making process, respecting a patient's preferences as much as possible is of great importance and healthcare professionals engage to fulfil those wishes whenever conditions allow.[3]

A recent review confirmed that most people - patients, caregivers and the general public – would choose to die at home and thispreference remains stable for four-fifths of patients.[4] Across countries, these figures ranged from 66.1% in Spain, to 71.6% in Flanders, Belgium, 76.1% in Italy and 83.1% in the Netherlands.[5] However, that wish is often unfulfilled[6] and a population-based study[7] on cancer patients' place of death in the UK showed that hospital remained the most common place of death for many patients. Therefore, meeting cancer patients' home death wishes continues to be a challenge and understanding the factors influencing preference met on home death will provide important information about how clinical practices might be improved.

Most existing studies have been focused on studying place of death and its associated factors, without taking into account people's preferences. These studies highlight the importance of environmental, illness-related and individual factors such as family support, gender and the availability of home care services.[8-16]A number of studies also examined determinants affecting the congruence of place of death, including factors like distance to hospitals and individual preferences.[15-17]However, past studies vary in research design and few provide cross-country perspectives on factors associated with meeting patient preferences or their sample sizes remained small. In addition, these factors appear to interact with one another,[14] complicating interpretations. Original research focusing on the factors related to meeting home preference is essential to disentangle the mechanism behind the reality.

Despite globalisations and progress in benchmarking, healthcare remains a domain heavily laden with country-specific characteristics.[18] It has been argued that localisation is essential for designing healthcare policies, including taking into account culture and existing service infrastructure.[19] Since the majority of cancer patients wish to die at home, a cross-country study on factors associated with meeting such preferences could contribute to knowing what types of intervention would help meeting that preference , thus potentially inform policy-makers about appropriate planning in end-of-life care.

In this study, utilising representative GP networks[20], the authors explored factors associated with cancer patients dying at home as a preferred place of death. We hypothesise factors of care characteristics are associated with meeting a known home death preference.

The study aims are:

1) To explore clinical and care factors associated with fulfilling preferences for dying at home among cancer patients in a mortality follow-back study Belgium, the Netherlands, Italy and Spain

2) To describe cross-country differences on factors facilitating meeting the known preferences

Methods

Design

We performed mortality follow-back study with the European Sentinel GP Networks Monitoring End-of-Life Care (EURO SENTI-MELC) 2009-2011 (2009-2010 in Belgium[BE], the Netherlands[NL] and Italy[IT], and 2010-2011 in Spain[ES]), which continuously monitored end-of-life care via the use of representative networks of general practitioners (GPs).[20]A sentinel network of GPs can be understood as “a network of general practices or primary care physicians who monitor one, several or an exhaustive list of health problems on a regular or continuing basis”.[20]GPs were asked to report all deaths of patients in their practice (age≥18 years) on a weekly basis and reported on preferences and end of life care provided in the final three months of life using a standardised registration form.

Setting and participants

The sampled GP networks represented from 0.8% (NL) to 4% (IT) of the population in the surveyed areas. Apart from Italy, networks in all countries had been in existence for a long time prior to enrolment in the project. A new network was established in Italy for the study. All countries were sampled nationwide, except for Spain, where only two regions (North: Castilla y León and South: Valencia) were included. Details concerning these representative GP networks have been published previously.[19]

Using the registration form, GPs registered whether or not the death was ‘sudden and totally unexpected’. For the present study, we included:

- all non-sudden deaths of people aged 18 years or older
- who died from cancer (cancer being the underlying cause of death according to the GP)
- whose actual place of death and home death preference was known by the GP (Were you informed of the patient’s preference regarding place of death? If YES, where did this patient prefer to die?).Information from both verbal and written communications was regarded as valid evidence of a patient’s indication of his/her preferred place of death.

Nursing home deaths from the Netherlands were excluded since GPs discontinued regular patient care after a patient’s transition to a nursing home.[20,23]

General practitioners and palliative care in the four countries

Within Europe, general practice is highly accessible. In some countries (e.g. the Netherlands, Spain), GPs are gatekeepers for healthcare delivery i.e. primary care providers who coordinate patient care and provide referrals to specialist services. In other countries (e.g. Belgium, Italy) they are not gatekeepers but do have a central coordinating role in the healthcare system with almost all of the population having a GP whom they consult regularly.[20-21]

With regard to GP palliative care provision, there are hardly any studies describing and comparing GPs’ roles in palliative care in these countries. Earlier reports on palliative care delivery in Belgium and the Netherlands have shown that GPs consult specialist palliative care providers more often in Belgium while they indicate they provide palliative care themselves more often in the Netherlands.[22] However, according to the latest EAPC

Atlas[21], palliative care services are generally covered by the public health systems in all countries, so most patients do not have to pay out-of-pocket for access to palliative care services, except sometimes a small fee for medications.

Data Collection Procedure

Participating GPs completed a weekly standardised registration form registering deaths in their practices. In order to minimise recall bias, they recorded deaths immediately after their patients died. Paper-based forms were administered in Belgium, the Netherlands and Castilla y León, whereas a web-based registration was adopted in Italy and an electronic registry in Valencia.

Measurements

Most items were pooled from existing registration forms used in the SENTI-MELC study in Belgium and the Netherlands.[20,23-24] Questions were first developed in Dutch and subsequently translated into French and English, and from English to Italian and Spanish through forward-backward procedures.[20] The questionnaire consisted of 22 questions concerning the final three months of life. They were classified into six domains: places of care and death and transitions between care settings, end-of-life care communications (i.e. physical and psychological distress), palliative care provision, symptoms in the last week of life and costs/burden of end-of-life care.

Twelve variables were tested for their association with preference met, i.e. age, gender, type of malignancy, the patient’s decision-making capacity in the last week of life, communication of options about palliative care,the patient’s expressed wishes about medical treatment, number of GP contact with the patient in the fourth to second week before death (last 28 to 8 days before death), GP provision of palliative care to the patient, initiation of specialist palliative care in the last three months, provision of specialist home care, difficulty for family in covering costs of care and the perceived burden to the informal caregiver(as observed and judged by GPs).

GP’s provision of palliative care is a modified binary variable (yes/no) to the question ‘did you provide palliative care to this patient?’ A ‘yes’ includes both GPs answering ‘yes, until death’ and ‘yes, but not until death’.

Two variables were created from the question ‘which specialist palliative care initiatives were involved in the last three months of this patient’s life?’ containing pre-defined categorical answers (different per country depending on the available services). The variable “Specialist palliative care initiated” refers to all types of palliative care services, and may include hospice care, palliative care units, day care centre as well as home care teams. And ”specialist palliative care at home” is a dichotomous variable (yes/no), and refers solely to the use of specialist palliative care at home.

Ethical approval

Ethical approval, including the consent procedures, was granted in Belgium and Italy, by the ethical review board of Brussels University Hospital (2004) and the local ethical committee in Grosseto (2008) respectively.. No specific ethical approvals were needed in the Netherlands or Spain because of the retrospective anonymous data collection, which conforms to the local legislations

Statistical analyses

The reported actual and preferred place of death was used to create a variable ‘preference met’ and other items from the questionnaire were tested as factors associated with preference met on home deaths. The analyses explored the potential associated factors related to meeting the known home death preferences.

Bivariate analyses (logistic regression on home preference met or not) were conducted separately for each country and for each of the 12 items selected for the analysis. Percentages (proportions of preference met in respect to the categorical variables) were calculated, then odds ratios (ORs) and 95% confidence interval (95% C.I.) from the bivariate analyses on each factor associated were reported. Multivariate logistic regressions (backward stepwise) were then fitted separately for each country, to identify independent associations of those covariates with preference met. The final model considered the variables that showed a significant association with the studied outcome in the adjusted model on a country by country basis. No model was fitted for Spain because of smaller sample size and lack of variability on some of the variables considered. Interaction terms between the covariates were tested through Likelihood Ratio test. All analyses were completed with STATA 12.0. (StataCorp, College Station, TX).

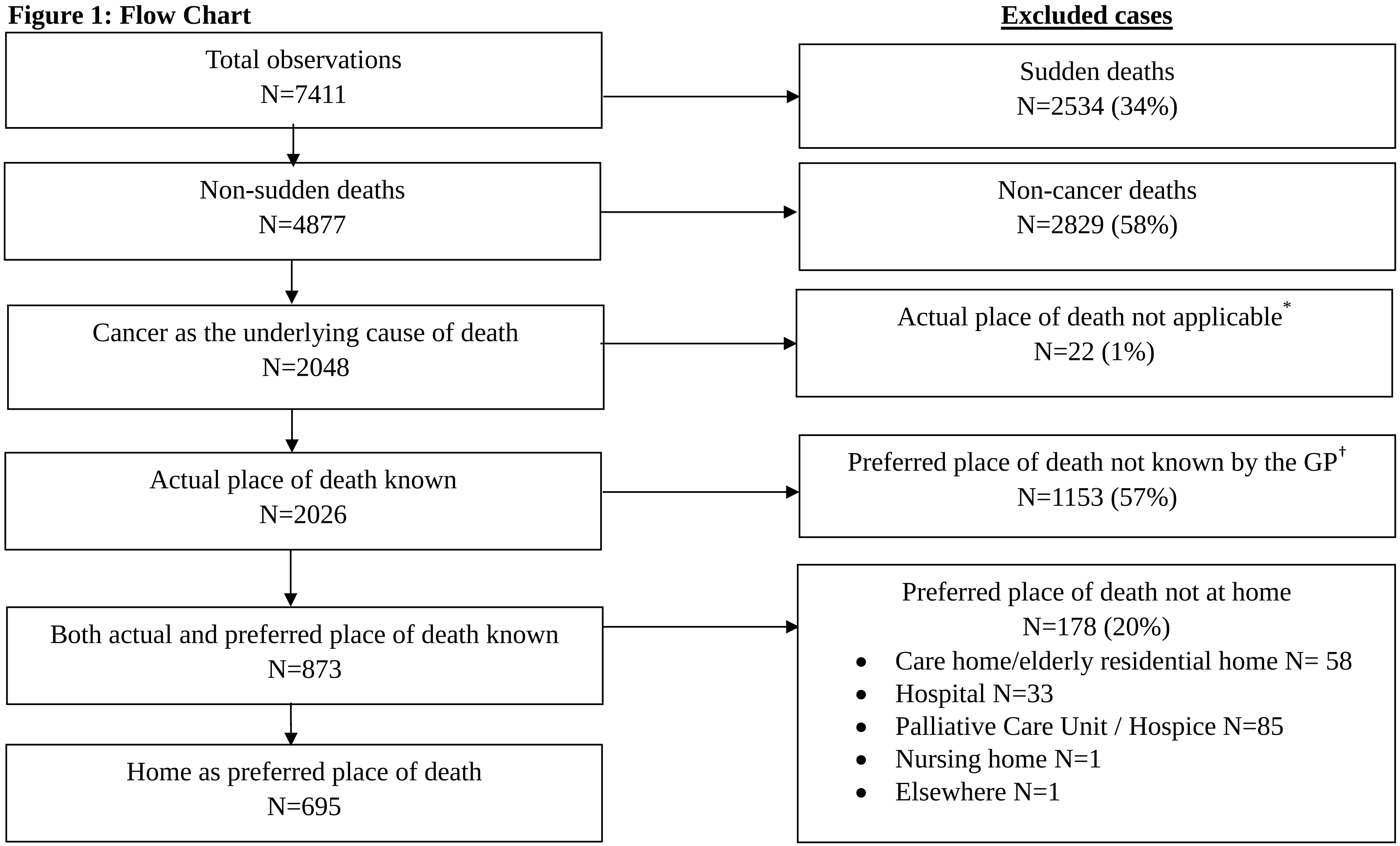
Results

Data for 7,411deceased patients were collected from four countries over the two-year periods of which 2,048died with cancer; and for 873 (42.6%) patients their place of death preference was known to their GPs (Figure 1). A vast majority of deceased patients (N=695, 79.8%: BE: 206 (70.8%), NL: 188(77.4%), IT: 235(89%), ES 66(90.4%)) preferred dying at home. Palliative Care Unit/ Hospice was the second most preferred place of death (N=85, 9.8%). While most patients died at home, hospital deaths ranged from less than one-tenth (NL, ES) to over one-third (IT) across the countries.

Patient sample and characteristics

No cross-country differences were found on gender or the type of malignancies among the 695 cancer patients who preferred to die at home (Table 1). There was a higher percentage (22.7%) of patients who died at 86 or above in Spain. Across countries three out of four patients died at age 65 or above. Differences were observed on actual place of death ($p<.001$). The proportions dying at home for those who preferred to ranged from 65.5% in Italy, 73.3% in Belgium, to 86.7% in the Netherlands and 90.9% in Spain.

Figure 1: Flow Chart



*****actual place of death not answered or nursing home deaths in the Netherlands

†preferred place of death not known by GPs (n=1139), not answered (n=14)

Table 1: Characteristics of cancer patients with a home death preference as known by the GP (N=695)

	Belgium (N=206)	**The Netherlands** (N=188)	**Italy** (N=235)	**Spain** (N=66)	**p-value**[§]
Age group[*]	N (%)	N (%)	N (%)	N (%)	*p=0.021*
18-64	66 (32.2)	51 (27.1)	49 (20.9)	14 (21.2)	
65-85	111 (54.2)	118 (62.8)	144 (61.3)	37 (56.1)	
86 or above	28 (13.7)	19 (10.1)	42 (17.9)	15 (22.7)	
Gender[†]					*p=0.302*
Male	116 (56.3)	96 (51.6)	138 (58.7)	42 (63.6)	
Female	90 (43.7)	90 (48.4)	97 (41.3)	24 (36.4)	
Type of Malignancy[‡]					*p=0.341*
Lung	54 (26.2)	42 (23.2)	51 (25.9)	10 (15.4)	
Breast	14 (6.8)	17 (9.4)	14 (7.1)	4 (6.2)	
Colorectal	27 (13.1)	23 (12.7)	25 (12.7)	15 (23.1)	
Prostate	10 (4.9)	13 (7.2)	11 (5.6)	8 (12.3)	
Others	101 (49.0)	86 (47.5)	96 (48.7)	28 (43.1)	
Place of death					*p<0.001*
Home (home preference met proportions)	151 (73.3)	163 (86.7)	154 (65.5)	60 (90.9)	
Care home/ Residential home for elderly	3(1.5)	2 (1.1)	3 (1.3)	----	
Hospital	26 (12.6)	15 (8.0)	70 (29.8)	5 (7.6)	
Palliative Care Unit/Hospice	25 (12.1)	8 (4.3)	8 (3.4)	1 (1.5)	
Elsewhere	1 (0.5)	----	----	----	

[*] missing: n=1

[†] not answered: n=2

[‡] missing or not answered: n=46

[§] χ^2test on cross-country differences

Bivariate analyses on factors associated with preference for dying at home met

In the bivariate analyses (Table 2), only one variable was found consistently associated with preference met for two countries(estimation not possible in Spain and borderline significant in Italy), i.e. GP provision of palliative care (ORs: BE: 9.2[95% C.I. 3.6-23.8], NL: 7.2[2.2-23.9]).

Two variables yielded country-specific results. Gender was associated with meeting preferences in the Netherlands. A Dutch female patient had a lower chance of dying at home when preferred (OR 0.2[0.1-0.7]). Having a caregiver (whether the caregiver felt burdened or not) increased a Belgian patient’s odds of achieving a home death preference (ORs 8.9 [1.7-47.2] and 9.4 [1.8-49.3] respectively).Estimations for some variables were not possible due to the lack of variability in the data.

When looking more closely into the data (results not shown in tables), the proportions of patients receiving both GP care and specialist palliative care at home were 59.9% (BE), 20% (NL) and 37.2%(IT). However, 75.3% of patients in the Netherlands received GP care exclusively, and the numbers were 40.1% and 62.3% in Belgium and Italy respectively. Lastly, 20.8% (BE) and 32.6% (IT) of patients were cared for at home only by specialist palliative care teams, but no cases were found in the Netherlands.

Factors independently associated with preference for dying at home met

Multivariate logistic regressions were performed separately for each country (Table 3). GP provision of palliative care was independently associated with preference met in all countries when other covariates such as age, gender, number of GP contacts in previous weeks and patient capable of decision making were controlled for, the strongest in Belgium (OR 9.9[3.7-26.6]), followed by the Netherlands (OR 9.7 [2.4-39.9]) and Italy (OR 2.6[1.2-5.5]).

A few country-specific associations were found. Older Belgian patients had a lower likelihood of having their home death preference met compared with their younger peers (aged 65-85 OR 0.4[0.2-0.97]). Two variables were distinctive for Dutch patients. Being female significantly reduced one’s chance of achieving home death preference (OR 0.1[0.04-0.4]). Decision-making capacity increased the likelihood of fulfilment of preference in the Netherlands (OR 6.7[1.5-29.0]). In Italy, patients who had two or more contacts with their GPs in the final second to fourth week of life had a lower chance of having their home death preference met. (OR 0.1[0.01-0.9]).

Table 2: Bivariate Analyses of factors associated with fulfilling preference of dying at home as known by the GP(N=695)

	Belgium(N=206)		**The Netherlands (N=188)**		**Italy (N=235)**		**Spain (N=66)**	
Variables[*]								
	%[†]	OR(95% C.I.)	%[†]	OR(95% C.I.)	%[†]	OR(95% C.I.)	%[†]	OR(95% C.I.)
Age group								
18-64	83.3	ref	86.3	ref	61.2	ref	78.6	ref
65-85	70.3	0.5(0.2-1.0)	89.0	1.3(0.5-3.4)	66.0	1.2(0.6-2.4)	97.3	9.8(0.9-104.2)
86 or above	64.3	0.4(0.1-1.0)	73.7	0.4(0.1-1.6)	69.1	1.4(0.6-3.4)	86.7	1.8(0.2-12.6)
Gender								
Male	71.6	ref	93.8	ref	65.9	ref	88.1	ref
Female	75.6	1.2(0.6-2.3)	78.9	**0.2(0.1-0.7)**	65.0	0.96(0.6-1.7)	95.8	3.1(0.3-28.3)
Type of malignancy								
Lung	81.5	ref	88.1	ref	68.6	ref	90.0	ref
Breast	71.4	0.6(0.1-2.2)	88.2	1.0(0.2-5.8)	71.4	1.1(0.3-4.2)	100	Not estim.[‡]
Colorectal	70.4	0.5(0.2-1.6)	82.6	0.6(0.2-2.7)	72.0	1.2(0.4-3.4)	93.3	1.6(0.1-28.1)
Prostate	80.0	0.9(0.2-5.0)	92.3	1.6(0.2-15.3)	81.8	2.1(0.4-10.6)	75.0	0.3(0.02-4.5)
Others	69.3	0.5(0.2-1.1)	84.9	0.8(0.3-2.3)	58.3	0.6(0.3-1.3)	92.9	1.4(0.1-17.9)
Capable of decision making								
No	71.4	ref	69.2	ref	64.2	ref	100	ref
Yes/Sometimes	75.7	1.2(0.5-3.0)	88.5	3.4(0.96-12.2)	67.9	1.2(0.6-2.3)	86.4	Not estim.[‡]
Communication PC options								
No	65.2	ref	83.3	ref	65.8	ref	90.0	ref
Yes	73.6	1.5(0.6-3.7)	86.6	1.3(0.1-11.5)	66.4	1.0(0.6-1.8)	89.1	0.9(0.1-8.8)
Wishes about treatment								
No	71.4	ref	83.8	ref	63.1	ref	91.3	ref
Yes	74.8	1.2(0.6-2.3)	88.1	1.4(0.5-3.9)	67.1	1.2(0.7-2.2)	84.6	0.5(0.1-3.2)
Average number of GP contact (n) in 2nd to 4th week before death								
0	64.7	ref	75.0	ref	90.9	ref	100	ref
0<n<2	70.6	1.3(0.4-3.8)	87.5	2.3(0.6-9.0)	71.2	0.2(0.03-2.1)	87.1	Not estim.[‡]

2 or more	80.0	2.2(0.7-6.9)	88.0	2.4(0.7-8.7)	60.9	0.2(0.02-1.2)	93.3	Notestim.[‡]
GPs' provision of PC								
No	29.2	ref	53.9	ref	53.5	ref	100	ref
Yes	79.1	**9.2 (3.6-23.8)**	89.4	**7.2 (2.2-23.9)**	68.6	1.9 (1.0-3.7)	90.2	Notestim.[‡]
Specialist palliative care initiated								
No	81.2	ref	89.8	ref	71.9	ref	96.3	ref
Yes	69.3	0.5(0.3-1.1)	80.3	0.5(0.2-1.1)	61.2	0.6(0.4-1.1)	87.2	0.3(0.03-2.4)
Specialist palliative care at home								
No	64.8	ref	84.9	ref	65.3	ref	92.1	ref
Yes	80.7	1.5(0.8-2.6)	91.2	2.0(0.7-5.9)	67.1	0.9(0.6-1.3)	89.3	0.7(0.1-3.8)
Difficulty for family to cover costs of care								
Difficulty/very difficult	80.0	ref	86.5	ref	59.8	ref	100	ref
Not difficult at all	74.5	0.7(0.3-1.8)	84.7	0.9(0.3-2.2)	71.1	1.7(0.9-2.9)	87.8	Not estim.[‡]
Patient did not need care	100	Not estim.[‡]	82.6	0.7(0.2-2.6)	50.0	0.7(0.04-11.1)	92.9	Not estim.[‡]
Burden of informal caregiver								
No caregiver	25.0	ref	n/a[§]	ref	81.8	ref	n/a[§]	ref
Caregiver feeling burdened	74.7	**8.9(1.7-47.2)**	83.1	0.6(0.2-1.4)	63.8	0.4(0.1-1.9)	93.1	1.9(0.3-11.0)
Caregiver not feeling burdened	75.7	**9.4(1.8-49.3)**	89.7	Not estim.[‡]	77.8	0.8(0.1-4.4)	87.9	Not stim.[‡]

[*] missing: age: n=1, gender: n=2, Type of malignancy: n=46, Capable of decision making: n=32, Communication PC options: n=35, Wishes about treatment: n=44,GPs' provision of PC till death: n=6, Specialist home care: n=12, Difficulty for families to cover costs of care: n=63, Burden of informal caregiver: n=35

[†] row percentages of preference met

NOTE: ORs in bold are statistically significant at $p<0.05$,

[‡] not estim.: insufficient variation in the outcome variable to make estimates of correlations: one category of the variable has 100% of preference met

[§] n/a: no observation was found in the category of a variable

Table 3: Multivariate Analyses of factors associated with fulfilling preference of dying at home as known by the GP(N=629)

	Belgium (N=206)	**The Netherlands (N=188)**	**Italy (N=235)**
Variables	OR(95% C.I.)	OR(95% C.I.)	OR(95% C.I.)
Age group			
18-64	ref	ref	ref
65-85	**0.4 (0.2-0.97)**	-----	-----
86 or above	0.4 (0.1-1.1)	-----	-----
Gender			
Female	-----	**0.1 (0.04-0.4)**	-----
GPs’ provision of PC			
Yes	**9.9 (3.7-26.6)**	**9.7 (2.4-39.9)**	**2.6 (1.2-5.5)**
Average number of GP contact (n) in 2nd to 4th week before death			
0	ref	ref	ref
0<n<2	-----	-----	0.2 (0.02-1.8)
2 or more	-----	-----	**0.1 (0.01-0.9)**
Capable of decision making			
Yes/Sometimes	-----	**6.7 (1.5-29.0)**	-----

[*] missing: age: n=1, gender: n=2, Type of malignancy: n=46, Capable of decision making: n=32, Communication PC options: n=35, Wishes about treatment: n=44,GPs’ provision of PC till death: n=6, Specialist home care: n=12, Difficulty for families to cover costs of care: n=63, Burden of informal caregiver: n=35

NOTE: ORs in bold are statistically significant at $p<0.05$

Discussion

Our results showed that on average, almost four out of five deceased patients for whom the GP was informed about their preferences for place of death in the surveyed countries wanted to die at home, confirming the conventional wisdom about people’s preference for home death.[4,10] However, cross-country differences were observed on the actual place of death of these patients, with proportions of meeting home death preference ranging from 65.5% for Italy to 90.9% in Spain, also corresponding to findings in existing literature where congruence on place of death ranged from 30-90% across countries.[25]Spain presents a high proportion of home deaths (if the preference was known) and lower proportions of deaths in hospitals, palliative care units or hospices. Apparently, if Spanish GPs indicate to be aware of a home death preference, care was coordinated in such a way that the home death wishes could be achieved. However, it might also signify that, in case people are able to stay at home in Spain and in case all conditions are met to achieve home death, the home death wishes is more often expressed or elicited.Among our sampled cancer patients, those receiving palliative care from their GPs were found to have a higher chance of dying at home when preferred in three of the studied countries.

A first reading of this finding demonstrates the importance of GPs' provision of palliative care to patients. On the one hand, this may be due to the long established relationship between GPs and their patients (and families), enabling them to have an overall picture of the home conditions, and thus facilitating the essential steps for meeting the home death preference. However, it may also mean that if patients are able to stay in their preferred place due to other factors such as availability of family support, GPs are consequently able to provide palliative care at home – or care which they perceived as being palliative care. Furthermore, patients who explicitly expressed a preference for home death might have a better-than-average relationship with their GPs and depend strongly on that to stay at home till the last moment. Regardless of the direction of the association between GP palliative care provision and dying in their preferred place, the results do show that GP palliative care and dying at home as are intrinsically related. Policies aiming to support people dying in their preferred place need to consider the role of and resources available to primary end-of-life care. The strength of the association with the provision of palliative care by GPsdid vary across the countries, being stronger in BE and NL and weaker in IT, which might reflect the fact that palliative care is a young discipline in Italy, and future research should study these findings in more depth. Although previous literature highlighted the high proportions of home deaths in some countries might reflect a lack of access to acute care or palliative care[7], we believe this is unlikely for the four countries studied since access to healthcare in general is free. On the other hand, other information, like distance of assisted patients from acute care settings and cultural perceptions on professional care settings, if available, will enhance understanding our results, i.e. disentangle the relationships of different factors.

Interestingly, 'specialist palliative care at home' was not a factor independently associated with achieving a home death preference. This finding is intriguing because it had been argued that in spite of increasing specialisation of palliative care as a discipline, the current trend is that most of the care worldwide is provided by GPs[11, 26] and it is unlikely that specialists will take over all patients receiving palliative care[27-28], given the time and resource constraints, further indicating the vital role of GPs[27-30]. These results not only reflect the different organisations of palliative care services[31-34] such as the role of GPs in the Netherlands, the frequent use of specialist palliative care in Belgium, and the middle-ground position of Italy, but may also support the concept of optimal division of labour between generalists and specialists[25,35]. In Spain, an integrated plan for palliative care in Valencia recommends the most complex patient to receive hospital palliative care alongside with other services. While most patients typically receive palliative care at home by their GPs or palliative care teams visiting patients at home. Nevertheless, intra-regional variations are expected. The differences in service provision but general high proportions of home death preference met suggest the importance of good communication between GPs and specialist teams, particularly of making due time referrals[36] and exploring a patient's preferences in a timely manner.[37]

Apart from the association with GPs found across countries, the country-specific associations identified in the data remind us of the caution needed totranslate the findings directly into practice. For example, the association with decision-making might be pointing to something specific in the medical culture of the Netherlands, i.e.the emphasis on patient autonomy in end-of-life decisions,which possibly enhances the chance of dying at home if that desire was communicated to healthcare professionals. Also, the correlation with the number of GPs' contacts in Italy requires future investigation to understand the organisation of care for the dying in the final weeks of life. It was observed thatan increased number of contacts with GPs in the last few weeks reduced the odds of meeting home death preference, opening up the possibility of whether these patients had a greater symptom burden and more needs and were thus transferred to a hospital in the final hours of life for these reasons, thus decreasing the home death preference met.

Current literature noted that clinical factors such as types of tumour (i.e. having a haematological tumour) [9,38] and need for symptom control (i.e. inability to control pain) decrease the congruence on achieving a preferred place of death.[7] Social factors like costs and the burden on others were quoted as indicators of equitable access to palliative care services.[8,39-40] Even though our present study did not find the same associations, this was perhaps due to the small sample. It is also possible that our sampled cancer type belonged to a special group (i.e. preferred place of death was known, with a lower symptom burden and having access to high quality of palliative care). The country specific factors, such as decision-making capacity, also reflect findings in the literature about the concept of autonomy in the Netherlands[41] and the reduced chances of dying at home for older patients.[42]

Finally, home death has been promoted as a major quality marker in palliative care, by both the research community[43] and policy makers,[10,44] yetthe notion of home death as the gold standard is controversial[45] and preferences could change in time for some people.[24,46] It is important to respect a patient’s preferences[47] while taking into account other factors like costs and the burden imposed on informal caregivers.[48] As this study is about patients’ preference on place of death and the factors associated with it, the best way would be to have a study asking patients directly to indicate their preference on place of death and to assess if that preference was met. Also, one should be reminded that patients’ preferences might change over their disease trajectory.

GPs were used as proxies in reporting items such as costs and burden of caregivers. And this data could be less accurate compared to patient-reported outcomes or routinely collected administrative data.

Strengths and weaknesses

This study offers an overview of how preferences for home death among deceased cancer patients had been met in the four countries surveyed, allowing for cross-national comparisons. The sentinel GP networks were nationally and/or regionally representative and thus were able to provide a macro-picture of how end-of-life care was arranged in these countries. Focusing specifically on determinants of preference met, this study can help understanding of how current practice could be improved.

However, the study also has several limitations. Firstly, only patients whose wish to die at home was known to the GP were included in the analyses, so we could not interpret univocally the relationship between GP provision of palliative care and meeting home death preference. It was possible that this group of patients had a better-than-average relationship with their GPs, making their preferences more explicit and allowing their GPs to care for them at home. Therefore, it was very likely that patients included in the analyses were receiving GP-oriented palliative care, making it easier for GPs to elicit preferences of place of care and death, and also to avoid frequent transitions between settings, thus making a home death more feasible. The higher congruence of home death preference than other studies (30-90%)[25] might also reflect the limitations of using GP as respondents, i.e. if patients preference for place of death in unknown by the GP, they more often die in a hospital which is often not the preferred place of death according to other preference studies[49].

Furthermore, the low proportion of known preferences might point to a more fundamental gap in communicating about end-of-life preferences. Also, for patients whose home death preference was known but not met, we did not have sufficient information to conclude what happened in their final months or days of life that made it no longer feasible for them to die at home. Moreover, making use of GPs as a source of information is not unproblematic. Costs and emotional burden of caregivers were measured as perceived by GPs, which might have underestimated or overestimated the actual burden. Lastly, the questionnaire design did not allow us to know further details of what GPs did when they claimed they were providing palliative care: this may include referrals to specialist care, home visits and engaging in discussions on end-of-life decisions. GPs have a long lasting relationship with patients, often until the end of life in the participating countries. Hence, while death certificates might not always be reliable because often filled in by attending specialists, the identification of patients who died with cancer as underlying cause of death will be more reliable when performed by the treating GPs, as was done in this study. A prospective study design directly interviewing the patients and their family is advisable to disentangle the role of each aspect of care and to overcome the majority of these limitations.

Conclusion

In spite of differences in both culture and healthcare systems,66-92% of cancer patients died at home with this as their preferred location. We discovered that GP provision of palliative care is related to meeting cancer patients' preference for home death across all countries studied. This is an important finding as GPs are expected to play an increasing role in ensuring access to palliative care for all patients. Policies aiming to achieve people dying in their preferred place need to include consideration of the role of and resources available for primary end-of-life care.

References

1. Malvezzi M, Bertuccio P, Levi F, La Vecchia C, Negria E. European cancer mortality predictions for the year 2013. Ann Oncol 2013; 24(3): 792-800.
2. Ferlay J, Steliarova-Foucher E, Lortet-Tieulent J et al. Cancer incidence and mortality patterns in Europe: Estimates for 40 countries in 2012. Eur J Cancer 2013; 49(6):1374-1403.
3. Hofmann JC, Wenger NS, Davis RB, et al. Patient preferences for communication with physicians about end-of-life decisions. SUPPORT Investigators. Study to Understand Prognoses and Preference for Outcomes and Risks of Treatment. Ann Intern Med 1997; 127(1): 1-12.
4. Gomes B, Calanzani N, Gysels M, Hall S, Higginson IJ. Heterogeneity and changes in preferences for dying at home: a systematic review. BMC Palliat Care 2013; 12:7.
5. Gomes B, Higginson IJ, Calanzani N, et al. Preferences for place of death if faced with advanced cancer: a population survey in England, Flanders, Germany, Italy, the Netherlands, Portugal and Spain. Ann Oncol 2012; 23(8): 2006-2015.
6. Higginson IJ, Sarmento VP, Calanzani N, Benalia H, Gomes B. Dying at home-is it better: A narrative appraisal of the state of the science. Palliat Med 2013. May 22 [Epub ahead of print]
7. Gao W, Ho YK, Verne J, Glickman M, Higginson IJ and on behalf of the GUIDE_Care project. Changing Patterns in Place of Cancer Death in England: A Population-Based Study. PLoS Med 2013. 10: e1001410.
8. Gomes B and Higginson IJ. Factors influencing death at home in terminally ill patients with cancer: systematic review. BMJ 2006; 332(7540): 515-521.
9. Higginson IJ and Costantini M. Dying with cancer, living well with advanced cancer. Eur J Cancer 2008; 44(10): 1414-1424.
10. NHS Critical success factors that enable individuals to die in their preferred place of death. 2012. Available from: http://www.endoflifecareforadults.nhs.uk/publications/critical-success-factors. Accessed November 19, 2012.
11. Hinton J. Which patients with terminal cancer are admitted from home care? Palliat Med 1994; 8(3):197-210.

12. Grande GE, Addington-Hall JM and Todd CJ. Place of death and access to home care services: are certain patient groups at a disadvantage? SocSci Med 1998; 47(5):565-579.
13. Gatrell AC, Harman JC, Francis BJ, Thomas C, Morris SM and Mclllmurray M. Place of death: analysis of cancer deaths in part of North West England. J Public Health Med 2003; 25(1):53-58.
14. Wachterman MW and Sommers BD. The impact of gender and marital status on end-of-life care: evidence from the National Mortality Follow-Back Survey. J Palliat Med 2006; 9(2): 343-352.
15. Tang ST, and Mccorkle R. Determinants of Congruence between the Preferred and Actual Place of Death for Terminally Ill Cancer Patients. J Palliat Care 2004; 19(4):230-237.
16. Bell CL, Somogyi-Zalud E, MasakiKH. Factors Associated with Congruence Between Preferred and Actual Place of Death. J Pain Symptom Manage 2010; 39(3): 591-604.
17. Brogaard T, Neergaard MA, Sokolowski I, Olesen F, Jensen AB. Congruence between preferred and actual place of care and death among Danish cancer patients. Palliat Med 2012; 27(2): 155-164.
18. Lachenmann G. Globalisation and Localisation of Health Care in Poor Countries in Africa. Nord-Südaktuell 2002; 16(3): 456-461.
19. Whitehead M, Dahlgren Gand Gilson L. Developing the Policy Response to Inequalities in Health: A Global Perspective. In: Evans T, Whitehead M, Diderichsen F, Bhuiya A and Wirth M, eds. Challenging inequities in health: from ethics to action. New York: Oxford University Press; 2002.
20. Van den Block L, Onwuteaka-Philipsen B, Meeussen K et al. Nationwide continuous monitoring of end-of-life care via representative networks of general practitioners in Europe. BMC Palliative Care 2013; 14(1):73.
21. Lynch T, Connor S and Clark D. Mapping Levels of Palliative Care Development: A Global Update. J Pain Symptom Manage 2013. 45(6): 1094-1106.
22. Meeussen K, Van den Block L, Echteld MA et al. End-of-life care and circumstances of death in patients dying as a result of cancer in Belgium and the Netherlands: a retrospective comparative study. J Clin Oncol 2011; 29(32): 4323-4334.

23. Van den Block L, Van Casteren V, Deschepper R et al. Nationwide monitoring of end-of-life care via the Sentinel Network of General Practitioners in Belgium: the research protocol of the SENTI-MELC study. BMC Palliative Care 2007; 6:6.
24. Donker GA. Continuous Morbidity Registration Dutch Sentinel General Practice Network 2011. Annual report. Utrecht, NIVEL, 2012. www.nivel.nl/peilstations.
25. Bell CL, Somogyi-Zalud E, Masaki KH. Methodological review: measured and reported congruence between preferred and actual place of death. Palliat Med 2009; 23(6): 482-490.
26. Mitchell GK. How well do general practitioners deliver palliative care? A systematic review. Palliat Med 2002; 16(6):457-464.
27. Gardiner C, Gott M, Ingleton C. Factors supporting good partnership working between generalist and specialist palliative care services: a systematic review. Br J Gen Pract 2012; 62(598): e353-362. doi: 10.3399/bjgp12X641474.
28. Schneider N, Mitchell GK and Murray SA. Palliative care in urgent need of recognition and development in general practice: the example of Germany. BMC FamPract 2010; 11:66.
29. Bajwah S and Higginson IR. General practitioners’ use and experiences of palliative care services: a survey in south east England. BMC Palliative Care 2008; 7:18.
30. Michiels E, Deschepper. Van DerKelen G, et al. The role of general practitioners in continuity of care at the end of life: a qualitative study of terminally ill patients and their next of kin. Palliat Med 2007. 21(5):409-415.
31. Sbanotto A and Burnhill R. Palliative care in Italy: the current situation. Support Care Cancer 1998; 6(5):426-429.
32. Desmedt M. Palliative care services in Belgium: benefits and shortcomings of a legal framework. Support Care Cancer 1999; 7(3):109-112.
33. Desmedt MS, De la Kethulle YL, Deveugele MI et al. Palliative inpatients in general hospitals: a one day observational study in Belgium. BMC Palliat Care 2011; 10:2. doi:10.1186/1472-684X-10-2
34. Gomez-Batiste X, Tuca A, Corrales E et al. Resource consumptions and costs of palliative care services in Spain: a multicentre prospective study. J Pain Symptom Manage 2006; 31(6):522-532.

35. Quill TE, Abernethy AP. Generalist plus Specialist Palliative Care-Creating a More Sustainable Model. N Engl J Med 2013;368(13): 1173-1175.
36. Poulose JV, Do YK, Neo PS. Association Between Referral-to-Death Interval and Location of Death of Patients Referred to a Hospital-Based Specialist Palliative Care Service. J Pain Symptom Manage 2013; 46(2): 173-181.
37. Galushko M, Romotzky V and Voltz R. Challenges in end-of-life communication. Curr Opin Support Palliat Care 2012; 6(3):355-364.
38. Hong CY, Chow KY, Poulose J, et al. Place of death and its determinants for patients with cancer in Singapore: an analysis of data from the Singapore Cancer Registry, 2000-2009. J Palliat Med 2011; 14(10):1128-1134.
39. Barclay JS, Kuchibhatla M, Tulsky JA et al. Association of Hospice Patients' Income and Care Level With Place of Death. JAMA Intern Med 2013; 173(6): 450-456.
40. Howell DM, Abernathy T, Cockerill R, et al. Predictors of Home Care Expenditures and Death at Home for Cancer Patients in an Integrated Comprehensive Palliative Home Care Pilot Program. Healthc Policy 2011; 6(3): e73-92.
41. Rietjens JA, van der Heide A, Onwuteaka-Philipsen BD, van der Maas PJ, van der Wai G. Preferences of the Dutch general public for a good death and associations with attitudes towards end-of-life decision-making. Palliat Med 2006; 20(7): 685-692.
42. Cohen J, Bilsen J, Hooft P, Deboosere P, van der Wal, Deliens L. Dying at home or in an institution using death certificates to explore the factors associated with place of death. Health Policy 2006; 78(2-3): 319-329.
43. Houttekier D, Cohen J, Van den Block L, Bossuyt N, Deliens L. Involvement of palliative care services strongly predicts place of death in Belgium. J Palliat Med 2010; 13(12): 1461-1468.
44. National EOL Framework Forum. Health system reform and care at the end of life: A guidance document. Canberra, Australia: Palliative Care Australia 2010.
45. Barclay S, Arthur A. Place of death: how much does it matter? The priority is to improve end-of-life care in all settings. Br J Gen Pract 2008; 58(549):229-231.
46. Luckett T, Davidson PM, Lam L, et al. Do Community Specialist Palliative Care Services That Provide Home Nursing Increase Rates of Home Death for People With Life-Limiting Illnesses? A Systematic Review and Meta-Analysis of Comparative Studies. J Pain Symptom Manage 2013; 45(2):279-297.

47. Borreani C and Miccinesi G. End of life care preferences. CurrOpin Support Palliat Care 2008; 2(1):54-59.
48. Stajduhar KI, Martin WL, Barwich D, Fyles G. Factors influencing family caregivers' ability to cope with providing end-of-life cancer care at home. Cancer Nurs 2008; 31(1):77-85.
49. Ko W, Beccaro M, Miccinesi G, et al. Awareness of general practitioners concerning cancer patients' preferences for place of death: evidence from four European countries. Eur J Cancer; 49(8): 1967-1974.

Part III Advanced lung cancer patients: place of death and quality of life

Chapter 6 **Differences in place of death between lung cancer and COPD patients: A 14-country study using death certificate data.**

(submitted)

“Death is no more than passing from one room into another.
But there’s a difference for me, you know.
Because in that other room I shall be able to see.”
--- Helen Keller

Title: Differences in place of death between lung cancer and COPD patients: A 14-country study using death certificate data.

Authors: Winne Ko[1], Dirk Houttekier[1], Lieve Van den Block[1,2] Lucas Morin[3], Katherine Hunt[4], Guido Miccinesi[5], Marylou Cardenas-Turanzas[6],Bregje Onwuteaka-Philipsen[7], Rod MacLeod[8], Miguel Ruiz-Ramos[9], Donna M Wilson[10], Martin Loucka[11], Agnes Csikos[12], Yong-Joo Rhee[13], Joan Teno[14], Luc Deliens[1,7], Joachim Cohen[1] ,on behalf of IPoD and EURO IMPACT

[1]Vrije Universiteit Brussel (VUB) and Ghent University, End-of-Life Care Research Group, Brussels, Belgium
[2]Vrije Universiteit Brussel (VUB), Department of Family Medicine and Chronic Care, Brussels, Belgium
[3]National Observatory of End of Life Care, Paris, France
[4]University of Southampton, Health Sciences, Southampton, United Kingdom
[5]Cancer Prevention and Research Institute, ISPO, Clinical and Descriptive Epidemiology Unit, Florence, Italy
[6]The University of Texas MD Anderson Cancer Center, Houston, TX, United States
[7]EMGO Institute for Health and Care Research, Public and Occupational Health, and Palliative Care Expertise Centre, VU Medical Centre, Amsterdam, Netherlands
[8]HammondCare and University of Sydney, Australia
[9]Ministry of Health, Government of Andalusia, Seville, Spain
[10]University of Alberta, Faculty of Nursing, Edmonton, AB, Canada
[11]Center for Palliative Care, Third Faculty of Medicine, Charles University in Prague, Prague, The Czech Republic
[12]University of Pécs Medical School, Pécs, Hungary
[13]Dongduk Women's University, Health Sciences, Seoul, Republic of Korea
[14]Brown University, Community Health, Providence, RI, United States

Funding information: The **I**nternational **P**lace of **D**eath (IPoD) study is supported by a fund from the Research Foundation Flanders. This work was supported by EURO IMPACT (FP7/2007-2013, under grant agreement n° [264697]). Joachim Cohen and Lieve Van den Block are supported by a postdoctoral grant from the Research Foundation – Flanders, Belgium.

Abstract

Introduction

Chronic obstructive pulmonary disease (COPD) and lung cancer are leading causes of death with comparable symptoms at the end of life. This study compares the place of death of people dying from COPD or lung cancer in 14 countries.

Methods

Population death certificate data from 2008 were collected from 14 countries covering place of death, underlying cause of death and demographic information. We included patients dying from lung cancer or COPD and used descriptive statistics and multivariate logistic regressions to describe patterns in place of death.

Results

Of 5,568,827 deaths, 5.8% were from lung cancer and 4.4% from COPD. Among lung cancer decedents, home deaths ranged from 12.5% in South Korea to 57.1% in Mexico while hospital deaths ranged from 27.5% in New Zealand to 77.4% in France. In COPD patients, the proportion dying at home ranged from 10.4% in Canada to 55.4% in Mexico while hospital deaths ranged from 41.8% in Mexico to 78.9% in South Korea.

Conclusion

Controlling for age, sex and marital status, patients with COPD were significantly less likely die at home rather than in hospital in nine countries. This might be due to differences in disease trajectories and prognostication.

Introduction

Lung cancer and chronic obstructive pulmonary disease (COPD) are two major causes of death in many countries, appearing as the fifth and third most common cause of death globally.[1] Both illnesses affect patients quality of life with various stages of functional decline before death. Studies suggested that patients from both disease groups suffer from considerable dyspnoea and pain.[2-3]Other studies have indicated that people with COPD have severe symptoms causing major disruptions to normal life but these are often perceived and accepted asa ‘way of life’ rather than an illness.[4] Despite similar problems, existing literature has reported a disadvantage for people with COPD compared with those with lung cancer in receiving end-of-life(EOL) care.[3,5-6] Lung cancer patients seem to receive a more holistic palliative approach to care. [3] Fewer palliative care resources were used by people with COPD[3] and EOL care discussions occurred later in their disease trajectories.[7-8] Those with COPD also seem to face unmet care needs to a larger extent[9-10] and appear to have less access to palliative care services.[11-12] The historical focus of palliative care on cancer patients may be one of the main reasons for this.[5]

Previous research comparing EOL care for COPD and lung cancer patients has focused on symptom management[13-15] and communication,[16-18] little is known about how place of death differs between them. Place of death is often seen as a contributing factor in quality of dying, particularly because most people prefer to be cared for and to die at home[19-20] while the setting of dying has been shown to influence the characteristics of care and the dying experience.[21] From research using Medicare data from the USA, we know that COPD patients were more likely to die in hospital than were lung cancer patients.[22] Nonetheless, cross-national comparisons for both populations remain scarce and such studies encourage mutual learning across borders by shedding alight on how patients with the same or different diseases die in different countries. Even neighbouring countries with relatively similar cultures may organise EOL care differently and this evidence is valuable for evidence-based health policy-making.

The research aims of this study were firstly to compare and describe place of death of those persons diagnosed with lung cancer compared with those diagnosed with COPD in 14 countries and secondly to examine to what extent place of death differences between the two disease groups are due to confounding socio-economic and residential factors.

Materials and Methods

Study design and data

This study is part of the International Place of Death (IPoD) study, which is a study of population level death certificate data. An open call was launched by the principal investigators and candidate partners negotiated a full year’s death certificate data for inclusion. An exploration by all candidate partners revealed the most recent available year in all targeted countries was or would be 2008, which was chosen as the reference year. Exceptions were the USA (2007) and Spain (no data were recorded prior to 2010). Fourteen out of the 27 candidate countries obtained permission for data use and their data were integrated into an international database. The principal investigators pooled all data guaranteeing uniform coding throughout the database.

Death certification was executed in similar ways in the 14 countries: a physician or a qualified person such as a nurse completes the part of the death certificate indicating cause of death, time and place of death[23] along with a limited range of demographic information (e.g. sex) for the deceased. In some countries another part of the death certificate, containing more socio-demographic information about the deceased, is completed by a civil servant. All information is then processed by trained coders, following strict coding protocols, with the necessary quality checks. The death certificate data were linked across a number of countries with similar population databases such as the Census Data to include more socio-demographic information about the decedents in the database. For this study we used the death certificate data of all 14 countries included in the IPoD study: Belgium, France, Italy, Spain (Andalusia), the Netherlands, Czech Republic, Hungary, England, Wales, New Zealand, United States, Canada, Mexico and Korea.

Data

We selected cases where lung cancer (ICD10 codes[24] C33-C34) or COPD (ICD-10 codes J40-44, J47) was an underlying cause of death. The outcome for our study was the place of death as recorded in the death certificate. The available categories of place of death were: hospital, home, nursing home/residential long-term care, hospice, or others. In Hungary the death certificate only contains two categories of place of death, hospital and others, whereas hospice (e.g. palliative care institution) was only available as a category in England, Wales, New Zealand, Canada and the United States.

Independent variables used in the multivariate analyses included demographics and healthcare resources. Demographic factors included age (categories 0-17, 18-64, 65-85, 85 or above), sex and marital status (unmarried, married, widowed or divorced).

Statistical analysis

Descriptive statistics were used to examine differences in the place of death between patients dying from lung cancer and those from COPD. Crude ratios (the percentages of lung cancer deaths divided by the percentages of COPD deaths) were calculated to compare the differences in place of death between the two disease groups.

There are five categories of place of death, home, hospital, nursing home, PC institutions or other places. Multivariate binary logistic regression models were constructed to determine the odds ratios of dying at home (comparing home vs all other places), (comparing home vs hospital), hospital deaths (vs all other places), in nursing home (vs hospital) and PC institutions (vs all other places). All analyses used lung cancer as the reference group. Relevant confounders and covariates in the models were entered using a forward stepwise selection method with p<0.05 set as an entry criterion. All statistical analyses were conducted using IBM-SPSS Statistics version 20 (SPSS Inc., Chicago, Illinois, 2010). For all analyses, significance was set at *p*<.05 (two tailed).

Results

A total of 5,568,827 deaths were documented in the 14 countries. In all countries, except New Zealand and Mexico, more people died from lung cancer than COPD (Table 1, country abbreviations explained). Lung cancer deaths ranged from 1.2% of all in Mexico to 7.6% in the Netherlands. Deaths from COPD ranged from 1.7% in France to 5.3% in the USA.

Table 1: Deaths from COPD and lung cancer in 14 countries during the year 2008 (N=5,568,827)

Country	Abbreviations	Total Number of deaths	COPD deaths N(% of all deaths)	Lung cancer deaths N(% of all deaths)
France	FR	541,135	9274(1.7)	29221(5.4)
Italy	IT	578,192	21356(3.7)	33004(5.7)
Spain (Andalusia)	ES	57,380	2564(4.5)	3198(5.6)
Belgium	BE	102,924	4751(4.6)	6491(6.3)
The Netherlands	NL	135,136	6303(4.9)	9918(7.6)
Czech Republic	CZ	101,804	2161(2.1)	5310(5.2)
Hungary	HU	130,027	4875(3.7)	8330(6.4)
England	ENG	475,763	25143(5.3)	28222(5.9)
Wales	WAL	32,066	1730(5.4)	2032(6.3)
New Zealand	NZ	29,312	1837(6.3)	1634(6.0)
Canada	CA	182,134	8185(4.5)	12902(7.1)
United States of America	USA	2,428,343	128021(5.3)	158889(6.5)
Mexico	MX	528,093	21804(4.6)	6563(1.2)
Korea	KR	247,757	7349(3.0)	14883(6.0)
Total		**5,568,827**	**245,345 (4.4)**	**320,591(5.8)**

COPD, Chronic obstructive pulmonary disease

As compared with people dying from lung cancer, those dying from COPD were more often older, female and widowed or divorced (Table 2). Most lung cancer patients were married (ENG: 51.3% to IT: 69.3%) whereas the majority of COPD sufferers were widowed/divorced (ES: 37.6% to USA: 57.5%).

Table 2: Demographic characteristics of people with COPD or lung cancer who died during 2008 in 14 countries (N=562,151)

		Age (%)			Sex(%)	Marital Status (%)		
		18-64	65-84	85 or above	Female	Unmarried	Married	Widowed/ Divorced
FR	**COPD**	10.2	30.0	59.6	37.5	12.4	40.4	47.3
	Lung cancer	40.4	40.3	19.3	23.6	11.4	60.8	27.8
IT	**COPD**	3.5	26.2	70.3	39.3	10.8	42.5	46.7
	Lung cancer	22.3	50.7	27.0	23.4	8.1	69.3	22.6
ES	**COPD**	6.0	38.7	55.2	20.6	9.1	53.3	37.6
	Lung cancer	33.1	47.1	19.8	13.7	8.5	71.6	19.9
BE	**COPD**	11.5	37.2	51.2	36.5	8.2	43.0	48.8
	Lung cancer	30.9	47.3	21.8	23.8	7.1	61.3	31.7
NL	**COPD**	9.4	36.8	53.7	44.2	59.7	40.3	N/A
	Lung cancer	31.5	48.5	20.0	35.6	38.9	61.1	N/A
CZ	**COPD**	21.4	42.4	36.2	39.7	8.0	39.9	52.1
	Lung cancer	39.6	46.7	13.6	27.4	5.7	57.2	37.1
HU	**COPD**	15.8*	48.4*	35.7*	40.9	9.5	36.3	54.1
	Lung cancer	33.5*	55.5*	10.9*	32.8	7.5	53.6	38.9
ENG	**COPD**	10.5	39.2	50.1	48.7	7.8	36.9	55.3
	Lung cancer	22.3	48.2	29.5	43.2	6.8	51.3	41.9
WAL	**COPD**	9.1	40.8	50.1	50.8	6.0	39.0	54.9
	Lung cancer	22.5	49.2	28.3	42.4	6.1	51.8	42.1
NZ	**COPD**	12.2	37.8	49.9	50.2	†	†	†
	Lung cancer	28.8	47.1	24.1	45.6	†	†	†
CA	**COPD**	8.5	34.3	57.1	46.9	7.7	36.8	55.6
	Lung cancer	26.7	47.7	25.7	46.0	6.8	55.5	37.7
USA	**COPD**	14.2	40.2	45.4	52.1	6.3	36.2	57.5
	Lung cancer	28.8	47.1	24.1	44.3	6.0	51.0	43.0
MX	**COPD**	11.8	35.9	51.4	44.5	11.2	44.6	44.2
	Lung cancer	31.3	47.3	21.3	33.7	10.8	61.8	27.4
KR	**COPD**	7.9	42.8	49.3	38.7	2.8	47.7	49.7
	Lung cancer	25.3	56.3	18.4	26.4	2.3	69.2	28.5

Percentages are row percentages.

* For age, the Hungarian file was delivered using a different aggregation: 0-17,18-59,60-79(65-84), 80 or above(85 or above)

†Variable not available not available for the country; N/A: category within variable not presented on the data file of the Netherlands; variable was dichotomized into married or not.

Note: Percentages may not add up to 100 due to rounding

From 12.5% (KR) to 57.1% (MX) of persons diagnosed with lung cancer died at home (Table 3). Hospital deaths accounted for 27.5% (NZ) to 86.5% (KR) of lung cancer deaths. Another 0.9% (KR) to 22.5% (NZ) of lung cancer deaths occurred in nursing homes. For countries where the category hospice (i.e.palliative care institution) was available (England, Wales, New Zealand and the USA), from 5.2% (USA) to 17.6% (NZ) of lung cancer deaths took place there. Of the COPD deaths, 10.4% (CA) to 55.4% (MX) took place at home, 41.8% (NL) to 78.9% (KR) in hospital, 1.5% (KR) to 35.4% (NL) in nursing homes and 0.2% (WAL) to 2.9% (US) in palliative care institutions. As compared with COPD sufferers, those with lung cancer had better crude chances of dying at home in nine out of 13 countries (data on home death not available from Hungary), with the difference particularly large in the Netherlands (2.34) and New Zealand (1.93). In six of these nine countries, lung cancer patients were less likely to die in hospitals. In France, Italy, Spain, Belgium, Canada and Korea lung cancer patients had relatively higher chances of dying in hospital but they were less likely to die in hospital in seven out of 13 countries. In three countries - Belgium, Italy and Canada - persons with lung cancer had both a higher ratio of dying at home and in hospital compared with people with COPD. Except in Czech Republic, those with lung cancer in all countries were less likely to die in a nursing home. In countries where hospice (i.e.palliative care institutions)was available as a category of place of death, lung cancer sufferers were more likely than COPD ones to die there [risk ratios: 17.93 (ENG), 36.82 (WAL), 9.52 (NZ) and 1.78 (US)].

Table 3: The place of death of deceased patients with COPD and lung cancer during 2008 by country (N=562,151)

	Place of death	FR	IT	ES	BE	NL	CZ	HU	ENG	WAL	NZ	CA	US	MX	KR
		%	%	%	%	%	%	%	%	%	%	%	%	%	%
Lung Cancer	**Home**	17.0	44.2	33.1	28.8	48.0	17.3	/[*]	28.2	28.1	29.9	16.3	40.3	57.1	12.5
	Hospital	77.4	49.5	64.5	63.9	28.0	66.4	72.1	45.8	57.5	27.5	69.0	33.9	40.1	86.5
	Nursing home	3.0	2.9	2.1	6.8	15.3	15.5	/	9.0	4.2	22.5	9.9	15.0	/	.9
	PC institutions	/	/	/	/	/	/	/	15.3	8.5	17.6	/	5.2	/	/
	Others	2.7	3.5	.2	0.6	8.7[+]	.8	27.9	1.7	1.6	2.6	4.9	5.7	2.8	.1
COPD	**Home**	25.6	41.6	36.3	22.0	20.5	17.2	/	19.8	16.9	15.5	10.4	26.2	55.4	19.4
	Hospital	60.2	47.4	56.7	52.8	41.8	66.8	69.8	67.5	73.9	44.7	65.4	44.5	41.8	78.9
	Nursing home	11.2	7.5	6.2	24.4	35.4	14.7	/	10.8	8.2	34.0	20.7	22.7	/	1.5
	PC institutions	/	/	/	/	/	/	/	.9	.2	1.9	/	2.9	/	/
	Others	3.0	3.5	.8	.8	2.4	1.3	30.2	1.0	.8	4.0	3.6	3.7	2.8	.3
Crude risk ratios: % of LC deaths/ % of COPD deaths	**Home**	0.66	1.06	0.91	1.31	2.34	1.00	/	1.42	1.67	1.93	1.57	1.54	1.03	0.64
	Hospital	1.28	1.04	1.14	1.21	0.67	0.99	0.40	0.68	0.78	0.61	1.05	0.76	0.96	1.10
	Nursing home	0.26	0.38	0.34	0.28	0.43	1.06	/	0.83	0.51	0.66	0.48	0.66	/	0.59
	PC institutions	/	/	/	/	/	/	/	17.93	36.82	9.52	/	1.78	/	/
	Others	0.91	1.00	0.28	0.71	3.66	0.59	0.92	1.71	2.16	0.64	1.37	1.55	0.99	0.49

Percentages are column percentages.

[*] Category not presented on death certificate. In Hungary, the death certificate registry only coded hospital or others as the place of death and nursing home does not exist as a separate health service in Mexico.

[+] Others: in the Netherlands are mostly hospices, so could be understood as a type of PC institution

Note: Percentages may not add up to 100 due to rounding

Controlling for confounders (age, sex, marital status), using binary logistic regression analyses (Table 4), persons dying of COPD were significantly less likely than lung cancer patients to die at home (vs any other place of death) in 10 countries [OR from 0.4(NL) to 0.8 (BE, ES and MX)]. An opposite pattern was found in France (OR 1.7) and Korea (OR 1.5), with COPD sufferers there more likely to die at home. When only comparing home to hospital as a place of death, lower odds ratios for home death (less than one) were observed in COPD decedents in nine countries [OR from 0.3 (NL and NZ) to 0.9 (ES)] with France (OR 1.8) and Korea (OR 1.6) showing patients with COPD more likely to die in hospitals. Compared with those with lung cancer, COPD patients were significantly more likely to die in hospital instead of outside a hospital in seven countries [OR from 1.2 (IT) to 2.7 (NZ)], but the opposite was observed in France (OR 0.5), Korea (OR0.7) and Belgium (OR 0.8). Czech Republic was the only country showing no differences between the two disease groups with regard to place of death. COPD patients were more likely than lung cancer patients to die in a nursing home (as compared to hospital) in five countries [OR from 1.5 (CA) to 2.4 (BE)], while in five other countries (NL, CZ, ENG, NZ, USA), COPD decedents died more often in hospitals than did lung cancer decedents. Lastly, a comparison between palliative care institutions and other places of death for England, Wales, New Zealand and the United States showed that in all these countries, COPD decedents had a significantly lower chance of dying in a palliative care institution compared with lung cancer decedents (ORs ranging from 0.1-0.9).

Table 4: Odds ratios of COPD vs lung cancer patients (reference) stratified by place of death: binary multivariate logistic regression models of death certificates data from 14 countries during 2008(N=562,151)

Country	**Home (vs all others) N=562,151**	**Home (vs Hospital) N=447,537**	**Hospital (vs all others) N=562,151**	**Nursing home (vs Hospital) N=345,463**	**PC institutions (vs others) N=41,092**
	OR (95% CI)	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
BE	**0.8(0.77-0.93)**	0.97 (0.9-1.07)	**0.8(0.71-0.84)**	**2.4 (2.09-2.73)**	/*
FR	**1.7(1.58-1.80)**	**1.8(1.71-1.94)**	**0.5 (0.52-0.58)**	**2.1 (1.89-2.33)**	/*
IT	**0.9 (0.87-0.94)**	**0.9 (0.88-0.96)**	**1.0 (1.00-1.08)**	**1.6 (1.42-1.72)**	/*
ES	**0.8(0.75-0.96)**	0.9(0.79-1.01)	1.0 (0.91-1.17)	**1.9 (1.34-2.67)**	/*
NL	**0.4(0.33-0.39)**	**0.3(0.27-0.33)**	**2.4(2.23-2.59)**	**0.9 (0.81-0.98)**	/*
CZ	1.1(0.96-1.26)	1.1(0.92-1.22)	1.1 (0.95-1.19)	**0.8 (0.68-0.92)**	/*
HU	/*	/*	0.9(0.85-1.01)	/*	/*
ENG	**0.7 (0.68-0.74)**	**0.5 (0.50-0.54)**	**2.5 (2.42-2.60)**	**0.6 (0.55-0.62)**	**0.1 (0.07-0.11)**
WAL	**0.6(0.49-0.68)**	**0.5 (0.43-0.61)**	**2.1(1.80 -2.40)**	1.1 (0.82-1.48)	**0.1 (0.01-0.20)**
NZ	**0.5(0.43-0.60)**	**0.3(0.27-0.40)**	**2.7 (2.28-3.10)**	**0.6 (0.51-0.75)**	**0.1 (0.05-0.14)**
US	**0.6(0.56-0.58)**	**0.5(0.47-0.49)**	**1.8(1.81-1.87)**	**0.8 (0.77-0.81)**	**0.9 (0.87-0.98)**
CA	**0.7(0.63-0.76)**	**0.7(0.67-0.80)**	0.98 (0.92-1.05)	**1.5 (1.40-1.66)**	/*
MX	**0.8(0.72-0.82)**	**0.8(0.72-0.81)**	**1.3 (1.21-1.37)**	/*	/*
KR	**1.5 (1.43-1.68)**	**1.6(1.43-1.69)**	**0.7 (0.60-0.71)**	1.2 (0.90-1.57)	/*

Bold denotes a significant difference between lung cancer and COPD patients.

*Category did not exist on death certificate

Variables included in model: age, sex, marital status (except NZ, where marital status was not available)

Discussion

Our study found that patients dying from COPD were more likely to die in hospital than at home (or in a hospice) than those dying from lung cancer, even when consideringcharacteristics in terms of age, gender and marital status. France and Korea were the exceptions.

Few population-based studies compare the outcomes of EOL care across countries globally, specifically about place of death. This study captures variations in place of death of people dying from lung cancer and COPD, two major causes of death, across different health care systems. Nonetheless, there are limitations in our study design because the use of robust population level data reflects a loss of information at the individual level. For instance, the death certificate does not provide information on important aspects of the EOL process such as preferences of place of death, choices of place of care and course of decision-making levels i.e. patients, family, health care professionals and/or healthcare policy makers. The use of a single underlying cause of death might underestimate the number of people dying with rather than from COPD[25] thus having a similar dying trajectory but being recorded as dying from other underlying diseases or multi-morbidities[26] An additional limitation is that statistical interpretations about country differences in place of death are subject to country-specific choices regarding the organisation and use of health care settings. Nevertheless, the statistical patterns about place of death do reflect important differences in the health care organisational choices countries have made regarding end-of-life care in lung cancer versus COPD and inspire further qualitative studies to provide us with a deeper understanding of observed patterns and the cross-national differences underlying those patterns.

Previous studies have found on average 75% of respondents prefer to die at home, among the terminally ill and the general public.[19] However, for the majority of the countries in our study, COPD decedents were substantially more likely than lung cancer decedents to die in hospital even after controlling for confounders; this may suggest a lack of options for COPD patients to die at home in most countries.

This is likely to be due to a combination of factors, including a long-standing cancer focus in palliative care services in many countries and the more uncertain disease trajectory and prognosis of COPD.COPD is an illness characterised by unpredictable exacerbations[26] and the number of acute exacerbations has been shown to be the best way of estimating the end-of-life phase in COPD.[27] Perhaps these exacerbations could be windows of opportunity for end-of-life discussions about preferences for place of terminal care. A number of issues have been identified and if tackled, might ameliorate the quality of death of COPD patients. A recent qualitative study shows that many end-stage COPD patients suffer from fluctuating episodes of breathlessness[28] and this complicates healthcare professionals' judgement of the ideal time to move from a curative approach to the start of palliative care. An additional barrier, as indicated by Beernaert[8] and Pinnock,[6] is that some COPD sufferers and their families do not see COPD as a life-threatening disease but as an inevitable decline of old age and therefore do not discuss palliative care options with their health care providers. Removing some of the barriers to timely initiation of a palliative care approach (including the making of advance care plans and establishing contact with end-stage care services) could possibly result in a reduction of hospitalisations of advanced COPD patients at the end of life and increase the opportunity to honour their preferences for place of death. Previous experiences have indicated that working with a co-ordinator for care planning may also be a way to improve EOL care for persons diagnosed with COPD.[29]

The percentages of COPD patients dying in nursing homes are substantially higher compared with lung cancer. This finding may reflect their older age and their disability or loss of functional performance in home management.[30] This functional performance was found to be higher in older females,[30] often leading to admission to a nursing home, and might explain why female COPD patients are more likely to die in a nursing home.

However, the role of the nursing home as a place of EOL care and death is not well understood. Previous studies highlighted barriers to performing EOL care in long-term care settings because of a lack of communication and failure to initiate a palliative trajectory in good time.[31-32] This is an important consideration as hospital deaths can potentially be avoided if location preferences are known through optimal advance care planning. Improving the quality of EOL care in nursing homes, including policies to reduce hospitalizations at the end of life, thus seems to be an important policy priority for COPD sufferers as opposed to simply focusing all efforts on enabling them to die at home.

Furthermore, social disadvantage is common in COPD (certainly in the UK) and is associated with a reduced likelihood of achieving preferences for place of death.[33] For instance, hospital admissions due to COPD are higher in lower socio-economic groups,[34] and area deprivation is associated with a longer hospital stay for COPD.[35]

While the differences in terms of place of death between COPD and lung cancer decedents were large in most countries, they were very small in Italy, Spain, and Mexico. In these three countries, a relatively large proportion of both COPD and lung cancer patients died at home. This is probably due to a culture of family (or community) care-giving rather than the result of specific public health policies to facilitate home deaths. In spite of the observed general patterns of differences in place of death across the two groups of patients in each country, there were some additional cross-border differences. Home deaths were generally high for all decedents in Mexico (55.4-57.1%) and Italy (41.6-44.2%), whereas hospital deaths were high in France (60.2-77.4%) and South Korea (78.9-86.5%). The trend in France might be a result of the continued dominance of hospital-centred care and the insufficient training of oncologists and pulmonologists in palliative care. This might be understood in the light of different cultures of caregiving as well as of the surrounding medical culture. In those countries where hospice was recorded as a category, lung cancer patients were found to die there in far greater numbers than COPD patients. However, this was not the case in the US and it might reflect how countries differ in placing the long-term focus of their palliative care services on cancer as opposed to other illnesses eligible for palliative care.[5] More wider structural country specific factors, such as insurance and reimbursement systems and regulations might, however, also play a role.

Conclusions and Implications

Our study found an almost uniform disadvantage across the countries under study for COPD sufferers as compared with lung cancer sufferers in terms of being able to die at home or outside a hospital. At the same time, we found considerable variation between countries in the extent of that disadvantage as well as in the overall proportions dying in those places. These findings suggest strong intra- and cross-country differences in the organisation of EOL care for COPD and lung cancer sufferers, along with different attitudes towards the appropriateness of a palliative care approach and care planning in COPD versus lung cancer. In order to create equal opportunities for access to palliative care for COPD sufferers, improvements may particularly need to be made in improving the ability to predictthe disease trajectory of COPD, create a ‘palliative care’ culture for COPD and initiate early discussions about EOL care preferences with COPD sufferers and their families. The fluctuating trajectory of COPD might call for even more awareness among medical staff of the need to take the initiative to talk about EOL wishes (because patients and families might not realise the severity of the condition). More clinical staff could be educated to provide appropriate EOL care during the final stages of COPD and thus avoid unplanned EOL hospitalizations and hospital death. Family education could also prove critical, so that family members are able to care for people who live at home with COPD who may wish to remain at home until death.

References

1 Lozano R, Naghavi M, Foreman K et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012;380:2095–2128.

2 White P, White S, Edmonds P et al. Palliative care or end-of-life care in advanced chronic obstructive pulmonary disease. *Br J Gen Pract*2011;61:e362–370.

3 Gore JM, Brophy CJ, Greenstone MA. How well do we care for patients with end stage chronic obstructive pulmonary disease (COPD)? A comparison of palliative care and quality of life in COPD and lung cancer. *Thorax* 2000;55:1000–1006.

4 Edmonds P, Karlsen S, Khan S et al. A comparison of the palliative care needs of patients dying from chronic respiratory diseases and lung cancer. *Palliat Med* 2001;15:287–295

5 Addington-Hall J and Hunt K. ‘Non-cancer patients as an under-served group’ in Cohen J and Deliens L (eds) *A Public Health Perspective on End of Life Care.*Oxford University Press, New York, 2012:151–167.

6 PinnockH, Kendall M, Murray SA et al. Living and Dying with severe chronic obstructive pulmonary disease: multi-perspective longitudinal qualitative study. *BMJ* 2011.342:d142

7 Carlucci A, Guerrieri A, Nava S. Palliative care in COPD patients? Is it only an end-of-life issue? *EurRespir Rev* 2012;21:347–354.

8 Beernaert K, Cohen J, Deliens L et al. Referral to palliative care in COPD and other chronic diseases: A population-based study. *Respir Med* 2013; 107:1731–1739.

9 Strang S, Ekberg-Jansson A, Strang P et al. Palliative care in COPD-web survey in Sweden highlights the current situation for a vulnerable group of patients. *Ups J Med Sci* 2013;118:181–186.

10 Classens MT, Lynn J, Zhong Z et al. Dying with lung cancer or chronic obstructive pulmonary disease: insights from SUPPORT. Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments. *J Am GeriatrSoc*2000;48:S146–S153.

11 Au DH, Udris EM, Fihn SD et al. Differences in health care utilization at the end of life among patients with chronic obstructive pulmonary disease and patients with lung cancer. *Arch Intern Med* 2006;166:326–331.

12 Levy MH, Adolph MD, Back A et al. Palliative care. *J Natl Comp CancNetw*2012;10:1284–1309.

13 Seamark DA, Seamark CJ, Halpin DM. Palliative care in chronic obstructive pulmonary disease: a review for clinicians. *J R Soc Med* 2007;100:225–233.

14 Philip J, Lowe A, Gold M et al. Palliative care for patients with chronic obstructive pulmonary disease: exploring the landscape. *Internal Medicine Journal* 2012;42:1053–1057.

15 Janssen DJ, Spruit MA, Alsemgeest TP et al. A patient-centred interdisciplinary palliative care programme for end-stage chronic respiratory diseases. *Int J PalliatNurs* 2010;16:189–194.

16 Curtis JR. Palliative and end-of-life care for patients with severe COPD. *EurRespir J* 2008;32:796–803.

17 Curtis JR, Wenrich MD, Carline JD et al. Patients’ Perspectives on Physician Skill in End-of-Life Care. *Chest* 2002;122:356–362.

18 Au DH, Udris EM, Engelberg RA et al. A randomized trial to improve communication about end-of-life care among patients with COPD. *Chest* 2012;141:726–735.

19 Gomes B, Calanzani N, Gysels Met al. Heterogeneity and changes in preferences for dying at home: a systematic review. *BMC Palliat Care* 2013;12:7

20 Bilingham MJ and Bilingham SJ. Congruence between preferred and actual place of death according to the presence of malignant or non-maliganant disease: a systematic review and meta-analysis. *BMJ Support Palliat Care* 2013;3:144–154.

21 Quality of care at the end of life varies with cause and place of death. http://www.ons.gov.uk/ons/rel/subnational-health1/national-bereavement-survey--voices-/2012/sty-care-at-the-end-of-life.html (Accessed 8 Nov 2013)

22 Teno JM, Gozalo PL, Bynum JPE et al. Change in End-of-Life Care for Medicare Beneficiaries: site of death, place of care, and health care transitions in 2000, 2005, and 2009. *JAMA* 2013;309:470–477.

23 Cohen J, Houttekier D, Onwuteaka-Philipsen B et al. Which patients with cancer die at home? A study of six European countries using death certificate data. *J ClinOncol* 2010;28:2267-2273.

24 International Statistical Classification of Diseases and Related Health Problems 10th Revision http://apps.who.int/classifications/icd10/browse/2010/en (accessed 15 Aug 2013)

25 C Fuhrman, E Jougla, J Nicolau et al.Deaths from chronic obstructive pulmonary disease in France, 1979–2002: a multiple cause analysis, *Thorax* 2006;61:930–934.

26 Calverley PMA, Anderson, JAet al. Salmeterol and fluticasone propionate and survival in chronic obstructive pulmonary disease. *New Engl J Med*, 2007;356:775–89.

27 Gruffudd-Jones and Loveridge. The 2010 NICE COPD guidelines: how do they compare with the GOLD guidelines? *Primary Care Respiratory Journal* 2011;**20**: 199–204.

28 Simon ST, Higginson IJ, Benalia H et al. Episodes of breathlessness: types and patterns- a qualitative study exploring experiences of patients with advanced diseases. *Palliat Med* 2013; **27:** 524-532.

29 Epiphaniou E, Shipman C, Harding R, et al. Coordination of end-of-life care for patients with lung cancer and those with advanced COPD: are there transferable lessons? A longitudinal qualitative study. *Prim Care Respir* J 2014. doi: 10.4104/pcrj.2014.00004.

30 Skumlien S, Haave E, Morland L.Gender differences in the performance of activities of daily living among patients with chronic obstructive pulmonary disease. *ChronRespir Dis* 2006;3:141–148.

31 Habraken JM, van der Wal WM, Tier Riet G et al. Health-related quality of life and functional status in end-stage COPD: a longitudinal study. *EurRespir J* 2011;37:280–288.

32 Travis SS, Bernard M, Dixon S et al. Obstacles to Palliation and End-of-Life Care in a Long-Term Care Facility. *Gerontologist* 2002;42:342–349.

33 Deprivation and death: Variation in place and cause of death. National end of life care Intelligence Network. February 2012.

34 Prescott E, Vestbo J. Socioeconomic status and chronic obstructive pulmonary disease. *Thorax* 1999;54:737–741.

35 Agboado, G. Peters, J. Donkin, L. Factors influencing the length of stay among patients resident in Blackpool admitted with COPD: a cross-sectional study. *BMJ Open* 2012;2:5.

Chapter 7 **Quality of Life of Advanced Lung Cancer Patients: a longitudinal study**

“ The meaning of life is that it stops ”
--- Franz Kafka

Title: Quality of life of patients with advanced lung cancer. A longitudinal study in Flanders, Belgium

Winne Ko, MA[1], Koen Pardon, PhD[1], Jan L. Bernheim, MD,PhD[1], Luc Deliens, PhD[1,3], Lieve Van den Block, PhD[1,2]on behalf of EURO IMPACT*

1 End-of-Life Care Research Group, Vrije Universiteit Brussel (VUB) and Ghent University, Brussels, Belgium
2 Department of Family Medicine and Chronic Care, Vrije Universiteit Brussel (VUB), Brussels, Belgium
3 Department of Medical Oncology, Ghent University, Belgium

Email address:
WK: winne.ko@vub.ac.be
KP: koen.pardon@vub.ac.be
LVB: lvdblock@vub.ac.be
JLB: Jan.Bernheim@vub.ac.be
LD: Luc.Deliens@vub.ac.be

*Collaborators EURO IMPACT**

Van den Block Lieve, De Groote Zeger, Brearley Sarah, Caraceni Augusto, Cohen Joachim, Francke Anneke, Harding Richard, Higginson Irene, KaasaStein, Linden Karen, Miccinesi Guido, Onwuteaka-Philipsen Bregje, Pardon Koen, Pasman Roeline, Pautex Sophie, Payne Sheila, Deliens Luc

Abstract

Introduction

Advanced lung cancer is a condition with a median life expectancy of 1 year. However, little is known about the quality of life (QOL)– including symptomatology and functioning– of advanced lung cancer patients nor about the change of QOL over time, e.g. due to the difficulty of performing studies in a vulnerable population with limited life expectancy.

Methods

We performed a longitudinal study of a consecutive sample of newly diagnosed stage IIIb/IV non-small-cell lung cancer patients in Flanders, Belgium, between 2007 and 2011. Patients were recruited by physicians in 13 hospitals and interviewed every 2 months until the fourth and every 4 months until the sixth interview with the EORTC QLC C15-PAL.

Results

Sixty-seven patients were interviewed three times. The mean score on the overall QOL-scale of the EORTC was 60, on the physical functioning scale 81 and on the emotional functioning scale 80 (scores from 0 to 100, 100 is very good). Looking at the EORTC symptom scales, the most prevalent symptoms were: fatigue, appetite loss, pain and dyspnea. The mean scores on all scales did not significantly change over time at 2 and 4 months. There were however significant changes over time at an individual level: e.g. between baseline and 2 months, 40% to 83% of patients, depending on the scale, changed at least 11 points towards more or less quality of life.

Conclusion

Newly diagnosed advanced lung cancer patients in Flanders have a significantly diminished QOL and a high symptom burden. This indicates the need of early integration of palliative care – as an approach that addresses QOL via symptom management - in standard oncological care. Since QOL significantly changes over time, caregivers should measure it regularly and adapt their care accordingly.

Introduction

Lung cancer is one of most frequently occurring malignancy types[1] in many developed countries and its incidence is expected to rise among females and in developing countries due to the evolution of the smoking epidemic.[2] Prognosis of lung cancer is generally poor and patients diagnosed with non-small cell (NSC) lung cancer in stage IIIb or stage IV lung cancer have a 5-year survival rate of only 5% and 1% respectively.[3] For patients with NSC lung cancer Temel and colleagues have shown that they can benefit from early palliative care[4].

For patients with a limited life expectancy, maintaining their quality of life (QoL) might be at least as relevant a care goal than life-prolongation.[4] It has been said that quality of life "can only be described and measured in individual terms, and depends on present lifestyles, past experiences, hopes for the future, dreams and ambitions".[5] If QoL is understood cognitively as life satisfaction "a good quality of life can be said to be present when the hopes of an individual are matched and fulfilled by experience".[5] However, next to the cognitive dimension of life satisfaction, there is also the emotional dimension of wellbeing[6.]. Measuring patients' quality of life can be methodologically challenging, because of the multidimensional nature of the concept itself [6] and the difficulties in distinguishing statistical and clinical significances.[7] Therefore global (uni-scale) assessment has been proposed as an alternative to multi-item scales.[8] Understanding the evolution of a patient's QoL scores would bring the added-value of the overall well-being of the patient along the disease trajectory.

Longitudinal data have been scarce within palliative care research due to the ethical concerns on harming the patients as well as the high rate of dropping-out of patients due to their deteriorating condition.[9] Various constructs[10-13] have been developed to measure the overall QoL among patients with advanced cancer, one of them is the European Organisation of Research and Treatment of Cancer (EORTC). EORTC QLQ-C30.[13] Yet, adaptations were desirable since they might be considered to be too long and burdensome for a palliative care population, and this led to the development of the EORTC QLQ-C15-PAL. In spite of all these challenges, availability of this information is important for clinicians to know how things change over time in order to provide guidance for improving treatment.

A longitudinal study in measuring the QoL of patients diagnosed of advanced NSC lung cancer was carried out in Flanders, Belgium from 2007-2010.The EORTC QLQ-C15-PAL (module on assessing the QoL of palliative care patients) questionnaire[14-15] was administered. Also the Anamnestic Comparative Self-Assessment (ACSA) was applied.[8] The results comforted the EORTC QLQ-C15-PAL data and are not shown for brevity's sake. The interviewers felt the ACSA procedure was well received and contributed to the quality of report between investigator and responder.

The two research questions are:

1) What is the quality of life of advanced lung cancer patients?
2) How does the quality of life change in time among advanced lung cancer patients?

Methods

Data for analyses was collected for the End-Of-Life Information and Communication (EOLIC) study, which was a longitudinal study on information and participation preferences of patients with advanced lung cancer. The study was conducted from 2007 to 2010. This is a multi-centre study across Flanders, the Dutch-speaking part of Belgium.

Patients diagnosed with advanced NSC lung cancer (stage IIIb or stage IV) were invited by their oncologists to participate in the study. Informed consent was obtained from patients and patients completed the first interview at inclusion (shortly after diagnosis-T1). Subsequently, follow-up interviews were held at two (T2) and four months (T3). Due to the small numbers in the fourth, fifth and sixth interview, only patients completing the first three interviews were included into the analyses.

Instrument: the EORTC QLQ-C15-PAL questionnaire

The EORTC QLQ-C15-PAL questionnaire is a shortened version derived from the EORTC QLQ-C30 questionnaire on measuring the QOL of cancer patients. It was developed to adapt to cancer patients in palliative care who might be too sick to complete the standard C30 version. Items have been tested and merged as necessary, resulting in a 15-item questionnaire. The last question is on 'global wellbeing': a one item asking for the subjective overall well-being of patients in the previous week on a 1-7(very poor to excellent) scale.

Minimal important differences (MIDs)

Minimal important differences (MIDs) were used as a threshold for identifying clinically relevant changes among patients' scores on each item in the questionnaire. Analyses on changes were based on the findings of Bedard and colleagues.[16] They identified the thresholds of changes in symptoms and functioning scales that constitute a meaningful (clinically significant) change. We used these threshold changes to estimate the number and proportions of patients that improve, worsen or remain stable on each item, comparing shortly after diagnosis vs 2 months after diagnosis, 2 months after diagnosis vs 4 months after diagnosis and shortly after diagnosis vs 4 months after diagnosis.

Ethical approval

Patients offered written informed consent and were within two weeks of inclusion contacted by an interviewer to schedule an interview. After each interview, the patients were asked for their agreement to take part in another interview. Interviews took place at the patient's home or in another setting where the patient felt comfortable.

Data analysis

Descriptive statistics were used to show the global and dimensional quality of life scores of patients at different time points. All analyses were completed using SPSS 22.0. (IBM Corporation)

Results

A total of 128 patients were included in the study shortly after diagnosis. 97 and 67 patients completed the second and the third interview respectively at two months, and four months after initial diagnosis (Table 1).

Table 1: Inclusion of patients recently diagnosed of advanced lung cancer (Stage IIIb or Stage IV non-small-cell lung cancer)

Time of interview (months from diagnosis)	No. of patients
Shortly after recent diagnosis of advanced cancer	128
31 patients dropped out	
Two months after diagnosis	97
30 patients dropped out	
Four months after diagnosis	67

Patients' characteristics (Table 2)

Table 2 shows the characteristics of the patients at three time-points. The majority of the group were male (79-80%). The distribution of age was similar across the three time points. About 60% of the patients completed secondary education. Most patients were living with someone (75-76%) and had a partner (77-79%). 94-96% of patients indicated that they were religious. Slightly more than half of the patients (54-55%) received treatments in a general hospital, the others in a university hospital. With regard to clinical characteristics, the number of patients who were in chemotherapy or had just completed a cycle of chemotherapy decreased over time, from 89% shortly after diagnosis to 15% at four months after diagnosis. For radiotherapy, the number of patients in treatment fluctuated over time, with 68% shortly after diagnosis, 39% at two months after diagnosis and 42% at four months after diagnosis.

Table 2: Characteristics of Patients

[*] does not add to 100 due to round off
[†]missing values-religiosity: n=31
[a]No decision was made: Chemotherapy shortly after diagnosis: n=14, Chemotherapy two months after diagnosis: n=10, Chemotherapy four months after diagnosis: n=21, Radiotherapy shortly after diagnosis: n=72, Radiotherapy two months after diagnosis: n=64, Radiotherapy four months after diagnosis: n=43

Social-demographics		Shortly after diagnosis (N=128) N (%)	Two months after diagnosis (N=97) N (%)	Four months after diagnosis (N=67) N (%)
Sex	Male	102 (80)	78 (80)	53 (79)
	Female	26 (20)	19 (20)	14 (21)
Age	41-60	45 (35)	36 (37)	22 (33)
	61-70	44 (34)	32 (33)	26 (39)
	71 or above	39 (30)	29 (30)	19 (28)
Education[*]	Primary	24 (18)	18 (19)	12 (18)
	Lower secondary	42 (33)	27 (28)	17 (25)
	Higher secondary	40 (31)	34 (35)	25 (37)
	University/ higher education	22 (17)	18 (19)	13 (19)
Living status	Alone	31 (24)	24 (25)	17 (25)
	With someone	97 (76)	73 (75)	50 (75)
Presence of Partner	No	30 (23)	22 (23)	14 (21)
	Yes	98 (77)	75 (77)	53 (79)
Religiosity[†]	Not religious	6 (6)	3 (4)	2 (4)
	Religious	91 (94)	71 (96)	47 (96)
Hospital type	General hospital	69 (54)	52 (54)	37 (55)
	University hospital	59 (46)	45 (47)	30 (45)
Clinical				
Chemotherapy[a]	Start of a cycle	101 (89)	21 (24)	7 (15)
	Prolongation	10(9)	29 (33)	22 (48)
	No start/stopped	3 (3)	37 (43)	17 (37)
Radiotherapy[a]	Start	38 (68)	13 (39)	10 (42)
	Prolong	0 (0)	17 (52)	1 (4)
	Didn’t start/stop	18 (32)	3 (9)	13 (54)

Quality of life, Physical & Emotional Functioning and Symptoms Score

Tables 3a to 3c show the scores of interviewed patients on quality of life, physical and emotional functioning as well as various symptoms at the three time-points on a *group* level (mean scores). *Table 3a* shows the mean scores of the patients who completed the first interview (n=128), the mean scores of the patients who completed the second interview (n=97) and the mean scores of the patients who completed the third interview (n=67).

Table 3b compares patients who completed the first and second interview (n=97). *Table 3c and 3d* compare patients who completed three interviews (n=67), with *3c* presenting the scores of patients at the second and the third interview. *Table 3d* shows the comparisons between the first and third interview. These comparisons describe how the same group of patients (those who are alive at least 2 and at least 4 months after diagnosis of advanced lung cancer) evolve over time in quality of life.

No significant differences were found on the mean scores of any items in the EORTC QLQ-PAL 15 module between shortly after diagnosis (t1), two months after diagnosis (t2) and four months after diagnosis (t3). The mean global quality of life scores were 54.8, 50.9 and 57.0 respectively for patients who were alive at t1, t2 and t3 (scores on a total of 100 and the three time points with different number of patients) (Table 3a). Physical functioning scores were 73.7(t1), 71.0(t2) and 76.8(t3). Emotional functioning scores were74.6, 77.7 and 82.6. Regarding the various symptoms, fatigue was the most burdensome symptom at the three time points of measurement. Patients rated their fatigue at 43.8(t1), 44.2(t2) and 38.3(t3). The aggregate pain scores did not change. Insomnia was improved initially (35.2[t1],32.6 [t2]) and went up again (33.4)[t3]. Appetite loss (38.5[t1]>32.3[t2]>22.9[t3]), nausea (20.6[t1]>18.9[t2]>12.4[t3]) and constipation (24.5[t1]>20.6[t2]>14.4[t3]) were consistently improving across the three time points and the appetite loss score was statistically significant at $p<0.05$. Therefore at T2, most scores were seemed consistently slightly worse.

The comparisons of the various scores between shortly after diagnosis and two months after diagnosis were shown in *Table 3b (two time points with the same number of patients)*. The global quality of life score (58.6[t1]>50.9[t2]) and physical functioning (76.1[t1]>71.0[t2]) significantly deteriorated during this period. On the other hand, insomnia (28.5[t1]>21.6[t2]) was a symptom that was rated as significantly improving in this period. Between two months and four months after diagnosis, none of the items was statistically different (*Table 3c*). When comparing patients shortly after diagnosis and 4 months after diagnosis, appetite loss was a symptom that was rated as significantly improved. (34.8[t1]>22.9[t3]) (*Table 3d*)

Table 3a: Quality of life scores of advanced lung cancer patients shortly after diagnosis, two months after diagnosis and four months after diagnosis

Global Quality of Life Score[1]	**Shortly after diagnosis** (N=128)	**Two months after diagnosis**(N=97)	**Four months after diagnosis** (N=67)
Mean score (S.D.)	54.8 (23.0)	50.9 (23.5)	57.0 (21.9)
	p=0.196[‡]		
Physical functioning[1]			
Mean score (S.D.)	73.7 (24.3)	71.0 (27.3)	76.8 (24.2)
	p=0.422		
Emotional functioning[1]			
Mean score	74.6 (28.8)	77.7 (29.2)	82.6 (23.1)
	p=0.163		
Dyspnoea[2]			
Mean score (S.D.)	32.6 (33.1)	35.4 (35.3)	33.3 (33.3)
	p=0.825		
Pain[2]			
Mean score (S.D.)	30.3 (31.4)	29.0 (31.3)	27.1 (32.4)
	p=0.795		
Insomnia[2]			
Mean score (S.D.)	29.9 (35.2)	21.6 (32.6)	22.9 (33.4)
	p=0.137		
Appetite loss[2]			
Mean score (S.D.)	38.5 (38.4)	32.3 (36.1)	22.9 (32.9)
	p=0.014		
Nausea[2]			
Mean score (S.D.)	20.6 (29.9)	18.9 (27.2)	12.4 (23.1)
	p=0.146		
Constipation[2]			
Mean score (S.D.)	24.5 (34.1)	20.6 (31.0)	14.4 (24.8)
	p=0.197		
Fatigue[2]			
Mean score (S.D.)	43.8 (28.1)	44.2 (30.5)	38.3 (31.8)
		p=0.615	

[*] does not add up to 100 due to round up

[‡] ANOVA with repeated measures test used among the 67 patients present at all three time-points

Notes: all scales range from 0-100

[1] From 0-100, higher score means better quality of life

[2] From 0-100, higher score means more severe symptom burden

Table 3b: Quality of life scores of advanced lung cancer patients shortly after diagnosis and two months after diagnosis (N=97)

Global Quality of Life Score[1]	**Shortly after diagnosis**	**Two months after diagnosis**
Mean score (S.D.)	58.6 (21.5)	50.9 (23.5)
	p=0.002	
Physical functioning[1]		
Mean score (S.D.)	76.1 (21.7)	71.0 (27.3)
	p=0.031	
Emotional functioning[1]		
Mean score	74.7 (27.4)	77.7 (29.2)
	p=0.315	
Dyspnoea[2]		
Mean score (S.D.)	29.9 (32.1)	35.4 (35.3)
	p=0.077	
Pain[2]		
Mean score (S.D.)	31.3 (31.6)	29.0 (31.3)
	p=0.519	
Insomnia[2]		
Mean score (S.D.)	28.5 (34.7)	21.6 (32.6)
	p=0.045	
Appetite loss[2]		
Mean score (S.D.)	36.8 (38.0)	32.3 (36.1)
	p=0.339	
Nausea[2]		
Mean score (S.D.)	19.6 (28.8)	18.9 (27.2)
	p=0.779	
Constipation[2]		
Mean score (S.D.)	23.7 (34.3)	20.6 (31.0)
	p=0.431	
Fatigue[2]		
Mean score (S.D.)	42.1 (27.4)	44.2 (30.5)
	p=0.500	

Table 3c: Quality of life scores of patients two months and four months after diagnosis of advanced lung cancer (N=67)

Global Quality of Life Score[1]	**Two months after diagnosis**	**Four months after diagnosis**
Mean score (S.D.)	55.0 (23.8)	57.0 (21.9)
	p=0.474	
Physical functioning[1]		
Mean score (S.D.)	77.8 (24.8)	76.8 (24.2)
	p=0.642	
Emotional functioning[1]		
Mean score	81.1 (29.4)	82.6 (23.1)
	p=0.621	
Dyspnoea[2]		
Mean score (S.D.)	32.3 (34.3)	33.3 (33.3)
	p=0.704	
Pain[2]		
Mean score (S.D.)	22.6 (29.5)	27.1 (32.4)
	p=0.266	
Insomnia[2]		
Mean score (S.D.)	19.9 (29.8)	22.9 (33.4)
	p=0.282	
Appetite loss[2]		
Mean score (S.D.)	25.9 (33.7)	22.9 (32.9)
	p=0.457	
Nausea[2]		
Mean score (S.D.)	17.9 (25.5)	12.4 (23.1)
	p=0.187	
Constipation[2]		
Mean score (S.D.)	13.4 (25.9)	14.4 (24.8)
	p=0.896	
Fatigue[2]		
Mean score (S.D.)	41.3 (30.8)	38.3 (31.8)
	p=0.420	

Table 3d: Quality of life scores of advanced lung cancer survivors shortly after diagnosis and four months after diagnosis (N=67)

Global Quality of Life Score[1]	shortly after diagnosis	Four months after diagnosis
Mean score (S.D.)	60.0 (21.7)	57.0 (21.9)
	p=0.375	
Physical functioning[1]		
Mean score (S.D.)	81.3 (17.2)	76.8 (24.2)
	p=0.131	
Emotional functioning[1]		
Mean score	77.9 (23.3)	82.6 (23.1)
	p=0.150	
Dyspnoea[2]		
Mean score (S.D.)	26.9 (32.9)	33.3 (33.3)
	p=0.123	
Pain[2]		
Mean score (S.D.)	28.9 (31.5)	27.1 (32.4)
	p=0.722	
Insomnia[2]		
Mean score (S.D.)	24.9 (34.0)	22.9 (33.4)
	p=0.578	
Appetite loss[2]		
Mean score (S.D.)	34.8 (37.8)	22.9 (32.9)
	p=0.041	
Nausea[2]		
Mean score (S.D.)	19.9 (27.9)	12.4 (23.1)
	p=0.066	
Constipation[2]		
Mean score (S.D.)	20.4 (30.7)	14.4 (24.8)
	p=0.165	
Fatigue[2]		
Mean score (S.D.)	37.8 (26.8)	38.3 (31.8)
	p=0.950	

Minimal Important Differences (MIDs) of changes in scores

MIDs of two functioning scales and seven symptoms are presented in Table 4. These were scores of surviving individual changes over time. A lot of patients had changes (improve or worsen) over the three time points. From 16.5% to 37.1% of patients between T1 and T2 had changes. The corresponding figures were 14.9% to 26.9% between T2 and T3, and 16.4% to 32.8% between T1 and T3.

Between T1 and T2, emotional functioning was the most improved (N=36, 37.1% of patients improved) and dyspnoea the most worsened (30, 30.9% of patients worsened) measurement. Little changes (63, 64.9% of patients did not change) were found in pain among the patients in this period. Fatigue (16,16.5%) was the least improved symptom.

Between T2 and T3, the majority of patients did not experience a minimal important change in fatigue (43,64.2%) and constipation (44,65.7%), while fatigue was also the symptom with the least patients ratings being worsened(10, 14.9%). 26.9% of patients reported their nausea being improved in this period.

Finally, between T1 and T3, emotional functioning (27, 40.3%) and appetite loss (26, 38.8%) were the two aspects that were most frequently rated as improved. Physical functioning (38, 56.7%) and fatigue (44, 65.7%) showed the least changes. Emotional functioning (20, 29.9%) and dyspnoea (22, 32.8%) were the two scales that were most frequently rated as worsen.

Table 4: Changes in quality of life on an individual basis
Minimal important differences using the distribution-based method*

	N(%) of patients whose quality of life changed between T1 and T2 (N=97)			N(%) of patients whose quality of life changed between T2 and T3 (N=67)			N(%) of patients whose quality of life changed between T1 and T3 (N=67)		
SCALE (No of items)	**Improve**	**No change**	**Worsen**	**Improve**	**No change**	**Worsen**	**Improve**	**No change**	**Worsen**
EORTC QLQ C15-PAL scales									
Physical functioning	29 (29.9)	42 (43.3)	26 (26.8)	12 (17.9)	39 (58.2)	16 (23.9)	11 (16.4)	38 (56.7)	18 (26.9)
Emotional functioning	36 (37.1)	31 (32.0)	30 (30.9)	16 (23.9)	33 (49.3)	18 (26.9)	27 (40.3)	20 (29.9)	20 (29.9)
Dyspnoea	17 (17.5)	50 (51.5)	30 (30.9)	13 (19.4)	37 (55.2)	17 (25.4)	12 (19.9)	33 (49.3)	22 (32.8)
Insomnia	32 (33.0)	50 (51.5)	15 (15.5)	12 (17.9)	37 (55.2)	18 (26.9)	20 (29.9)	34 (50.7)	13 (19.4)
Fatigue	16 (16.5)	57 (58.8)	24 (24.7)	14 (20.9)	43 (64.2)	10 (14.9)	11 (16.4)	44 (65.7)	12 (17.9)
Nausea	22 (22.7)	53 (54.6)	22 (22.7)	18 (26.9)	38 (56.7)	11 (16.4)	19 (28.4)	34 (50.7)	14 (20.9)
Pain	18 (18.6)	63 (64.9)	16 (16.5)	12 (17.9)	37 (55.2)	18 (26.9)	17 (25.4)	34 (50.7)	16 (23.9)
Appetite loss	32 (33.0)	43 (44.3)	22 (22.7)	13 (19.4)	39 (58.2)	15 (22.4)	26 (38.8)	25 (37.3)	16 (23.9)
Constipation	23 (23.7)	54 (55.7)	20 (20.6)	11 (16.4)	44 (65.7)	12 (17.9)	20 (29.9)	35 (52.2)	12 (17.9)

*based on the minimal important differences (MIDs) estimated as in Bedard G et al, 2013.

Discussion

We followed 128 patients who were recently diagnosed of advanced lung cancer and measured their quality of life shortly after diagnosis, two months after diagnosis and four months after diagnosis. Over the interval of 4 months there were only small changes in physical functioning and global quality of life at the whole group level.

In contrast, when looking at the MIDs at an individual level, for the three scales (physical, emotional functioning and global quality of life) and several symptoms, such as insomnia, constipation and dypsnoea, 40% or more patients reported changes (improvements or worsening) between the three periods.

Group and individual differences

Comparing the results at the group level (Table 3a to d) and at an individual level (Table 4), a rather different picture emerges. At the group level, only a few scales showed significant changes (e.g. slightly deteriorating global quality of life and physical functioning over the first two months) and one might draw the conclusion that the overall quality of life of patients did not undergo major changes. However, it is essential to note that the attrition rate in the study was high and patients who were sicker were not retained in later interviews. Therefore the scores reflect only the conditions of surviving patients and thus the possible large changes in patients who dropped out were not shown. However, at an individual level, major changes appeared. For example, one-third of the patients rated dyspnoea as worsened between T1 and T2, and 40% rated their emotional well-being improved between T1 and T3. These results communicated a different message: many patients experienced fluctuations not only with regards to their symptoms, but also in their overall quality of life..

Strengths and limitations

This is one of the few studies that utilised patient-reported data over time in a population with a poor prognosis. Patients were enrolled as a cohort from diagnosis until death, so the data could reflect the evolution of their quality of life. However, there were also a number of limitations. First, the number of subjects in the study remained modest, so readers have to be cautious in generalising the findings to the whole population of lung cancer patients. Importantly, the drop-out rate in the study was high and the remaining patients along the study are likely to represent the special group of longer survivors, with slower deterioration and a lower symptom burden, so these patients' quality of life scores must have inflated the overall scores.

Deterioration shortly after diagnosis of advanced cancer

One worth-noting result was the significant deterioration for some patients in many aspects of well-being a mere two months after diagnosis. Close to one-third of patients reported a decline in their physical functioning, 25% of patients had worse fatigue and 17% had worsened pain. On the other hand, in the period T2 to T3, the proportions of 'no change' increased for all scales except pain. One possible explanation is that in the period T2 to T3 only responders to treatment or other longer-survivors because of less aggressive disease remained in the study. However, these results might also reflect some patients became more stable by adjusting to the disease and effect of treatments.

Quality of life

Our results illustrate the complexities of quality of life as a measurement tool as well as the interpretations of the different elements. Nonetheless, it remains an important and valid concept to understand performances of patients in various aspects. Medical professionals gain an overview of the patient's well-being through the overall quality of life scores, while the current results also point to the importance of fluctuation for particular items, such as fatigue and insomnia that have to be addressed.

Conclusion

Longitudinal cohort studies had a higher attrition rate because of progressive disease such as this one cannot reflect the deterioration that inevitably befalls many of the patients. In effect, measures at sequential time points represent cross-sections of different populations. Initially, it is a heterogeneous population including both patients who will soon drop out by progressive disease, but who at that time have not yet deteriorated and future responders to treatment and long survivors, At later times, one sees only the relatively invariable subpopulation of longer survivors and responders to treatment.

Newly diagnosed advanced lung cancer patients in Flanders have a significantly diminished QOL and a high symptom burden This indicates the need of early integration of palliative care – as an approach that addresses QOL via symptom management in standard oncological care. Since QOL significantly changes over time, caregivers should measure it regularly and adapt their care accordingly.

References

1. Malvezzi M, Beruccio P, Levi F, La Vecchia C and Negri E. European cancer mortality predictions for the year 2014. AnnOncol 2014. doi: 10.1093/annonc/mdu138

2. Bosetti C, Malvezzi M, Rosso T et al. Lung cancer mortality in European women: Trends and predictions. Lung Cancer 2012. 78(3): 171-178.

3.http://www.cancer.org/cancer/lungcancer-non-smallcell/detailedguide/non-small-cell-lung-cancer-survival-rates

4. Temel JS, Greer JA, Muzikansky A et al. Early Palliative Care for Patients with Metastatic Non-Small-Cell Lung Cancer. New Eng J Med 2010. 363(8): 733-742.

5. Bernheim, J.L.. How to get serious answers to the serious question: “How have you been?”: Subjective quality of life (QOL) as an individual experiential emergent construct. *Bioethics* 13(3–4): 272–287, 1999.

6. Aaronson NK. Methodological Issues in Assessing the Quality of Life of Cancer Patients. Cancer 1991.

7. McCabe C, Begley C, Collier S, McCann S. Methodological issues related to assessing and measuring quality of life in patients with cancer: implications for patient care. Eur J Cancer Care (Engl) 2008. 17(1): 56-64.

8. Theuns P, Hofmans J, Bernheim JL .Anamnestic Comparative Self Assessment (ACSA). In: Michalos AC (Ed.). Encyclopedia of Quality of Life and Well-Being Research. Springer, Dordrecht, Netherlands: Springer, pp 160-169; 2014. DOI.10.1007/978-94-007-0753-5, Springer, Heidelberg, New York

9. Sloan JA, Loprinzi CL, Kuross SA et al. Randomized comparison of four tools measuring overall quality of life in patients with advanced cancer. J ClinOncol 1998. 16(11): 3662-3673.

10. Cella DF, Tulsky DS, Gray G et al. The Functional Assessment of Cancer Therapy scale: development and validation of the general measure. J Clin Oncol 1993. 11(3): 570-579.

11. Aaronson NK, Ahmedzai S, Bergman B et al. The European Organization for Research and Treatment of Cancer QLQ-C30: A Quality-of-Life Instrument for Use in International Clinical Trials in Oncology. JNCI J Natl Cancer Inst 1993. 85(5): 365-376.

12. Goerling U, Stickel A. ‘Quality of Life in Oncology’ in Psycho-Oncology (ed) Goerling U. Springer Berlin Heidelberg 2014, pp. 137-152.

13. EORTC QLQ-C30. http://groups.eortc.be/qol/eortc-qlq-c30 (accessed 10 April 2014)

14. EORTC QLQ-C15-PAL. http://groups.eortc.be/qol/eortc-qlq-c15-pal (accessed 10 April 2014)

15. Groenvold M, Petersen MA, Aaronson NK et al. The development of the EORTC QLQ-C15 PA1L: a shortened questionnaire for cancer patients in palliative care. Eur J Cancer 2006. 42(1): 55-64.

16. Bedard G, Zeng L, Zhang L et al. Minimal important differences in the EORTC QLQ-C15-PAL to determine meaningful change in palliative advanced cancer patients. Asia Pac J Clin Oncol 2013. doi: 10.1111/ajco.12069. [Epub ahead of print]

Chapter 8 General discussion

“Each of us is merely a small instrument, all of us, after accomplishing our mission, will disappear”--- Mother Teresa

8.1 Strengths and limitations of methodology

European Sentinel GP Networks Monitoring End-of-Life Care (EURO SENTI-MELC)[1-3]

Strengths

1) **The use of a standardised questionnaire across countries in existing GPs Sentinel Networks**

EURO SENTI-MELC study is the only known study that measures GPs provision of palliative care across different countries using a standardised questionnaire and using existing Sentinel Networks of GPs for data collection. The advantage of this is the potential of accessing a broad population since most residents in the four countries have a regular GP. GPs often maintained long term relationships with their patients until death, and therefore GPs is a valid unit to provide reliable and macro-level information about palliative care services in those countries. GPs participating in the study were not selected based on their interests in palliative care, and thus the bias of selecting GPs with better knowledge or experiences concerning palliative care was minimised. While countries differ on their organisation of palliative care services, the design adopted in the present study shows the feasibility of such approach. Through comprehensive and extensive pilot testing, the research team finalised the questionnaire and included the key domains deemed important to understand the quantity (e.g. number of GPs contact and transitions in the last months and week) and the quality of palliative care (e.g. preferred and actual place of death, level of physical and psychological distress) in these countries. Data collected in different years (i.e. comparisons of results between 2005 and 2010 in Belgium) can be used for future cross-country comparisons in palliative care development.

2) **Generating representative population-based data**

The EURO SENTI MELC study is going into its tenth year of data collection. More countries are expected to be included in the study and the feasibility and reliability of the data showed the potential to generate representative population-based data in end-of-life care across the country. While some specific information (concerning care provided in hospitals or sudden and totally unexpected deaths for example) might be less well represented via these networks, they were able to report on many issues in end of life of patients dying non-suddenly. So the current study design has the potential to expand to other countries wishing to collect data in monitoring palliative care development.

3) Challenges of cross-country comparisons

Interpreting differences in results between countries is challenging due to the differences in healthcare organisation. For example, nursing homes is understood as a long term care institution managed by GPs in many countries, while in the Netherlands, once these patients moved into nursing homes, the care will be taken over by the nursing home physicians so GPs could no longer provided information on the care of the patients. Also, differences in health care institutions, like home, hospitals, hospices, nursing homes could mean something slightly different in different countries, i.e. how they’re associated with the perceived quality for the dying, and we can only try to understand the data within such a context. Furthermore, palliative care might be practiced very differently between as well as within countries, therefore when comparing the results, consultations with local experts might be useful. Nevertheless, challenges in interpreting differences considering that the health care systems are different, our study remains unique in its attempt to study the provision of primary palliative care across countries using a standardised framework.

Limitations

1) Unavoidable recall bias and interpretations in a retrospective study

One limitation of the study is memory bias because it is by default a limitation of a retrospective study. Even though GPs reported weekly immediately after a patient in their practice passed away, there might still be inaccuracies on items such as distress symptoms or details of communications, thus the validity of these items might be questioned. These weaknesses might create difficulties when interpreting the results, such as the higher missing frequencies on lack of appetite than pain might be due to a recall bias, the difficulty for GPs to assess or other reasons. Therefore, results from our study might be different if patient outcomes assessments were used.

2) **GPs may miss out information on hospitalised patients**

Items such as costs of palliative and burden of care were perceived judgement by GPs, and the accuracy could be affected by the frequency of timing of the GP visits. A few items in the EURO SENTI-MELC data like symptoms in the last week of life, costs and burden of care have more missing values, which might reflect that some patients were hospitalised and therefore GPs did not have access to these information. Though GPs were able to offer a range of information about palliative care received by their patients in the final months, their assessments of symptoms like physical and psychological distresses could also be less accurate as would have been assessed by others (specialists, nurses, family). So the interpretation of the data is from the perspective of the GP (eg the symptoms that GPs are aware of or the burden they perceive) and transferring the results directly into clinical practices should be cautious.

International Study of Place of Death (IPOD) [4-5]

Strength

1) **Population-based data gives a good overview of palliative care organisation**

From a public health point of view, place of death has been used as an indicator of the quality of palliative care because most patients prefer dying at home while most died in hospitals.[1,3] Many countries included place of death as one of the items on their death certificates and thus provided an opportunity to use a standardised category (home/hospital/nursing homes etc) to compare the patterns of place of death across the different countries. Moreover, death certificate data provide an overview of the pattern of place of death in these countries without the problem of sampling issue or biases from proxies. The data could inform us something about the final destination of a dying trajectory of the patient. The underlying cause of death also provides an alternative perspective of how people with different diseases die differently in the different countries.

Limitations

1) Limited information available on death certificates

One major shortcoming of utilising death certificate data for research is the limited amount of information available. This is likely due to the fact that death certificate was designed for administrative purposes and not for research, so it is kept short with only the most important variables. It is known from the literature that place of death is influenced by many factors, such as distance to hospitals, socio-economic status of the patient, availability of family caregivers, the underlying illnesses etc. However, death certificates often only contain a few variables, such as age, gender and cause(s) of death and therefore making it difficult to interpret these results fully. This is further complicated by the fact that the different categories on death certificates were affected by the different coding of care settings across countries. If a particular type of care institution is not available in certain countries, a comparison between the countries could not be made.

2) Accuracy of cause of death, underlying cause of death and co-morbidity issues

One concern of using death certificates for research is the validity and reliability of the certified cause of death. For diseases such as malignancies, a diagnosis is often clear and a physician could identify it as the underlying or direct cause of death relatively easy. However, for chronic conditions such as chronic obstructive pulmonary disease (COPD) or dementia where multiple morbidities can be present, filling in a single cause of death can be rather arbitrary, a family physician or a specialist might even disagree on the most direct cause of death. This means the types of research questions are limited by the nature of data.

End of Life Information and Communication (EOLIC)[6-7]

Strengths

1) The rarity of longitudinal data in palliative care research

Due to the vulnerability of the palliative care population (i.e. patients too unwell and feeling over-burdened), a lot of the literature rely on medical professionals or caregivers to report symptoms or well-being of the patients in the final months or weeks of life. The EOLIC study tries to overcome this by approaching patients who were recently diagnosed of advanced lung cancer and measured the changes of their quality of life over time. Therefore, the results not only provide information of patients' quality of life at a particular time. i.e. subsequent to immediate diagnosis or too close to death. The data also offers a rare opportunity to understand how the physical, emotional and the overall well-being of lung cancer patients changed over the entire period of the disease. The longitudinal design of the study also means that we can study both similarities and differences at the group level as well as at an individual level, which might possibly give us some general insights into the changes in quality of life of lung cancer patients as a group over time, but more importantly, paying attention to specific individuals who were performing significantly worse than the group as a whole.

Limitation

1) Small sample size and drop outs

It is known that advanced lung cancer diagnosis is often associated with a poor prognosis, and many patients had dropped out from the study after the first interview (two months after diagnosis, N=31) and the second interview (four months after diagnosis, N=30), out of the 128 who enrolled initially. The implication is that only a small group of patients was retained in the remaining study and no information was available on patients who dropped out. Therefore, the results of the study have to be interpreted very carefully because there was a risk that patients who left the study (death or too ill to continue) might represent a group of patients having a very different trajectory on their changes of quality of life, especially possible that patients staying in the study had a slower deterioration and might inflate the quality of life scores of the group.

8.2 Summary of the results

Part I: Care provided to cancer patients in the final months of life

1) What was the type of care and communication that cancer patients had in their last months of life?

Existing literature has shown that access to palliative care differs both inter and intra-countries and that communication about palliative care with terminally ill cancer patients can be challenging for healthcare professionals.[8-12] This thesis focuses on inter-countries differences and we examined a few aspects of GPs' provision of palliative care to dying cancer patients in four different countries (Belgium, the Netherlands, Italy and Spain). Cross-country differences were observed in care provided in the last months and last week of life. GPs provision of palliative care was more prevalent in the Netherlands than in other countries while specialist palliative care services were less often used in the Netherlands. In all countries, palliative care was adopted as an important treatment goal (versus curative or prolonging life) for most patients in the last three months (58-76%) and in the last week of life (80-95%) although with some variations between countries.

Specifically examining the communication processes at the end of life, clear cross-country differences were also observed. For seven out of ten of the communication topics asked in the questionnaire, GPs in the Netherlands and Belgium were more likely than their Italian and Spanish counterparts to have discussed issues like primary diagnosis, possible medical complications, options for palliative care etc. What is interesting is the differences found between Belgium and the Netherlands, the two countries are geographically close and share the same language, yet Dutch GPs engaged in end of life communication more often than Belgian GPs. Similarly, patients in Italy and Spain less often expressed a preference for place of death or medical treatment to their GPs. These results show the different organisation and GPs' involvement in palliative care in the four countries.

2) What were the number of final transitions and the types of care settings transitions of cancer patients at the end of life, and how often were final transitions to the place of death based on patients' or families' wishes?

Looking at cancer patients who died non-suddenly across the four countries in their final three months of life, we found that at least 50% of patients in all countries had a transition between care settings during this period. From 17% to 27% of patients had a care setting transition in the last week of life. There were four main types of transitions between care settings for these cancer patients in Belgium, the Netherlands, Italy and Spain, and they were: hospital death from home (25-47%), PCU/hospice death from home(11-16%), PCU/hospice death from hospital (4-18%) and home death from hospital(16-30%). In the four countries studied, terminal hospital admission was significantly less often in the Netherlands. While research had been done on the frequencies of hospitalisations or hospital admissions for dying patients[13-14], and these final transitions could at times be burdensome[13,15], little is known to what extent these transitions were congruent with patients or family wishes. We tried to answer this question by showing how often patients or families wishes were cited by GPs as reasons for occurrence of the final transitions. Wishes from both patients and family were found to a lesser extent in Italy(4%) and Spain(1%) than in Belgium(14%) or the Netherlands(8%). Cross-country differences on the wishes with regard to the types of transitions were found. For home death from hospital, patient wishes were most frequently expressed in Belgium, followed by the Netherlands, Italy and Spain. These results demonstrate that the four countries varied on how the final transitions for cancer patients were based upon patients or family wishes as well as how often these wishes were known by the GPs.

Part II: Preferences of place of death of cancer patients according to GPs

3) How often are GPs aware of cancer patients' preferred place of death and what was the preferred place of death as expressed to GPs?

Among the GPs we surveyed, except for the Netherlands (28%), the majority of GPs in the other three countries was not informed about patients' preferred place of death (BE: 56%, IT: 73%, ES: 64%). The data also confirmed that when GPs were informed, cancer patients from the four countries (N=389) often preferred dying at home (71-90%), followed by palliative care unit/hospice (3-13%), care home (1-11%) and hospital (1-6%). On the other hand, some cross-country differences had been observed on the actual place of death of cancer patients. On average, hospital was the most common place of death, followed by home, palliative care unit/hospice and care home. And among GPs (N=389) who knew the patients' preferred place of death, a different pattern was found across the four countries. In Belgium and the Netherlands, GPs were often informed by the patient only (63-72%) or both patient and family (20-21%). On the other hand, in Italy and Spain, GPs were more often informed by a family member only (53-54%) and to a lesser extent to the patient himself/herself (32-40%).

4) How often are cancer patient preferences for place of death met, if known to GPs,
and what are the factors associated with a preference to die at home?

Another contribution our research added to the literature is the role of GPs in fulfilling these wishes on place of death. Examining how often these preferences met were showed that the overall preference met was high in all countries in case GPs were aware of the preference, ranging from 68% in Italy, 81% in Belgium, 91% in the Netherlands to 92% in Spain. Patients whose home death wishes were not achieved often died in hospitals (the Netherlands, Italy, Spain) or PCU/hospices (Belgium). Finally, we tried to answer the research question by comparing the outcomes on place of death for patients whose preferred place of death is known or unknown by their GPs. When patients' preferred place of death was unknown, they were more likely to die in hospitals (34-53%) compared to 4-34% when the preference was known. Our analyses showed that age group, GPs' provision of palliative care and decision-making capability were the factors associated with a known home death preference. GPs' provision of palliative care is a consistent factor that appears significant in facilitating home death in Belgium, the Netherlands and Italy, after controlling for all other factors such as age, the type of malignancies etc. Factors such as communication about palliative care options, wishes about treatment, specialists' palliative care or burden of informal caregivers did not emerge as factors associated with achieving home death wish if known in advance. Nonetheless, the studies in this thesis could only produce hypotheses for future testing but no causal relationships about GPs' involvement could be inferred.

Part III: Place of death and quality of life of patients with advanced lung cancer

5) What is the international pattern of place of death for lung cancer and COPD patients?

To answer this research question, we conducted an international study on place of death using death certificate data from 14 countries. The most commonly found places of death were home, hospital, hospices and nursing homes. Our study had a focus on comparing the place of death of lung cancer and COPD patients. And we found that across all countries studied, lung cancer patients more often died at home than COPD patients, and this remained valid after controlling for variables such as age, sex, socio-economic statuses and healthcare resources available in the country (if the information was available). The final database included 5,568,827 deaths from all countries and COPD death represented 4.4% of all deaths while lung cancer represented 5.8% of all deaths.

With regard to place of death, most deceased patients with COPD or lung cancer died at home, in hospitals, nursing home or palliative care institutions. A small proportion died in the category of others, i.e. on ambulances or in offices. The overview of the pattern of place of death of the two groups of patients illustrated that lung cancer patients were more likely to die at home than COPD patients in 9 out of 13 countries. On the other hand, lung cancer patients were less likely to die in hospitals in 7 out of 13 countries. In countries where palliative care institution was available as a category of place of death, more lung cancer patients than COPD patients died there. In a nutshell, though the two patient groups had similar symptoms and issues at the end of life, the dying pattern of place of death varied consistently in all countries studied.

6) What is the quality of life of patients diagnosed with advanced lung cancer?

Last but not least, this thesis included a longitudinal study on the changes of quality of life (QoL) among patients diagnosed of advanced lung cancer in Flanders, Belgium. Information from 128 patients on their quality of life scores was collected using the EORTC QLQ-C15-PAL questionnaire. Large drop outs had been experienced in the study due to both deterioration and death of patients, but collected data showed few changes in the physical and emotional well-being, as well as the global quality of life scores of patients at different time points of interviews. Biggest changes were found when patients were interviewed shortly after diagnosis and two months after diagnosis, such as the global quality of scores dropped from 58.6 to 50.9 and insomnia changed from 28.5 to 21.6 in the same period of time. When the analyses were done at the individual level with the use of minimal important differences (MIDs), more 'changes' were recognised. The percentages of patients who had an improvements or worsening were on average 40% or more of the population.

8.3 Interpretations of results

This section provides a discussion on the main findings of this thesis with respective to the themes outlined in the introduction.

8.3.1 Care provided to cancer patients in the last months of life

One notable finding from this thesis is the cross-country differences as well as some commonalities shared by countries. We will address these separately below.

Similarities among countries studied

First examining similarities between countries, our data showed that most patients resided at home in the last months of life, but they were also often transferred between home and hospitals. Some patients even had three or more transitions in the last three months of life. Although it is important that cancer patients receive active treatments in the hospital over the course of their illness, we studied patients with cancer as the underlying cause of death of whom the GP indicated that death was non-sudden or expected. Hence considering that in many cases of cancer, it becomes clear towards the end of life that additional curative or life-prolonging treatment might not benefit the patient[16], the rationale of these high numbers of moves between settings is questionable, in particular considering research has consistently shown that patients prefer dying at home.[17-18] At present, unlike managing pain or sedation, there is no consensus guideline or standardised protocol[19-20] about transfers or hospitalisation of dying cancer patients, and from existing research, we understand that these decisions might reflect healthcare provider's behaviour of services policy rather than patients' preferences or needs.[21-22] For example, healthcare professionals might want to spend more time with patients and families in end-of-life care communication but are constrained with the large number of patients and limited amount of available time. Thus, the pattern we found on care settings transitions is most likely the result of a combination of factors, such as the symptoms of the patients, distance from home to hospitals/palliative care units, the availability of carers etc.

Mentioning patient preferences, a certain proportion (about one in ten) of patients or families had a wish for hospital transfers when we asked GPs to indicate the reasons for the final transition from home to hospital (this was excluding palliative care units). This looks like a contradiction to the conventional understanding that patients do not prefer dying in hospitals. Although the proportion was small, one might still wonder what the thoughts were of these patients or families. Were they in acute medical situations that require hospital care? Were they prepared or aware that hospital might be the place where they would die? Was it the impression of the GP that hospital admission would be better? Did patients or relatives did not see any alternative? One related idea with this phenomenon is the idea that ‘hospitals provide the best care’. Studies showed that other than home, inpatient hospice care is also often a preferred place of care for advanced illnesses.[17] It is documented in the literature that some clinicians indicated that hospitals are not the best place for providing palliative care[23] and that more staff training is needed to improve the quality of care[24-25]. However, the transfers from our results were towards acute hospital settings, excluding palliative care units. The preferences from patients and families to have to be transferred to the hospital might be an example of little knowledge about palliative care among the public as reflected in recent surveys.[26-27] One possible interpretation is that patients and families believe hospitals offer the best type of care, even caring for the dying, and that is why they wish for a hospital transfer at the end of life. Nonetheless, this is just one possible hypothesis to explain the frequent hospital transfers we found and further future research on understanding the public’s and patients’ views is needed.

Cross-country differences

Cross-country differences were also found in our studies. Our data illustrated the cross-country differences about discussions of end-of-life care topics. Many research have shown the important role of communication in end of life care with cancer patients, with differences of care provided in the last phase of life such as less aggressive care and better quality of life.[28-29] Discussions about wishes and treatment goals can only be known if care professionals elicited these choices from patients early enough. The fact that some topics were more often discussed than others (i.e. primary diagnosis was more often discussed than life expectations in all four countries we studied) might be interpreted that communication on some topics (i.e. social and spiritual problems) remains a challenge for many healthcare professionals. Talking about death and dying is not easy and requires a lot of skills.[30-31]

End-of-life communication is one area where cross-country differences are notable. Our current data seem to suggest that in countries like the Netherlands, GPs more often discussed end-of-life care topics than in countries like Italy and Spain.

Furthermore, variations across countries on the wishes for transitions were also found. For example, GPs in Belgium and the Netherlands more often recorded a wish from patients and families about a preference for a care setting transition than in Italy and Spain. This might be referring to cultural differences (i.e. prognostication and life expectancy disclosures) in end of life care provision.[32-33] In spite of cultural differences, eliciting patients' wishes is a crucial part of delivering patient-centred end-of-life care, and therefore the discrepancies (more transitions to hospitals and fewer patients wishes in Italy and Spain) we found might be evidence that some clinicians can further improve their work by having early discussions about end-of-life care choices i.e. place of care and minimising the number of transitions, not only improving patient-centred care, but also facilitating the work of care professional, i.e. knowing the goals of care and what to do when patients become unconscious.

Finally, although our results seem to suggest that palliative care was more developed into primary care in Belgium and the Netherlands than in Italy and Spain, which had also been reflected in the quality of death index published by a commissioned report[34], readers should not forget that inter and intra-country differences exist. Studies in this thesis present a lot of cross-country differences in GPs' provision of palliative care on a national level, differences within the countries could well exist. For instance, Italy and Spain are larger countries than Belgium and the Netherlands, while the networks were representative, the former countries only cover parts of the countries, thus the cross-country differences we found could have been under/over-estimated due to the averaging effect. This is also to take into consideration the variations within the countries themselves, such as urban and rural, distribution of hospices or palliative care institutions (such as hospices are more populated in Northern Italy than the South). Therefore, it is possible that a cancer patient from southern Italy does not receive the level of palliative care as described in our studies because of a lack of access to such services.

8.3.2 Preferences of place of death of cancer patients according to GPs

Results from the IPOD study provide an international perspective on the pattern of place of death for lung cancer and COPD patients. Existing evidence show that factors such as the distance to hospitals, one's socio-economic status and the use of specialist palliative care had been previously reported[35-37] to be associated to the increased chance of a patient dying at home. Though those information was not available for more in-depth analyses, the cross-country variations of place of death with two identical diseases may mean that the way end-of-life care is organised varies vastly in different countries, such as depending on the existence of a palliative care culture and the training of medical staff.

The EURO SENTI-MELC data[38] and other international literature[18-19] confirm that cancer patients prefer dying at home, while what was surprising was that most of the GPs caring for their dying patients were unaware of the preference. Although our data could only show an association between knowing a preference and meeting it, care professionals could still try to elicit that preference in advance to have that information ready. Nevertheless, it would be useful to understand why these GPs were unaware of the preference for place of death for patients. Was it because the patients deteriorated rapidly and there was not sufficient time anymore? We know from the literature[39-40] that preference itself is a fluid concept and it is contingent upon many mediating factors, such as the role of families, availability of resources, patients' perception about his/her own control of the situation etc. Therefore, it was also possible that patients had a preference of place of death but their GPs did not elicit it for various reasons.

Finally, though our studies align with existing wisdom that terminally ill cancer patients wish to die at home, we could not provide the reasons behind this ideal of a 'home death'. It might be related to the familiar environment that the patients were used to or the importance of being with their closed ones in the final hours of death. The first results from the 'Unpacking the Home' study in the UK offer evidence that support for informal carers is vital for home death.[41] Knowing the reasons for asking for a home death and barriers could help create alternatives for patients where dying at home is difficult, i.e. lack of informal carers, time constraints etc. For patients with high risks of being transferred i.e. facing imminent deaths and deaths might occur on ambulance transfers, by re-creating a more 'home-like' environment for patients and sometimes, is the 'second-best' option for patients and families. Understandably, many unexpected situations might occur at the end of life and patients' preferences could change even if they have been expressed earlier in a disease trajectory. For example, a patient who had indicated a home death preference previously might revoke the decision because circumstances change, for instance, symptoms control becomes more difficult and there is a perceived increasing burden on one's carers. And this is why it is necessary for care professionals to continuously assess and ask for patients' preferences to detect changes as death is closer.

8.3.3 Advanced lung cancer: place of death and quality of life

Finally, the thesis looked at two domains, the quality of life and the place of death of lung cancer patients as a subgroup of cancer patients. In recent years, there was an exponential growth in the amount of research in quality of life[42-44], both reflecting the increasing amount of people dying as well as the growing awareness of the relevance of the concept itself. People diagnosed with advanced cancer could sometimes live for years, but the side effects of treatments, i.e. surgery or chemotherapy, might substantially compromise their daily living abilities. And therefore quality of life is both a conceptual construct[45] (a theoretical concept) as well as an empirical tool[46] (a scale of scores) to help clinicians understand the performance (and changes) of patients in the overall, physical and psychological well-being, and the various symptoms.

The EOLIC study in the thesis used the EORTC quality of life survey in a specific population, patients diagnosed with advanced lung cancer and scores were recorded at three time points. The results reveal that quality of life is a complicated concept because the single question on 'how do you feel this week' might encompass physical, psychological, social as well as spiritual dimensions of the patient. And these different aspects might sometimes conflict with one another. For instance, the patient might rate oneself 'well' but still suffering from symptoms like pain and dyspnoea.

Furthermore, one interesting finding is that a lot of individual fluctuations were found when the data was analysed using the minimal important differences (MIDs) methods, but fewer differences were found on a group level. These results might be interpreted as an example of the need for patient-centred assessment. Although there are symptoms prevalence indicators such as percentage of patients suffered from pain etc, each patient is different and the large individual fluctuations found in our study are proof to support the claim that clinicians need to ask or assess patients more often to address the potentially missing or fluctuating physical or psychological symptoms.

Lastly, the IPOD study presented the differences on place of death between patients with lung cancer and COPD. Across the 14 countries we studied, lung cancer patients more often died at home (than in hospitals) than COPD patients. However, existing death certificate studies could not inform us the reasons behind these patterns, questions such as ‘was more lung cancer patients receiving palliative care’ and ‘how did receiving palliative care relate to the place of death of lung cancer patients’ remain unanswered. Nonetheless, the fact that these patterns were found across the countries might be signs that many healthcare systems handle terminally ill lung cancer patients and COPD patients differently.

8.4 Implications: Practice, Policy and Research

Practice

Routine assessments on cancer patients

Studies in this thesis show that in spite of existence of different assessment tools on symptoms and overall quality of life, there is still a lack of a culture of routine assessment of terminally ill cancer patients’ physical and psychological conditions. This for example is presented by the high number of missing symptoms reported by GPs from the EURO SENTI-MECL study. This might be related to many different factors, such as the lack of time, the patient is too ill or simply that the assessment procedure is not part of the standard care. Yet, without valid and reliable data, clinicians might risk missing treatable symptoms and the opportunities for patients and families to have a better quality of life. Results from the EOLIC study call for the integration of routine assessments into standard care of cancer patients, this means that clinicians (both generalists and specialists) should be trained to assess symptoms of cancer patients (ideally) at every visit, and provide assistance as soon as possible. One of the insights from our study is that there can be differences when patients are viewed as a group and when their conditions are viewed individually. This is an important reminder to clinicians that each patient is different and a balance between adhering to protocols and personalised care is needed in each case.

Timely Communication about end-of-life care preferences

Secondly, our studies on preferences and place of death highlighted the association between general practitioners' knowledge of preference and meeting a patient's preference. Although our studies are limited to the topic of place of death, this could be relevant for many domains in end-of-life care, such as wishes for (or forgoing) treatments and the assignment of a surrogate. Discussing issues related to death and dying is not easy, due to reasons such as social taboo or the feeling of uneasiness from both sides (clinicians and patients/families).[47] Therefore, if practitioners and policy-makers wish to improve the outcome of care (more open discussions and better preference met on indicators i.e. place of death), more trainings and public education work are required. First of all, clinical staff (nurses, general practitioners as well as specialists) should possess the skills and the mentality to conduct these conversations.[48-49] Then, through public education programmes (social media, outreach work)[50-51], the public might have a better awareness of communicating at the end-of-life and become more willing to have such conversations when the time comes. Although palliative care might be considered something special as it involves sensitive and emotional conversations, it shares some similarities to topics such as organ donation, where both require advanced consent. The countries we studied had integrated palliative care into the routine health care system at varied extent, yet there is still room for improving healthcare professionals' general palliative care skills, so that these discussions become a more routine part in caring for terminally ill patients.[52] Since with the ageing population, palliative care provided by generalists will be in high demand in the near future, improving under and postgraduate education of healthcare providers about palliative care would be urgently needed.[53]

Policy

A public health approach in monitoring palliative care

Our studies highlight the importance of developing a future public health perspective in monitoring palliative care nationally and internationally. This means aspects of assurance, assessment and policy development (which are the main function of public health) are all crucial to enable patients having access to high quality of end of life care with policies coherent with the healthcare system. Measures had been developed in comparing countries' performances in palliative care, such as the EAPC Atlas[54] or the Quality of Death index by the Lien Foundation Report[34]. Reaching a consensus on the core components in end of life care is the first step to improve surveillance and enable valid comparisons of end of life care across countries around the world. Policy makers might also use the different quality indicators[55-56] developed to evaluate performances of different services and settings in end-of-life care.

Currently there is a lack of good data in monitoring death and dying both at a country level and at an international level. The few existing initiatives include the EURO SENTI-MELC, the IPOD study and the European Palliative Care Research Collaborative (EPCRC)[57], yet they have limitations like the restricted scope of care or only provide information at a particular care setting i.e. hospital or GPs. Cross-country data can offer a good overview of palliative care. Palliative care might benefit from examples of large databases such as the National Bereavement Survey (VOICE)[58], the World Value Surveys (WVS)[59] and the Survey of Ageing and Retirement in Europe (SHARE)[60]. Though these are existing population-based instruments in measuring the access and quality of palliative care, they are being underused. Future work could focus on establishing registries recording the use and evaluation of palliative care services across settings, and including patients dying from different diseases, at both regional, national, as well as the international level. For instance, policy makers could also make use of existing efforts and expand them, such as the EURO SENTI-MELC methodologies, and linking socio-demographic census data to electronic medical records, utilising GPs or hospital networks in collecting data, as shown by an initiative in Sweden.[61]

Adopting a public health approach in palliative care not only implies more funding is needed for both service development and research, palliative care should also be more embedded in basic medical education, but also palliative care has to be given more weight in the current discussions of ageing and societal challenges facing by all countries.[62] One example is the 2014 European Declaration on Palliative Care[63] which is used to raise awareness among policy makers the potential benefits of mainstreaming palliative care into standard health care delivery all across the continent. Other useful policies include establishing registries of palliative care services, integrating palliative care in ageing policies[62] and encourage public participation in healthcare policy decision-making.

Research

More cross-country studies in cancer palliative care

Studies in this thesis found both similarities (i.e. frequent care settings transitions) and differences (i.e. GPs in Belgium and the Netherlands were more informed about patients' preferred place of death) in the four European countries' (Belgium, the Netherlands, Italy and Spain) organisation and the use of palliative care for cancer patients. Nonetheless, we also learned that there are still many unsolved puzzles and more cross-country studies are needed.

There might be many possible explanations for the differences found, such as the different historical development of palliative care, how palliative care was introduced into the existing healthcare systems or the general public's attitudes towards palliative care. Furthermore, there is also evidence suggesting that the Netherlands seem to be the country standing out among the countries, and this could be due to the strong emphasis of developing primary palliative care and the existence of national palliative care guidelines as well as the use of specialist palliative care.

In the future, comparative studies with robust study design might help us better understand the strengths and weaknesses of different palliative care systems. This could be done through examples like large-scale epidemiological studies with follow-up on patients and bereaved relatives receiving palliative care, and the differences on healthcare outcomes. On the other hand, studies could look at the different roles of generalists and specialists in delivering palliative care, and the associated costs implications to healthcare financing.

The International Place Of Death (IPOD) study showed the potential of making use of routine administrative data in research (i.e. death certificates and electronic medical records). Nowadays, a large amount of patients' information is collected and pooled together in electronic systems, such as data on prescriptions, demographic data of patients and families, and sometimes history of advance care planning like the signing of an advance directive. However, due to different privacy legislations in countries, this information was often not available for further analyses, which could help improve healthcare services. For instance, in death certificate studies, only a few variables were recorded (age, sex, underlying cause of death and place of death), and therefore, conclusions might sometimes be difficult to be drawn on clinical practices, questions such as why did a cancer patient die in a palliative care unit? Besides, if the procedures allowing the anonymous linkages of death certificates data to other information systems are made easier, such as social insurance and hospital use in the last months of life, researchers could better understand the social and clinical conditions of a typical patient who died at home, and more evidence-based recommendations could be derived from the data.

Quality and access to palliative care for cancer patients

Palliative care was traditionally born from caring for cancer patients, so cancer patients remain the largest disease group of people receiving palliative care in many countries. Even though many studies had been conducted on topics like patients' symptoms, place of death and advance care planning, future research can be oriented towards measuring the quality and access to palliative care among cancer patients. The recent problems with the 'Liverpool Care Pathway'[64-66] (a number of cases reported in the UK about the inappropriate use of a standard palliative care pathway for dying patients in the final days or hours) showed the danger of quick expansion of palliative care services without appropriate checks, where medical staff's reputation is tarnished, patients suffering and families were left with a bad experience of dying. Moreover, while palliative care services have been slowly expanding to different age (i.e. paediatrics) and disease groups (i.e. dementia, organ failure), there is little information on how the rate of access is matching with the needs of patients and families. And the situation can be varied on a country-to-country basis, bigger countries might utilise mobile teams for more efficient services provision, more densely populated countries might enjoy the privilege of centralised services. However, in all cases, assessing the quality of palliative services (i.e. patients and family satisfaction, quality of death) and comparing different models of care will tell us the room for improvement as well as what works and what does not. Access to palliative care involves the concept of health equity, that every patient and family is entitled the equally high quality of care regardless of factors like race, socio-economic class and geographical locations. Quality and access to palliative care should be the two areas of future research because these studies will inform us whether resources had been efficiently and effectively applied. Quality indicators found by on-going research[67-68] like quality and safety, access, infrastructure and education will be useful for evaluating service provided by hospitals, hospices and community care facilities. Questions such as "did adding two palliative care specialists help improve patients' experience of a service?, and "how are preferences from patients and families integrated into regular staff meetings?" remain to be answered with high quality data. And at present, evidence in this domain is scarce.

Mixed-methods, longitudinal study in palliative care

Another recommendation for future research in cancer palliative care is the urgent need to conduct more mixed-methods, longitudinal studies. Studies in this thesis are quantitative in nature and one weakness is the lack of information on some aspects of healthcare, such as the experiences of interacting with a general practitioner, the details of an end-of-life care discussion or medical staff's difficulties in providing care. Quantitative and qualitative designs are equally important to rational healthcare policies making; numbers give us information like costs, required workforce and training needs, while qualitative data offers another side of a story, such as how a particular patient encountered problems in getting a palliative care referral or the stress of palliative care staff. Researchers in palliative care increasingly see the advantages to adopt a mixed-method study design because the two types of data not only complementary, but also enhance our understanding of the messages from the data. On the other hand, longitudinal studies remain scant in palliative care mostly due to the frailty of patients. Yet, these researches are of great value to the community because they are able to capture the evolution of a patient, family or healthcare staff's experience in a disease trajectory. Many of the existing studies can only describe or analyse events at one particular time point and longitudinal study offer a new perspective of viewing an experience, by connecting the different time-points to create a bigger picture. For instance, longitudinal study could track how a patient's psychological well-being or changes of preferences evolves from diagnosis until death. And this information can be matched with the care received by the patient so as to see if these items are coherent. Therefore, it is encouraged that future work in the field could consider more using mixed methods and longitudinal designs.

Trials in cancer palliative care

Last but not least, only a few trials[29,69-71] had been conducted in the area of palliative care due to various methodological issues, the vulnerability of patients and gatekeeping from some clinicians. Nonetheless, trials are useful in evaluating the quality of services development. Evidence generated from trial studies will offer us high quality of evidence for better practices. For instance, proof of cost-saving using palliative care (over other inappropriate use of intensive care used at the end of life) will be of utmost importance for persuading policy-makers in supporting more palliative care initiatives and more evidence is also needed in disentangling how patients and families benefit from early integration of palliative care into the disease trajectory.

References

1. Van den Block L, Onwuteaka-Philipsen B, Meeussen K et al. Nationwide continuous monitoring of end-of-life care via representative networks of general practitioners in Europe. BMC Pam Pract 2013; 14:73.
2. Van den Block L, Van Casteren V, Deschepper R et al. Nationwide monitoring of end-of-life care via the Sentinel Network of General Practitioners in Belgium: the research protocol of the SENTI-MELC study. BMC Palliat Care 2007; 6:6.
3. Meeussen K, Van den Block L, Echteld MA, et al: End-of-Life Care and Circumstances of Death in Patients Dying As a Result of Cancer in Belgium and the Netherlands: A Retrospective Comparative Study. J ClinOncol2011,29:4327-4334.
4. Cohen J, Bilsen J, Miccinesi G et al. Using death certificate data to study place of death in 9 European countries: opportunities and weaknesses. BMC Public Health 2007; 7:283.
5. Chambaere K, Bilsen J, Cohen J et al. A post-mortem survey on end-of-life decisions using a representative sample of death certificates in Flanders, Belgium: research protocol. BMC Public Health 2008; 8:299.
6. Pardon K, Deschepper R, Stichele RV et al. Preferences of advanced lung cancer patients for patient-centred information and decision-making: a prospective multicentre study in 13 hospitals in Belgium. Patient Educ Couns 2009; 77(3): 421-429.
7. Pardon K, Deschepper R, Vander Stichele R et al. Changing preferences for information and participation in the last phase of life: a longitudinal study among newly diagnosed advanced lung cancer patients. Support Care Cancer 2012; 20(10): 2473-2482.
8. Hudson PL, Aranda S and Kristjanson. Meeting the Supportive Needs of Family Caregivers in Palliative Care: Challenges for Health Professionals. J Palliat Med 2004; 7(1): 19-25.
9. Cherny NI, Catane R. Attitudes of medical oncologists toward palliative care for patients with advanced and incurable cancer: report on a survey by the European Society of Medical Oncology Taskforce on Palliative and Supportive Care. Cancer 2003; 98(11): 2502-2510.
10. Griffiths J, Ewing G, Wilson C, Connolly , Grande G. Breaking bad news about transitions to dying: A qualitative exploration of the role of the District Nurse. Palliat Med 2014. pii: 0269216314551813. [Epub ahead of print]
11. Beccaro M, Costantini M, Merli DF and the ISDOC Study Group. Inequity in the provision of and access to palliative care for cancer patients. Results from the Italian survey of the dying of cancer (ISDOC). BMC Public Health 2007; 7:66.
12. Walshe C, Todd C, Caress A, Chew-Graham C. Patterns of Access to Community Palliative Care Services: A Literature Review. J Pain Symptom Manga 2009; 37(5): 884-912.

13. Burge FI, Lawson B, Critchley P and Maxwell D. Transitions in care during the end of life: changes experienced following enrolment in a comprehensive palliative care program. BMC Palliat Care 2005; 4:3.

14. Reyniers T, Houttekier D, Cohen J, Pasman HR, Deliens L. What justifies a hospital admission at the end of life? A focus group study on perspectives of family physicians and nurses. Palliat Med 2014. doi:10.1177/0269216314522317

15. Gonzalo P, Teno JM, Mitchell SL, et al. End-of-Life Transitions among Nursing Home Residents with Cognitive Issues. N Engl J Med 2011; 365: 1212-1221.
16. Ahearn DJ, Nidh N, Kallat A, Adenwala Y, Varman S. Offering Older Hospitalised Patients the Choice to Die in Their Preferred Place. Postgrad Med J 2013. 89(1047): 20-24.
17. Gomes B, Higginson IJ, Calanzani N, et al. Preferences for place of death if faced with advanced cancer: a population survey in England, Flanders, Germany, Italy, the Netherlands, Portugal and Spain. Ann Oncol 2012; 23(8): 2006-2015.
18. Beccaro M, Costantini M, Giorgi RP, Miccineso G, Grimaldi M, Bruzzi P, ISDOC study Group. Actual and preferred place of death of cancer patient. Results from the Italian survey of the dying of cancer (ISDOC). J Epidemiol Community Health 2006. 60(5): 412-416.
19. WHO's cancer pain ladder for adults. http://www.who.int/cancer/palliative/painladder/en/ (accessed 11/12/2014)
20. Cherny NI, Radbruch L, The Board of the European Association for Palliative Care. European Association for Palliative Care (EAPC) recommended framework for the use of sedation in palliative care. Palliat Med 2009; 23(7): 581-593.
21. Peruselli C, Giulio PD, Toscani F et al. Home palliative care for terminal cancer patients: a survey on the final week of life. Palliat Med 1999; 13(3): 233-241.
22. West E, Barron DN, Reeves R. Overcoming the barriers to patient-centred care: time, tools and training. J Clin Nurs 2005; 14(4): 435-443.
23. Cassel CK, Ludden JM, Moon GM. Perceptions of barriers to high-quality palliative care in hospitals. Health Aff (Millwood) 2000; 19(5): 166-172.
24. Reyniers T, Houttekier D, Pasman HR, Stichele RV, Cohen J, Deliens L. The family physician's perceived role in preventing and guiding hospital admissions at the end of life: a focus group study. Ann Fam Med 2014; 12(5): 441-446.
25. Frey R, Gott M, Raphael D et al. Clinical staff perceptions of palliative care-related quality of care, service access, education and training needs and delivery confidence in an acute hospital setting. BMJ Support Palliat Care 2014. 4(4): 381-389.
26. McIlfatrick S, Hasson F, McLaughlin D et al. Public awareness and attitudes toward palliative care in Northern Ireland. BMC Palliat Care 2013; 12:34.
27. Center to Advance Palliative Care: Public Opinion Research on Palliative Care a Report Based on Research by Public Opinion Strategies. America: Research Commissioned by the Center to Advance Palliative Care Support Provided by the American Cancer Society and the American Cancer Society Cancer Action Network; 2011:2011.
28. 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(14): 1665-1673.
29. Bakitas M, Lyons KL, Hegel MT et al. Effects of a Palliative Care Intervention on Clinical Outcomes in Patients With Advanced Cancer. The Project ENABLE II Randomized Controlled Trial. JAMA 2009; 302(7): 741-749.
30. Clayton JM, Butow PN, Terrersall MHN. When and How to Initiate Discussion About Prognosis and End-of-Life Issues with Terminally Ill Patients. J Pain Symptom Manage 2005; 30(2): 132-144.
31. Kumar P, Temel JS. End-of-life care discussions in patients with advanced cancer. J Clin Oncol 2013; 31(27): 3315-3319.
32. Evans N, Pasman HR, Payne SA et al. Older patients' attitudes towards and experiences of patient-physician end-of-life communication: a secondary analysis of interviews from British, Dutch and Belgian patients. BMC Palliat Care 2012; 11:24.
33. Koffman J. Servicing multi-cultural needs at the end of life. J Ren Care 2014; 40(Suppl 1):

6-15.
34. Quality of Death Index, Lien Foundation. http://www.lifebeforedeath.com/qualityofdeath/ (accessed 12/12/2014)
35. Gomes B, Higginson IJ. Factors influencing death at home in terminally ill patients with cancer: systematic review. BMJ 2006; 332: 515.
36. Bell CL, Somogyi-Zalud E, Masaki KH. Factors Associated with Congruence Between Preferred and Actual Place of Death. J Pain Symptom Manage 2010; 39(3): 591-604.
37. Grande GE, Addington-Hall JM, Todd CJ. Place of death and access to home care services: are certain patient groups at a disadvantage? Soc Sci Med 1998; 47(5): 565-579.
38. Ko W, Beccaro M, Miccinesi G et al. Awareness of general practitioners concerning cancer patients' preferences for place of death: evidence from four European countries. Eur J Cancer 2013; 49(8); 1967-1974.
39. Butow PN, Maclean M, Dunn SM, Tarreesall MHN and Boyer MJ. The dynamics of change: Cancer patients' preferences for information, involvement and support. Ann Oncol 1997; 8(9): 857-863.
40. Pruchno RA, Rovine MJ, Carwright F, Wilson-Genderson M. Stability and change in patient preferences and spouse substituted judgements regarding dialysis continuation. J Gerontol B Psychol Sci Soc Sci 2008; 63(2): 5S81-90.
41. Payne S, Turner M, Seamark D et al. Managing end of life medications at home- accounts of bereaved family carers: a qualitative interview study. BMJ Support Palliat Care 2014; doi: 10.1136/bmjspcare-2014-000658. [Epub ahead of print]
42. Duijts SFA, Faber MM, Oldenburg HAS, van Beurden M and Aaronson NK. Effectiveness of behavioral techniques and physical exercise on psychosocial functioning and health-related quality of life in breast cancer patients and survivors – a meta-analysis. Psycho-Oncology 2011; 20(2): 115-126.
43. Wright AA, Keating NL, Balboni TA et al. Place of Death: Correlations With Quality of Life of Patients With Cancer and Predicators of Bereaved Caregivers' Mental Health. J Clin Oncol 2010; 28(29): 4457-4464.
44. Akin S, Can G, Aydiner A, Ozdilli K, Durna Z. Quality of life, symptom experience and distress of lung cancer patients undergoing chemotherapy. Eur J Oncol Nurs 2010; 14(5): 400-409.
45. Moons P, Budts W, De Geest S. Critique on the conceptualisation of quality of life: A review and evaluation of different conceptual approaches. Int J Nurs Stud 2006; 43(7): 891-901.
46. Aaronson NK. Methodological issues in assessing the quality of life of cancer patients. Cancer 1991; 67(3 Suppl): 844-850.
47. Rabow MW, Schanche K, Petersen J, Dibble SL, McPhee SJ. Patient perceptions of an outpatient palliative care intervention. J Pain Symptom Manage 2003; 26(5): 1010-1015.
48. Block SD, Bernier GM, Crawley LM et al. Incorporating Palliative Care into Primary Care Education. J Gen Intern Med 1998; 13(11): 768-773.
49. Wessel EM, Rutlesge DN. Home Care and Hospice Nurses' Attitudes Toward Death and Caring for the Dying: Effects of Palliative Care Education. J Hospice Palliat Nursing 2005; 7(4): 212-218.
50. The Conversation Project, http://theconversationproject.org/ (accessed 5/1/2015)
51. Mcllfatrick S, Nobie H, McCorry NK et al. Exploring public awareness and perceptions of palliative care: a qualitative study. Palliat Med 2014; 28(3): 273-80.
52. Quill TE, Abernethy AP. Generalist plus Specialist Palliative Care-Creating a More Sustainable Model. N Engl J Med 2013;368(13): 1173-1175.
53. Pype P, Stes A, Wens J, Van den Eynden B, Deveugele M. The landscape of postgraduate education in palliative care for general practitioners: results of a nationwide survey in

Flanders, Belgium. Patient Educ Counc 2012; 86(6): 220-225.
54. Centeno C, Lynch T, Donea O, et al: EAPC Atlas of Palliative Care in Europe 2013. Full edition. Milan: EAPC Press; 2013
55. Leemans K, Cohen J, Francke AL et al. Towards a standardized method of developing quality indicators for palliative care: protocol of the Quality indicators for Palliative Care (Q-PAC) study. BMC Palliat Care 2013; 12:6.
56. De Roo ML, Leemans K, Claessen SJ et al. Quality indicators for palliative care: update of a systematic review. J Pain Symptom Manage 2013; 46(4): 556-572.
57. Rayment C, Hjermstad MJ, Aass N et al. Neuropathic cancer pain: Prevalence, severity, analgesics and impact from the European Palliative Care Research Collaborative-Computerised Symptom Assessment study. Palliat Med 2013; 27(8): 714-721.
58. National Bereavement Survey (VOICES), (accessed 12/12/2014)
59. World Values Survey (WVS), www.worldvaluessurvey.org (accessed 12/12/2014)
60. The Survey of Health, Ageing and Retirement in Europe (SHARE), www.share-project.org (accessed 12/12/2014)
61. Martinsson L, Furst CJ, Lundtrom S, Nathanaelsson L, Axelsson. Registration in a quality register: a method to improve end-of-life care-- a cross-sectional study. BMJ Open 2012; 2:e001328.
62. Van den Block L. The need for integrating palliative care in ageing and dementia policies. Eur J Public Health 2014; 24(5): 705-706.
63. 2014 European Declaration on Palliative Care. http://www.palliativecare2020.eu/declaration/
64. Independent Review of the Liverpool Care Pathway, https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/212450/Liverpool_Care_Pathway.pdf (accessed 12/12/2014)
65. Liverpool Care Pathway: ‘They told my family I was dying’. http://www.bbc.com/news/health-23698071 (accessed 12/12/2014)
66. Liverpool care pathway for dying patients to be abolished after review. http://www.theguardian.com/society/2013/jul/15/liverpool-care-pathway-independent-review (accessed 12/12/2014)
67. Van Riet Paap J, Vernooij-Dassen M, Droes RM et al. Consensus on quality indicators to assess the organization of palliative cancer and dementia care applicable across national healthcare systems and selected by international experts. BMC Health Serv Res 2014; 14:396.
68. Leemans K, Deliens L, Francke AL et al. Quality indicators for palliative care services: Mixed-method study testing for face validity, feasibility, discriminative power and usefulness. Palliat Med 2015; 29(1): 71-82.
69. Temel JS, Greer JA, Muzikansky A et al. Early Palliative Care for Patients with Metastatic Non-Small-Cell Lung Cancer. N Engl J Med 2010; 363:733-742.
70. Costantini M, Romoli V, Di Leo S et al. Liverpool Care Pathway for patients with cancer in hospital: a cluster randomized trial. Lancet 2014; 383(9913): 226-237.
71. Bakitas MA, Tosteson TD, Li Z et al. Early versus Delayed Initiation of Concurrent Palliative Oncology Care: Patient Outcomes in the ENABLE III Randomized Controlled Trial. J Clin Oncol 2015. pii: JCO.2014.58.6362. [Epub ahead of print]