Potentially inappropriate treatments at the end of life in nursing home residents: Findings from the PACE cross-sectional study in six European countries

Abstract

Context
Certain treatments are potentially inappropriate when administered to nursing homes residents at the end of life and should be carefully considered. An international comparison of potentially inappropriate treatments allows insight into common issues and country-specific challenges of end-of-life care in nursing homes and helps direct health care policy in this area.

Objectives
To estimate the prevalence of potentially inappropriate treatments in the last week of life in nursing home residents, and analyze the differences in prevalence between countries.

Methods
A cross-sectional study of deceased residents in nursing homes (2015) in six European countries: Belgium (Flanders), England, Finland, Italy, the Netherlands and Poland. Potentially inappropriate treatments included: enteral administration of nutrition, parental administration of nutrition, artificial fluids, resuscitation, artificial ventilation, blood transfusion, chemotherapy/radiotherapy, dialysis, surgery, antibiotics, statins, antidiabetics, new oral anticoagulants. Nurses were questioned about whether these treatments were administered in the last week of life.

Results
We included 1,384 deceased residents from 322 nursing homes. In most countries, potentially inappropriate treatments were rarely used, with a maximum of 18.3% of residents receiving at least one treatment in Poland. Exceptions were antibiotics in all countries (between 11.3% in Belgium and 45% in Poland), artificial nutrition and hydration in Poland (54.3%) and Italy (41%) and antidiabetics in Poland (19.7%).

Conclusion
Although the prevalence of potentially inappropriate treatments in the last week of life was generally low, antibiotics were frequently prescribed in all countries. In Poland and Italy, the prevalence of artificial
administration of food/fluids in the last week of life was high, possibly reflecting country differences in legislation, care organization and culture, and the palliative care competences of staff.

Key words: potentially inappropriate treatments, nursing homes, end-of-life care, Europe.

Key message:
Potentially inappropriate treatments in the last week of life of nursing homes residents are uncommon in most countries except for the use of antibiotics. In Italy and Poland these treatments are more prevalent, especially artificial nutrition and fluid treatments and antibiotics, possibly due to country differences in legislation, organization, culture and staff competence.

Running title: Potentially inappropriate treatments in last week
Introduction

In Europe, an increasing number of older people spend their last months in nursing homes and up to 38% of people over 65 years die there(1). We conducted the PACE (Palliative Care for Older People) cross-sectional study in nursing homes in Belgium, England, Finland, Italy, the Netherlands and Poland(2), and demonstrated that residents in these countries die at a mean age of 85 years, often with advanced dementia, multiple comorbidities and clinical complications(1,3,4). This makes them a particularly vulnerable population for whom providing appropriate treatments at the end of life is crucial, albeit challenging(1,3–8). The difficulty of predicting death in older people complicates the decision on whether a treatment or medication is still appropriate(9); staff are sometimes too optimistic about the benefits of such treatments(10,11), and residents are often poorly informed of the possible complications(12).

Recent studies show that certain treatments are potentially inappropriate when administered to older people at the end of life, in particular those with dementia and those living in nursing homes, and should therefore be carefully considered(13–15). Antibiotics and medications like anti-diabetics, statins or oral anticoagulants have no or questionable benefit in short-term use in the last week of life(13). In long-term use, polypharmacy, comorbidities and age-related alterations in drug metabolism can result in side-effects that cause functional and cognitive impairment in older adults(16–18). Artificial nutrition and hydration(19–21), resuscitation(22,23) and artificial ventilation(24–26) can have deleterious effects on quality of life when used in the last week and can complicate the dying process while blood transfusion, chemo/radiotherapy, dialysis or surgery can be futile and burdensome with low survival rates and resulting in poor quality of life(10–12,14).

Earlier studies on potentially inappropriate treatments are limited to describing prevalence in one country or comparison between countries in specific settings such as home care(27) or during the last month of life(28). So far, there are no studies that have compared prevalence of potentially inappropriate treatments in the last week of life between European countries. An international comparison would allow deeper insight into common issues and country-specific challenges in nursing homes and could help direct health care policy and decision-makers. The aim of the current
study was to estimate the prevalence of potentially inappropriate treatments in the last week of life in nursing home residents in six European countries and to study the differences in prevalence of these treatments between countries.

**Methods**

*Study design and sampling*

A cross-sectional study of deceased residents in nursing homes was conducted in 2015 in six European countries: Belgium (Flanders), England, Finland, Italy, the Netherlands and Poland(2), using proportional stratified random sampling. In each country, nursing homes were stratified by region (provinces or other large regions), by type and by bed capacity (above/below country median), and sampled randomly to cover the entire country. For each one that declined participation, another from the same stratum was sampled. Available national (or regional in Belgium) lists were used for recruitment. In England, we also used the ENRICH (Enabling Research in Care Homes) network(29). In Italy, a previously created cluster interested in research was used as the basis for the sample since no national list was available. We aimed to include at least 48 nursing homes per country, to identify a minimum of 192 residents per country or 1,152 in total(2). The PACE protocol provides more details(2).

*Setting and participants*

The term nursing home in this paper refers to ‘collective institutional settings where care, on-site provision of personal assistance with activities of daily living, and on-site or off-site provision of nursing and medical care, is provided for older people who live there, 24 hours a day, seven days a week, for an undefined period of time’ (30). Participating nursing homes reported on all deceased residents over the preceding three months. Questionnaires on each were sent to the nurse/care assistant most involved in their care, the manager, and the resident’s general practitioner (GP); the manager was asked to fill in a questionnaire about the nursing home.

*Data collection*
Nursing homes received a letter presenting the PACE project and a call for participation. Further contact was made via phone or email. The manager nominated an internal contact who provided an overview of all deceased residents in the preceding three months and a list of the key respondents for each (staff member, i.e. nurse/care assistant most involved in care, manager/administrator, GP); these received a paper questionnaire with an anonymous code and an attached document that guaranteed full anonymity and confidentiality with questionnaires returned directly to the researchers who monitored them using excel files. In case of non-response, up to two reminders were sent after three and six weeks.

**Measurements**

Questionnaires from all three key respondents were used to report on the characteristics of the resident: age, gender, length of stay in the nursing home, place of death, presence and stage of dementia at time of death, diseases at time of death and functional and cognitive status during last month of life (Table 1). Presence of dementia was based on the estimation of the GP, nurse or both; stage was based on the Global Deterioration Scale and the Cognitive Performance Scale, as estimated by nursing staff(3) with CPS scores of 5-6 and GDS stage 7 considered as advanced dementia. The score for functional and cognitive status during last month of life was computed with the Bedford Alzheimer Nursing Severity Scale (BANS-S)(31), ranging between 7 and 28. Higher scores indicated greater severity.

In this study, we refer to inappropriate treatments as treatments and/or medication for which ‘the negative consequences (such as mortality and symptom burden) outweigh the expected health benefits (such as increased life expectancy or pain relief)’(32). We first performed an extensive literature search. Next, during multiple meetings with the PACE consortium (i.e. geriatricians, nurses, psychologists) and palliative care researchers, we discussed the list of potentially inappropriate treatments and made a final selection based on the following criteria: 1) used as a standard treatment for older people, 2) considered potentially life-prolonging, and 3) can be easily recalled by a nurse filling in the questionnaire. The final selection agreed by the consortium partners, was: artificial enteral administration of nutrition (e.g. tube feeding, percutaneous endoscopic gastrostomy i.e. PEG), parenteral administration of nutrition, artificial fluids, resuscitation, artificial ventilation, blood transfusion, chemotherapy/radiotherapy, dialysis,
surgery, antibiotics, statins, antidiabetics, new oral anticoagulant (33–38). Nurses were asked whether, to their knowledge, these were administered in the last week of life or not (meaning either ‘not at all’ or ‘in the last month except the last week’). The treatments were then subdivided into five categories: artificial nutrition and hydration treatments (enteral administration nutrition, parental administration nutrition, artificial fluid), critical treatments (resuscitation and artificial ventilation), antimicrobial treatments (antibiotics), medications (statins, antidiabetics, new oral anticoagulants) and other (blood transfusion, chemotherapy/radiotherapy, dialysis, surgery).

Statistical analysis

Analyses were conducted for deceased residents for whom an assessment by the nurse was made retrospectively, using IBM SPSS version 25(39). To investigate the effect of missing data (up to 24% missing values for some treatments), sensitivity analyses were conducted via imputation of incomplete cases with fully conditional specification (shown in Results and Table 2) and complete cases (Table 1A in Appendix). The imputation method estimates each missing value based on associations with other covariates from the dataset using regression analysis (age of resident, gender of resident, availability and number of visits by GP, comorbidity and cause and place of death). Demographic and clinical characteristics are reported as mean and standard deviation (SD) for continuous variables, or median and range in case of skewness, and count and percentage for categorical variables. Linear and logistic mixed-effects regression was used to compute differences in demographic characteristics of residents between countries. These models were used for the analyses because of the clustering of data (in countries and nursing homes). Country was included as a fixed effect and nursing home as a random effect in each model. We present frequencies and total numbers for all potentially inappropriate treatments in each country (Table 1).

To determine differences in the prevalence between countries, we conducted logistic mixed-effects regression analyses (Table 2). Country was again included as a fixed effect and nursing home as a random effect in each model. To correct for differences in demographic and clinical characteristics, we included age, length of stay, place of death, dementia at time of death, diseases (cancer, cardiovascular, pulmonary and others) and functional/cognitive status as fixed effects.
Missing values for each treatment were excluded. This allowed for a fair comparison between countries. An alpha level of $p < 0.05$ represents statistical significance.

Ethical aspects

The relevant ethics committee of each country approved the study protocol (2), except for Italy and the Netherlands, where no additional ethical approval was needed since retrospective data of deceased residents was used.

Results

In 322 participating nursing homes, 1,707 deaths were reported. For 11 cases, no staff member could be identified (Figure 1). Of the 1,696 staff members sent a questionnaire, 1,384 responded (overall response rate 81.6%). Response rates per country are reported in the footnotes of Figure 1. Sensitivity analyses using only complete cases (Table 1A in Appendix) did not result in different conclusions.

Characteristics of the study sample

At the time of death, mean age ranged between 81 years in Poland and 87 years in Belgium and England (Table 1). Residents were mostly female, ranging from 63.5% in Poland to 75% in England. The shortest median stay (145 days) was found in Poland, the longest (745 days) in Belgium. Residents died mainly in the nursing home (80% in Poland – 89.3% in the Netherlands). Dementia was most prevalent in Finland (82.5%) and least in England (60.2%), with between 42.9% (England) and 64% (Poland) being advanced. Severe cardiovascular disease was most often reported as the disease at time of death in all countries (34.7% in Belgium – 55.7% in Poland) except England, where this was malignant cancer (42.9%). The poorest functional and cognitive status was found in Poland (BANS-S mean score of 21.9) and the best in England (BANS-S mean score of 17.5).

Differences in the prevalence of potentially inappropriate treatments in the last week of life in six countries
Use of at least one potentially inappropriate treatment in the last week ranged from 19.9% in Belgium to 68.2% in Poland (p<0.001). Artificial nutrition and/or hydration were most frequent in Poland (54.3%) and least in the Netherlands (2.7%; p<0.001). In advanced dementia use was low in England (0%), the Netherlands (1.7%), Finland (3.8%) and Belgium (4.8%) but higher in Italy (43.9%) and Poland (59.4%; not in tables), artificial fluids being used most (p<0.001), in particular in Poland (48.6%) and Italy (24.5%). Artificial enteral nutrition was administered mainly in Poland (17%; p>0.001) whereas parenteral nutrition was more prevalent in Italy (21.5%; p>0.001). Use of critical care treatments was limited, ranging from 8.7% in Poland to 1.4% in Belgium (p<0.001), with resuscitation being most frequent in England (5.5%; p=0.05) and artificial ventilation in Poland (7.1%; p>0.001). Of all treatments, antibiotics were the most commonly used in all countries, from 11.3% in Belgium to 45% in Poland (p<0.001). At least one of antibiotics, antidiabetics, statins, and anticoagulants was used in 18.3% of residents in Poland and 4.8% in Belgium (p<0.001). Antidiabetic medications were administered in from 2.2% in England to 13.2% in Poland (p<0.001) and statins from 1% in Belgium to 4.4% in England (p=0.23). No use of oral anticoagulants was reported in England while in Poland use was reported for 5.5% of residents (p<0.001). Other treatments like blood transfusions, chemotherapy or radiotherapy, dialysis and surgery were rarely used, from England where no usage was reported to Poland where 3.2% of residents underwent at least one of these treatments (p<0.001). Dialysis was rarely used (p<0.001) ranging between 0% (England and Finland) and 1.6% (Poland). Surgery was performed on none of the residents in England and on up to 1.4% in the Netherlands (p<0.001). No blood transfusions were reported in England with 1% in Poland (p<0.001). Chemotherapy and radiotherapy were almost never used in the last week of life in any country, ranging from 0% in Belgium, England, the Netherlands and Poland to 1% in Italy. The risk adjustment procedure ruled out these differences being due to resident characteristics, implying they reflected differences in appropriate care between countries. Results of the complete case analysis were similar to the results from the imputed data (Table 1A in Appendix).

Discussion

Main findings
Artificial ventilation, resuscitation, blood transfusions, chemotherapy or radiotherapy, dialysis and surgery were rarely used in the last week of life of nursing home residents in most of the studied countries. However, the prevalence of most treatments differed statistically significantly between countries. Poland had the highest percentage of residents receiving at least one potentially inappropriate treatment in the last week of life. Artificial nutrition and/or hydration were common in Poland and Italy, in particular the administration of artificial fluids, even in residents with advanced dementia. Antibiotics were frequently administered in all countries, albeit with the highest rates in Poland and Italy, and antidiabetics were most often administered in Poland.

**Strengths and limitations**

This study is the first to compare the use of potentially inappropriate treatments in the last week of life of nursing home residents in representative samples of nursing homes in different countries. We were able to include data on 1,384 residents from 322 nursing homes in six European countries with different healthcare systems and palliative care cultures. The risk adjustment procedure assured that our results reflected differences in prevalence between countries and were not influenced by differences in resident characteristics.

This study also has important limitations. Firstly, it is not possible to infer from survey data when a particular treatment is ‘inappropriate’. The data may lead to the assumption that, in retrospect, all treatments administered in the last week of life were inappropriate. However, death is difficult to predict so at the time it was given, a treatment may not have been considered inappropriate. Nevertheless, this study compares the use of treatments on a country level and does not aim to evaluate their appropriateness on an individual level. Secondly, the data were collected from nurses rather than directly from resident files. There is a possibility of recall bias, though nurses were instructed to consult patient records where necessary. Thirdly, we did not collect information about when treatments were initiated or the clinical indications for them, which would have provided a more detailed understanding. Fourthly, we were dealing with high quantities of missing data for some treatments (up to 24%). Therefore, sensitivity analyses were conducted via regression imputation of incomplete and complete cases. These showed mainly similar results,
indicating that the missing data influence was small. Finally, when a resident died in hospital, the
nursing home may not have had information on hospital treatments in the last week of life, leading
to a possible underestimation. However, given that only 15% of the residents died in-hospital, the
possible bias caused by this is likely to be small.

What this paper adds
This study showed that the prevalence of most potentially inappropriate treatments in the last
week of life was low in nursing home residents in Belgium, England, Finland and the Netherlands
and particularly low compared with earlier studies in the United States and Canada. For instance,
up to 23% of residents with severe cognitive impairment in Canada received statins in their last
week of life, and anticoagulants were used in 52% of nursing home residents with dementia.
However, comparison of data is difficult when study designs and data collection are different (data
from medical records and administrative databases using prospective samples)(42–45). Besides
the variation in data collection and study design, differences might be explained by the North
American medical culture that tends to favor more aggressive treatments for terminally ill
people(46).

The use of antibiotics in the last week of life was high in all countries, from one in ten in Belgium
to four in ten in Poland. There is an ongoing debate on the indications for antibiotics at the end of
life(47,48) and guidelines on antimicrobial stewardship in palliative care do not yet exist(48). While
some researchers consider antibiotic treatment in the last days of life to be pointless(49–51),
others consider it part of symptom control(52). Earlier research on the use of antibiotics in nursing
homes revealed a similar prevalence at the end of life(53–58). It is challenging to predict when
someone will die(41) and whether an antimicrobial treatment will have a positive effect on
symptom control, which complicates the decision(47), particularly in residents with cognitive
impairments for whom expressing symptoms is difficult(48). Better recognition of the terminal
phase might help with these decisions. Finally, more research is needed to guide the use of
antibiotics at the end of life of nursing home residents.
The low prevalences in Belgium, England and the Netherlands might be partly explained by the culture of palliative care. In those countries many nursing homes provide palliative care and have more palliative care implementation activities (6), with high regional and national activity at policy, finance, legislation and regulation levels and a longer tradition of advance care planning than in Poland and Italy, making nursing home staff more aware of the resident’s preferences at the end of life.

In contrast with other countries, the prevalence of most potentially inappropriate treatments was highest in Poland and Italy, especially for enteral and parenteral administration of nutrition and artificial fluid administration, even with advanced dementia. There are several possible explanations for this. Firstly, the high rate in Italy might be related to law enforcement. In 2009, a bill was passed(59) mandating that hydration and nutrition must always be provided, and by any means, because they are considered basic support measures and fundamental to life. In Poland, artificial feeding is considered an admission criterion for nursing homes (60). Nevertheless, their appropriateness is questionable (61), especially for those with advanced dementia(15). Taking into account the relatively high numbers with advanced dementia in our sample, with the highest rates in Poland and Italy (64% and 55%), our findings are particularly striking.

Secondly, care culture in these countries rarely includes advance care planning, leaving the administration or discontinuation of certain treatments undiscussed(62). This may lead to more pressure from family members to use all possible treatments(62,63). The decision about discontinuation may also cause ethical problems when there is no advance care planning in place. In addition, because of the greater taboo about death and dying in these countries, nursing home staff may not feel competent to discuss end-of-life issues with residents and family members(5,64,65). A third possible explanation may be the low level of basic knowledge of end-of-life care among nursing home staff. An earlier report of the PACE study(7) showed that knowledge of the basic physical aspects of end-of-life care among nurses and care assistants in nursing homes was lowest in Poland and Italy, particularly of indications for the use of feeding tubes(7). Fourthly, GPs in Poland and Italy recognize the terminal phase less often than in Belgium, England, Finland and the Netherlands(66). Nursing home residents in Poland and Italy also least often had palliative care as their main treatment goal in the last week of life, indicating a focus on
life-sustaining treatments. This might lead to negative consequences such as more futile or invasive
treatments, more ‘in bed’ time and higher healthcare costs(67). At the same time, one could argue
that treatment choices also have to be culturally sensitive to be appropriate. Although ESPEN
(European Society of Clinical Nutrition and Metabolism) has elaborated European nutrition
recommendations(68), there are country-specific approaches to artificial nutrition, which not only
depend on legislation or health care policy and organization, but also on culture. It is also plausible
that a difference in prescribing habits between countries is responsible for difference in
treatments. However, this was not examined in this study and should be included in future
research

Implications

Our findings are a potential starting point for the improvement of end-of-life care treatments in
nursing homes. Practices where there is more room for improvement (e.g. artificial nutrition and
hydration treatments), require particular attention. Substantial country differences call for the
development of guidelines to assist nursing home staff and GPs in treatment decision-making and
in recognizing the terminal phase, taking into account cultural differences. Further, greater
attention needs to be paid to advance care planning in nursing homes as this may help residents,
relatives and caregivers to discuss goals and preferences for future care. Finally, there is a need for
staff training in end-of-life care conversations and the physical aspects of end-of-life care. Our
results can be used by policy and other decision-makers to develop public health policies and
interventions to improve the appropriateness of end-of-life care in nursing homes and allow the
exchange of good practices across national borders.

Conclusion

The prevalence of potentially inappropriate treatments in the last week of life of nursing home
residents was low in most studied countries, except for the use of antibiotics which was common.
In Italy and Poland, all treatments were more prevalent, specially the administration of artificial
nutrition and fluids and antibiotics. These differences may reflect country-specific differences in
legislation, care organization, culture and the knowledge and skills of nursing home staff regarding
palliative care.
Figure 1: Flowchart of identified deceased residents for whom an assessment by staff° was made in six countries.

Deaths of residents from 322 nursing homes
n=1707

No Staff member could be identified
n=11 residents

Staff identified
n=1696

No questionnaire received from Staff
n=312 residents

Questionnaire received from Staff
n=1384
Response rate: 81.6%

Study population n=1384

° staff = nurse or care assistant most involved in resident’s care

Response rates per country: Belgium (85.1% (N=291/342)); England (54.2% (N=91/168)); Finland (95.1% (N=269/283)); Italy (91.7% (N=200/229)); the Netherlands (67.5% (N=222/329)); Poland 87.4% (N=311/356).
Table 1: Demographic and clinical characteristics of deceased residents for whom an assessment by staff* was made in six countries: (N=1384)

<table>
<thead>
<tr>
<th></th>
<th>BE (N=291)</th>
<th>EN (N=91)</th>
<th>FI (N=269)</th>
<th>IT (N=200)</th>
<th>NL (N=222)</th>
<th>PL (N=311)</th>
<th>P-value*</th>
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</thead>
<tbody>
<tr>
<td><strong>Age – years</strong></td>
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<tr>
<td>Mean (SD) years old at time of death</td>
<td>87 (7)</td>
<td>87 (9)</td>
<td>85 (9)</td>
<td>86 (8)</td>
<td>86 (9)</td>
<td>81 (11)</td>
<td>&lt;0.001</td>
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<tr>
<td><strong>Gender</strong></td>
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<tr>
<td>Female Count (%)</td>
<td>174 (64.0)</td>
<td>66 (75.0)</td>
<td>169 (64.3)</td>
<td>136 (68.3)</td>
<td>132 (66.7)</td>
<td>195 (63.5)</td>
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</tr>
<tr>
<td>Male Count (%)</td>
<td>98 (36.0)</td>
<td>22 (25.0)</td>
<td>94 (35.7)</td>
<td>63 (31.7)</td>
<td>66 (33.3)</td>
<td>112 (36.5)</td>
<td>0.387</td>
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<tr>
<td><strong>Length of stay</strong></td>
<td></td>
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<td>&lt;0.05</td>
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<tr>
<td>Median (min-max) number of days</td>
<td>745 (2-9706)</td>
<td>600 (2-4952)</td>
<td>581 (1-9218)</td>
<td>416 (2-10171)</td>
<td>710 (1-6290)</td>
<td>145 (1-12365)</td>
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<tr>
<td><strong>Place of Death</strong></td>
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<tr>
<td>Nursing home Count (%)</td>
<td>226 (82.2)</td>
<td>71 (81.6)</td>
<td>224 (84.8)</td>
<td>170 (86.7)</td>
<td>176 (89.3)</td>
<td>248 (80.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hospital Count (%)</td>
<td>48 (17.5)</td>
<td>16 (8.6)</td>
<td>24 (9.1)</td>
<td>26 (13.3)</td>
<td>12 (6.1)</td>
<td>60 (19.4)</td>
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<tr>
<td><strong>Dementia at time of death (yes)</strong></td>
<td></td>
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<td>&lt;0.001</td>
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<tr>
<td>Count (%)</td>
<td>183 (62.9)</td>
<td>53 (60.2)</td>
<td>222 (82.5)</td>
<td>154 (77.0)</td>
<td>135 (61.4)</td>
<td>207 (67.9)</td>
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<tr>
<td><strong>Diseases at time of death†‡¶</strong></td>
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<tr>
<td>Malignant cancer‡</td>
<td>30 (15.5)</td>
<td>9 (42.9)</td>
<td>41 (19.4)</td>
<td>26 (17.2)</td>
<td>27 (18.5)</td>
<td>10 (4.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Severe cardiovascular disease‡</td>
<td>67 (34.7)</td>
<td>2 (9.5)</td>
<td>79 (37.4)</td>
<td>71 (47.0)</td>
<td>45 (30.8)</td>
<td>141 (55.7)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Cerebrovascular accident (CVA)‡</td>
<td>40 (20.7)</td>
<td>3 (14.3)</td>
<td>49 (23.2)</td>
<td>34 (22.5)</td>
<td>25 (17.1)</td>
<td>70 (27.7)</td>
<td>0.483</td>
</tr>
<tr>
<td>Severe pulmonary disease‡</td>
<td>33 (17.1)</td>
<td>3 (14.3)</td>
<td>17 (8.1)</td>
<td>40 (26.5)</td>
<td>17 (11.6)</td>
<td>18 (7.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Severe neurological disease (not dementia)‡</td>
<td>15 (7.8)</td>
<td>0 (0.0)</td>
<td>26 (12.3)</td>
<td>18 (11.9)</td>
<td>11 (7.5)</td>
<td>32 (12.6)</td>
<td>0.381</td>
</tr>
<tr>
<td>Severe renal disease‡</td>
<td>19 (9.8)</td>
<td>2 (9.5)</td>
<td>13 (6.2)</td>
<td>22 (14.6)</td>
<td>19 (13.0)</td>
<td>29 (11.5)</td>
<td>0.420</td>
</tr>
<tr>
<td>Severe diabetes‡</td>
<td>11 (5.7)</td>
<td>1 (4.8)</td>
<td>16 (7.6)</td>
<td>18 (11.9)</td>
<td>17 (11.6)</td>
<td>33 (13.0)</td>
<td>0.177</td>
</tr>
<tr>
<td>Other severe disease‡</td>
<td>31 (16.1)</td>
<td>3 (14.3)</td>
<td>51 (24.2)</td>
<td>33 (21.9)</td>
<td>4 (2.7)</td>
<td>33 (13.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Functional/cognitive status one month before death (BANS-S)†¶</strong></td>
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<td></td>
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<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>18.5 (4.9)</td>
<td>17.5 (4.2)</td>
<td>19.6 (4.3)</td>
<td>21.8 (3.7)</td>
<td>17.7 (4.7)</td>
<td>21.9 (4.6)</td>
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</tbody>
</table>

* Generalized linear mixed model reporting p-value for differences between countries, α =0.05
|| Reported by administrator/manager of nursing home. For 44 out of 1,384 residents no questionnaire was returned by the administrator/manager of care home; these are not included as missing values reported below.
† Reported by staff member (nurse/care assistant) most involved in care.
‡ Reported by general practitioner (GP). For 397 out of 1,384 residents no questionnaire was returned by the GP, these are not included as missing values below.
§ When either the physician or the nurse (or both) considered the resident to have dementia, this was coded as yes.
* staff = nurse or care assistant most involved in resident’s care
^Other categories: facility hospice/PC unit or other
¶ Scores on BANS-S range from 7 to 28; higher scores indicate greater severity.
Percentages may not always add up to 100 because of rounding.
Abbreviations: BANS-S = Bedford Alzheimer Nursing Severity Scale, SD = Standard Deviation
Missing values: age=13, sex=13, size=60, length of stay=36, place of death=11, dementia =11, stage of dementia=187 (419 not applicable because resident did not have dementia), diseases at time of death=12, BANS-S=86 missing data on at least one item.
Table 2. Prevalence of potentially inappropriate treatments in the last week of life in six countries

<table>
<thead>
<tr>
<th>Artificial nutrition and hydration treatments</th>
<th>BE (N=291)</th>
<th>EN (N=91)</th>
<th>FI (N=269)</th>
<th>IT (N=200)</th>
<th>NL (N=222)</th>
<th>PL (N=311)</th>
<th>Country range (%)</th>
<th>Corrected p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Count (%)</td>
<td>Count (%)</td>
<td>Count (%)</td>
<td>Count (%)</td>
<td>Count (%)</td>
<td>Count (%)</td>
<td>Count (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enteral administration of nutrition</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>13</td>
<td>3</td>
<td>53</td>
<td>0.7% - 17%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(0.7%)</td>
<td>(1.1%)</td>
<td>(0.7%)</td>
<td>(6.5%)</td>
<td>(1.4%)</td>
<td>(17%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parenteral administration of nutrition</td>
<td>3</td>
<td>1</td>
<td>4</td>
<td>43</td>
<td>0</td>
<td>40</td>
<td>0.0% - 21.5%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(1%)</td>
<td>(1.1%)</td>
<td>(1.5%)</td>
<td>(21.5%)</td>
<td>(0.0%)</td>
<td>(12.9%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Artificial (non-oral) fluid administration</td>
<td>17</td>
<td>6</td>
<td>19</td>
<td>45</td>
<td>5</td>
<td>151</td>
<td>2.3% - 48.6%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(5.8%)</td>
<td>(6.6%)</td>
<td>(7.1%)</td>
<td>(24.5%)</td>
<td>(2.3%)</td>
<td>(48.6%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At least one artificial nutrition and hydration treatment</td>
<td>19</td>
<td>7</td>
<td>22</td>
<td>82</td>
<td>6</td>
<td>169</td>
<td>2.7% - 54.3%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(6.5%)</td>
<td>(7.7%)</td>
<td>(8.2%)</td>
<td>(41%)</td>
<td>(2.7%)</td>
<td>(54.3%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Critical care treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resuscitation</td>
<td>2</td>
<td>5</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>7</td>
<td>0.5% - 5.5%</td>
<td>0.05</td>
</tr>
<tr>
<td>(0.7%)</td>
<td>(5.5%)</td>
<td>(1.5%)</td>
<td>(1%)</td>
<td>(0.5%)</td>
<td>(2.3%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Artificial ventilation</td>
<td>3</td>
<td>4</td>
<td>7</td>
<td>3</td>
<td>22</td>
<td></td>
<td>1% - 7.1%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(1%)</td>
<td>(4.4%)</td>
<td>(2.6%)</td>
<td>(3.6%)</td>
<td>(1.4%)</td>
<td>(7.1%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At least one critical care treatment</td>
<td>4</td>
<td>8</td>
<td>11</td>
<td>9</td>
<td>27</td>
<td></td>
<td>1.4% - 8.7%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(1.4%)</td>
<td>(8.8%)</td>
<td>(4.1%)</td>
<td>(4.9%)</td>
<td>(1.8%)</td>
<td>(8.7%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antimicrobial treatment</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antibiotics of any type</td>
<td>33</td>
<td>18</td>
<td>48</td>
<td>74</td>
<td>38</td>
<td>140</td>
<td>11.3% - 45%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(11.3%)</td>
<td>(19.8%)</td>
<td>(17.8%)</td>
<td>(37%)</td>
<td>(17.1%)</td>
<td>(45%)</td>
<td></td>
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<tr>
<td>At least one medication</td>
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</tr>
<tr>
<td>Statins</td>
<td>3</td>
<td>4</td>
<td>10</td>
<td>4</td>
<td>9</td>
<td>13</td>
<td>1% - 4.4%</td>
<td>0.23</td>
</tr>
<tr>
<td>(1%)</td>
<td>(4.4%)</td>
<td>(3.7%)</td>
<td>(2%)</td>
<td>(4.1%)</td>
<td>(4.2%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antidiabetics</td>
<td>12</td>
<td>2</td>
<td>18</td>
<td>7</td>
<td>14</td>
<td>41</td>
<td>2.2% - 13.2%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(4.1%)</td>
<td>(2.2%)</td>
<td>(6.7%)</td>
<td>(3.5%)</td>
<td>(6.3%)</td>
<td>(13.2%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral anticoagulants</td>
<td>1</td>
<td>0</td>
<td>3</td>
<td>4</td>
<td>7</td>
<td>17</td>
<td>0.0% - 5.5%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(0.3%)</td>
<td>(0.0%)</td>
<td>(1.1%)</td>
<td>(2%)</td>
<td>(3.2%)</td>
<td>(5.5%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At least one anticoagulant</td>
<td>14</td>
<td>5</td>
<td>28</td>
<td>11</td>
<td>20</td>
<td>57</td>
<td>4.8% - 18.3%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(4.8%)</td>
<td>(5.5%)</td>
<td>(10.4%)</td>
<td>(5.5%)</td>
<td>(9%)</td>
<td>(18.3%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other treatments</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>0.0% - 1%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(0.3%)</td>
<td>(0.0%)</td>
<td>(0.4%)</td>
<td>(1%)</td>
<td>(0.5%)</td>
<td>(1%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chemotherapy/radiotherapy</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0.0% - 1%</td>
<td>0.01</td>
</tr>
<tr>
<td>(0.0%)</td>
<td>(0.0%)</td>
<td>(0.4%)</td>
<td>(1%)</td>
<td>(0.0%)</td>
<td>(0.0%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dialysis</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>1</td>
<td>5</td>
<td>0.0% - 1.6%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(0.3%)</td>
<td>(0.0%)</td>
<td>(0.0%)</td>
<td>(1%)</td>
<td>(0.5%)</td>
<td>(1.6%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgery</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td>2</td>
<td></td>
<td>0.0% - 1.4%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Generalized linear mixed model reporting p-value for differences between countries, $\alpha = 0.05$

All treatments are reported by staff member (nurse/care assistant) most involved in care.

°Results from regression imputation.

* To correct for differences in demographic and clinical characteristics, we included age, length of stay, place of death, dementia at time of death, diseases at time of death (cancer, cardiovascular, pulmonary and other diseases) and functional/cognitive status as fixed effects.

<table>
<thead>
<tr>
<th>At least one of the other treatments</th>
<th>(0.3%)</th>
<th>(0.0%)</th>
<th>(0.4%)</th>
<th>(0.5%)</th>
<th>(1.4%)</th>
<th>(0.6%)</th>
<th>0.0% - 3.5%</th>
<th>&lt;0.001</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3</td>
<td>0</td>
<td>3</td>
<td>7</td>
<td>5</td>
<td>10</td>
<td>0.0% - 3.5%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>At least one potentially inappropriate treatment</td>
<td>58</td>
<td>28</td>
<td>75</td>
<td>106</td>
<td>51</td>
<td>212</td>
<td>19.9% - 68.2%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

(0.3%) (0.0%) (0.4%) (0.5%) (1.4%) (0.6%) 0.0% - 3.5% <0.001

At least one of the other treatments

At least one potentially inappropriate treatment

Generalized linear mixed model reporting p-value for differences between countries, $\alpha = 0.05$

All treatments are reported by staff member (nurse/care assistant) most involved in care.

*Results from regression imputation.

* To correct for differences in demographic and clinical characteristics, we included age, length of stay, place of death, dementia at time of death, diseases at time of death (cancer, cardiovascular, pulmonary and other diseases) and functional/cognitive status as fixed effects.
Disclosure Statement
Miss Honinx reports funding from Polish Ministry of Science and Higher Education based on the decision no 3202/7PR/2014/2, grants from European Union’s Seventh Framework Programme (FP7/2007e2013), during the conduct of the study.

Ethics approval and consent to participate
Ethics approval from the relevant ethics committees were obtained in all participating countries. Belgium: Commissie Medische Ethiek UZBrussel, 27/05/2015; England: NHS – NRES Committee North West-Haydock, 10/09/2015; Finland: Terveyden ja hyvinvoinnin laitos, Institutet för hälsa och välfärd, 30/6/2015; Italy: Comitato Etico, Universitativa Cattolica del Sacro Cuore, 6/11/2017; Netherlands: Medisch Ethische Toetsingscommissie VUMedisch Centrum, 2/7/2015; Poland: Komisja Bioetyczna, Uniwersytetu Jagiellonskiego, 25/6/2015; Switzerland: Commission cantonale d’éthique de la recherche scientifique de Genève (CCER), 6/8/2015.

All persons participating in the study (facility managers, care staff, GPs) have to give their prior informed consent in writing. If residents are unable to give informed consent, they will not be involved in the study. In some countries, such as Poland and the Netherlands, a separate informed consent is not required if questionnaires are filled in anonymously.

Consent for publication
Not applicable.

Availability of data and material
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests
The authors declare that they have no competing interests.

Funding
Project has been co-funded by Polish Ministry of Science and Higher Education in the years 2014-2019 based on the decision no 3202/7PR/2014/2 dated on Nov. 25th, 2014. This work was supported by the European Union’s Seventh Framework Programme (FP7/2007e2013) under grant agreement 603111 (PACE project Palliative Care for Older People). The funders had no role in study design, collection, analysis or interpretation of the data, nor in writing and the decision to submit this article for publication.

Authors’ contributions
EH, TS, RP, SVK, BDOP, SP, KS, GG, HFS, DL and LVDB were involved in the study design. TS, BDOP, SP, KS, GG, HFS, DL and LVDB are involved in data acquisition. EH, TS, RP, SVK, LD, and LVDB were involved in developing the data analysis plan. EH, TS, RP, SVK, BDOP, SP, KS, GG, HFS, DL and LVDB were involved in writing of the manuscript. All authors read and approved the final manuscript.

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*Other PACE collaborators not in the list: Yuliana Gatsolaeva, Rose Miranda, Lara Pivodic, Marc Tanghe, Hein van Hout, Nele Van Den Noortg, Katherine Foggatt, H. Roeline W. Pasman, Ilona Baranska, Mariska Oosterveld-Vlug, Anne B. Wichmann, Yvonne Engels, Myrta Vernooij-Dassen, Jo Hockley, Sui Leppäaho, Sophie Pautex, Catherine Bassal, Federica Mammarella, Martina Mercuri, Paola Rossi, Ivan Segat, Agata Stodolska, Eddy Adang, Marika Kylänen, Paula Andreasen, Outi Kuitunen-Kaija, Danni Collingridge Moore, Agnieszka Pac, Violetta Kijowska, Maud ten Koppel, Jenny T. van der Steen, Emilie Morgan de Paula, and the European Association for Palliative Care vzw, European Forum For Primary Care, Age Platform Europe, and Alzheimer Europe.
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### Prevalence of potentially inappropriate treatments in the last week of life in six countries (complete case analysis)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>BE (N=291)</th>
<th>EN (N=91)</th>
<th>FI (N=269)</th>
<th>IT (N=200)</th>
<th>NL (N = 222)</th>
<th>PL (N=311)</th>
<th>Country range (%)</th>
<th>Corrected p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Artificial nutrition and hydration treatments</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enteral administration of nutrition</td>
<td>2 (0.7%)</td>
<td>1 (1.4%)</td>
<td>2 (0.8%)</td>
<td>13 (7.7%)</td>
<td>3 (1.4%)</td>
<td>53 (24.9%)</td>
<td>0.7% - 24.9%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Parenteral administration of nutrition</td>
<td>3 (1.1%)</td>
<td>1 (1.4%)</td>
<td>4 (1.7%)</td>
<td>43 (25.6%)</td>
<td>0 (0.0%)</td>
<td>40 (19.8%)</td>
<td>0.0% - 19.8%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Artificial (non-oral) fluid administration</td>
<td>16 (6%)</td>
<td>6 (8.1%)</td>
<td>19 (8%)</td>
<td>45 (26.8%)</td>
<td>4 (2%)</td>
<td>125 (52.1%)</td>
<td>6% - 52.1%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>At least one artificial nutrition and hydration treatment</td>
<td>18 (6.8%)</td>
<td>7 (9.5%)</td>
<td>22 (8.6%)</td>
<td>81 (49.7%)</td>
<td>6 (2.9%)</td>
<td>163 (66.3%)</td>
<td>2.9% - 66.3%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Critical care treatment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resuscitation</td>
<td>2 (0.8%)</td>
<td>5 (6.7%)</td>
<td>4 (1.7%)</td>
<td>2 (1.3%)</td>
<td>1 (0.5%)</td>
<td>7 (4%)</td>
<td>0.5% - 4%</td>
<td>0.16</td>
</tr>
<tr>
<td>Artificial ventilation</td>
<td>3 (1.1%)</td>
<td>4 (5.4%)</td>
<td>7 (3%)</td>
<td>7 (4.6%)</td>
<td>3 (1.5%)</td>
<td>22 (11.8%)</td>
<td>1.1% - 11.8%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>At least one critical care treatment</td>
<td>4 (1.5%)</td>
<td>8 (10.8%)</td>
<td>11 (4.7%)</td>
<td>9 (5.9%)</td>
<td>4 (1.9%)</td>
<td>27 (14.8%)</td>
<td>1.5% - 14.8%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Antimicrobial treatment</strong></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antibiotics of any type</td>
<td>33 (12%)</td>
<td>18 (22%)</td>
<td>46 (18.5%)</td>
<td>71 (38.4%)</td>
<td>35 (17%)</td>
<td>107 (44.2%)</td>
<td>12% - 44.2%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>At least one medication</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Statins</td>
<td>3 (1.2%)</td>
<td>4 (6.1%)</td>
<td>10 (4.4%)</td>
<td>4 (2.7%)</td>
<td>9 (4.5%)</td>
<td>13 (8.1%)</td>
<td>1.2% - 8.1%</td>
<td>0.22</td>
</tr>
<tr>
<td>Antidiabetics</td>
<td>12 (4.6%)</td>
<td>2 (2.9%)</td>
<td>18 (7.8%)</td>
<td>7 (4.5%)</td>
<td>14 (7%)</td>
<td>38 (19.7%)</td>
<td>2.9% - 19.7%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Oral anticoagulants</td>
<td>1 (0.4%)</td>
<td>0 (0.0%)</td>
<td>3 (1.3%)</td>
<td>4 (2.7%)</td>
<td>7 (3.5%)</td>
<td>17 (9.6%)</td>
<td>0.0% - 9.6%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>At least one medication</td>
<td>14 (5.8%)</td>
<td>5 (7.9%)</td>
<td>28 (12.4%)</td>
<td>11 (7.5%)</td>
<td>20 (10.2%)</td>
<td>57 (31%)</td>
<td>5.8% - 31%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Other treatments</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>1 (0.4%)</td>
<td>0 (0.0%)</td>
<td>1 (0.4%)</td>
<td>2 (1.3%)</td>
<td>1 (0.5%)</td>
<td>3 (1.7%)</td>
<td>0.0% - 1.7%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Chemotherapy/radiotherapy</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>1 (0.4%)</td>
<td>2 (1.3%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0.0% - 1.3%</td>
<td>0.07</td>
</tr>
<tr>
<td>Dialysis</td>
<td>1 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>2 (1.0%)</td>
<td>1 (0.5%)</td>
<td>5 (2.9%)</td>
<td>0.0% - 2.9%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Generalized linear mixed model reporting p-value for differences between countries. \( \alpha = 0.05 \)
All treatments are reported by staff member (nurse/care assistant) most involved in care.
* To correct for differences in demographic and clinical characteristics, we included age, length of stay, place of death, dementia at time of death, diseases at time of death (cancer, cardiovascular, pulmonary and other diseases) and functional/cognitive status as fixed effects.
Percentages may not correspond with count due to missing values.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Surgery</th>
<th>(0.4%)</th>
<th>(0.0%)</th>
<th>(0.0%)</th>
<th>(1.3%)</th>
<th>(0.5%)</th>
<th>(2.9%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>At least one of the other treatments</td>
<td></td>
<td>3</td>
<td>0</td>
<td>3</td>
<td>7</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>