1 # Potentially inappropriate treatments at the end of life in nursing home residents:
2 # Findings from the PACE cross-sectional study in six European countries
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4
5 ## Abstract
6
7 *Context*

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

12
13 *Objectives*

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

16
17 *Methods*

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

24
25 *Results*

26 We included 1,384 deceased residents from 322 nursing homes. In most countries, potentially
27 inappropriate treatments were rarely used, with a maximum of 18.3% of residents receiving at least one
28 treatment in Poland. Exceptions were antibiotics in all countries (between 11.3% in Belgium and 45% in
29 Poland), artificial nutrition and hydration in Poland (54.3%) and Italy (41%) and antidiabetics in Poland
30 (19.7%).

31
32 *Conclusion*

33 Although the prevalence of potentially inappropriate treatments in the last week of life was generally low,
34 antibiotics were frequently prescribed in all countries. In Poland and Italy, the prevalence of artificial

35 administration of food/fluids in the last week of life was high, possibly reflecting country differences in

36 legislation, care organization and culture, and the palliative care competences of staff.

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

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40

41 **Key message**:

42 Potentially inappropriate treatments in the last week of life of nursing homes residents are uncommon in

43 most countries except for the use of antibiotics. In Italy and Poland these treatments are more prevalent,

44 especially artificial nutrition and fluid treatments and antibiotics, possibly due to country differences in

45 legislation, organization, culture and staff competence.

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47 **Running title**: Potentially inappropriate treatments in last week

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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

105   study was to estimate the prevalence of potentially inappropriate treatments in the last week of

106   life in nursing home residents in six European countries and to study the differences in prevalence

107   of these treatments between countries.

108   **Methods**

109   *Study design and sampling*

110   A cross-sectional study of deceased residents in nursing homes was conducted in 2015 in six

111   European countries: Belgium (Flanders), England, Finland, Italy, the Netherlands and Poland(2),

112   using proportional stratified random sampling. In each country, nursing homes were stratified by

113   region (provinces or other large regions), by type and by bed capacity (above/below country

114   median), and sampled randomly to cover the entire country. For each one that declined

115   participation, another from the same stratum was sampled. Available national (or regional in

116   Belgium) lists were used for recruitment. In England, we also used the ENRICH (Enabling Research

117   in Care Homes) network(29). In Italy, a previously created cluster interested in research was used

118   as the basis for the sample since no national list was available. We aimed to include at least 48

119   nursing homes per country, to identify a minimum of 192 residents per country or 1,152 in total(2).

120   The PACE protocol provides more details(2).

121
122   *Setting and participants*

123   The term nursing home in this paper refers to 'collective institutional settings where care, on-site

124   provision of personal assistance with activities of daily living, and on-site or off-site provision of

125   nursing and medical care, is provided for older people who live there, 24 hours a day, seven days

126   a week, for an undefined period of time' (30). Participating nursing homes reported on all deceased

127   residents over the preceding three months. Questionnaires on each were sent to the nurse/care

128   assistant most involved in their care, the manager, and the resident's general practitioner (GP); the

129   manager was asked to fill in a questionnaire about the nursing home.

130   *Data collection*

131 Nursing homes received a letter presenting the PACE project and a call for participation. Further

132 contact was made via phone or email. The manager nominated an internal contact who provided

133 an overview of all deceased residents in the preceding three months and a list of the key

134 respondents for each (staff member, i.e. nurse/care assistant most involved in care,

135 manager/administrator, GP); these received a paper questionnaire with an anonymous code and

136 an attached document that guaranteed full anonymity and confidentiality with questionnaires

137 returned directly to the researchers who monitored them using excel files. In case of non-response,

138 up to two reminders were sent after three and six weeks.

139 *Measurements*

140 Questionnaires from all three key respondents were used to report on the characteristics of the

141 resident: age, gender, length of stay in the nursing home, place of death, presence and stage of

142 dementia at time of death, diseases at time of death and functional and cognitive status during last

143 month of life (Table 1). Presence of dementia was based on the estimation of the GP, nurse or

144 both; stage was based on the Global Deterioration Scale and the Cognitive Performance Scale, as

145 estimated by nursing staff(3) with CPS scores of 5-6 and GDS stage 7 considered as advanced

146 dementia. The score for functional and cognitive status during last month of life was computed

147 with the Bedford Alzheimer Nursing Severity Scale (BANS-S)(31), ranging between 7 and 28. Higher

148 scores indicated greater severity.

149 In this study, we refer to inappropriate treatments as treatments and/or medication for which 'the

150 negative consequences (such as mortality and symptom burden) outweigh the expected health

151 benefits (such as increased life expectancy or pain relief)'(32). We first performed an extensive

152 literature search. Next, during multiple meetings with the PACE consortium (i.e. geriatricians,

153 nurses, psychologists) and palliative care researchers, we discussed the list of potentially

154 inappropriate treatments and made a final selection based on the following criteria: 1) used as a

155 standard treatment for older people, 2) considered potentially life-prolonging, and 3) can be easily

156 recalled by a nurse filling in the questionnaire. The final selection agreed by the consortium

157 partners, was: artificial enteral administration of nutrition (e.g. tube feeding, percutaneous

158 endoscopic gastrostomy i.e. PEG), parenteral administration of nutrition, artificial fluids,

159 resuscitation, artificial ventilation, blood transfusion, chemotherapy/radiotherapy, dialysis,

160 surgery, antibiotics, statins, antidiabetics, new oral anticoagulant (33–38). Nurses were asked

161 whether, to their knowledge, these were administered in the last week of life or not (meaning

162 either 'not at all' or 'in the last month except the last week'). The treatments were then subdivided

163 into five categories: artificial nutrition and hydration treatments (enteral administration nutrition,

164 parental administration nutrition, artificial fluid), critical treatments (resuscitation and artificial

165 ventilation), antimicrobial treatments (antibiotics), medications (statins, antidiabetics, new oral

166 anticoagulants) and other (blood transfusion, chemotherapy/radiotherapy, dialysis, surgery).

167

168 *Statistical analysis*

169 Analyses were conducted for deceased residents for whom an assessment by the nurse was made

170 retrospectively, using IBM SPSS version 25(39). To investigate the effect of missing data (up to 24%

171 missing values for some treatments), sensitivity analyses were conducted via imputation of

172 incomplete cases with fully conditional specification (shown in Results and Table 2) and complete

173 cases (Table 1A in Appendix). The imputation method estimates each missing value based on

174 associations with other covariates from the dataset using regression analysis (age of resident,

175 gender of resident, availability and number of visits by GP, comorbidity and cause and place of

176 death). Demographic and clinical characteristics are reported as mean and standard deviation (SD)

177 for continuous variables, or median and range in case of skewness, and count and percentage for

178 categorical variables. Linear and logistic mixed-effects regression was used to compute differences

179 in demographic characteristics of residents between countries. These models were used for the

180 analyses because of the clustering of data (in countries and nursing homes). Country was included

181 as a fixed effect and nursing home as a random effect in each model. We present frequencies and

182 total numbers for all potentially inappropriate treatments in each country (Table 1).

183 To determine differences in the prevalence between countries, we conducted logistic mixed-

184 effects regression analyses (Table 2). Country was again included as a fixed effect and nursing home

185 as a random effect in each model. To correct for differences in demographic and clinical

186 characteristics, we included age, length of stay, place of death, dementia at time of death, diseases

187 (cancer, cardiovascular, pulmonary and others) and functional/cognitive status as fixed effects.

188   Missing values for each treatment were excluded. This allowed for a fair comparison between

189   countries. An alpha level of p<0.05 represents statistical significance.

190

191   *Ethical aspects*

192   The relevant ethics committee of each country approved the study protocol (2), except for Italy

193   and the Netherlands, where no additional ethical approval was needed since retrospective data of

194   deceased residents was used.

195

196   Results

197

198   In 322 participating nursing homes, 1,707 deaths were reported. For 11 cases, no staff member

199   could be identified (Figure 1). Of the 1,696 staff members sent a questionnaire, 1,384 responded

200   (overall response rate 81.6%). Response rates per country are reported in the footnotes of Figure

201   1. Sensitivity analyses using only complete cases (Table 1A in Appendix) did not result in different

202   conclusions.

203

204   *Characteristics of the study sample*

205   At the time of death, mean age ranged between 81 years in Poland and 87 years in Belgium and

206   England (Table 1). Residents were mostly female, ranging from 63.5% in Poland to 75% in England.

207   The shortest median stay (145 days) was found in Poland, the longest (745 days) in Belgium.

208   Residents died mainly in the nursing home (80% in Poland – 89.3% in the Netherlands). Dementia

209   was most prevalent in Finland (82.5%) and least in England (60.2%), with between 42.9% (England)

210   and 64% (Poland) being advanced. Severe cardiovascular disease was most often reported as the

211   disease at time of death in all countries (34.7% in Belgium – 55.7% in Poland) except England,

212   where this was malignant cancer (42.9%). The poorest functional and cognitive status was found

213   in Poland (BANS-S mean score of 21.9) and the best in England (BANS-S mean score of 17.5).

214

215   *Differences in the prevalence of potentially inappropriate treatments in the last week of life in six*

216   *countries*

217   Use of at least one potentially inappropriate treatment in the last week ranged from 19.9% in

218   Belgium to 68.2% in Poland (p<0.001). Artificial nutrition and/or hydration were most frequent in

219   Poland (54.3%) and least in the Netherlands (2.7%; p<0.001). In advanced dementia use was low

220   in England (0%), the Netherlands (1.7%), Finland (3.8%) and Belgium (4.8%) but higher in Italy

221   (43.9%) and Poland (59.4%; not in tables), artificial fluids being used most (p<0.001), in particular

222   in Poland (48.6%) and Italy (24.5%). Artificial enteral nutrition was administered mainly in Poland

223   (17%; p>0.001) whereas parenteral nutrition was more prevalent in Italy (21.5%; p>0.001). Use of

224   critical care treatments was limited, ranging from 8.7% in Poland to 1.4% in Belgium (p<0.001),

225   with resuscitation being most frequent in England (5.5%; p=0.05) and artificial ventilation in Poland

226   (7.1%; p>0.001). Of all treatments, antibiotics were the most commonly used in all countries, from

227   11.3% in Belgium to 45% in Poland (p<0.001). At least one of antibiotics, antidiabetics, statins, and

228   anticoagulants was used in 18.3% of residents in Poland and 4.8% in Belgium (p<0.001).

229   Antidiabetic medications were administered in from 2.2% in England to 13.2% in Poland (p<0.001)

230   and statins from 1% in Belgium to 4.4% in England (p=0.23). No use of oral anticoagulants was

231   reported in England while in Poland use was reported for 5.5% of residents (p<0.001). Other

232   treatments like blood transfusions, chemotherapy or radiotherapy, dialysis and surgery were rarely

233   used, from England where no usage was reported to Poland where 3.2% of residents underwent

234   at least one of these treatments (p<0.001). Dialysis was rarely used (p<0.001) ranging between 0%

235   (England and Finland) and 1.6% (Poland). Surgery was performed on none of the residents in

236   England and on up to 1.4% in the Netherlands (p<0.001). No blood transfusions were reported in

237   England with 1% in Poland (p<0.001). Chemotherapy and radiotherapy were almost never used in

238   the last week of life in any country, ranging from 0% in Belgium, England, the Netherlands and

239   Poland to 1% in Italy. The risk adjustment procedure ruled out these differences being due to

240   resident characteristics, implying they reflected differences in appropriate care between countries.

241   Results of the complete case analysis were similar to the results from the imputed data (Table 1A

242   in Appendix).

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244   **Discussion**

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246   *Main findings*

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248 Artificial ventilation, resuscitation, blood transfusions, chemotherapy or radiotherapy, dialysis and

249 surgery were rarely used in the last week of life of nursing home residents in most of the studied

250 countries. However, the prevalence of most treatments differed statistically significantly between

251 countries. Poland had the highest percentage of residents receiving at least one potentially

252 inappropriate treatment in the last week of life. Artificial nutrition and/or hydration were common

253 in Poland and Italy, in particular the administration of artificial fluids, even in residents with

254 advanced dementia. Antibiotics were frequently administered in all countries, albeit with the

255 highest rates in Poland and Italy, and antidiabetics were most often administered in Poland.

256
257 *Strengths and limitations*
258
259 This study is the first to compare the use of potentially inappropriate treatments in the last week

260 of life of nursing home residents in representative samples of nursing homes in different countries.

261 We were able to include data on 1,384 residents from 322 nursing homes in six European countries

262 with different healthcare systems(6) and palliative care cultures(40). The risk adjustment

263 procedure assured that our results reflected differences in prevalence between countries and were

264 not influenced by differences in resident characteristics.

265

266 This study also has important limitations. Firstly, it is not possible to infer from survey data when a

267 particular treatment is 'inappropriate'. The data may lead to the assumption that, in retrospect, all

268 treatments administered in the last week of life were inappropriate. However, death is difficult to

269 predict(41) so at the time it was given, a treatment may not have been considered inappropriate.

270 Nevertheless, this study compares the use of treatments on a country level and does not aim to

271 evaluate their appropriateness on an individual level. Secondly, the data were collected from

272 nurses rather than directly from resident files. There is a possibility of recall bias, though nurses

273 were instructed to consult patient records where necessary. Thirdly, we did not collect information

274 about when treatments were initiated or the clinical indications for them, which would have

275 provided a more detailed understanding. Fourthly, we were dealing with high quantities of missing

276 data for some treatments (up to 24%). Therefore, sensitivity analyses were conducted via

277 regression imputation of incomplete and complete cases. These showed mainly similar results,

278   indicating that the missing data influence was small. Finally, when a resident died in hospital, the

279   nursing home may not have had information on hospital treatments in the last week of life, leading

280   to a possible underestimation. However, given that only 15% of the residents died in-hospital, the

281   possible bias caused by this is likely to be small.

282

283   *What this paper adds*

284   This study showed that the prevalence of most potentially inappropriate treatments in the last

285   week of life was low in nursing home residents in Belgium, England, Finland and the Netherlands

286   and particularly low compared with earlier studies in the United States and Canada. For instance,

287   up to 23% of residents with severe cognitive impairment in Canada received statins in their last

288   week of life, and anticoagulants were used in 52% of nursing home residents with dementia.

289   However, comparison of data is difficult when study designs and data collection are different (data

290   from medical records and administrative databases using prospective samples)(42–45). Besides

291   the variation in data collection and study design, differences might be explained by the North

292   American medical culture that tends to favor more aggressive treatments for terminally ill

293   people(46).

294

295   The use of antibiotics in the last week of life was high in all countries, from one in ten in Belgium

296   to four in ten in Poland. There is an ongoing debate on the indications for antibiotics at the end of

297   life(47,48) and guidelines on antimicrobial stewardship in palliative care do not yet exist(48). While

298   some researchers consider antibiotic treatment in the last days of life to be pointless(49–51),

299   others consider it part of symptom control(52). Earlier research on the use of antibiotics in nursing

300   homes revealed a similar prevalence at the end of life(53–58). It is challenging to predict when

301   someone will die(41) and whether an antimicrobial treatment will have a positive effect on

302   symptom control, which complicates the decision(47), particularly in residents with cognitive

303   impairments for whom expressing symptoms is difficult(48). Better recognition of the terminal

304   phase might help with these decisions. Finally, more research is needed to guide the use of

305   antibiotics at the end of life of nursing home residents.

306

307   The low prevalences in Belgium, England and the Netherlands might be partly explained by the

308   culture of palliative care. In those countries many nursing homes provide palliative care and have

309   more palliative care implementation activities (6), with high regional and national activity at policy,

310   finance, legislation and regulation levels and a longer tradition of advance care planning than in

311   Poland and Italy, making nursing home staff more aware of the resident's preferences at the end

312   of life.

313   In contrast with other countries, the prevalence of most potentially inappropriate treatments was

314   highest in Poland and Italy, especially for enteral and parenteral administration of nutrition and

315   artificial fluid administration, even with advanced dementia. There are several possible

316   explanations for this. Firstly, the high rate in Italy might be related to law enforcement. In 2009, a

317   bill was passed(59) mandating that hydration and nutrition must always be provided, and by any

318   means, because they are considered basic support measures and fundamental to life. In Poland,

319   artificial feeding is considered an admission criterion for nursing homes (60). Nevertheless, their

320   appropriateness is questionable (61), especially for those with advanced dementia(15). Taking into

321   account the relatively high numbers with advanced dementia in our sample, with the highest rates

322   in Poland and Italy (64% and 55%), our findings are particularly striking.

323   Secondly, care culture in these countries rarely includes advance care planning, leaving the

324   administration or discontinuation of certain treatments undiscussed(62). This may lead to more

325   pressure from family members to use all possible treatments(62,63). The decision about

326   discontinuation may also cause ethical problems when there is no advance care planning in place.

327   In addition, because of the greater taboo about death and dying in these countries, nursing home

328   staff may not feel competent to discuss end-of-life issues with residents and family

329   members(5,64,65). A third possible explanation may be the low level of basic knowledge of end-

330   of-life care among nursing home staff. An earlier report of the PACE study(7) showed that

331   knowledge of the basic physical aspects of end-of-life care among nurses and care assistants in

332   nursing homes was lowest in Poland and Italy, particularly of indications for the use of feeding

333   tubes(7). Fourthly, GPs in Poland and Italy recognize the terminal phase less often than in Belgium,

334   England, Finland and the Netherlands(66). Nursing home residents in Poland and Italy also least

335   often had palliative care as their main treatment goal in the last week of life, indicating a focus on

336 life-sustaining treatments. This might lead to negative consequences such as more futile or invasive

337 treatments, more 'in bed' time and higher healthcare costs(67). At the same time, one could argue

338 that treatment choices also have to be culturally sensitive to be appropriate. Although ESPEN

339 (European Society of Clinical Nutrition and Metabolism) has elaborated European nutrition

340 recommendations(68), there are country-specific approaches to artificial nutrition, which not only

341 depend on legislation or health care policy and organization, but also on culture. It is also plausible

342 that a difference in prescribing habits between countries is responsible for difference in

343 treatments. However, this was not examined in this study and should be included in future
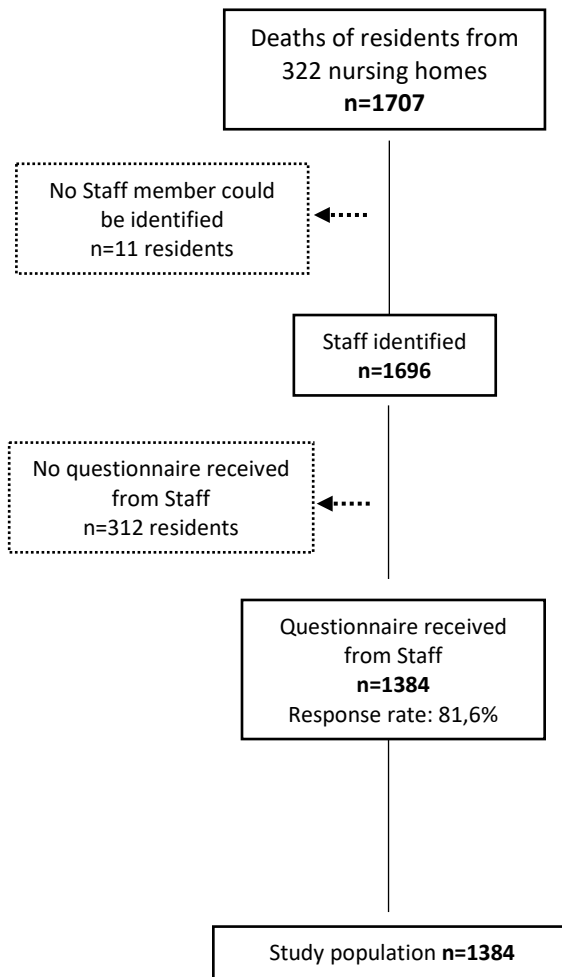
344 research

345

346 *Implications*

347 Our findings are a potential starting point for the improvement of end-of-life care treatments in

348 nursing homes. Practices where there is more room for improvement (e.g. artificial nutrition and

349 hydration treatments), require particular attention. Substantial country differences call for the

350 development of guidelines to assist nursing home staff and GPs in treatment decision-making and

351 in recognizing the terminal phase, taking into account cultural differences. Further, greater

352 attention needs to be paid to advance care planning in nursing homes as this may help residents,

353 relatives and caregivers to discuss goals and preferences for future care. Finally, there is a need for

354 staff training in end-of-life care conversations and the physical aspects of end-of-life care. Our

355 results can be used by policy and other decision-makers to develop public health policies and

356 interventions to improve the appropriateness of end-of-life care in nursing homes and allow the

357 exchange of good practices across national borders.

358

359 **Conclusion**

360 The prevalence of potentially inappropriate treatments in the last week of life of nursing home

361 residents was low in most studied countries, except for the use of antibiotics which was common.

362 In Italy and Poland, all treatments were more prevalent, specially the administration of artificial

363 nutrition and fluids and antibiotics. These differences may reflect country-specific differences in

364 legislation, care organization, culture and the knowledge and skills of nursing home staff regarding

365 palliative care.

366   Figure 1: Flowchart of identified deceased residents for whom an assessment by staff° was made in six countries


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              ┌─────────────────────────────┐
              │  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   │
              └─────────────────────────────┘
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° 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).

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Table 1: Demographic and clinical characteristics of deceased residents for whom an assessment by staff° was made in six countries: (N=1384)

	BE (N=291)	EN (N=91)	FI (N=269)	IT (N=200)	NL (N=222)	PL (N=311)	P-value*
Age – years ‖							
Mean (SD) years old at time of death	87 (7)	87 (9)	85 (9)	86 (8)	86 (9)	81 (11)	**<0.001**
Gender ‖							
Female Count (%)	174 (64.0)	66 (75.0)	169 (64.3)	136 (68.3)	132 (66.7)	195 (63.5)	
Male Count (%)	98 (36.0)	22 (25.0)	94 (35.7)	63 (31.7)	66 (33.3)	112 (36.5)	0.387
Length of stay ‖							
Median (min-max) number of days	745 (2-9706)	600 (2-4952)	581 (1-9218)	416 (2-10171)	710 (1-6290)	145 (1-12365)	**<0.05**
Place of Death ‖^							
Nursing home Count (%)	226 (82.2)	71 (81.6)	224 (84.8)	170 (86.7)	176 (89.3)	248 (80.0)	
Hospital Count (%)	48 (17.5)	16 (8.6)	24 (9.1)	26 (13.3)	12 (6.1)	60 (19.4)	**<0.001**
Dementia at time of death (yes) †‡ §							
Count (%)	183 (62.9)	53 (60.2)	222 (82.5)	154 (77.0)	135 (61.4)	207 (67.9)	**<0.001**
Advanced dementia							
Count %	83 (52.5)	18 (42.9)	78 (43.8)	66 (55.0)	60 (46.2)	96 (64.0)	0.676
Diseases at time of death‡¶							
Malignant cancer‡	30 (15.5)	9 (42.9)	41 (19.4)	26 (17.2)	27 (18.5)	10 (4.0)	**<0.001**
Severe cardiovascular disease‡	67 (34.7)	2 (9.5)	79 (37.4)	71 (47.0)	45 (30.8)	141 (55.7)	**<0.05**
Cerebrovascular accident (CVA)‡	40 (20.7)	3 (14.3)	49 (23.2)	34 (22.5)	25 (17.1)	70 (27.7)	0.483
Severe pulmonary disease‡	33 (17.1)	3 (14.3)	17 (8.1)	40 (26.5)	17 (11.6)	18 (7.1)	**<0.001**
Severe neurological disease (not dementia) ‡	15 (7.8)	0 (0.0)	26 (12.3)	18 (11.9)	11 (7.5)	32 (12.6)	0.381
Severe renal disease‡	19 (9.8)	2 (9.5)	13 (6.2)	22 (14.6)	19 (13.0)	29 (11.5)	0.420
Severe diabetes‡	11 (5.7)	1 (4.8)	16 (7.6)	18 (11.9)	17 (11.6)	33 (13.0)	0.177
Other severe disease‡	31 (16.1)	3 (14.3)	51 (24.2)	33 (21.9)	4 (2.7)	33 (13.0)	**<0.001**
Functional/cognitive status one month before death (BANS-S) † ¶							
Mean (SD)	18.5 (4.9)	17.5 (4.2)	19.6 (4.3)	21.8 (3.7)	17.7 (4.7)	21.9 (4.6)	**<0.001**

* 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°

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

(0.3%)	(0.0%)	(0.4%)	(0.5%)	(1.4%)	(0.6%)		
3	0	3	7	5	10		
At least one of the other treatments (1%)	(0.0%)	(1.1%)	(3.5%)	(2.3%)	(3.2%)	*0.0% - 3.5%*	<0.001
58	28	75	106	51	212		
At least one potentially inappropriate treatment (19.9%)	(30.8%)	(27.9%)	(53%)	(23%)	(68.2%)	*19.9% - 68.2%*	<0.001

Generalized linear mixed model reporting p-value for differences between countries, **α** =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.

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Table 1A Prevalence of potentially inappropriate treatments in the last week of life in six countries (complete case analysis)

	BE (N=291) Count (%)	EN (N=91) Count (%)	FI (N=269) Count (%)	IT (N=200) Count (%)	NL (N = 222) Count (%)	PL (N=311) Count (%)	Country range (%)	Corrected p-value*
Artificial nutrition and hydration treatments								
Enteral administration of nutrition	2 (0.7%)	1 (1.4%)	2 (0.8%)	13 (7.7%)	3 (1.4%)	53 (24.9%)	0.7% - 24.9%	<0.001
Parenteral administration of nutrition	3 (1.1%)	1 (1.4%)	4 (1.7%)	43 (25.6%)	0 (0.0%)	40 (19.8%)	0.0% - 19.8%	<0.001
Artificial (non-oral) fluid administration	16 (6%)	6 (8.1%)	19 (8%)	45 (26.8%)	4 (2%)	125 (52.1%)	6% - 52.1%	<0.001
At least one artificial nutrition and hydration treatment	*18 (6.8%)*	*7 (9.5%)*	*22 (9.6%)*	*81 (49.7%)*	*6 (2.9%)*	*163 (66.3%)*	*2.9% - 66.3%*	<0.001
Critical care treatment								
Resuscitation	2 (0.8%)	5 (6.7%)	4 (1.7%)	2 (1.3%)	1 (0.5%)	7 (4%)	*0.5% - 4%*	0.16
Artificial ventilation	3 (1.1%)	4 (5.4%)	7 (3%)	7 (4.6%)	3 (1.5%)	22 (11.8%)	*1.1% - 11.8%*	<0.001
At least one critical care treatment	*4 (1.5%)*	*8 (10.8%)*	*11 (4.7%)*	*9 (5.9%)*	*4 (1.9%)*	*27 (14.8%)*	*1.5% - 14.8%*	<0.001
Antimicrobial treatment								
Antibiotics of any type	33 (12%)	18 (22%)	46 (18.5%)	71 (38.4%)	35 (17%)	107 (44.2%)	*12% - 44.2%*	<0.001
At least one medication								
Statins	3 (1.2%)	4 (6.1%)	10 (4.4%)	4 (2.7%)	9 (4.5%)	13 (8.1%)	*1.2% - 8.1%*	0.22
Antidiabetics	12 (4.6%)	2 (2.9%)	18 (7.8%)	7 (4.5%)	14 (7%)	38 (19.7%)	*2.9% - 19.7%*	<0.001
Oral anticoagulants	1 0.4%	0 (0.0%)	3 (1.3%)	4 (2.7%)	7 (3.5%)	17 (9.6%)	*0.0% - 9.6%*	<0.001
At least one medication	*14 (5.8%)*	*5 (7.9%)*	*28 (12.4%)*	*11 (7.5%)*	*20 (10.2%)*	*57 (31%)*	*5.8% - 31%*	<0.001
Other treatments								
Blood transfusion	1 (0.4%)	0 (0.0%)	1 (0.4%)	2 (1.3%)	1 (0.5%)	3 (1.7%)	*0.0% - 1.7%*	<0.001
Chemotherapy/radiotherapy	0 (0.0%)	0 (0.0%)	1 (0.4%)	2 (1.3%)	0 (0.0%)	0 (0.0%)	*0.0% - 1.3%*	0.07
Dialysis	1	0	0	2	1	5	*0.0% - 2.9%*	<0.001

		(0.4%)	(0.0%)	(0.0%)	(1.3%)	(0.5%)	(2.9%)		
Surgery	1	0	1	1	3	2	0.0% - 1.5%	<0.001
	(0.4%)	(0.0%)	(0.4%)	(0.7%)	(1.5%)	(1.3%)		
At least one of the other treatments	*3*	*0*	*3*	*7*	*5*	*10*	*0.0% - 6.5%*	<0.001
	(1.2%)	*(0.0%)*	*(1.3%)*	*(4.8%)*	*(2.6%)*	*(6.5%)*		

Generalized linear mixed model reporting p-value for differences between countries, α =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.

Missing values for each treatment: enteral administration: 214, parenteral administration: 233, artificial fluid: 194, resuscitation: 272, ventilation: 261, antibiotics: 146, statins: 328, antidiabetics: 274, anticoagulants: 317, blood transfusion: 274, chemotherapy/radiotherapy: 278, dialysis: 285, surgery: 329