CHAPTER 2

CHANGES IN PRESCRIBING SYMPTOMATIC AND PREVENTIVE MEDICATIONS IN THE LAST YEAR OF LIFE IN OLDER NURSING HOME RESIDENTS

Helene G van der Meer, Katja Taxis, Lisa G Pont

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ABSTRACT

Background At the end of life goals of care change from disease prevention to symptom control, however little is known about the patterns of medication prescribing at this stage.

Objectives To explore changes in prescribing of symptomatic and preventive medication in the last year of life in older nursing home residents.

Methods A retrospective cohort study was conducted using pharmacy medication supply data of 553 residents from 16 nursing home facilities around Sydney, Australia. Residents received 24-h nursing care, were aged ≥ 65 years, died between June 2008 and June 2010 and were using at least one medication 1 year before death. Medications were classified as symptomatic, preventive or other. A linear mixed model was used to compare changes in prescribing in the last year of life.

Results 68.1% of residents were female, mean age was 88.0 (SD: 7.5) years and residents used a mean of 9.1 (SD: 4.1) medications 1 year before death. The mean number of symptomatic medications per resident increased from 4.6 medications 1 year before death to 5.1 medications at death (95% CI 4.4–4.7 to 5.9–5.2, p = 0.000), while preventive medication decreased from 2.0 to 1.4 medications (95% CI 1.9–2.1 to 1.3–1.5, p = 0.000). Symptomatic medications were used longer in the last year of life, compared to preventive medications (336.3 days (95% CI 331.8–340.8) versus 310.9 days (95% CI 305.2–316.7), p = 0.000).

Conclusions Use of medications for symptom relief increased throughout the last year of life, while medications for prevention of long-term complications decreased. But changes were slight and clinical relevance can be questioned.

INTRODUCTION

At all stages across the life span, the decision to prescribe a medication should be based on weighing potential benefits and harms of the medication considering the individual’s treatment goals. Goals range from decreasing mortality and morbidity, prevention of future conditions or complications, or minimisation of symptoms. Toward the end of life, in addition to considerations around potential medication related benefits and harms, treatment choice should also take life expectancy into consideration. As life expectancy decreases, the goals of care may change from decreasing mortality and morbidity, to symptom control. [1] Long-term residential aged care or nursing home residents are among the frailest of all older populations. They are generally medically complex, using a high number of medications, and this complexity together with age-related pharmacokinetic- and dynamic puts them at high risk of adverse outcomes related to medication. [2–4]

Of all aged care residents, 91% die in the nursing home after an average stay of 168 weeks for women and 110 weeks for men, indicating that the majority of residents have limited life expectancy following nursing home admission. [3] Adjusting prescribing according to a decreasing life expectancy involves deprescribing, defined as the process of withdrawing inappropriate medications. [5, 6] Hence in this population a decrease in preventive and an increase in the use of medications for symptom control and palliation could be expected. [7]

To date few studies exploring changes in the use of symptomatic and preventive medications have been conducted in older nursing home populations at the end of life. A recent systematic review found that use of preventive medications in patients with limited life expectancy was common. [8] Only few studies focused on deprescribing and there was no consensus on how to optimise medication use at the end of life. Of the 15 studies included, three were performed in a nursing home setting. [8]
These studies included only a small study population [9] or had a
cross-sectional study design. [10, 11] In order to consider optimi-
sation of medication use at the end of life we need to understand
the current patterns of use as life expectancy decreases. Therefore,
the aim of this study was to explore changes in prescribing of
symptomatic and preventive medications in the last year of life
among older nursing home residents.

METHODS

Study design and setting
A retrospective cohort study of 3876 nursing home residents liv-
ing in 26 residential aged care (RAC) facilities in New South Wales,
Australia between 1st June 2008 and 10th June 2010. The RAC fa-
cilities varied from low care to high care. High care facilities pro-
vided 24 h nursing care including medication administration. All
residents received medical care from the general practitioner of
their choice and were eligible to receive annual medication re-
views by a pharmacist. Each facility has a contracted pharmacy for
medication supply.

Study population
Recruitment was done at the facility level. All residents aged 65
years or older who died in one of the 26 RAC facilities between
2nd of June 2008 and 10th of June 2010 were included in the co-
hort. To allow medication changes in the year prior to death to
be explored, only those residents who were taking at least one
medication 1 year prior to death were included in the cohort.
Residents who were discharged prior to death were excluded
from the study, as medication use could not be ascertained once
they left the facility.

Data source
Weekly pharmacy medication supply data, including all prescrip-
tion, non-prescription and complementary medications, were
used for the study. The dataset included generic name, dose, date
of commencement, date of cessation and if the use was regular
or ‘as needed’. The dataset also included limited demographic data
for each resident including age, sex, date of admission, date and
reason for discharge and facility.

Medication classification
Medications were coded using the World Health Organization
Anatomical Therapeutic Chemical (ATC) code. [12] Medications
were classified into three categories: symptomatic, preventive and
other. All medications recommended for symptom control in the
Australian national palliative care guidelines were considered as
symptomatic medications. [13, 14] Medications defined in the lit-
erature for primary or secondary prevention of all-cause mortality
were defined as preventive medications. [15] Preventive medica-
tions included antihypertensive medications, [16] antithrombotic
agents, [17] osteoporosis medication [18] and lipid modifying
agents. [19] Medications that were not considered as either pre-
ventive or symptomatic were classified as other. Antibiotics, top-
ical preparations, ophthalmological and otological medications
were excluded due to the episodic nature of the use of these med-
ications. Vaccines were also excluded as they were administered
by the general practitioner and not supplied by the pharmacy. A
list of included medications can be found in the Appendix.

Outcomes
Three main outcome measures were determined. Firstly, we com-
pared the mean number of symptomatic, preventive and other
medications per resident at 1 year, 6 months, 1 month and 1 week
(8 days) before death and on the day of death. Secondly, we com-
pared the type of symptomatic, preventive and other medication
used 1 year before death versus on the day of death. For this anal-
ysis we included all medications, grouped by ATC level 2, which
were used by at least 10% of the population either 365 days before
death or on the day of death. Thirdly, we compared the duration
of use of symptomatic, preventive and other medications in the
last year of life. We included all medications used 365 days before death, and calculated the days of treatment during the last year of life.

All medications used 7 or fewer days before death were considered to be taken on the day of death. This was done for two reasons. Firstly, medication was supplied per week, therefore the last medication might have been supplied up to 7 days before death. Secondly, we assumed some inaccuracies in recording the date of death due to a delay in nursing home staff notifying pharmacy staff.

Statistical analysis
Medication changes were analysed with a linear mixed model to account for clustering of medications within one resident. Our data did not allow clustering for general practitioners. Therefore we performed clustering on the level of facility, to account for possible intra-facility culture of medication prescribing. We included a random intercept and a random slope at the level of resident and facility in the analysis. Analyses were adjusted for age, gender, duration of admission and number of medications at 365 days before death, if the individual p-value in the univariate analysis was 0.25 or less. The number of medication and days of treatment were reported as estimated marginal means with their 95% confidence intervals. The second outcome was analysed using a McNemar test. We report on proportions and absolute numbers of residents. All analyses were conducted in IBM SPSS 24 on a significance level of 0.05.

Ethical approval
This study was approved by the Sydney South West Area Health Service Human Research Ethics Committee, the Concord Repatriation General Hospital (CH62/6/2010-49 HREC/10/CGRH/57).

RESULTS

Resident characteristics
The cohort comprised of 553 residents out of the 3876 residents contained in the dataset (Figure 1).

Residents were between 65 and 105 years of age and lived in 16 different facilities. The average facilities size was 35 (SD: 21) residents per facility (range: 5–71) (Table 1).

Number of symptomatic, preventive and other medications in the last year of life
The total number of medications per resident decreased from 9.1 (95% CI 8.9–9.3) medications 1 year prior to death to 8.5 (95% CI 8.5–8.9) medications at death (p = 0.002). Symptomatic

Figure 1: Flow chart of resident inclusion.
Preventive medications at the end of life in older nursing home residents

Identifying opportunities for deprescribing

medication use increased from 4.6 to 5.1 (95% CI 4.4–4.7 to 5.9–5.2, p = 0.000) medications, while preventive and other medication decreased, respectively 2.0 to 1.4 (95% CI 1.9–2.1 to 1.3–1.5, p = 0.000) and 2.6–2.2 (95% CI 2.4–2.7 to 2.1–2.4, p = 0.000), toward death (Figure 2).

Type of symptomatic, preventive and other medication used in the last year of life
Analgesics were the most frequently used type of medication over the last year of life. Analgesic use did not change significantly during the last year of life and was comparable at 1 year before death and at death, (85.0% to 86.1% of patients, p = 0.610). A shift in the type of analgesics used was seen, shifting from paracetamol to opioids, respectively 83.4% to 77.9% (p = 0.005) and 18.1% to 44.5% (p = 0.000). Other significant changes in use of symptomatic medications toward death were only seen for diuretics (30.2% to 26.0%, p = 0.009) and medications for gastrointestinal disorders (17.2% to 22.8%, p = 0.000). In contrast, all preventive medications decreased significantly from 1 year before death until death. The highest decrease was found in mineral supplements (including calcium), agents acting on the renin-angiotensin-aldosterone-system (RAAS) and lipid modifying agents, those respectively decreased by 9.2% (p = 0.000), 8.9% (p = 0.000) and 8.1% (p = 0.000) (Table 2).

However, at death about one third of all residents was using at least one antihypertensive medication (35.8%), one medication for osteoporosis (32.9%) or an antithrombotic medication (33.1%).

Duration of use of symptomatic, preventive and other medications in the last year of life
Symptomatic, preventive and other medications were used respectively for 363 [95% CI 331.8–340.8], 310.9 [95% CI 305.2–316.7] and 320.3 [95% CI 315.2–325.8] days in the last year of life. Preventive and other medications were ceased earlier than symptomatic medication, respectively 25.4 days earlier [EMM, 95% CI 31.0–19.7, P=0.000] and 15.8 days earlier [EMM, 95% CI 20.9–10.7, P=0.000] (Figure 3).

DISCUSSION
Key findings
Throughout the last year of life we saw little change in overall medication use. Medications commonly used for symptom control slightly increased, while a small decrease in medication for disease-prevention was seen. However at death, preventive medication such as antithrombotic agents, antihypertensive medications and osteoporosis medications were still prescribed to one third of all residents.

Table 1: Resident characteristics

| Characteristic                              | Residents (n = 553) |
|--------------------------------------------|---------------------|
| Age, mean years (SD)                       | 88.0 (7.5)          |
| Gender, % female (number)                  | 68.1 (374)*         |
| Length of stay in RAC facility, mean weeks (SD) | 187.9 (104.4)      |
| Number of medications 365 days before death, mean (SD) | 9.1 (4.5)          |
| Number of medications at death, mean (SD)  | 8.7 (5.1)           |

'n =549, gender was missing for 4 residents

Figure 2: Number of symptomatic, preventive, and other medication in the last year of life. Estimated marginal means (EMMs), adjusted for number of bed days in facility*, age†, and number of medication at 365 days before death‡.

Figure 3: Number of symptomatic, preventive, and other medication in the last year of life. Estimated marginal means (EMMs), adjusted for number of bed days in facility*, age†, and number of medication at 365 days before death‡.
changes in medication use at the end of life.

Table 2: Type of symptomatic, preventive and other medication used by residents 1 year before death versus at death

| Symptomatic | Preventive | Other |
|-------------|------------|-------|
| ATC code    | Medication group | At death % | Δ % | ATC code | Medication group | At death % | Δ % | ATC code | Medication group | At death % | Δ % |
| N02         | Analgesics | 86.1 | 1.1 | B01 | Antithrombotics | 31.1 | −6.0* | C01 | Cardiac therapy | 25.7 | −2.7* |
| A06         | laxatives  | 72.9 | −0.4 | A11 | Vitamins | 23.9 | −5.6* | N06 | Psychomimetics | 24.2 | −6.0* |
| N05         | Psycholeptics | 50.1 | −0.4 | C09 | Agents acting on the RAAS system | 21.3 | −8.9* | B03 | Medication for obstructive airway disease | 22.2 | 0.2 |
| A02         | Medication for gastrointestinal disorders | 38.1 | −3.1 | A12 | Mineral supplements including calcium | 17.9 | −9.2* | B03 | Anti-anemic medication | 15.9 | −2.9 |
| C03         | Diuretics | 26.0 | −4.2* | C07 | Beta blockers | 14.5 | −2.7* | A12 | Mineral supplements (not including calcium) | 14.6 | −1.4 |
| A03         | Medication for gastrointestinal disorders | 22.8 | 5.6* | C10 | Lipid modifying agents | 9.9 | −8.1* | H03 | Thyroid therapy | 11.8 | −11 |
| N03         | Antiepileptic medication | 11.2 | 2.2 | C08 | Calcium channel blocking agents | 7.1 | −4.3* | A10 | Drugs used in diabetes | 11.4 | −34* |
| H02         | Corticosteroids for systemic use | 8.3 | −1.8 | M05 | Drugs for treatment of bone disease | 5.6 | −6.5* |

*McNemar test (df = 552), P < 0.05. Δ: percentage of residents taking medication at death − percentage of residents taking medication 365 days before death. RAAS = Renin-angiotensin-aldosterone system.

Changes in medication use at the end of life.

The characteristics of our cohort of residents are similar to other studies in this setting, so we believe our sample is representative for the nursing home population in Australia. The resident's average duration of stay in the RAC facility was slightly higher than the national average, which might be a consequence of selecting patients who stayed at least 1 year in the RAC. [3] We found an increase in symptomatic medication toward death, which was also seen in a small study looking at the last 3 months of life. [9] and another study focusing at the last week of life. [21]

The increase was very subtle, however, and mostly caused by an increase in gastrointestinal medications. Overall use of analgesics, which are supposed to be the most prominent medication group in palliative care, [13] did not change. But the shift from paracetamol to opioid use indicates some awareness in the changing needs of residents at the end of life by the GP.
Despite some deprescribing, the use of antithrombotics, antihypertensives, and osteoporosis medications was very high at the end of life, similar to other studies. [10, 11, 21] An explanation for this high use could be the lack of consensus on what medications are considered solely preventive and therefore inappropriate at the end of life. [22] We included antithrombotics, lipid-modifying agents, antihypertensives and osteoporosis medication, but other studies have also included iron, antibiotics, acid reducers and medications used in diabetes. [8] An exception to preventive medications, are lipid-modifying agents. These medications, especially statins, were unanimously classified as preventive medication and have been explored the most. [8] This attention to statins might have led to growing awareness of its inappropriateness at the end of life, resulting in early deprescribing by GPs. This could explain the lower use of statins compared to other preventive medication we found in our study.

Strengths and limitations
This study is unique in investigating changes in prescribing of symptomatic and preventive medication in the last year of life in a relatively large group of residents. We based the classification of medications on current guidelines. Some limitations need be taken into consideration when interpreting our results. Firstly, we were using medication supply data and therefore were not able to ascertain actual medication intake. However, the weekly medication supply ensured that the dataset remained relatively sensitive to change. Secondly, in line with other studies using dispensing data, we had no recorded indication for prescribed medication and therefore our medication classification was an approximation. We used the palliative care guidelines for classification of medication and rely on prescribing following the guidelines for correct classification. Thirdly, we were not able to cluster our data at the level of prescriber since each nursing home resident in Australia has his or her own prescriber. Fourthly, by investigating prescribing in the last year of life we had to exclude residents who stayed in the nursing home facility for a shorter time. Our results may not be generalisable to residents who died within a few months of nursing home admission.

CONCLUSION AND IMPLICATIONS FOR FURTHER RESEARCH
The awareness of deprescribing inappropriate medication at the end of life is growing throughout the literature. Recent articles have been published guiding the process of deprescribing [5, 23, 24] and shared decision making at the end of life. [25] But there still remains a lack of high quality evidence guiding deprescribing at the end of life. [26] For example aspirin has a number needed to treat of 120 patients over 6 years to prevent one cardiovascular event and a number needed to harm of 73 for a non-trivial bleedings, based on a study population with a mean age of 57 years. [27] The figures are likely to be different in an older population. Furthermore, contradictory recommendations and variation in interpretations of guidelines leads to clinical uncertainty. [28] An example is the most recent discussion on blood pressure control in older patients. [29] Exploring the use of preventive and symptomatic medication at the end of life is a first step to improve the quality of medication use for these patients.
Identifying opportunities for deprescribing

REFERENCES

1. Holmes HM, Hayley DC, Alexander GC, Sachs GA. Reconsidering medication appropriateness for patients late in life. Arch Int Med. 2006;166(6):605–609.
2. Taxis K, O’Sullivan D, Cullinan S, Byrne S. Drug utilization in older people. In: Elsevier M, Wettermark B, Almársdóttir A, et al, editors. Drug utilization research: Methods and applications. London: Wiley-Blackwell; 2016. p. 259–269.

Netherlands. Public health systems. 2015. 14:181–185.
29. Williamson JD, Supiano MA, Applegate WB, et al. Intensive vs Standard Blood Pressure Control and Cardiovascular Disease Outcomes in Adults Aged >/=75 Years: A Randomized Clinical Trial. JAMA. 2016;315(24):2673–2682.
30. Clifford J, Egberts M, Verhees M, van den Hooven-Broekhuijsen F, van der Schans C. Effect of aspirin on vascular and nonvascular outcomes: meta-analysis of randomized controlled trials. Arch Intern Med. 2012;172(3):209–216.
31. Alhawassi TM, Kras I, Punt LJ. Hypertension in Older Persons: A Systematic Review of National and International Treatment Guidelines. J Clin Hypertens (Greenwich). 2015;17(6):486–492.
32. Williamson JD, Supiano MA, Applegate WB, et al. Intensive vs Standard Blood Pressure Control and Cardiovascular Disease Outcomes in Adults Aged >/=75 Years: A Randomized Clinical Trial. JAMA. 2016;315(24):2673–2682.

17. WHO Collaborating Centre for Drug Statistics Methodology. ATC/DDD Index — Antithrombotic agents. 2016. https://www.whocc.no/atc_ddd_index?code=B01A&showdescription=no. Accessed March 2017.
18. NPS Medicinewise. Medicines for osteoporosis. 2017. http://www.nps.org.au/conditions/hormones-metabolism-and-nutritional-problems/bone-disorders-and-calcium-metabolism/osteoporosis/for-individuals/medicines. Accessed Mar 2017.
19. WHO Collaborating Centre for Drug Statistics Methodology. ATC/DDD Index — Lipid modifying agents. 2016. https://www.whocc.no/atc_ddd_index/?code=C10. Accessed March 2017.

Netherlands. Public health systems. 2015. 14:181–185.
29. Williamson JD, Supiano MA, Applegate WB, et al. Intensive vs Standard Blood Pressure Control and Cardiovascular Disease Outcomes in Adults Aged >/=75 Years: A Randomized Clinical Trial. JAMA. 2016;315(24):2673–2682.

Netherlands. Public health systems. 2015. 14:181–185.
29. Williamson JD, Supiano MA, Applegate WB, et al. Intensive vs Standard Blood Pressure Control and Cardiovascular Disease Outcomes in Adults Aged >/=75 Years: A Randomized Clinical Trial. JAMA. 2016;315(24):2673–2682.

Netherlands. Public health systems. 2015. 14:181–185.
29. Williamson JD, Supiano MA, Applegate WB, et al. Intensive vs Standard Blood Pressure Control and Cardiovascular Disease Outcomes in Adults Aged >/=75 Years: A Randomized Clinical Trial. JAMA. 2016;315(24):2673–2682.

Netherlands. Public health systems. 2015. 14:181–185.
29. Williamson JD, Supiano MA, Applegate WB, et al. Intensive vs Standard Blood Pressure Control and Cardiovascular Disease Outcomes in Adults Aged >/=75 Years: A Randomized Clinical Trial. JAMA. 2016;315(24):2673–2682.

Netherlands. Public health systems. 2015. 14:181–185.
29. Williamson JD, Supiano MA, Applegate WB, et al. Intensive vs Standard Blood Pressure Control and Cardiovascular Disease Outcomes in Adults Aged >/=75 Years: A Randomized Clinical Trial. JAMA. 2016;315(24):2673–2682.

Netherlands. Public health systems. 2015. 14:181–185.
29. Williamson JD, Supiano MA, Applegate WB, et al. Intensive vs Standard Blood Pressure Control and Cardiovascular Disease Outcomes in Adults Aged >/=75 Years: A Randomized Clinical Trial. JAMA. 2016;315(24):2673–2682.

Netherlands. Public health systems. 2015. 14:181–185.
29. Williamson JD, Supiano MA, Applegate WB, et al. Intensive vs Standard Blood Pressure Control and Cardiovascular Disease Outcomes in Adults Aged >/=75 Years: A Randomized Clinical Trial. JAMA. 2016;315(24):2673–2682.
### Appendix: Classification of medications used by our cohort into symptomatic, preventive or other

| ATC code | Name                                      | Category   |
|----------|-------------------------------------------|------------|
| A01AD1   | Various agents for local oral treatment  | Other      |
| A02AB01  | Aluminium Hydroxide                       | Other      |
| A02AD01  | Ordinary salt combinations                | Other      |
| A02AF02  | Ordinary salt combinations and antiflatulents | Other      |
| A02BA03  | Famotidine                                | Other      |
| A02BX13  | Alginic acid                              | Other      |
| A03AA04  | Mebeverine                                | Other      |
| A03AX    | Other drugs for functional gastrointestinal disorders | Other |
| A05BA03  | Silymarin                                 | Other      |
| A06AA    | Softeners, emollients                     | Other      |
| A06AC03  | Sterculia                                 | Other      |
| A07C     | Electrolytes with carbohydrates           | Other      |
| A07EC01  | Sulfasalazine                             | Other      |
| A07EC02  | Mesalazine                                | Other      |
| A09A     | Digestives, including enzymes             | Other      |
| A10AB    | Fast-acting insulins                      | Other      |
| A10AC    | Intermediate-acting insulins              | Other      |
| A10AD    | Intermediate- or long-acting combined with fast-acting insulins | Other |
| A10BA02  | Metformin                                 | Other      |
| A10BB01  | Glibenclamide                             | Other      |
| A10BB07  | Glipizide                                 | Other      |
| A10BB09  | Glitazide                                 | Other      |
| A10BG03  | Pioglitazone                              | Other      |
| A11DA01  | Thiamine                                  | Other      |
| A11GB    | Ascorbic acid, combinations               | Other      |
| A11JD    | Other vitamin products, combinations      | Other      |
| A12BA    | Potassium                                 | Other      |
| A12BA01  | Potassium chloride                        | Other      |
| A12CA01  | Sodium chloride                           | Other      |
| A12CB01  | Zinc sulfate                              | Other      |
| A12CC    | Magnesium                                 | Other      |
| A12CC05  | Magnesium aspartate                       | Other      |
| B02BA01  | Phytomenadione                            | Other      |
| B03A     | Iron preparations                         | Other      |

### Preventive medications at the end of life in older nursing home residents

| ATC code | Name            | Category   |
|----------|-----------------|------------|
| B01BA01  | Cyanocobalamin  | Other      |
| B01BB    | Folic acid      | Other      |
| B01X20   | Darbepoetin alfa| Other      |
| C01AA05  | Digoxin         | Other      |
| C01BC04  | Flecainide      | Other      |
| C01BD01  | Amiodarone      | Other      |
| C01CA24  | Epinephrine     | Other      |
| C01DA02  | Glycerol Trinitrate | Other |
| C01DA08  | Isosorbide Dinitrate | Other |
| C01DA14  | Isosorbide Mononitrate | Other |
| C01DX16  | Nicorandil      | Other      |
| C01EB09  | Ubidecarenone   | Other      |
| G01AF02  | Clotrimazole    | Other      |
| G02CB03  | Cabergoline     | Other      |
| G03BA03  | Testosterone    | Other      |
| G03HA01  | Cyproterone     | Other      |
| G04BX    | Sodium citrotrate | Other     |
| H01AA01  | Levethyroxine sodium | Other  |
| H01BA02  | Propranolol      | Other      |
| H01BB01  | Carbamazepine   | Other      |
| H01AA01  | Glucagon        | Other      |
| J01AH02  | Oseltamivir     | Other      |
| L01AA02  | Chlorambucil    | Other      |
| L01BC02  | Fluorouracil    | Other      |
| L01BC06  | Capetitabine    | Other      |
| L01X20   | Hydroxycarbamide| Other      |
| L02AF02  | Leupotrexin     | Other      |
| L02AF03  | Goserelin       | Other      |
| L02BA01  | Tamoxifen       | Other      |
| L02BB02  | Nilutamide      | Other      |
| L02BG04  | Letrozole       | Other      |
| L02BG06  | Exemestane      | Other      |
| L03AA08  | Interferon beta-3b | Other   |
| L04AX03  | Methotrexate    | Other      |
| M01AC01  | Piroxicam       | Other      |
| M01AC06  | Meloxicam       | Other      |
| M01AH01  | Celecoxib       | Other      |
| ATC code | Name | Category |
|----------|------|----------|
| M01AX05 | Glucosamine | Other |
| M01AX25 | Chondroitin sulfate and Glucosamine | Other |
| M01BC01 | Orphenadrine citrate | Other |
| M04A01 | Allopurinol | Other |
| M04AC01 | Colchicine | Other |
| N02AC04 | Dextropropoxyphene | Other |
| N02AC54 | Dextropropoxyphene, combinations excl. psycholeptics | Other |
| N02AX02 | Tramadol | Other |
| N02A01 | Acetylsalicylic acid | Other |
| N03AA03 | Primidone | Other |
| N03AX09 | Lamotrigine | Other |
| N03AX14 | Levetiracetam | Other |
| N04AA01 | Trihexylphenidyl | Other |
| N04AA02 | Biperiden | Other |
| N04BA02 | Levodopa and decarboxylase inhibitor | Other |
| N04BA03 | Levodopa, decarboxylase inhibitor and COMT inhibitor | Other |
| N04BB01 | Amantadine | Other |
| N04BC02 | Pergolide | Other |
| N04BC05 | Pramipexole | Other |
| N04BC07 | Apomorphine | Other |
| N04RD01 | Selegine | Other |
| N04RY02 | Entacapone | Other |
| N05AB06 | Trifluoperazine | Other |
| N05AC01 | Pericyazine | Other |
| N05AC02 | Thioridazine | Other |
| N05AF01 | Flupenthixol | Other |
| N05AH04 | Quetiapine | Other |
| N05AN | Lithium | Other |
| N05AX12 | Anipiprazole | Other |
| N05BA08 | Bromazepam | Other |
| N05CF01 | Zopiclone | Other |
| N05CF02 | Zolpidem | Other |
| N06AA02 | Imipramine | Other |
| N06AA16 | Dosulepin | Other |
| N06AB03 | Fluoxetine | Other |

| ATC code | Name | Category |
|----------|------|----------|
| N06AB04 | Citalopram | Other |
| N06AB06 | Sertraline | Other |
| N06AB08 | Fluvoxamine | Other |
| N06AB10 | Escitalopram | Other |
| N06AF03 | Phenerazine | Other |
| N06AG02 | Moxibemide | Other |
| N06AX03 | Mianserin | Other |
| N06AX11 | Mirtazapine | Other |
| N06AX18 | Reboxetine | Other |
| N06AX23 | Dexamfetamine | Other |
| N06BA07 | Modafinil | Other |
| N06DA02 | Donepezil | Other |
| N06DA03 | Rivastigmine | Other |
| N06DA04 | Galantamine | Other |
| N06DX01 | Memantine | Other |
| N07BA01 | Nicotine | Other |
| N07CA01 | Betabistine | Other |
| P01BA02 | Hydrosoltothioquin | Other |
| P01BC01 | Quinidine | Other |
| P02CF01 | Ivermectin | Other |
| P03AC04 | Permethrin | Other |
| R03BA07 | Mometason | Other |
| R02A03 | Dichlohexytmethyl alcohol | Other |
| R02AD02 | Lidocaine | Other |
| R03AC02 | Salbutamol | Other |
| R03AC03 | Terbutaline | Other |
| R03AX06 | Fluticasone and Salmeterol | Other |
| R03AX07 | Formoterol and Budesonide | Other |
| R03BA01 | Beclomethasone | Other |
| R03BA02 | Budesonide | Other |
| R03BA05 | Fluticasone | Other |
| R03BB01 | Ipratropium bromide | Other |
| R03BB04 | Tiotropium bromide | Other |
| R03DA04 | Theophylline | Other |
| R05CA12 | Hederae helicis folium | Other |
| R05CB02 | Bromhexine | Other |
| R05DA04 | Codeine | Other |
### Preventive medications at the end of life in older nursing home residents

| ATC code | Name                                           | Category   |
|----------|------------------------------------------------|------------|
| R05DA08  | Pholcodine                                     | Other      |
| R05DA09  | Dextromethorphan                               | Other      |
| R05DA12  | Acetyldihydrocodeine                           | Other      |
| R06AA02  | Diphenhydramine                                | Other      |
| R06AB02  | Dexchlorpheniramine                            | Other      |
| R06AE07  | Cetirizine                                     | Other      |
| R06AX02  | Cyproheptadine                                 | Other      |
| R06AX11  | Loratadine                                     | Other      |
| R06AX26  | Fexofenadine                                   | Other      |
| V03AB33  | Hydroxycobalamin                               | Other      |
| V03AE01  | Polystyrene Sulfonate                          | Other      |
| V03AG    | Sodium itamine phosphate                       | Other      |
| A11CC    | Vitamin D and vitamin D analogues              | Preventive |
| A12A     | Calcium                                        | Preventive |
| B01      | Antithrombotic agents                          | Preventive |
| C02      | Antihypertensives                              | Preventive |
| C03      | Diuretics (except for hydrochlorothiazide, frusemide, spironolactone) | Preventive |
| C07      | Betablocking agents                            | Preventive |
| C08      | Calcium channel blockers (except for nifedipine and diltiazem) | Preventive |
| C09      | Agents acting on the renin angiotensin system | Preventive |
| C10A     | Lipid modifying agents (plain)                 | Preventive |
| C10B     | Lipid modifying agents (combinations)          | Preventive |
| G03C     | Estrogen                                       | Preventive |
| G03F     | Progesteron                                    | Preventive |
| G01XC01  | Ranolaxine hydrochloride                       | Preventive |
| G04CA03  | Terazosin hydrochloride                        | Preventive |
| H05AA02  | Teriparatide                                   | Preventive |
| H05BA    | Calcitonin                                     | Preventive |
| H05BX01  | Cinacalcet                                     | Preventive |
| M05BA    | Bisphosphonates (except for clodronic acid, pamidronate acid, ibandronic acid, zoledronic acid) | Preventive |
| M05BB    | Bisphosphonates combinations                    | Preventive |
| M05BX03  | Strontium ranelate                             | Preventive |
| M05BX04  | Denosumab (calcium & bone metabolism medicines) | Preventive |
| A01AD02  | Benzydamine                                    | Symptomatic |
| A02BA02  | Ranitidine                                     | Symptomatic |
| A02BC01  | Omeprazole                                     | Symptomatic |
| A02BC02  | Pantoprazole                                   | Symptomatic |
| A02BC03  | Lansoprazole                                   | Symptomatic |
| A02BC04  | Rabeprazole                                    | Symptomatic |
| A02BC05  | Esomeprazole                                   | Symptomatic |
| A02BX02  | Sucralfate                                     | Symptomatic |
| A03AA01  | Glycosurol bromide                             | Symptomatic |
| A03AA05  | Propantheline                                  | Symptomatic |
| A03AA01  | Atropine sulfate                               | Symptomatic |
| A03FA01  | Metoclopramid                                  | Symptomatic |
| A03FA02  | Cisapride                                      | Symptomatic |
| A03FA03  | Domperidone                                    | Symptomatic |
| A04AA01  | Ondansetron                                    | Symptomatic |
| A04AA02  | Granisetron                                    | Symptomatic |
| A04AA03  | Tropisetron                                    | Symptomatic |
| A04AA04  | Dolasetron                                     | Symptomatic |
| A04AD01  | Hyoscine hydrobromide                          | Symptomatic |
| A04AD10  | Dronabinol                                     | Symptomatic |
| A04AD11  | Nabilone                                       | Symptomatic |
| A04AD12  | Aprepitant                                      | Symptomatic |
| A06AA01  | Liquid paraffin                                | Symptomatic |
| A06AA02  | Docusate                                       | Symptomatic |
| A06AA02  | Bisacodyl                                      | Symptomatic |
| A06AB06  | Senna glycosides                               | Symptomatic |
| A06AB08  | Sodium picosulphate                            | Symptomatic |
| A06AB16  | Senna glycosides combinations                  | Symptomatic |
| A06AC01  | Ispagula (psylla seeds)                        | Symptomatic |
| A06AC51  | Stericula combinations                         | Symptomatic |
| A06AD11  | Lactulose                                      | Symptomatic |
| A06AD15  | Macrogol                                       | Symptomatic |
| A06AD17  | Sodium phosphate                               | Symptomatic |
| A06AD18  | Sorbitol                                       | Symptomatic |
| A06AG11  | Sorbitol Lauryl Sulfoacetate and combinations   | Symptomatic |
| A06AH01  | Methylsalazone                                 | Symptomatic |
| A06AH04  | Naloxone                                       | Symptomatic |
| A06AX01  | Glycerrhizin                                   | Symptomatic |
| A07DA01  | Loperamide                                     | Symptomatic |
| A09AA02  | Pancrelipase                                   | Symptomatic |
| A10AE04  | Long acting insulin                            | Symptomatic |
| B02AA02  | Tranexamic acid                                | Symptomatic |
| B05B     | I.V. solutions                                 | Symptomatic |
### Preventive medications at the end of life in older nursing home residents

| ATC code | Name                     | Category    |
|----------|--------------------------|-------------|
| C01BB02  | Mexiletine               | Symptomatic |
| C03AA01  | Hydrochlorothiazide      | Symptomatic |
| C03CA01  | Furosemide               | Symptomatic |
| C03DA01  | Spironolactone           | Symptomatic |
| C08CA05  | Nifedipine               | Symptomatic |
| C08DB01  | Diliazem                 | Symptomatic |
| G04BD04  | Oxybutynin               | Symptomatic |
| G04BD08  | Solifenacin succinate    | Symptomatic |
| G04CA02  | Tamsulosin               | Symptomatic |
| G04CB01  | Finasteride              | Symptomatic |
| H01CB02  | Octreotide               | Symptomatic |
| H01CB03  | Lanreotide               | Symptomatic |
| H02A02   | Fludrocortisone          | Symptomatic |
| H02A02   | Methylprednisolone       | Symptomatic |
| H02A06   | Prednisolone             | Symptomatic |
| H02A07   | Prednisone               | Symptomatic |
| H02A09   | Fludrocortisone          | Symptomatic |
| J02AC01  | Cortisone acetate        | Symptomatic |
| J02AC02  | Fluconazole oral         | Symptomatic |
| J02AC02  | Itraconazole oral        | Symptomatic |
| J05AB09  | Famciclovir              | Symptomatic |
| J05AB11  | Valaciclovir             | Symptomatic |
| M01AB01  | Indomethacin             | Symptomatic |
| M01AB05  | Diclofenac               | Symptomatic |
| M01AB55  | Diclofenac combinations  | Symptomatic |
| M01AE01  | Ibuprofen                | Symptomatic |
| M01AE02  | Naproxen                 | Symptomatic |
| M03BX01  | Baclofen                 | Symptomatic |
| M03CA01  | Dantrolene               | Symptomatic |
| M05BA02  | Clodronic acid           | Symptomatic |
| M05BA03  | Pamidronic acid          | Symptomatic |
| M05BA06  | Ibdedronic acid          | Symptomatic |
| M05BA08  | Zoledronic acid          | Symptomatic |
| M05BA08  | Diphosphonate mouthwash  | Symptomatic |
| N01AH03  | Sufentanil               | Symptomatic |
| N01AX03  | Ketamine                 | Symptomatic |
| N01BB02  | Lignocaine               | Symptomatic |
| N02AA01  | Morphine hydrochloride   | Symptomatic |

| ATC code | Name                     | Category    |
|----------|--------------------------|-------------|
| N02AA01  | Hydromorphone            | Symptomatic |
| N02AA05  | Oxycodone                | Symptomatic |
| N02AB03  | Fentanyl                 | Symptomatic |
| N02AE01  | Buprenorphine            | Symptomatic |
| N02BE01  | Paracetamol              | Symptomatic |
| N02BE02  | Codeine                  | Symptomatic |
| N03AB02  | Phenytoin                | Symptomatic |
| N03AE01  | Clonazepam               | Symptomatic |
| N03AF01  | Carbamazepine            | Symptomatic |
| N03AG01  | Sodium Valproate         | Symptomatic |
| N03AX12  | Gabapentin               | Symptomatic |
| N03AX16  | Pregabalin               | Symptomatic |
| N04AC01  | Benztropine              | Symptomatic |
| N05AA01  | Chlorpromazine           | Symptomatic |
| N05AA02  | Levomepromazine          | Symptomatic |
| N05AB04  | Prochlorperazine         | Symptomatic |
| N05AD01  | Haloperidol              | Symptomatic |
| N05AH03  | Olanzapine               | Symptomatic |
| N05AX08  | Risperidone              | Symptomatic |
| N05BA01  | Diazepam                 | Symptomatic |
| N05BA04  | Oxazepam                 | Symptomatic |
| N05BA06  | Lorazepam                | Symptomatic |
| N05BA12  | Alprazolam               | Symptomatic |
| N05CD02  | Nitrazepam               | Symptomatic |
| N05CD07  | Temazepam                | Symptomatic |
| N05CD08  | Midazolam                | Symptomatic |
| N06AA09  | Amitriptyline            | Symptomatic |
| N06AA10  | Nortriptyline            | Symptomatic |
| N06AA12  | Doxepin                  | Symptomatic |
| N06AB05  | Paroxetine               | Symptomatic |
| N06AX16  | Venlafaxine              | Symptomatic |
| N06AX21  | Duloxetine               | Symptomatic |
| N06BA02  | Dexamfetamine             | Symptomatic |
| N06BA04  | Methylphenidate          | Symptomatic |
| N07BC02  | Methadone                | Symptomatic |
| R06AD01  | Alimemazine              | Symptomatic |
| R06AD02  | Promethazine             | Symptomatic |
| R06AE01  | Cyclizine                | Symptomatic |