The European Institute For Innovation Thr~ugh Health Data

GHENT UNIVERSITY

Polypharmacy from a clincal perspective

Prof. Dr. R. Vander Stichele, MD, PhD
Clinical pharmacologist at Ghent University, Belgium
Senior Reseearch Coordinator at I~HD
Webinar for C3-Cloud, August 28, 2020

The European Institute For Innovation Through Health Data

GHENT UNIVERSITY

No conflicts of interest to declare

OVERVIEW

The problem of polypharmacy in older adults

How to assess (potentially) inappropriate medications (PIMs) ?

Focus on the aspects covered by PIMs lists

Evidence of association of potentially inappropriate medication with clinical outcomes

Evidence fo the impact of remedial actions using PIM-lists

Take home messages

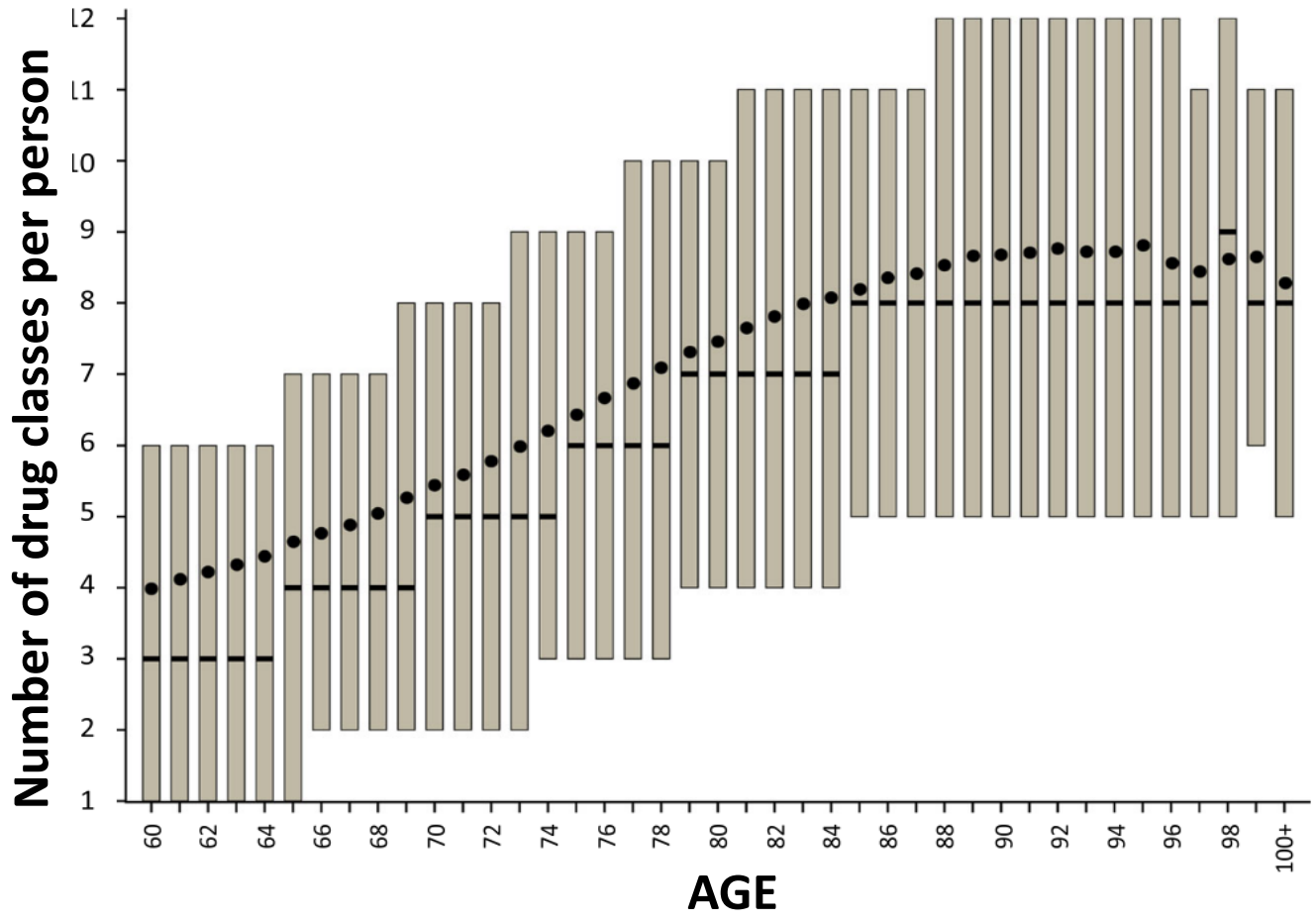
The problem of Polypharmacy in Older Adults

THE OLDER ADULTS (ELDERLY) AND MEDICATION

- In the developed world, 15 to 20% of the population is 65+ (and this percentage is growing).
- Among the population of 65+
  - Many of the healthy aging older adults take one or more chronic medication
  - Of the community-dwelling very old (80%) also more than half present polymorbidity and polypharmacy
  - Five to 8% reside in Nursing Homes (long-time care facilities LTCF)
    - In some countries these are home-replacing living, in other countries places to die
    - Up to 50% of the residents are cognitively impaired (and constitute half of the demented population)
    - Life expectancy is <1 to 4 years
    - Many of them have multiple chronic diseases
    - Most of them have polypharmacy (4 or more chronic medications with systemic action)
    - For 1 in 2 citizens, the end-of-life trajectory is going to a nursing home and die there,

A nation-wide appraisal of polypharmacy in Denmark

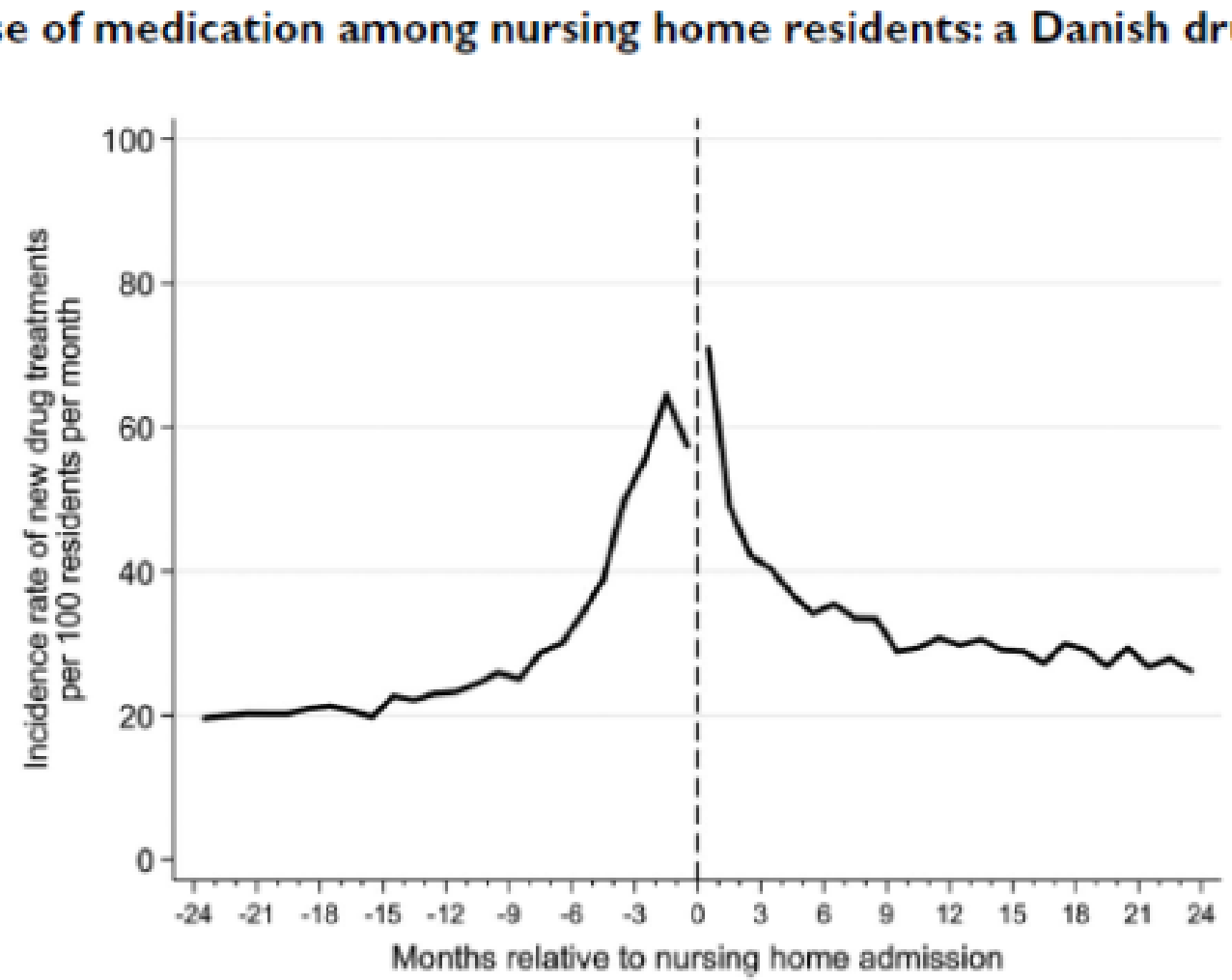
Fig. 1 Mean, median and IQR of the number of unique drug classes per older adult as a function of age. Boxes represent the interquartile range with the median score shown as a horizontal line and the means represented as circles



1,4 million
Danish residents 60+
(mean 70Y,
53% women)

(Christensen et al., 2019, Eur J Clin Pharmcol)

Incidence of new drug treatments rate during transition from communicty-dwelling to nursing home



A cohort of 5,179 individuals (63% women; median age of 84y) admitted into 94 nursing homes across Denmark during 2015–2017.

Lindby et al., 2020, Age and Aging

Polypharmacy is just a number

What is the number ?

the number of chronic medications (with systemic action)
taken by one patient at a given moment in time

What is polypharmacy ?

5 or more chronic medications (with systemic action)
taken by one patient at a given moment in time

What is excessive polypharmacy ?

10 or more chronic medication (with systemic action)
taken by one patient at a given moment in time

Some statements to consider

Not all polypharmacy is bad

It might be perfectly appropriate for a patient with 4 chronic conditions to take 5 different medications

Not every patient with less then 5 medications is well treated

It might be that a patient on 4 appropriate medications for 3 chronic conditions might have two more chronic conditions which are not treated as they should be

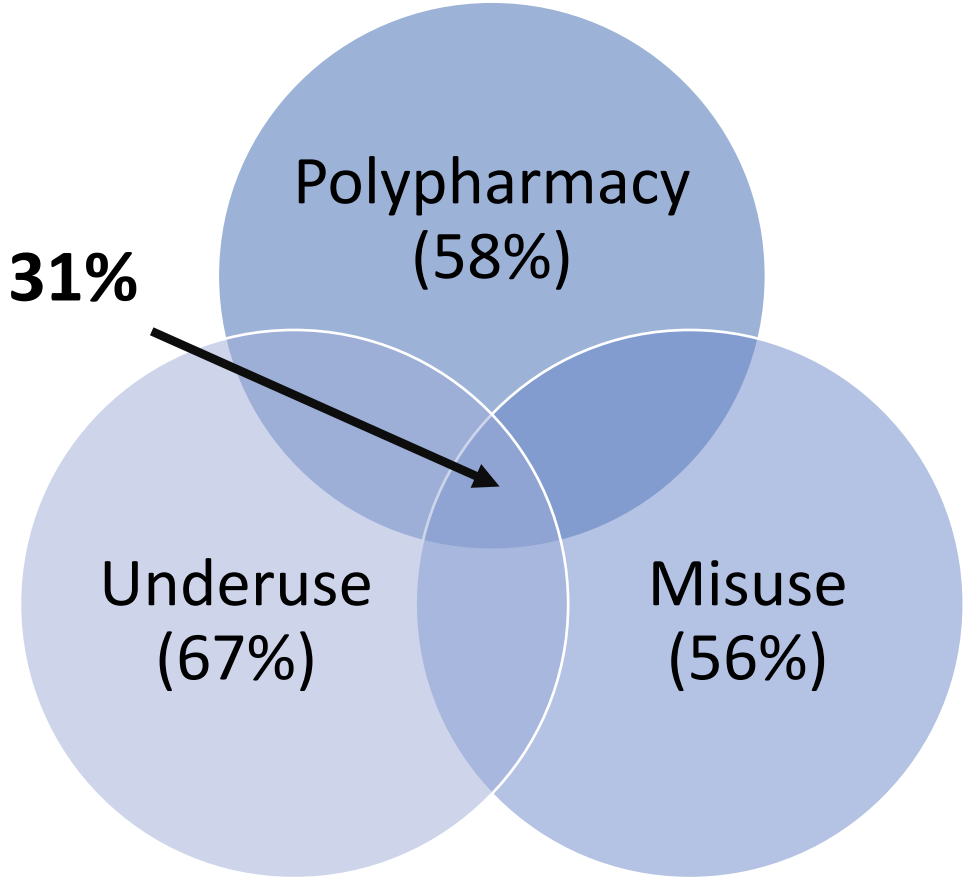
What counts is whether each chronic condition of the patient

- is not left untreated (underuse)
- and treated with appropriate medication (proper use)
  and not with inappropriate medication (misuse)

Most guidelines are directed to one clinical condition.

If a patient with multimorbidity is treated by the book, the number of medications may be high and become a problem in itself.

Prevalence of Potentially inappropriate medication in community-dwelling older adults (80+)



503 Belgian community dwelling 80+ (mean 84,4Y, 61,2% women)

Wauters et al., Brit J Clin Pharmacol, 2017

How to assess (potentially) inappropriate prescribing ?

Two different approaches

1. By having clinical experts assessing the medical records and medication lists
   Medication Appropriateness Index
   (ten questions for each medication line)
   Using validated lists of explicit criteria :
   Beers' list (US) ; STOPP-START list (EU)

   Note: This approach is time consuming, and
   expert resources might simply not be available

2. By combining multidisciplinary Medication Review
   with ICT assessement of (potentially) inappropriate medication (PIMs),
   assessed by explicit criteria
   Prima-EDS / OptiMeds / ….

Explicit criterion of (in)appropriate prescrbing : a decision rule

IF

A specific disease is present (ICD or SNOMED code)

And /OR

A specific drug is present (ATC code and/or PHPID)

THEN

A specific inappropriate medication should be

stopped or reduced in dosage OR

A specific appropriate medication sould be started

(BECAUSE)

there is evidence for this advice or

an expert panel said so

Validation of explicit criteria of Potentially (in)appropriate medication (PIM)

Mostly originated from expert panels using Delphi Methodology

Validated as lists of PIMs (not by individual PIM)

- In cross-sectional observational studies
- In Longitudinal observational studies
- In Randomised Clinical trials

Validity to assess the quality of pharmacotherapy of an individual patient remains

Selection of 650 explicit criteria from the 3 most important, validated, and current lists

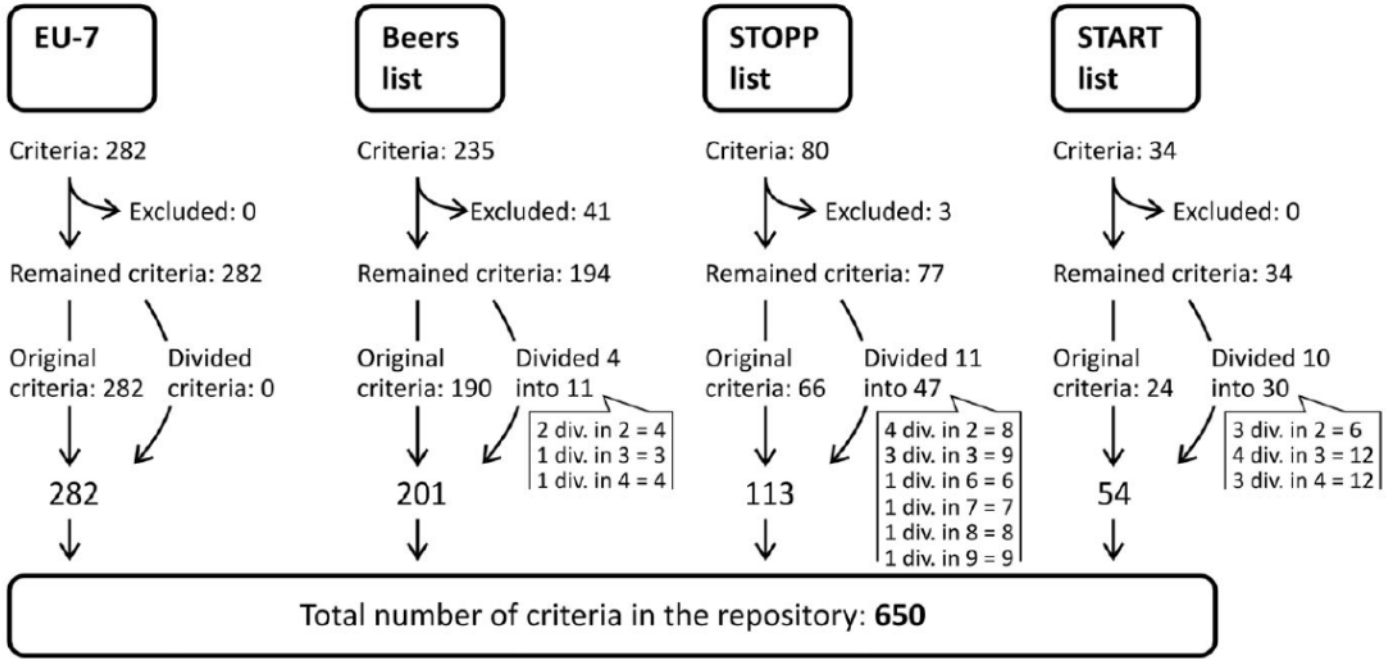


Figure 2 Flow chart of the selection of the criteria. All explicit criteria from the three included lists were considered for inclusion. We excluded explicit criteria focused on drug–drug interactions, as well as too general explicit criteria (not referring to a specific medication or definable drug group). Some of the criteria were divided for more operable use. From the original number of 641 criteria in the three lists, 44 criteria were excluded, and 25 criteria were divided for more operable use into 88 criteria. This resulted in a total number of 650 potentially inappropriate medications criteria included in the repository.

Ivana et al., 2018, Geriatr Gerontol

Prerequisites for wide spread use of PIMs-lists

- **Availablility of data** (reliable medication and clinical data)
  Access to the eMAR data (the nurse administration data)
  Access to Current Patient Summaries

- **Computerization** of PIMs

- **Interpretation in clinical context** of PIMs

- **Multidisciplinarity** (General Practitioner, community pharmacist, attending nurse)

- **Adequate ICT support** for communication of results between the multidisciplinary actors

- **Global identification of medicinal products** (UNICOM)
  Better application of decision rules, internationalization of CDS systems -

Focus on the aspects covered by
Potentially inappropriate medication lists

Focus on the aspects covered by Potentially Inappropriate medication Lists

- Underuse
- Obsolete drugs
- Dangerous drugs in the elderly
- Pharmacokinetic interactions
  (the additiotion of one drug leads to inactivity or toxicity of another drug)
- Pharmacodynamic interactions
  (two drugs reinforcing each others action or side-effect)
- Discontinuation of too long chronic therapy
  - Benzo's, Antipsychotics, PPIs
- Deprescribing near the end of life
  Statins, Calcium
- Compliance to complex guidelines in specific clinical conditions

Evidence of association of inappropriate medication with clinical outcomes

Evidence of association of inappropriate medication with clinical outcomes

- Mortality
- (Drug-related) unplanned hospitalisations
- Reduction of Quality of life
- Cognitive impairment
- Lack of alertness
- Falls
- Cost of health care
- …

Evidence fo the impact of remedial actions
Using PIM-lists

Methods of measuring impact

- With experts in research setting
  - using clinical insight and implicit criteria
  - using explicit criteria

- With computer generated PIMs evaluation in research setting

  - Based on medicaton data only (scratch the surface)
  - Based on medication data and on (reliable) clinical data

- With computer generated PIMs evaluation on Real World Data

Differences in method have an Impact on :

- estimates of prevalence of the problem
- estimates of effect size
- cost of the evaluation and cost benefit of the interventions

Results of outcome studies

OBSERVATIONAL STUDIES

Many studies showing impact on process indicators

Reduction of the mean number of PIMs per patient

Some studies show association with

mortality and hospitalisation

Most studies show no associaton with on falls (multicausality)

RANDOMIZED CLINICAL TRIALS

Many studies showing impact on process indicators

Reduction of the mean number of PIMs per patient

A few studies show association with

mortality and hospitalisation

Most studies fail to show association with quality of life

NOTE : ICT support, Multidiscpilary cooparation (General Practitioner, pharmacist, nurse, geriatrician) is important

Change in organisational culutre in health care services take time, and sufficient time frame is needed to evaluate outcome

Take home messages

Take home messages

- Complex morbitity patterns and polypharmacy are the fate of many older adults, whether residing in nursing homes or community-dwelling.

- These are vulnerable patients, often with insufficient clinical documentation

- A current Patient Summary with a reliable medication list is enough to unleash the power of ICT supported medication review.

- Good clinical data and ICT-Support will increase the efficiency of medication review, prevent alert fatigue, and facilitate interprofessional cooperation.

- Better quality of prescribing could make this vulnerable population more resilient to pandemics and may reduce pharmacodynamic interactions with impact on Quality of Life. The latter statement needs more evidence.

Take home messages

- Complex morbitity patterns and polypharmacy are the fate of many older adults, whether residing in nursing homes or community-dwelling.

Take home messages

- Complex morbitity patterns and polypharmacy are the fate of many older adults, whether residing in nursing homes or community-dwelling.

- These are vulnerable patients, often with insufficient clinical documentation

Take home messages

- Complex morbitity patterns and polypharmacy are the fate of many older adults, whether residing in nursing homes or community-dwelling.

- These are vulnerable patients, often with insufficient clinical documentation

- A current Patient Summary with a reliable medication list is enough to unleash the power of ICT supported medication review.

Take home messages

- Complex morbitity patterns and polypharmacy are the fate of many older adults, whether residing in nursing homes or community-dwelling.

- These are vulnerable patients, often with insufficient clinical documentation

- A current Patient Summary with a reliable medication list is enough to unleash the power of ICT supported medication review.

- Good clinical data and ICT-Support will increase the efficiency of medication review, prevent alert fatigue, and facilitate interprofessional cooperation.

Take home messages

- Complex morbitity patterns and polypharmacy are the fate of many older adults, whether residing in nursing homes or community-dwelling.

- These are vulnerable patients, often with insufficient clinical documentation

- A current Patient Summary with a reliable medication list is enough to unleash the power of ICT supported medication review.

- Good clinical data and ICT-Support will increase the efficiency of medication review, prevent alert fatigue, and facilitate interprofessional cooperation.

- Better quality of prescribing could make this vulnerable population more resilient to pandemics and may reduce pharmacodynamic interactions with impact on Quality of Life. The latter statement needs more evidence.

References

1. Wauters M, Elseviers M, Vaes B, et al. **Polypharmacy in a Belgian cohort of community-dwelling oldest old (80+).** *Acta Clin Belg*. 2016;71(3):158-166. doi:10.1080/17843286.2016.1148298
2. Ivanova I, Elseviers M, Wauters M, Christiaens T, Vander Stichele R**. European repository of explicit criteria of potentially inappropriate medications in old age**. *Geriatr Gerontol Int*. 2018;18(8):1293-1297. doi:10.1111/ggi.13331
3. Wauters M, Elseviers M, Dilles T, et al**. OptiMEDs Pilot Study** - Full Text View - ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT04142645 (accessed 29 Jun 2020).
4. Wauters M, Klamer T, Elseviers M, et al. **Anticholinergic Exposure in a Cohort of Adults Aged 80 years and Over: Associations of the MARANTE Scale with Mortality and Hospitalization**. *Basic Clin Pharmacol Toxicol*. 2017;120(6):591-600. doi:10.1111/bcpt.12744
5. Dilles T, Vander Stichele RH, Van Bortel LM, Elseviers MM**. The development and test of an intervention to improve ADR screening in nursing homes**. *J Am Med Dir Assoc*. 2013;14(5):379.e1-379.e3796. doi:10.1016/j.jamda.
6. Paque K, Elseviers M, Vander Stichele R, et al. **Balancing medication use in nursing home residents with life-limiting disease.** *Eur J Clin Pharmacol*. 2019;75(7):969-977. doi:10.1007/s00228-019-02649-6
7. Rapid Response: Vander Stichele RH, Elseviers M, Christiaens T, Wauters M, Kalra D. **Quality of prescribing to vulnerable nursing home residents: time to act.** Rapid response to: Use of an electronic decision support tool to reduce polypharmacy in elderly people with chronic diseases: cluster randomised controlled trial. *BMJ* 2020; 369 doi: https://doi.org/10.1136/bmj.m1822 (Published 18 June 20)
8. Fisman DN, Bogoch I, Lapointe-Shaw L, McCready J, Tuite AR. **Risk Factors Associated With Mortality Among Residents With Coronavirus Disease 2019 (COVID-19) in Long-term Care Facilities in Ontario, Canada**. *JAMA Netw Open*. 2020;3(7):e2015957. Published 2020 Jul 1. doi:10.1001/jamanetworkopen.2020.15957.
9. Geert Molenberghs, Christel Faes, Jan Aerts, Heidi Theeten, Brecht Devleesschauwer, Natalia Bustos Sierra, Toon Braeye, Francoise Renard, Sereina Herzog, Patrick Lusyne, Johan Van der Heyden, Herman Van Oyen, Pierre Van Damme, Niel Hens.**Belgian Covid-19 Mortality, Excess Deaths, Number of Deaths per Million, and Infection Fatality Rates (8 March - 9 May 2020)? doi:** https://doi.org/10.1101/2020.06.20.20136234
10. Miranda R, Bunn F, Lynch J, Van den Block L, Goodman C. **Palliative care for people with dementia living at home: A systematic review of interventions.** *Palliat Med*. 2019;33(7):726-742. doi:10.1177/0269216319847092
11. Christensen LD, Reilev M, Juul-Larsen HG, et al. Use of prescription drugs in the older adult population-a nationwide pharmacoepidemiological study. Eur J Clin Pharmacol. 2019;75(8):1125-1133
12. Lundby C, Jensen J, Larsen SP, Hoffmann H, Pottegård A, Reilev M. Use of medication among nursing home residents: a Danish drug utilisation study. Age Ageing. 2020;49(5):814-820
13. Zueger PM, Holmes HM, Calip GS, Qato DM, Pickard AS, Lee TA. Older Medicare Beneficiaries Frequently Continue Medications with Limited Benefit Following Hospice Admission. J Gen Intern Med. 2019;34(10):2029-2037.
14. Morin L, Laroche ML, Vetrano DL, Fastbom J, Johnell K. Adequate, questionable, and inadequate drug prescribing for older adults at the end of life: a European expert consensus. Eur J Clin Pharmacol. 2018;74(10):1333-1342.
15. Morin L, Wastesson JW, Laroche ML, Fastbom J, Johnell K. How many older adults receive drugs of questionable clinical benefit near the end of life? A cohort study. Palliat Med. 2019;33(8):1080-1090.
16. Aubert CE, Kerr EA, Maratt JK, Klamerus ML, Hofer TP. Outcome Measures for Interventions to Reduce Inappropriate Chronic Drugs: A Narrative Review [published online ahead of print, 2020 Aug 11]. J Am Geriatr Soc. 2020;10.1111/jgs.16697.