

# Rapid trajectories of polypharmacy over time are associated with a higher risk of death



Longitudinal trajectories of polypharmacy in older people, and their association with the risk of mortality: A joint latent class model analysis of real-world data from the UK and the Netherlands.

## Background

- Polypharmacy has been defined using cross-sectional thresholds (e.g.,  $\geq 10$  ingredients in a year).
- There are subgroups of the older population that may deteriorate faster than the rest.

## Objectives

- Identify clusters of distinct polypharmacy trajectories over five years in older people, and study their association with mortality.
- Characterise comorbidity burden and drug use in these clusters.
- Assess the generalisability of the resultant clusters in two external databases.

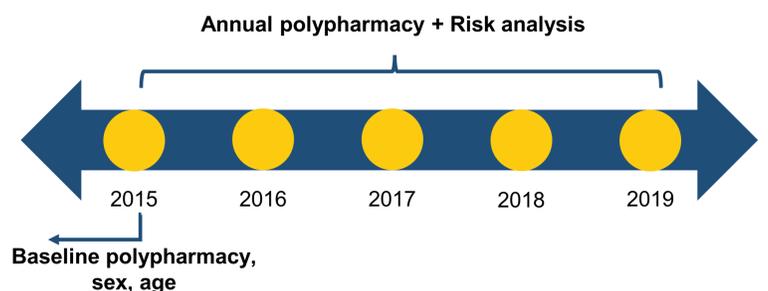
## Methods

**Population:** Random samples of patients aged  $> 65$  as of 31/12/2014, from OMOP-CDM mapped databases:

- Training set: UK Clinical Practice Research Datalink (CPRD) GOLD
- Validation set 1: CPRD AURUM
- Validation set 2: Dutch Integrated Primary Care Information (IPCI)

**Longitudinal exposure:** Polypharmacy, defined as the cumulative number of prescribed ingredients.

**Adverse outcome:** All-cause mortality



### Statistical methods:

- Joint latent class models divided the population into clusters with:
  - Different intercepts and slopes.
  - Different mortality risk profiles.

**Model validation:** 50% with posterior probability  $\geq 0.7$

## Results

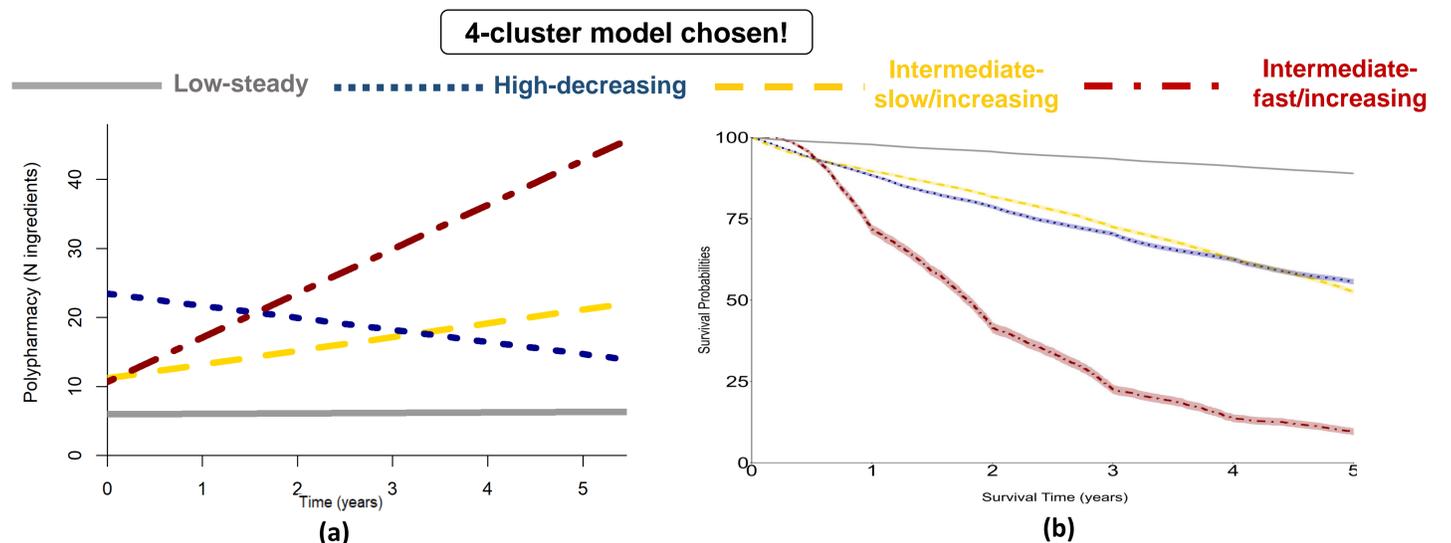
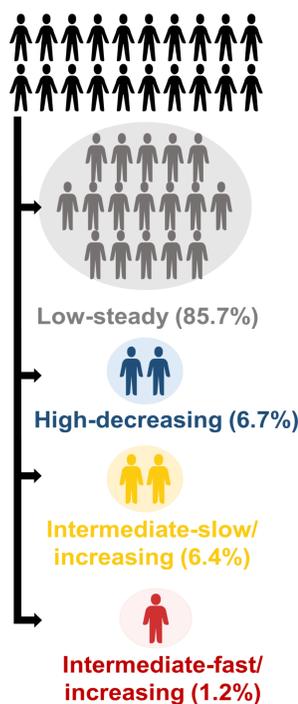


Figure: (a) intercepts and slopes of the four clusters, and (b) Survival curves of the four clusters

- Low-steady  $\rightarrow$  Healthiest group
- High-decreasing  $\rightarrow$  Highest drug use and chronic comorbidity prevalence at baseline
- Intermediate-slow/increasing  $\rightarrow$  Fastest accumulation of chronic comorbidities
- Intermediate-fast/increasing  $\rightarrow$  Highest prevalence and incidence of cancer

Table: Baseline characteristics of the overall population and the identified cluster in CPRD GOLD, Aurum and IPCI

	Intermediate-fast/increasing	Low-steady	Intermediate-slow/increasing	High-decreasing	Overall
<b>CPRD GOLD</b>					
n	3708 (1.2%)	256923 (85.7%)	19207 (6.4%)	20021 (6.7%)	299859
Sex = Male (%)	1838 (49.6%)	117450 (45.7%)	8745 (45.5%)	7987 (39.9%)	136020 (45.4%)
Age (mean (SD))	76.73 (7.56)	75.01 (7.90)	76.77 (7.85)	76.86 (7.88)	75.26 (7.91)
<b>CPRD Aurum</b>					
n	3766 (1.3%)	255788 (85.3%)	23064 (7.7%)	17320 (5.8%)	299938
Sex = Male (%)	1955 (51.9%)	116958 (45.7%)	10779 (46.7%)	6926 (40.0%)	136618 (45.5%)
Age (mean (SD))	76.95 (7.54)	75.02 (7.91)	77.21 (7.93)	77.40 (7.97)	75.35 (7.95)
<b>IPCI</b>					
n	1429 (1.0%)	125835 (90.3%)	8268 (5.9%)	3775 (2.7%)	139307
Sex = Male (%)	814 (57.0%)	56789 (45.1%)	4138 (50.0%)	1565 (41.5%)	63306 (45.4%)
Age (mean (SD))	75.29 (6.96)	74.10 (7.31)	75.09 (7.14)	75.29 (7.13)	74.21 (7.30)

Good model validation in AURUM and IPCI!



• Posterior probability  $\geq 0.7$  for more than 50%

- Similar:
  - ✓ Polypharmacy trajectories
  - ✓ Mortality risks
  - ✓ Comorbidity and drug use