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RESEARCH PAPER

Does polypharmacy shape dependency transitions in the very old? Findings from the Newcastle 85+ Study

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Abstract

Background: helping older people to maintain their independence, and identifying risk factors that compromise this, is of high importance. Polypharmacy is common in the very old (aged ≥ 85) but whether it can shape transitions in dependency in this fastest growing subpopulation is unclear.
Methods: using Newcastle 85+ Study data and multi-state modelling, we investigated the association between each additional medication prescribed and the progression of and recovery from dependency states, over 10 years (age 85–95). Participants were defined as either free from care (independent), requiring care less often than daily (low dependency), or requiring care at regular intervals each day or 24 hourly (medium/high dependency).
Results: each additional medication prescribed was associated with a 10% decreased chance of recovery from low dependence to independence (hazard ratio (HR): 0.90, 95% confidence interval (CI): 0.82–0.99).
Discussion: when a relatively able person visits the GP or clinical pharmacist, careful consideration should be given to whether the potential benefits from adding a new medication outweigh the risk to reduced recovery of independence.

Keywords: polypharmacy, very old, primary care, older people

Key Points

- We investigated whether polypharmacy shapes transitions between dependency states in the very old over 10 years.
- From age 85 to 95, the care requirements for very old people increased substantially.
- Each additional medication prescribed decreased the chance of recovery from low dependence to independence by 10%.

Background

Underpinning functional ability is the autonomous completion of activities of daily living (ADLs), such as shopping, dressing, toileting and bathing, though the number of ADLs that cannot be performed gives little indication of the intensity of social care support an individual requires [1]. A better measure is achieved by combining activities of daily living, continence and cognition, and measuring the time interval between necessary periods of help for these tasks (so-called 'dependency') [1].

Older age is often accompanied by an inability to self-care and live independently (i.e. dependency) [1, 2], and the world's population is ageing [3]; for example by mid-2045 in the UK, numbers of the very old (aged ≥85 years) will almost double to 3.1 million [4]. The loss of independence can profoundly affect quality of life [5, 6], and increase healthcare use [7], and many high-income countries are contending with how to finance social care to support their ageing populations [8, 9], making preservation of function for older people a public health priority [10].

To help maintain the independence of and/or prevent loss of function of older people, evidence for how risk factors shape transitions in dependency is required for example, and the role of complex multimorbidity has been identified in those aged 85 and over [11]. One possible consequence of multimorbidity is polypharmacy. Polypharmacy is generally understood as the concurrent use of multiple medicines [12] and is common in the very old. For instance, 85 year olds in English primary care are prescribed a median of six medicines, with 65% prescribed at least five medicines [13]. Polypharmacy is thought to be a potential modifier of the disablement process [14], but there is no evidence to quantify whether it can influence dependency transitions in the very old, despite co-occurrence, and potential mechanisms. These include (i) non-adherence leading to the onset or worsening of disabling diseases, and greater total disease, and (ii) cumulative medication side effects affecting cognition, continence status or the self-reported ability to do activities of daily living.

The prevalence of polypharmacy in growing older populations is also likely to rise in the coming years, because of rising multimorbidity [15], whilst the supply of caregivers, who support people with dependency, is expected to decline [16].

All this considered, we aim to examine, for the first time, the association between polypharmacy (defined as the number of prescribed medications) and transitions in dependency in the very old over 10 years using a rich dataset: the Newcastle 85+ Study.

Methods

Design and setting

The Newcastle 85+ Study is a population-based longitudinal study of people who were born in 1921, aged 85 in 2006 when the study began, and permanently registered with a participating general practice in Newcastle or North Tyneside [17]. The study has 10 years of follow-up, and data were collected in two ways over this time: multidimensional health assessments by trained research nurses in participants usual place of residence, inclusive of care homes, at baseline (wave 1), 18 months (wave 2), 36 months (wave 3), 60 months (wave 4) and 120 months (wave 5), and review of general practice medical records at baseline, waves 3, 4 and 5. Study questionnaires and the GP record review proforma are available on the Newcastle 85+ Study website https://research.ncl.ac.uk/85plus/. Full details of the study design and recruitment strategy have been published [17–19], and an overview of study recruitment and retention can be found in Appendix 1 (available in *Age and Ageing* online). Of the 849 people who were eligible for analyses at baseline, we constructed a measure of dependency on 806 individuals (497 women and 309 men).

Ethical approval

The Newcastle and North Tyneside Local Research Committee One approved the Newcastle 85+ Study (Ref: 06/Q0905/2).

Medication data

A detailed discussion characterising polypharmacy amongst the Newcastle 85+ Study participants has previously been presented [13]. Data on prescribed medications were obtained from general practice medical records and coded according to the British National Formulary [19]. From which polypharmacy was operationalised as a continuous variable, i.e. as a count of the number of prescribed medications, to account for potential nonlinearity within categorical thresholds [20]. Participant reported over-the-counter medications and items such as vaccines, wound-management products and catheter/stoma products were excluded from this analysis (Appendix 2 available in *Age and Ageing* online) [13].

Definition of dependency

Our measure of dependency comprises four categories based on the time interval between necessary periods of help with activities of daily living, urinary continence and cognition: (i) independent: free from care, (ii) low dependency: requiring help less than daily, (iii) medium dependency: requiring help at regular intervals each day and (iv) high dependency: requiring 24-hour care [1]. The logic statements for classifying participants and the items used are provided in Box 1.

Box 1. Definition of dependency

High dependency:
MMSE score of less than 10, or having severe or profound urinary incontinence with inability to dress or undress without help, or unable to perform, without help, any of: transfer to/from toilet, or transfer to/from a chair or feeding oneself.
Medium dependency:
Unable to perform, without help, any of: transfer to/from bed, dressing and undressing, preparing and cooking a hot meal, taking medication or washing face and hands.
Low dependency:
Unable to perform without help, any of: washing all over, shopping for groceries, light housework, heavy housework, managing money or cutting own toenails.
Independent:
The remainder of participants were defined as independent (free from care). Participants were classified as missing if they could not be categorised.

Statistical analysis

Participant characteristics were examined through descriptive statistics. To model transitions in dependency over 10 years, we fitted a multi-state model with four states: independent, low dependency, medium/high dependency and death (Appendix 3 available in *Age and Ageing* online). Medium- and high-dependency states were collapsed to enable model convergence. Age was used as the temporal metric to mitigate some of the effect of the Markov assumption i.e. that only the current state influences future progression. Survival time was calculated from the date of baseline interview to the date of death or censoring at 120 months (if a participant had taken part in the 10-year follow-up). Models were adjusted in stage as follows:

- Polypharmacy and age (model 1)
- Polypharmacy, age and sex (model 2)
- Polypharmacy, age, sex and years in education (model 3)
- Polypharmacy, age, sex, years in education and multiple long-term conditions (model 4)
- Polypharmacy, age, sex, years in education, multiple long-term conditions and body mass index (model 5).

Covariates (excepting sex and years in education) were treated as time varying. Full details of disease status construction can be found in Appendix 4 (available in *Age and Ageing* online). Analyses were conducted in R V.4.0.2 using the msm package [21].

Results

Changes in dependency levels between age 85 and 95

By age 95, the proportion of men and women who were independent reduced significantly (age 85: 58% of men, 31% of women; age 95: 23% of men, 5% of women). For women, the greatest increase in care needs was in the proportion with high dependency (requiring 24-hour care) (8% at age 85, 25% by age 95) whilst for men, the greatest increase was for those requiring care at regular intervals throughout the day (12% at age 85 and 27% by age 95) (medium levels of dependency) (Figure 1).

Prevalence of polypharmacy by dependency level

For men and women, median medication counts broadly increase with increased dependency (Table 1).

Multistate model

As shown in Table 2, each additional medication prescribed is associated with a 10% decrease in the chance of recovery from low dependence to independence (HR: 0.90, 95% CI: 0.82–0.99, model 5), but is not significantly associated with (i) the progression of dependency—be it transitions from independence to low dependence (HR: 1.02, 95% CI: 0.97–1.08), independence to medium/high dependence (HR: 0.49, 95% CI: 0.20–1.19), or low to medium/high dependence (HR: 1.03, 95% CI: 0.96–1.10) –, or (ii) recovery from medium/high to low dependency (HR: 1.03, 95% CI: 0.91–1.16) (model 5).

Discussion

Principle findings

From age 85 to 95, the care requirements for very old people increased substantially. Each additional medication prescribed decreased the chance of recovery from low dependence to independence by 10%.

Comparison with existing literature

The decreased chance of reablement associated with each additional prescribed medication at the point of low dependency might reflect cumulative side effects with the potential to affect manual dexterity and balance, such as drowsiness or dizziness. Adverse drug reactions are more common in older people [22, 23] and also increase with the number of prescribed medications for example [24], and such effects can be ascribed to frailty, existing diagnoses or new medical problems [25]. Indeed in this study in the North East, approximately 30% of participants with low dependency were frail at baseline (Appendix 5 available in *Age and Ageing* online), and multimorbidity is the norm in the very old [26]. Our findings might also stem from non-adherence following rising medication counts [27], leading to the onset or progression of disabling diseases, especially as older people and their family carers often struggle to manage medicines with little or no support [28]. The reason why each additional prescribed medication reduced the chance of recovery from low but not medium or high care needs also reflects the disability hierarchy. Indeed low dependency is the optimal point at which reablement is possible; beyond this, in the very old, the chances of recovery are slim to nothing (Appendix 3 available in *Age and Ageing* online).

Strengths and limitations

To our knowledge, this is the first study to examine how polypharmacy shapes dependency transitions in the very old, over long-term follow-up, with medication and disease data obtained from general practice medical records as opposed to the less reliable method of self-report [19]. Multistate modelling has previously been used to examine how polypharmacy shapes frailty transitions over time in older community-dwelling men [29], so our analysis extends the existing literature.

However our work has limitations, mainly, we could not isolate the medication classes or combinations that hinder the recovery of independence, and previous research describes medication count as a reductionist measure [30]. Secondly, we could not reliably calculate hazard ratios separately by sex due to the reduced number of transitions, and

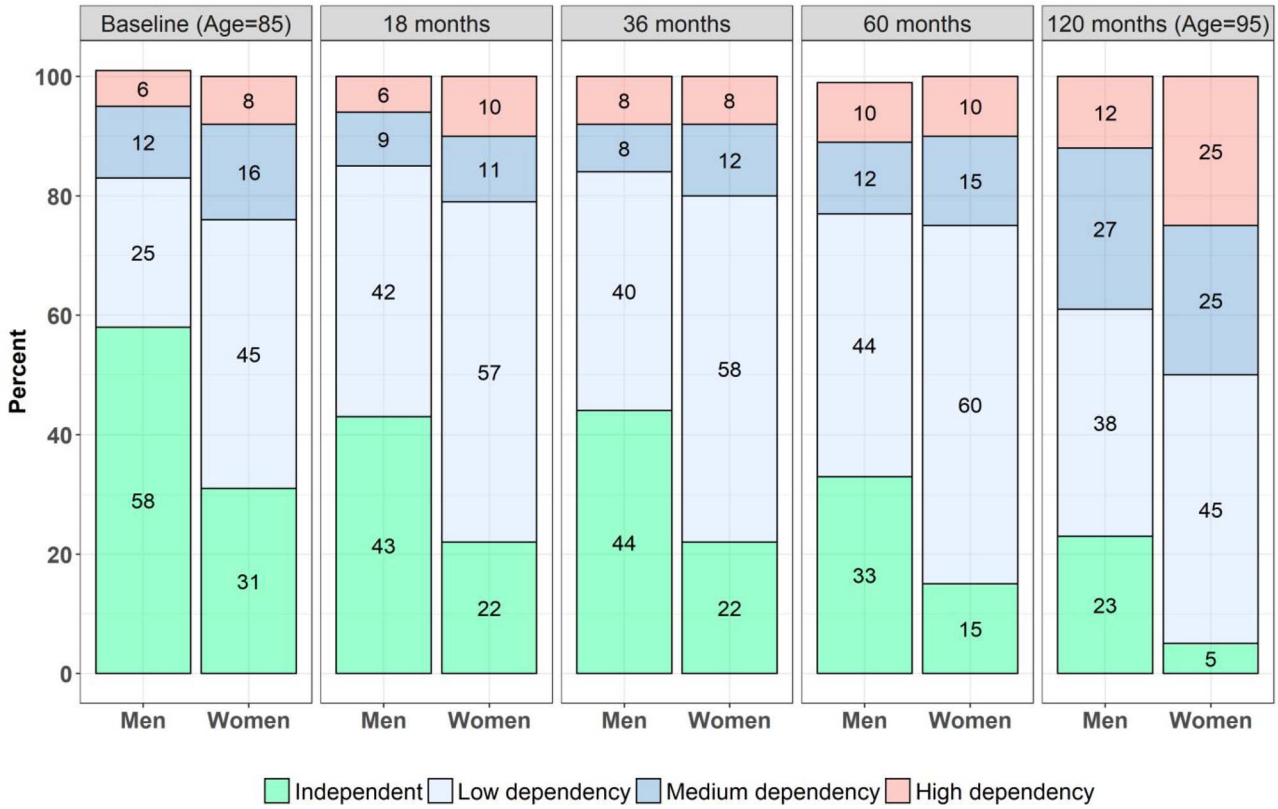

Figure 1. Prevalence of dependency from 85 to 95 years of age.

Table 1. Median medication counts by dependency level from 85–95 years of age

		Mediation medication count (interquartile range)			
Dependency level	Sample	Baseline (age = 85)	Wave 3 (age = 88.5)	Wave 4 (age = 90)	Wave 5 (age = 95)
Independent	All	5 (2–7)	5 (2.5–7)	5 (3–7.25)	4 (3–9)
	Men	5 (3–7)	5 (3–7)	5 (3–7.5)	6.5 (3.25–9.75)
	Women	4 (2–6)	4 (2–6.25)	4 (1–7)	2 (1.5–4)
Low	All	6 (4–9)	6 (4–9.25)	7 (4.5–10)	8 (5–10)
	Men	6 (4–8)	6 (4–9)	7 (4.75–9)	7.5 (5.25–9)
	Women	6 (4–9)	6 (5–10)	6 (4.5–10)	8 (5–10)
Medium	All	8 (5–10)	6 (4–9.5)	8 (4–11)	7 (5–10)
	Men	7 (5–10)	4.5 (3.25–7)	4.5 (3–10.25)	6 (5–9.5)
	Women	8 (6–10)	7 (5–10)	8 (5–10.5)	7.5 (6–10.5)
High	All	7 (4.5–9)	8 (6–10.5)	7 (5–9)	6 (5–10)
	Men	6 (4–9)	8 (6–8)	8.5 (6.75–9.5)	8 (6–9)
	Women	7 (5–10)	8 (6–11)	6.5 (5–8.75)	6 (5.25–9.5)

there are known differences in prescribing [13] and dependency [2] between very old men and women. Whilst we adjusted for changes in multimorbidity as a count over time, we had no information on disease progression or severity for example, so residual confounding cannot be excluded as is the case with all observational studies. Our results also predate the COVID-19 pandemic. In order to model all transitions that are clinically plausible (for example transitioning from independence to a heightened state of unhealthiness following a catastrophic event), we merged participants with medium or high dependency on the basis of their similar characteristics (i.e. both need intensive levels of care and help with personal care). We could not capture prescribing changes outside of data collection points, which could overlook fluctuations in medication prescription (such as medications prescribed for short-term use). We also cannot confirm whether medications were taken as prescribed; to measure non-adherence, a linked prescribing and dispensing

Table 2. The association between each additional medication prescribed and dependency transitions over 10 years (age 85–95)

	Hazard ratio (95% confidence interval)				
Dependency transitions	Model 1	Model 2	Model 3	Model 4	Model 5
Independent to low	1.04 (0.99–1.09)	1.06 (1.01–1.11)	1.06 (1.01–1.11)	1.02 (0.97–1.07)	1.02 (0.97–1.08)
Independent to medium/high	0.62 (0.38–1.03)	0.62 (0.31–1.25)	0.59 (0.34–1.04)	0.42 (0.18–1.00)	0.49 (0.20–1.19)
Independent to death	1.13 (1.01–1.25)	1.02 (0.89–1.18)	1.02 (0.89–1.18)	0.94 (0.81–1.10)	0.98 (0.84–1.15)
Low to medium/high	1.01 (0.96–1.07)	1.00 (0.95–1.06)	1.01 (0.96–1.06)	1.02 (0.97–1.08)	1.03 (0.96–1.10)
Low to independent	0.88 (0.81–0.96)	0.88 (0.80–0.95)	0.88 (0.81–0.96)	0.89 (0.81–0.97)	0.90 (0.82–0.99)
Low to death	1.03 (0.96–1.10)	1.05 (0.98–1.12)	1.04 (0.97–1.11)	1.02 (0.95–1.09)	1.04 (0.98–1.10)
Medium/high to low	1.00 (0.91–1.10)	1.00 (0.91–1.11)	1.00 (0.90–1.10)	1.03 (0.92–1.15)	1.03 (0.91–1.16)
Medium/high to death	1.04 (1.01–1.08)	1.05 (1.02–1.08)	1.05 (1.02–1.09)	1.04 (1.00–1.07)	1.03 (0.98–1.08)

Notes: Model 1 is adjusted for polypharmacy and age. Model 2 is adjusted for polypharmacy, age and sex. Model 3 is adjusted for polypharmacy, age, sex and years in education. Model 4 is adjusted for polypharmacy, age, sex, years in education and multiple long-term conditions. Model 5 is adjusted for polypharmacy, age, sex, years in education, multiple long-term conditions and body mass index.

dataset is believed to be optimal, though such linkage is not routine or straightforward [31]. Finally, whilst waves 1–4 of the Newcastle 85+ Study lay within a five-year time window, the interval between waves four and five was five years—we may therefore have missed transitions in dependency between the ages of 90 and 95.

Implications and conclusion

For very old people with low dependency, each additional medication prescribed is associated with a 10% decrease in their chance of reablement. In the future, absolute numbers of people aged 85 and over with low care needs are projected to increase [2], whilst family care networks (the mainstay of support) [16] are expected to become more fragile for reasons including extended working life, greater female labour market participation and more geographically disparate families [1]. Previous research also suggests that low dependency is the optimal point at which reablement is possible [1]. Older people often emphasise the importance of retaining independence for their quality of life [5], fearing disability and dependency more than death itself [32], and whilst life expectancy in most developed countries has increased over previous decades [33], attention is now focussing more on the quality of those extra years lived [34]. Recent reports also state that older people are prescribed too many medicines [35, 36], for which disease-specific clinical guidelines are one explanation [37].

Our findings therefore suggest that when a relatively able person visits the GP or clinical pharmacist, careful consideration must be given to whether the benefits from adding a new medication outweigh the potential for it to impact the capacity to live independently. Given that interventions at the point of low dependency (or even earlier) have the most chance of slowing down decline [1], our findings also advocate the promotion of physical reconditioning programs for older people with polypharmacy and low care needs, though not during the experience of or before resolution of medication side effects.

In terms of future work, evidence for de-prescribing is building [38, 39], and most older people would be willing to stop their medicines if their doctor deemed it appropriate to do so [40]. Future studies could therefore examine whether deprescribing medication in older people with low dependency promotes the transition to independence. If it does, this group could be targeted for medication reviews with the view to deprescribe if appropriate according to individual patient circumstances. If future studies were to also identify the medication classes that hinder the recovery of independence in the very old, this could focus deprescribing in this age group.

Supplementary Data: Supplementary data mentioned in the text are available to subscribers in *Age and Ageing* online.

Data Availability Statement: Data cannot be shared publicly because of data governance, GDPR and contractual arrangements with outside organisations who provide individual level data to the study (NHS Digital). Data are available from the Newcastle 85+ Data Guardians (contact via https://research.ncl.ac.uk/85plus/datarequests/) for researchers who meet the criteria for access to confidential data.

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