Research Report

Trajectories of Late-Life Disability Vary by the Condition Leading to Death

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Abstract

Background: Previous research suggested that there might be distinct patterns of functional decline in the last years of life depending on the condition leading to death, but the validity of these results and hence the explanatory value of the condition leading to death for late-life disability are uncertain.

Methods: A total of 636 decedents from a cohort of 754 community-living persons, 70+ years of age (Yale PEP Study) provided 33 700 monthly observations of self-/proxy-reported disability during the last 5 years of life. Nonlinear trajectories and short-term fluctuations of late-life disability by condition leading to death (cancer, organ failure, frailty, severe dementia, sudden death, other) were estimated with flexible mixed spline regression models.

Results: Disability trajectories at the end of life varied distinctively by the condition leading to death. Estimated disability trajectories among cancer deaths increased gradually up until about 6 months before death, after which a steep terminal decline set in. Among those with organ failure, frailty, and dementia, in contrast, disability was higher, increased more gradually, and there was no clear-cut terminal phase. Adding the condition leading to death to other known risk factors increased the amount of explained between-person variation in late-life disability from $R^2 = 0.35$ to 0.49. Short-term fluctuations in disability were not specific for decedents with organ failure.

Conclusions: The condition leading to death is an important determinant of trajectories of late-life disability. These trajectories follow distinct patterns partially resembling a previously outlined theoretical typology.

Keywords: Cause of death, Disability trajectories, End of life, Terminal decline

There is substantial variation in functioning including disability in the last years of life (1,2) between individuals, and knowledge about different clinical types of trajectories could help tailor care programs to patients' needs and assist in end-of-life decision making (3). Based on clinical experience, Lunney and colleagues (4) suggested 4 distinct end-of-life trajectories: (i) sudden death: high functioning until death, (ii) terminal cancer: high functioning followed by a steep decline in the last 3–6 months, (iii) organ failure: intermediate functioning and continuous decline intersected by repeated short-term decline-recovery cycles, and (iv) frailty and dementia: low functioning and gradual decline.

The empirical evidence for this influential typology, however, is mixed. Studies (eg, (5–8)) supporting distinct trajectories of

functioning by clinical conditions often rely on descriptive plots, analyses of a single cause of death, or simple logistic/linear regression models with few repeated observations per person, all of which do not allow the nonlinear trajectories outlined to be assessed. In contrast, 2 studies (2,8) which compared latent disability trajectory types—for example, progressive, late, or persistent disability—with groupings based on the condition leading to death found only partial agreement; for example, that frail older adults followed several disability trajectory types rather than just one or two. The authors thus concluded that disability during the last year(s) of life does not follow or only partially follows a predictable trajectory according to the condition leading to death. In conclusion, the validity and explanatory value of the

clinical condition leading to death for late-life disability are currently uncertain.

In this analysis, we use monthly disability data during the last 5 years of life and advanced mixed regression analyses to (i) directly model the nonlinear shape of disability trajectories by the condition leading to death, (ii) quantify the added explanatory value of the condition leading to death in addition to known predictors of disability (eg, sociodemographics, chronic diseases, hospital stays) (9,10), and (iii) assess whether short-term fluctuations in functioning (11) are indeed more prevalent among older adults suffering from organ failure compared to other causes of death due to episodic exacerbations of their illness (4).

Method

Data

The Yale PEP Study provides comprehensive face-to-face assessments at 18 months intervals and monthly telephone-based disability assessments among 754 health plan members 70 years or older in greater New Haven, CT (12). As of November 2018, 688 (91.2%) participants had died (100% complete mortality follow-up) as determined from local obituaries and informants. We used monthly disability assessments during the last 5 years of life from decedents who did not withdraw from the study permanently before death, and who provided at least 6 disability assessments and information on all variables, which resulted in 636 participants and 33 700 monthly observations (=53 repeated observations per person on average). When respondents were unable to answer themselves, proxy respondents provided information on disability (29.7% of observations). Concordance between proxy- and self-reported ADL disability in the PEP Study was assessed previously in both cognitively intact and mildly impaired participants over the course of 6 months and was found excellent ($\kappa = 1.0$).

Variables

The primary outcome of this study was monthly disability (range 0–12), measured with an index based on the need for personal assistance (no = 0, yes = 1) in 4 basic activities of daily living (ADLs: bathing, dressing, walking inside the house, transferring from a chair), 5 instrumental activities of daily living (IADLs: shopping, housework, meal preparation, taking medications, managing finances), and 3 mobility limitations (walking 1/4 mile, climb flight of stairs, lift/carry 10 pounds). The 3 subindices (ADLs, IADLs, mobility disability) were used separately as secondary outcomes.

Based on information from death certificates and the last comprehensive assessment, the immediate or underlying condition leading to death was classified according to a previous protocol (2) as: cancer, organ failure, frailty, severe dementia, sudden death, or other (see [Supplementary Methods](#)). In case of multiple conditions leading to death, assignment to a unique cause of death was forced hierarchically in the following order: cancer, dementia, organ failure, frailty.

Covariates from the comprehensive assessments included sex (male/female), race (White/non-White), married (no/yes), years of education, the age at death (years), the number of chronic diseases (0–9), and low social support (MOS social support survey < 18: no/yes). From monthly telephone-based interviews, we included

overnight hospital stays (0/1) as a lag variable referring to the respective month before the disability measurement.

Statistical Analysis

First, we modeled mean disability trajectories by condition leading to death using Poisson mixed regression models. The models included time to death, the condition leading to death, and an interaction term between these two as independent variables, as well as all covariates. To allow for nonlinear trajectories, the effect of time to death was modeled with a flexible thin-plate regression spline. Second, to assess the added explanatory value of the condition leading to death, we compared the model fit (R^2) of the full model with a reference model containing all variables except the condition leading to death. Third, and finally, we assessed short-term disability fluctuations based on observation-level residuals from the fully adjusted Poisson mixed regression model of overall disability which describe vertical deviations from individual disability growth curves based on random intercept and slope effects (11). The extracted absolute values of observation-level residuals were then modeled with a linear mixed regression model.

All models were fitted with a Bayesian estimation procedure via package *brms* (v2.11.1), a front-end for *Stan* (v2.19.2) in *R* (v3.6.3).

Results

About 63.1% of the sample were women and mean age at death was 87.2 years ($SD = 6.3$) for women and 86.6 ($SD = 5.7$) for men. The most common condition leading to death was frailty (28.0%), followed by organ failure (21.2%), severe dementia (20.6%), and cancer (16.5%). Only 2.2% ($n = 14$) were classified as sudden deaths. “Other” conditions leading to death (11.6%) mostly included diseases of the circulatory system as well as respiratory or infectious diseases as the immediate or underlying condition of death.

[Figure 1](#) shows estimated disability trajectories by cause of death for overall disability as well as for the 3 disability domains based on the nonlinear mixed regression models. Average trajectories of disability clearly varied between different causes of death, resembling the theorized typology. [Table 1](#) shows the estimated disability levels by condition leading to death at 5 years, 3 years, 1 year, 6 months, and 1 month before death based on the fully adjusted model. Among respondents who died a sudden death, overall functioning was good and hardly changed until 6 months before death, when terminal decline set in. Their level of disability in the last month before death was considerably lower compared to participants with other causes of death. Cancer patients were characterized by few initial disabilities and a gradual increase up until 6 months before death, after which a steep terminal decline set in. In contrast, there was no clear-cut terminal phase and disability was higher and increased more gradually among those with organ failure and frailty. Disability levels were highest throughout the last 5 years of life among those with dementia, and also without a clear terminal phase. The trajectory of the residual category “other” resembled a mixture of the sudden and cancer death trajectories. Compared to IADLs and mobility disability, ADL disability occurred later and the decline was generally steeper.

Including cause of death improved model fit substantially compared to the reference model: R^2 : 0.35 (CI-95% = 0.32–0.38) versus 0.49 (CI-95% = 0.46–0.51). In addition to the condition leading to death, females showed 32% (CI-95% = 16%–49%) more disabilities, disabilities increased by 3% (CI-95% = 2%–4%) per year

(age at death), each additional chronic disease was associated with a 3% (CI-95% = 1%–6%) increase, and overnight hospital stays were associated with a subsequent increase in disability by 32% (CI-95% = 29%–36%).

Median short-term vertical deviations from individual's disability trajectories amounted to 0.78 (on 12-point scale), and

Figure 1. Estimated mean disability trajectories by condition leading to death during the last 5 years. Estimated values are based on the Poisson mixed regression model adjusted for all covariates (sex, race, married, low education, hospital admission, age at death, number of chronic diseases, cognitive impairment, and low social support). For this plot, all effect-coded dichotomous variables were kept constant at value zero, and all continuous variables were kept at mean value. Overall disability refers to the composite index of disability, ADL disability = basic activities of daily living (bathing, dressing, walking inside the house, transferring from a chair), IADL disability = instrumental activities of daily living (shopping, housework, meal preparation, taking medications, managing finances), mobility disability = walking 1/4 mile, climb flight of stairs, lift/carry 10 pounds. Solid lines refer to point estimates, dotted lines refer to 95% credible intervals.

these fluctuations were smaller among decedents with dementia (median = 0.65) or a sudden death (=0.57) compared to those with organ failure (=0.86), frailty (=0.85), and cancer (=0.81). Similar results were seen in the model on short-term fluctuations ($R^2 = 0.03$, CI-95% = 0.02–0.03): such fluctuations were 18% (CI-95% = 8%–30%) higher among decedents with organ failure compared to those with dementia, and 39% (CI-95% = 14%–72%) higher compared to those with sudden deaths, but differences were not observed between organ failure, frailty, or cancer.

Discussion

In contrast to previous studies (5–8), which relied on bivariate statistics and plots or simple regression analyses, we directly modeled nonlinear disability trajectories by the condition leading to death. Without specifying the shape of the growth curves in advance, the flexible regression spline approach uncovered distinctive patterns of end-of-life functional decline which mostly resembled the typology outlined by Lunney et al (4). In contrast to earlier work (6) where frailty was operationalized via a nursing home stay, we assessed phenotypic frailty and differentiated it from severe dementia. We also included chronic kidney disease and cirrhosis in addition to congestive heart failure and chronic lung disease (2). In consequence, the disability trajectories of those with organ failure and those with frailty are more alike in our study, whereas the dementia trajectory in our study compares with the outlined (4) frailty trajectory type. The otherwise close correspondence of our results with the theoretical typology contrasts with the results of 2 previous studies (2,8), which first derived latent types of disability trajectories and then cross-tabulated the trajectories with different causes of death. While these studies highlighted the variation of disability trajectories *within* conditions leading to death, our study focused on mean differences in nonlinear disability trajectories *between* causes of death, and thus provides a more direct test of the theoretical typology (4).

In our study, we accounted for a number of risk factors for disability, and found that the condition leading to death explained a substantial additional proportion of interindividual variation in late-life disability. Nonetheless, older age at death, female sex, the number of chronic diseases, and overnight hospital stay(s) were important as well, which is in line with previous studies (eg, (1,9,10)). The effect of the condition leading to death might be even higher as adjusting for hospital admission blocks indirect effects on disability in the model, that is, when the underlying condition leads to hospital stays which in turn result in disability increases.

Table 1. Estimated Disability Levels During the Last 5 Years of Life by the Condition Leading to Death

	Time before death				
	5 y	3 y	1 y	6 mo	1 mo
Sudden deaths	0.7 (0.2–1.7)	0.9 (0.4–1.7)	1.5 (0.9–2.4)	2.0 (1.2–3.1)	4.1 (2.4–6.6)
Cancer	0.6 (0.4–0.8)	1.4 (1.1–1.8)	3.3 (2.7–4.0)	4.5 (3.7–5.4)	10.2 (9.1–11.0)
Organ failure	1.7 (1.2–2.3)	3.1 (2.4–3.9)	6.2 (5.3–7.2)	8.0 (6.9–9.0)	10.9 (10.2–11.5)
Frailty	1.9 (1.4–2.6)	4.0 (3.2–4.8)	7.4 (6.4–8.3)	8.5 (7.6–9.4)	10.9 (10.3–11.4)
Dementia	3.3 (2.3–4.5)	7.0 (5.7–8.5)	10.8 (10.1–11.4)	11.4 (10.9–11.8)	11.9 (11.5–12.2)
Other	0.5 (0.3–0.8)	1.2 (0.9–1.5)	2.8 (2.2–3.4)	4.1 (3.3–5.0)	8.7 (7.2–10.0)

Notes: Estimated values based on fully adjusted Poisson mixed regression model (636 participants, 33 700 observations, $R^2 = 0.49$). Values in parentheses refer to 95% credible intervals. All covariates were held constant, that is, they were set to zero in case of effect-coded categorical variables and to the mean in case of continuous variables.

In this study, we assessed overall disability and specific domains (ADLs, IADLs, mobility disability). We found that late-life functional decline is time-delayed, with the ability to live independently in the community (IADL) and then mobility deteriorating first, followed later by dependence in basic self-care activities (ADLs), which supports the hierarchic relation between these measures of disability. A phase of terminal decline for decedents with sudden death and cancer was most visible in ADLs, which renders these the most proximate markers of subsequent mortality. For frailty and severe dementia, which together accounted for almost half of the study's sample, no discrete terminal phase was discernible, which is also in line with previous studies (5,6). On the other hand, sudden deaths—a small and residual category—appear less “sudden” when IADL and mobility disability are also considered, although these participants did die with considerably fewer estimated disabilities compared to all others.

Our study assessed the last 5 years of life, which is longer than previous studies (1,2,5–7), to provide a more extended picture of late-life functional decline. Also, it was documented in a systematic review of end-of-life trajectories (13) that the transition to the terminal phase may occur several years before death. A study on motor function (14), for example, located the onset of terminal decline 2.5 years before death. The longer time period also illustrates the time delay in functional decline according to the underlying condition and the substantial heterogeneity of disability during the last years of life (8): The same degree of overall disability that showed in sudden deaths right before death, showed half a year before death for cancer patients, at about 2.5 years for those with organ failure, at about 3 years for those suffering from frailty, and 4.5 years before death for those with severe dementia. These results add to our understanding of late-life decline and this information can be helpful to describe to patients the expected impact of the illness progression on their daily living, which in turn could help tailor care programs to patients' needs, and assist in end-of-life decision making (3). Although no clear-cut terminal phase was found among those who died from organ failure, frailty, or dementia—which account for the majority of decedents in our sample—it is important that these patient groups also have access to adequate palliative treatment, as studies (15–17) have shown that these patients have symptom burdens comparable to cancer patients.

Next to long-term trajectories, we also assessed short-term disability fluctuations, which were hypothesized specifically for decedents who died from organ failure (4). We found slightly elevated fluctuations among this group, but also among those with cancer and frailty compared to those with dementia or sudden deaths. Such fluctuations could in principle result from oscillating acute symptoms such as shortness of breath or pain and subsequent hospital stays in those suffering from organ failure (4), positive/negative effects of palliative oncological treatment in cancer patients (3), and the cumulative physiological decline in frailty giving rise to unstable disability (18). However, the magnitude of these fluctuations was modest in summary, the differences between the clinical conditions small and the overall model fit poor. In any case, short-term disability fluctuations appear not to be a specific characteristic among decedents who died from organ failure, which contrasts with the original typology (4) but is in line with 2 more recent studies (8,19) which did not find such evidence either.

To our knowledge, this is the first study that modeled nonlinear trajectories of late-life functioning by cause of death explicitly while adjusting for known risk factors of disability. Further strengths of

this analysis include the assessment of overall disability as well as by domain over the last 5 years of life; assessment of both long-term trajectories and short-term fluctuations; a limited number of unclassified (“other”) decedents and few sudden deaths; and the overall high data quality (monthly disability assessments, high proxy-respondent reliability, and low rate of loss-to-follow-up). A central limitation of our study arises from the retrospective analysis of deceased participants and causes of death, which does not permit prospective prediction of disability trajectories. Although predicting mortality, let alone cause of death, is notoriously difficult, future studies could combine information on past and current disability levels and specific chronic diseases to predict mortality risk dynamically, for example, by using joint models for longitudinal and time-to-event data. Another limitation comes from the inherent difficulty of assigning only one condition leading to death in the presence of prevalent multiple comorbidities (20). Finally, as the study participants were members of a single regional health plan aged 70 and older, who were initially nondisabled, our results might not be widely generalizable to the older U.S. population or those younger than 70 years. Nonetheless, the demographic characteristics of greater New Haven, CT are comparable to those of the U.S. population except for underrepresentation of non-White older adults.

In conclusion, we found that late-life disability trajectories during the last 5 years of life vary according to the condition leading to death, which follows a distinctive pattern partially supporting a previously outlined theoretical typology.

Supplementary Material

Supplementary data are available at *The Journals of Gerontology, Series A: Biological Sciences and Medical Sciences* online.

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Conflict of Interest

None declared.

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Author Contributions

E.S. planned the study, performed all statistical analysis, and wrote the article. T.M.G. contributed to the planning of the study, provided access to the data, and critically reviewed the manuscript. H.M. contributed to the methodological approach and critically reviewed the manuscript. E.R. contributed to the interpretation of results and critically reviewed the article. W.F. supervised the analysis, contributed to the planning of the study, and critically reviewed the article.

References

- Smith AK, Walter LC, Miao Y, Boscardin WJ, Covinsky KE. Disability during the last two years of life. *JAMA Intern Med.* 2013;173:1506–1513. doi:[10.1001/jamainternmed.2013.8738](https://doi.org/10.1001/jamainternmed.2013.8738)
- Gill TM, Gahbauer EA, Han L, Allore HG. Trajectories of disability in the last year of life. *N Engl J Med.* 2010;362:1173–1180. doi:[10.1056/NEJMoa0909087](https://doi.org/10.1056/NEJMoa0909087)
- Murray SA, Kendall M, Boyd K, Sheikh A. Illness trajectories and palliative care. *BMJ.* 2005;330:1007–1011. doi:[10.1136/bmj.330.7498.1007](https://doi.org/10.1136/bmj.330.7498.1007)
- Lunney JR, Lynn J, Hogan C. Profiles of older Medicare decedents. *J Am Geriatr Soc.* 2002;50:1108–1112. doi:[10.1046/j.1532-5415.2002.50268.x](https://doi.org/10.1046/j.1532-5415.2002.50268.x)
- Covinsky KE, Eng C, Lui LY, Sands LP, Yaffe K. The last 2 years of life: functional trajectories of frail older people. *J Am Geriatr Soc.* 2003;51:492–498. doi:[10.1046/j.1532-5415.2003.51157.x](https://doi.org/10.1046/j.1532-5415.2003.51157.x)
- Lunney JR, Lynn J, Foley DJ, Lipson S, Guralnik JM. Patterns of functional decline at the end of life. *JAMA.* 2003;289:2387–2392. doi:[10.1001/jama.289.18.2387](https://doi.org/10.1001/jama.289.18.2387)
- Chen JH, Chan DC, Kiely DK, Morris JN, Mitchell SL. Terminal trajectories of functional decline in the long-term care setting. *J Gerontol A Biol Sci Med Sci.* 2007;62:531–536. doi:[10.1093/gerona/62.5.531](https://doi.org/10.1093/gerona/62.5.531)
- Lunney JR, Albert SM, Boudreau R, et al; Health Aging and Body Composition Study. Mobility trajectories at the end of life: comparing clinical condition and latent class approaches. *J Am Geriatr Soc.* 2018;66:503–508. doi:[10.1111/jgs.15224](https://doi.org/10.1111/jgs.15224)
- Stuck AE, Walther JM, Nikolaus T, Büla CJ, Hohmann C, Beck JC. Risk factors for functional status decline in community-living elderly people: a systematic literature review. *Soc Sci Med.* 1999;48:445–469. doi:[10.1016/s0277-9536\(98\)00370-0](https://doi.org/10.1016/s0277-9536(98)00370-0)
- Gill TM, Gahbauer EA, Han L, Allore HG. The role of intervening hospital admissions on trajectories of disability in the last year of life: prospective cohort study of older people. *BMJ.* 2015;350:h2361. doi:[10.1136/bmj.h2361](https://doi.org/10.1136/bmj.h2361)
- Stolz E, Gill TM, Mayerl H, Freidl W. Short-term disability fluctuations in late life. *J Gerontol B Psychol Sci Soc Sci.* 2019;74:e135–e140. doi:[10.1093/geronb/gbz089](https://doi.org/10.1093/geronb/gbz089)
- Gill TM. Disentangling the disabling process: insights from the precipitating events project. *Gerontologist.* 2014;54:533–549. doi:[10.1093/geront/gnu067](https://doi.org/10.1093/geront/gnu067)
- Cohen-Mansfield J, Skornick-Bouchbinder M, Brill S. Trajectories of end of life: a systematic review. *J Gerontol B Psychol Sci Soc Sci.* 2018;73:564–572. doi:[10.1093/geronb/gbx093](https://doi.org/10.1093/geronb/gbx093)
- Wilson RS, Segawa E, Buchman AS, Boyle PA, Hibel LP, Bennett DA. Terminal decline in motor function. *Psychol Aging.* 2012;27:998–1007. doi:[10.1037/a0028182](https://doi.org/10.1037/a0028182)
- Janssen DJ, Spruit MA, Wouters EF, Schols JM. Daily symptom burden in end-stage chronic organ failure: a systematic review. *Palliat Med.* 2008;22:938–948. doi:[10.1177/0269216308096906](https://doi.org/10.1177/0269216308096906)
- Stow D, Spiers G, Matthews FE, Hanratty B. What is the evidence that people with frailty have needs for palliative care at the end of life? A systematic review and narrative synthesis. *Palliat Med.* 2019;33:399–414. doi:[10.1177/0269216319828650](https://doi.org/10.1177/0269216319828650)
- van der Steen JT. Dying with dementia: what we know after more than a decade of research. *J Alzheimers Dis.* 2010;22:37–55. doi:[10.3233/JAD-2010-100744](https://doi.org/10.3233/JAD-2010-100744)
- Campbell AJ, Buchner DM. Unstable disability and the fluctuations of frailty. *Age Ageing.* 1997;26:315–318. doi:[10.1093/ageing/26.4.315](https://doi.org/10.1093/ageing/26.4.315)
- Lunney JR, Albert SM, Boudreau R, Ives D, Newman AB, Harris T. Fluctuating physical function and health: their role at the end of life. *J Palliat Med.* 2019;22:424–426. doi:[10.1089/jpm.2018.0289](https://doi.org/10.1089/jpm.2018.0289)
- Tinetti ME, McAvay GJ, Murphy TE, Gross CP, Lin H, Allore HG. Contribution of individual diseases to death in older adults with multiple diseases. *J Am Geriatr Soc.* 2012;60:1448–1456. doi:[10.1111/j.1532-5415.2012.04077.x](https://doi.org/10.1111/j.1532-5415.2012.04077.x)