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Research Article

Heterogeneous Long-Term Trajectories of Dependency in Older Adults: The PAQUID Cohort, a Population-Based Study over 22 years

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Abstract

Background: A critical step toward successful aging is to identify opportunities for prevention of functional decline. Our aim was to describe the heterogeneity in trajectories of dependency preceding death in elders and to identify factors associated with this heterogeneity.

Methods: The study relied on 3,238 participants of the prospective population-based PAQUID cohort aged 65+ at baseline in 1988. Dependency was defined from an 11-item scale of basic and instrumental activities of daily living (ADL: bathing, dressing, toileting, continence, eating, and transferring; instrumental activities of daily living (IADL): telephoning, shopping, using transport, handling medication, and managing finances) collected over 22 years. Heterogeneous trajectories were estimated using a longitudinal item response theory model including latent classes.

Results: Five distinct profiles of functional dependency were identified over the two last decades of life: persistently high (12%), moderate (26%), persistently low (40%), and accelerated high dependency (15%), and no dependency (8%). Main factors associated with heterogeneity included age at death, sex, education, initial cognition (Mini-Mental State Examination [MMSE] score and dementia), initial disability, and poly-medication.

Conclusions: In the two last decades of life, more than 9 elders in 10 were characterized as functional decliners. On average, around half of the elders died with no or mild dependency, while 27% live several years with a high level of limitations and would need assistance in activities of daily living, at least for 2–4 years preceding death. The identified factors associated with these trajectories are important to understand functional heterogeneity in elders and to propose interventions to postpone or prevent "chronic" disability.

Keywords: Activities of daily living, Functional trajectories, Item Response Theory, Latent class analysis

Despite the improvement of health highlighted over the last decades in the older population, the baby boomers generation's aging and the life expectancy increase, projections predict an increasing number of people with chronic diseases and dependency (1). In such context, ensuring that the added years of life are of good quality becomes more and more challenging. A critical step toward successful aging is to identify the factors associated with functional decline on which it is possible to act. Yet, the natural history of dependency is possibly highly heterogeneous. Indeed, some studies have highlighted heterogeneous functional trajectories in late life, notably with progressive, accelerated, stable, or catastrophic paths (2–8). However, while central for a better understanding and prevention of dependency, none of them explored the heterogeneity of the natural history of dependency over aging until death in the general older population. Contributions mainly focused on limited windows of time (eg, 2–14 years (6,7,9)), selected populations either at the end of life (eg, in nursing homes or hospices), or in young elders (50+) (10).

In the older adults, functional dependency is mainly assessed by limitations in basic activities of daily living (ADL) and instrumental activities of daily living (IADL). Despite a preexisting hierarchy, dependency is often analyzed as a degree, while it is a continuous process, or by raw scores which assume equivalence between each

activity, meaning for instance that consequences between a limitation in toileting or in telephoning would be the same on the daily living and, by overstating the rationale, in terms of burden for the eventual informal caregivers.

It was previously shown that such simple scores might be not accurate enough to finely discriminate proximate levels of dependency between individuals (11), somewhat limiting the adequacy of care support. Without disqualifying results provided by the use of aggregate scores, a more refined definition of dependency could be used that would fully exploit (with minimum assumptions) the information provided by items of (I)ADL as meaningful "clinical" manifestations to construct the underlying continuum of dependency. This is the purpose of the Item Response Theory (IRT) (12), which consists of relating the latent process of interest (here, the dependency) to its observable manifestations (here, (I)ADL limitations). This method provides an identification of clinical stages in the natural history of dependency (time of onset and duration).

In this context, our objectives were to describe the heterogeneity of functional trajectories of dependency over a maximum of 24-year period preceding death among the 65+ community-dwellers of the PAQUID French population-based study and to investigate the associated factors. To do so, we combined the IRT methodology that defined dependency as a continuum with a latent class mixed modeling to identify the different profiles of functional trajectories in this general population. Analyses were done according to years preceding death rather than chronological age to better reflect the complete natural history of dependency (13).

Methods

Study Population

The participants were drawn from the French PAQUID cohort, an ongoing epidemiological prospective study on cerebral and functional aging conducted in the general population and previously described in full (14). At baseline in 1988, 3,777 participants aged ≥65 and older, initially all community-dwellers, were randomly recruited from the electoral rolls of two administrative areas in southwestern France. The eligible sample included 3,238 deceased participants (86% of the cohort) with at least one available (I)ADL information over the 22-year follow-up. The 539 subjects still alive after 24 years of follow-up were thus excluded.

Informed consent was obtained for all participants and the ethics committee of the University Hospital in Bordeaux approved the research according to the principles embodied in the Declaration of Helsinki.

Data Collection

Face-to-face interviews were conducted at home every 2–3 years by specially trained neuropsychologists. Sociodemographic, environmental, and health-related data were prospectively collected at each wave with the participant or a proxy, when self-assessment was impossible or invalid. The PAQUID program included a systematic and regular record and check of deaths with the administrative data of death certificates obtained from GPs and the city administrative department (date and cause of death). Unlike functional assessments that were collected at planned follow-ups over 22 years, deaths occurred continuously up to 24 years after the first functional assessment.

Functional Assessment

The IADL were assessed using the French version of the Lawton scale (15) including ability to perform: telephoning, shopping, using transport, handling medication, and managing finances. The basic ADL were assessed by the French version of the Katz Index (16) including: bathing, dressing, toileting, continence, eating, and transfer from bed to chair. For both scales, limitation was defined as having no, partial or total limitation to perform the task. This corresponded to the original three-graded response of ADL. In contrast, for IADL, we considered the minimum and maximum original grades (no and total limitation) and merged the intermediate original grades into a single partial limitation. Based on previous studies (17–20), we assumed that the combined Lawton and Katz scales assessed a single underlying dimension of dependency with enhanced range and sensitivity.

Explanatory Variables

Variables related to demographics, material and social environments were: age at baseline and at death, sex, marital status, occupation, educational level, satisfaction with income level, household tenure, rural living area, comfortable housing, informal help, professional assistance, geographic proximity with family, and associative activities. Lifestyle variables included physical activity and smoking. At each visit, health status data were collected: depressive symptomatology assessed by the Center for Epidemiologic Studies Depression (CES-D) scale (21), visual and hearing impairments, disability level, cognitive functioning assessed by the Mini-Mental State Examination (MMSE) (22), self-reported history of health (diabetes, hypercholesterolemia, hypertension, stroke sequels, joint pain, cardiovascular diseases, dyspnea, Parkinson's disease, poly-medication), and perceived health and subjective health. Finally, life satisfaction and feeling of freedom were also collected. All explanatory variables with their measurement instruments are detailed in Supplementary Table S1.

Statistical Methods

The dependency continuum

Rather than defining dependency (in a deterministic way) as a sumscore of (I)ADL limitations with equal weights, we defined dependency as the common latent trait underlying observed (I)ADL limitations in an IRT model, specifically a two-parameter probit IRT model for ordinal responses (23). In this probabilistic definition, dependency is a latent trait (or continuum) which is only observed through multiple noisy ordinal manifestations (ie, no, partial or total limitation). The link between each manifestation and the underlying continuum (ie, the probability to observe each manifestation for a given level of dependency), is characterized by two parameters to estimate: the mean location of the (I)ADL limitation along the dependency continuum which corresponds to the severity of the loss, and the discrimination ability of the item to distinguish individuals with proximate levels of latent dependency which corresponds to the inverse of item error variance. The IRT model thus assumes a unique mean pattern of losses in daily activities between individuals.

Heterogeneous trajectories

We investigated heterogeneous trajectories of the dependency continuum by estimating a Latent Class Mixed Model (24) simultaneously with the IRT model. We assumed that a finite number of mean profiles of latent dependency trajectory existed, and considered quadratic shapes of trajectories over time to take into account that functional decline may accelerate at the approach of death. The models were estimated for a number of latent classes varying from 1 to 6 and the optimal number of classes was guided by the Bayesian Information Criterion (BIC, with a lower value indicating a better

fitting model), the size of the classes and the discriminatory performances. The report was done by following Guidelines for Reporting on Latent Trajectory Studies (GRoLTS) (25). See Supplementary Methods section in Supplementary Material for further details.

Factors associated with trajectories

Factors associated with trajectory profiles were identified using multinomial logistic regressions weighted by the posterior probabilities of class-membership and adjusted for age at baseline, sex, and education (26). Each variable was firstly considered in univariate analyses. Significant variables ($p < .05$) were then introduced into a backward stepwise multivariate multinomial logistic model to identify the factors significantly ($p < .05$) associated with the latent classes.

Analyses were performed with the SAS software, version 9.1.3 (SAS institute Inc., Cary, NC) and the Fortran90 HETMIXSURV program (free download at "http://www.isped.u-bordeaux.fr/biostat").

Results

Participants' Characteristics

As presented in Table 1, at baseline, the mean age was 76.5 (±6.8 *SD*), 44% were male, 63% were high-educated (≥7 years of schooling) with a higher educational level in men (69% in men vs 59% in women), and 37% were widowed. The four main causes of death were: tumors (19.5%); pulmonary circulation diseases, and other forms of cardiopathy (19.4%); symptoms, signs and ill-defined conditions (14.2%); and cerebrovascular diseases (11.9%); and the mean age at death was 86.7 (±6.8 *SD*). The level of initial (I)ADL limitation was quite low (see Supplementary Table S2 for more details). The median length of follow-up until death was 9.8 years (IQR: 4.9–14.9), and the median elapsed time between baseline and the last visit, where (I)ADL information was obtained, was 5.2 years. The median number of repeated measures for (I)ADL was 5.0.

The excluded participants were significantly younger (mean age, 69.4 [±3.4 SD]) at baseline, less often males (28.9%), more highly educated (74.4%), without limitations (48.1%), and less often demented (0.2%), but more often polymedicated (66.2%).

Table 1. Baseline Participants' Characteristics of The PAQUID Cohort (n = 3,238), France (1988–2012)

Characteristics	*N* = 3,238
Age at baseline (years), mean (*SD*)	76.5 (6.8)
Age at death (years), mean (*SD*)	86.7 (6.8)
Men, *n* (%)	1,420 (43.9)
High educational level[a], *n* (%)	2,033 (62.8)
Marital status, *n* (%)	
Married or in couple	1,780 (55.0)
Single, divorced, separated, other	245 (7.6)
Widowed	1,212 (37.4)
No. of IADL limitation (partial or total), mean (*SD*)	0.9 (1.4)
No. of ADL limitation (partial or total), mean (*SD*)	0.4 (1.0)
MMSE score, mean (*SD*)	25.2 (4.2)
Dementia diagnosis, *n* (%)	101 (3.1)
Poly-medication[b], *n* (%)	1,814 (56.0)
Cause of death[c], *n* (%)	
Malignant, benign and other tumors	445 (19.5)
Pulmonary circulation diseases and other forms of cardiopathy	443 (19.4)
Symptoms, signs, and ill-defined conditions	325 (14.2)
Cerebrovascular diseases	272 (11.9)
Other causes of death	756 (33.6)
Elapsed time between baseline and the last visit (years), mean (*SD*)	6.8 (6.0)
Elapsed time between baseline and death (years), mean (*SD*)	10.2 (6.1)

Note: ADL = activity of daily living; IADL = instrumental activity of daily living; MMSE = Mini-Mental State Examination; SD, standard deviation.
[a]>7 years of schooling; [b]> 3 drugs intake; [c]Missing data: 30.1%.

Item (I)ADL-Mapping Along the Continuum

The pattern of losses in (I)ADL along the dependency continuum is graphically reported in Figure 1 (see Supplementary Table S3 for items parameters). On average, individuals entered into mild dependency with partial limitations in shopping and transporting; shopping was the first total limitation (corresponding to entry into moderate dependency). The first ADL limitation was partial limitation in bathing followed by partial limitation in managing medication. The first total ADL limitations (characterizing entry into severe dependency) were in bathing and dressing and occurred at the same time. Finally, the continuum ended with the four total limitations in toileting, continence, eating, and transfer.

Heterogeneous Functional Trajectories

Although the six-class model reported the lowest BIC (BIC = 91,062.81), one represented a very small class (2.3%). We therefore retained the five-class model (BIC = 91,138.41). The quality of classification was moderate with mean posterior probabilities between 0.68 and 0.76 (see Supplementary Table S4). The five mean trajectories preceding death are presented in Figure 2 along with the corresponding (I)ADL-mapping (Figure 1) and a summary of class characteristics in Figure 3. The five classes were distinguishable by their level of dependency 22 years preceding death and by their trajectories over time:

- Persistently low dependent (*PersistLowD*) participants (in black) started 22 years before death in mean at the lowest level in the continuum and died at a mild level of dependency with only partial limitations in shopping. It concerned 39.7% of the sample.
- Persistently moderate dependent (*ModeratD*) participants (in blue) reported a mildly progressive decline with moderate dependency and concerned 25.6% of the sample. They started 22 years before death at a higher level in the continuum compared to the other participants, but experienced a weaker progression and died at a moderate level with, on average, total limitation in shopping and partial limitations in transport, handling finances and bathing.
- Persistently high dependent (*PersistHighD*) participants (in red) reported an early-progressive high dependency. They started 22 years before death at the highest level in the continuum compared to others, experienced an accelerated decline and died at a severe level of dependency with, on average, total limitation in shopping, finances, bathing, dressing, handling medication, and toileting. This class included 11.7% of the sample.
- Accelerated high dependent (*AccHighD*) participants (in green) reported a late-accelerated decline with high dependency. This class included 14.8% participants. They began on average at a lower level than *PersistHighD* and *ModeratD*, but experienced a severe accelerated decline 10 years before death and died at a

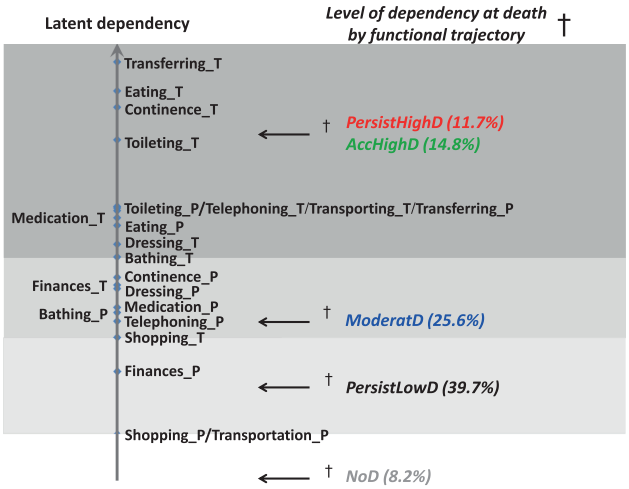

Figure 1. Pattern of losses in (I)ADL of the 3,238 deceased participants along the dependency continuum. The PAQUID cohort, France (1988–2012). Item mapping provided by the Item Response Theory (IRT) model is reported on the vertical axis (with "_P" for partial limitation, "_T" for total limitation). The background gray gradient represents the dependency severity from no (in white), mild, moderate, to severe (dark gray) dependency.

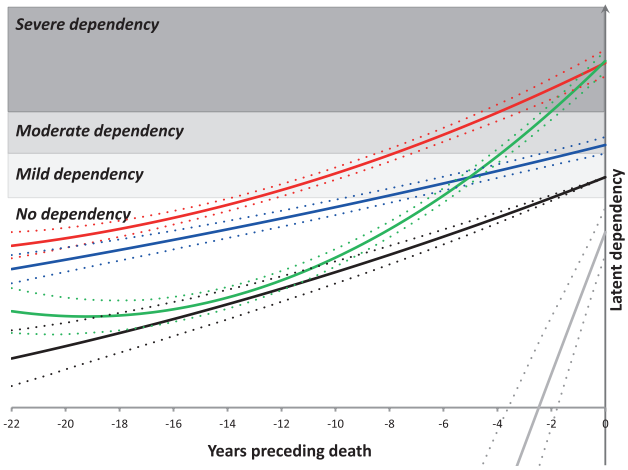

Figure 2. Twenty-two-year heterogeneous mean trajectories (and 95% confident bands) of latent dependency preceding death in the 3,238 participants. Latent class model with quadratic trajectories over time. The PAQUID cohort, France (1988–2012).

severe level of dependency with, on average, total limitation in shopping, finances, bathing, dressing, handling medication, and toileting.

- No dependent (*NoD*) participants (in gray) were totally outside the dependency process, dying before reaching any limitation. This class included 8.2% of the sample.

This analysis highlights different patterns of limitations over time. Four of the five profiles entered into mild dependency (with partial limitation in shopping) at different times of the process, from 2.0 to 13.5 before death according to the profile. Moderate dependency (with total limitation in shopping) was experienced by *PersistHighD*, *ModeratD*, and *AccHighD* participants and occurred on average at about 8.5, 4.0, and 2.0 years preceding death, respectively. Finally, only *PersistHighD* and *AccHighD* participants entered into severe

	PersistLowD Persistently low (39.7%) Class1 (n=1,287)	*NoD* No dependent (8.2%) Class 2 (n=264)	*PersistHighD* Persistently high (11.7%) Class 3 (n=378)	*ModeratD* Moderate (25.6%) Class 4 (n=829)	*AccHighD* Accelerated high (14.8%) Class 5 (n=480)
Profile description	Persistently low level of dependency with the last 2 years in mild dependency	Not in the dependency process	An accelerated decline from the highest level of dependency with 6.5 years in mild dependency, 3.5 in moderate dependency and the last 4.5 years in severe dependency	A weak decline from a high level of dependency with 8.5 years in mild dependency and the last 1.5 years in moderate dependency	An accelerated decline 10 years preceding death with a 2.5-year period of mild dependency, 1.5 years of moderate dependency and then the last 2.5 years with severe dependency
At baseline					
Characteristics	Male, high-educated, married, good subjective health	Male, high-educated, married	Female, low-educated, widowed, visual and hearing impairments	Female, low-educated, widowed, cardiovascular diseases	Female, high-educated, married
Disability	Mild	No/mild	Moderate/severe	Moderate	Mild
Age*	74.4±5.9	70.9±4.1	80.6±6.3	78.8±6.9	76.6±6.3
MMSE*	26.1±3.2	27.3±2.8	23.2±5.1	24.6±3.8	24.1±5.7
Dementia	1.7%	0.4%	7.1%	1.9%	7.3%
At the last visit					
MMSE*	25.4±4.3	26.5±5.6	15.8±8.6	23.5±4.2	15.7±9.8
At death					
Predicted consecutive losses	From partial shopping to transporting	None	From partial shopping to total toileting	From partial finances to total shopping	From partial shopping to total toileting
Age*	83.6±5.5	76.4±4.8	93.9±4.7	90.1±4.6	88.9±4.8
Main cause of death	Malignant, benign and other tumors		Pulmonary circulation diseases and other forms of cardiopathy		Symptoms, signs and ill-defined conditions
Dementia	8.9%	5.3%	54.2%	16.0%	52.1%
Follow-up (in years)					
Total*	9.2±5.8	5.5±3.9	13.3±5.9	11.2±6.2	11.4±5.8
In dependency	2	-	6	8.5	13.5
Associated factors					
Model **	*reference*	Male+, HE+, younger at baseline, no physical limitation due to a health problem ++	Female+++, LE++, older at death, dementia+, moderate (++) and severe (+++) baseline disability, polymedication	Female++, LE++, older at death, dementia, mild, moderate (++) and severe (++) baseline disability, polymedication	Female+, LE, older at death, dementia+, moderate and severe (+) baseline disability

Figure 3. Summary of main characteristics of the five classes drawn from the linear latent class model ($n = 3,238$). The PAQUID cohort, France (1988–2012). *Mean±SD, **Multivariate logistic regression adjusted for age at baseline and sex (OR: " "= In] 1-5[; "+"= in [5-20[; "++"= in [20-50[; "+++" > 50).

dependency (with total limitation in bathing) on average 4.5 and 2.5 years before death, respectively.

Characteristics of the Classes

Classes' characteristics are summarized in Figure 3 and reported in Supplementary Table S5. *PersistHighD* and *ModeratD* were the oldest (both at baseline and death), mostly female, low-educated, and more often widowed. They more frequently reported moderate disability at baseline and lower MMSE scores (23.2 (±5.1 *SD*) and 24.6 (±3.8 *SD*), respectively). Compared to *ModeratD*, *PersistHighD* participants were more likely to have severe disability (15.8% vs 2.2%), dementia diagnosis (7.1% vs 1.9%), stroke sequels, visual and hearing impairments, and depressive symptomatology. At the last visit (data not shown), *PersistHighD* showed increased frequencies in severe disability (35.4%), poly-medication (82.5%), dementia (54.2%), and a decreased mean MMSE score (15.8 [±8.6 *SD*]) compared to baseline.

With a mean age of 74.4 (±5.9 *SD*), the majority of *PersistLowD* were male, highly educated, in couple, with mild disability and had one of the highest MMSE score (26.1 [±3.2 *SD*]). Their mean age at death was 83.6 (±5.5 *SD*). Few were diagnosed with dementia (1.7%), half were poly-medicated, 6.3% experienced sequelae of stroke, and 15.8% depressive symptomatology. At the last visit, the mean MMSE score was 25.4 (±4.3 *SD*) with only 8.9% of the class diagnosed with dementia.

In contrast, at baseline, the majority of *AccHighD* participants, 77.6 (±6.3 *SD*) years old on average, were female, highly educated,

in couple, with mild disability and a mean MMSE score of 24.1 (±5.7 *SD*) with 7.3% diagnosed with dementia. Their mean age at death was 88.9 (±4.8 SD). At the last visit, the mean MMSE score was 15.7 (±9.8 *SD*) with 52.1% being diagnosed with dementia.

Finally, the majority of *NoD* participants were male, highly educated and in couple. They were the youngest at baseline and at death (70.9 [±4.1 *SD*] and 76.4 [±4.8 *SD*]), respectively, with consequently the smallest mean time of follow-up (3.7 [±4.0 *SD*] years compared to 6.8 [±6.0 *SD*] in the total sample). They also reported no or mild disability at baseline more frequently, had the highest MMSE scores (27.3 [±2.8 *SD*]), and the lowest frequencies in all health factors. Nevertheless, they were at baseline more often former or current smokers (72.2% compared to 38% in the total sample) and they died obviously prematurely and in the majority from malignant, benign and other tumors (40.9% compared to 19.5% in the total sample), pathologies more rapidly lethal than other chronic diseases such as dementia or heart failure. At the last visit, the mean MMSE score remained the highest (26.5 [±5.6 *SD*]) only 5.3% being diagnosed with dementia.

The more frequent causes of death were malignant, benign and other tumors in *PersitsLowD* (25.6%) and in *NoD* (40.9%), pulmonary circulation diseases and others forms of cardiopathies in *PersitHighD* (24.3%) and *ModeratD* (24.4%) and, symptoms, signs and ill-defined conditions in *AccHighD* (25.4%).

Profiles' Associated Factors

The multivariate multinomial logistic regression with the *PersistLowD* class as reference confirmed that the main factors associated with class membership were sex, educational level, age at death, MMSE score, dementia, disability, physical limitation due to a health problem, and poly-medication at baseline (Supplementary Table S6). Female gender was almost perfectly associated with *PersistHighD* and *ModeratD* profiles; participants with lower educational level were more likely to belong to *PersistHighD* and *ModeratD* profiles compared to *PersistLowD* and less likely to *AccHighD*. Compared to *PersistLowD*, participants with a higher age at death were more likely to be found in *PersistHighD* and less likely associated with *ModeratD* and *AccHighD*. Compared to *PersistLowD*, dementia was more strongly associated with *PersistHighD* and *AccHighD* profiles. Moderate disability at baseline was strongly associated with *PersistHighD* and *ModeratD*, whereas severe disability was more strongly associated with *PersistHighD*. No association was found with causes of death in this multivariate analysis ($p > .05$).

Discussion

During the last two decades of life, five main functional trajectories have been identified, with 9 elders in 10 experiencing a functional decline: around 12% were characterized by a persistently high dependency, 15% by an accelerated high dependency, 26% by a moderate dependency, and 40% by a persistently low dependency, while 8% were no dependent. According to the profile, the entry into dependency began in mean from 2.0 to 13.5 years preceding death. First, total limitation in shopping, marking the entry into moderate dependency, occurred on average between 2 and 9 years preceding death depending on the profile. On average, around half of the elders died with no or mild dependency, while 27% live several years with a high level of limitations and would need intensive care and assistance in activities of daily living, at least for 2–4 years preceding death. "Chronic" dependency (ie, with the highest dependency profiles at the beginning of the period) was more likely to be observed in women, low educated, poly-medicated, and moderately to severely disabled participants at baseline. Those initially diagnosed with dementia were more likely to belong to profiles with the highest dependency at death.

Comparable studies are sparse, conducted over shorter periods, and focused on different age periods and stages in life (2,8,10); any comparison with the present study is thus limited. For instance, a study on trajectories of (I)ADL disability over 10 years in younger American participants (50+) (10) also identified five groups but a majority of participants had excellent functional health. Consequently in that study, only 8% of the subjects experienced high disability, whereas in our general older population, a majority of our participants were decliners, 40% maintained mild dependency until death (*PersistLowD*), 26% moderate dependency (*ModeratD*), and less than 30% (*PersistHighD* and *AccHighD*) experienced severe dependency. Only 1 elder out of 10 would not experience dependency before death.

The disablement process (27) is recognized as being multifactorial (associated with older age, female gender, low education, and multiple comorbidities) (28,29), which was broadly confirmed in our findings. As others (8,30–32), we confirmed that neurodegenerative diseases caused the worst burden of dependency, with dementia being strongly associated with higher functional decline and persistently high levels of dependency. Indeed, while *ModeratD* and *PersistHighD* began with similar trajectories, dementia seemed to accelerate the evolution toward severe dependency in *PersistHighD* from 18 years before death. For the same reason, *AccHighD* pulled away from the *PersistLowD* to join the *PersistHighD* toward severe dependency from 9 years before death. In our study, comorbidities were not directly associated with class-membership. However, polymedication, a likely proxy for comorbidities, was associated. In our study, we confirmed the significant association of age at death with all the classes according to an increased gradient going from *NoD* to *PersistHighD* profiles. Female gender was more specific (to *PersistHighD* and *ModeratD*) showing that women remain a target population for care support and prevention, because they are associated with persistent high levels of dependency and accelerated decline. Indeed, women often experience a higher prevalence of disability probably due to an earlier incidence in the process, lower rates of recovery and a longer survival despite deteriorated status compared to men (33,34). In the present study, a low level of education was strongly associated to the persistent and the highest baseline dependency profiles (*PersistHighD* and *ModeratD*). Other studies have shown that education might be decisive for the onset of disability but less for its progression (35–37). Indeed, determined in early life, education might have a greater influence in preventing activity limitations by, for instance, limiting risky health behaviors, better management of chronic diseases, or greater access to health services and prevention. Furthermore, in our study, as previously shown elsewhere, profiles were also influenced by baseline disability, the worse the baseline disability the higher the trajectories of dependency (*PersistHighD,* then *ModeratD* and *AccHighD)*.

In the end, our study identified several potential leverages. Authorities should focus efforts on dementia preventing programs according to the latest recommendations of the Lancet commission on dementia prevention, intervention, and care (38): "active treatment of hypertension in middle aged and older people […]. Interventions for […] more childhood education, exercise, maintaining social engagement, reducing smoking, and (better) management of (vision) and hearing loss, depression, diabetes, and obesity" to impact functional trajectories and dependency by avoiding or postponing the

onset of disability. As reported in several studies (39–41), physical activity also constitutes a relevant preventive action easy to implement, to prevent or postpone disability in old age. In addition, physical activity promotes social interaction, limits isolation, postpones cognitive decline, and complements the management of chronic diseases in older adults (control weight, mental, and cardiovascular health) (42), all major risk factors for dependency. Nutrition therapies may constitute another significant mean to prevent functional decline. Indeed, a very recent 23-year longitudinal study showed (43) that dietary with higher protein intake across adulthood (and probably earlier in the life course) was associated with lower risk of losing functional integrity in aging whatever age, comorbidities, or age-related diseases, notably in women.

In a context of intense aging of the population, our results also have important public health implications. Indeed, more than 90% of elders are characterized as functional decliners with different heterogeneous profiles and various levels and durations of required assistance. This detailed information is relevant for decision making in terms of financial and human resources allocated to formal and informal care. It is known that the amount of care increases with the number and type of activity limitations, with informal care mainly allocated to IADL assistance and formal care to ADL (44). Moreover, in such a context, policies tend to promote the older people aging in place (45–47) to contain health expenditures, but consequently it results in pressure on informal care demand which is the predominant form of care provided to older people at home. However, this informal care has also a cost, with informal caregivers reporting greater burden, poorer perceived health, social isolation and lower productivity at work, compared to their counterparts not providing such care (48). With this kind of results, decision makers should anticipate policies targeting support to informal caregivers or optimize financial resources assigned to professional care and facilities.

This study has several strengths. Firstly, the study relies on a large representative sample of the older population with regular follow-up up to a maximum of 24 years, a systematic monitoring of activity limitations and a systematic prospective updating of deaths. We chose to focus on a sample of deceased individuals to investigate the trajectories of dependency according to a homogeneous time scale (from the entry into old age to death); it allowed capturing a larger proportion of the events eventually associated to dependency over the period preceding death. This retrospective timescale limited other sources of variability due to the heterogeneity of aging, and thus permitted an in-depth investigation of the natural history of functional dependency and its heterogeneity. Secondly, each interview was conducted at home by neuropsychologists, enabling an accurate assessment of activity limitations and the evaluation of participants even in case of frailty, disability, or poor health. Thirdly, the latent class mixed model allowed modeling the heterogeneous change of dependency over time, while taking into account the intra-individual correlation between the repeated and multiple measurements. It was combined with an IRT model to accurately describe the dependency process, taking into account each item properties (difficulty and discrimination). One of the innovative features of our study relies on, inter-alia, the mapping of the dependency process associated with longitudinal trajectories, providing not only accurate individual scores of dependency, but most of all, the clinical meaning of the dependency level, over time. Finally, our findings were coherent with studies using traditional counts of activity limitations.

This study has also limitations. Firstly, functional assessments were available for each participant only every 2–3 years, what could have impeded a finer description in the dynamic of dependency over time. However, by considering the whole deceased cohort and retrospective time as the timescale, assessments were distributed all over the two decades prior to death. Secondly, as many cohorts studying aging, PAQUID is prone to attrition and possible lack of follow-up at periods close to death, when an acceleration of the dependency process is likely to occur. Moreover, although the cohort was followed-up for up to 22 years, only a small proportion of participants (4%) were observed during this whole period due to incidence of death. However, with a long-term duration over more than two decades, our study is complementary to short-term studies such as Gill and colleagues (2,49,50). Thirdly, some data were not accurately measured in the cohort (eg, causes of death missing for 30%, or comorbidities only complemented by medication intake). Fourth, the exclusion of participants still alive at the end of the study might have introduced a selection bias in the description of the natural history of dependency, by missing those in a better functional status. However, due to the follow-up of 22 years in the cohort and the systematic death reporting, we expect minimum selection bias due to the censoring of the alive population. Fifth, the posterior classification of the participants into the profiles was not high (with mean posterior probability around 70%). This might have hampered the analysis of associated factors using the probability-weighted multinomial logistic regression. While the method shows good inference properties for identifying associated factors in case of moderate discrimination, the associations might have been underestimated as demonstrated in Clark and Muthèn (26). Finally, our study confirmed the great functional inequalities by gender; women presenting higher levels of dependency and greater declines than men. To study the own effect of gender, we chose to adjust the models on gender, but further research stratified on sex would be relevant to study the discrepancies between men and women.

Conclusion

This work highlighted the heterogeneity of functional trajectories during the last two decades of life in a population-based cohort. Each of the five trajectories identified was characterized by its prevalence in the general population, its duration, severity level of required assistance, and associated factors.

Apart from a deeper understanding of the natural history of dependency in older adults, such description of functional dynamic profiles in the older general population is crucial to (i) adapt societies to aging by anticipating public policies and expenditures or insurance coverage, (ii) provide appropriate care support in a heterogeneous older population, and (iii) conduct better targeted interventions at optimal stages of the dependency process such as promoting an appropriate management of medication, postpone or avoid "chronic" disability, and also at earlier stages in life course (childhood or middle age) to favor cognitive resilience and protective health factors in order to delay cognitive decline, dementia, and disability onset and thus prevent functional decline and promote successful aging, notably among women.

Supplementary Material

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

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Author Contributions

A.E., C.P.L., K.P., and J.F.D. designed the study. A.E. did the statistical analyses. C.P.L. supervised the statistical analyses and all authors contributed to the interpretation. A.E. draft the manuscript. All authors critically revised the manuscript for important intellectual content and are accountable for the parts of the work they have done.

Conflict of Interest

A.E., C.P.L., and K.P. report no conflict of interest, no support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work. F.D. reports personal fees from Novartis, outside the submitted work; no other relationships or activities that could appear to have influenced the submitted work. J.F.D. reports grants from CNSA, during the conduct of the study; grants and personal fees from IPSEN.

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