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Title

Clustering 5-year multidimensional healthcare trajectory patterns in Alzheimer's disease and related syndromes

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A nationwide cohort study among incident ADRS cases

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Brief summary

This nationwide study describes 5-year multidimensional healthcare utilization trajectories (HUT) and their determinants among incident ADRS cases. 25% of the patients presented

favorable HUT, with geographic variations. Individual and contextual determinants were identified.

1 ABSTRACT

2 **Objective:** After diagnosis of Alzheimer's Disease and Related Syndromes (ADRS),
3 personalized care adapted to each patient's needs is recommended in order to provide a
4 care plan and start symptomatic treatments according to guidelines. Over the last decade,
5 dedicated structures and care have been implemented in various settings. Equal access to
6 ADRS care, healthcare providers and services is crucial to ensure potential health benefits for
7 everyone. However, the extent of use of recommended services and favorable healthcare
8 utilization trajectories (HUT) may vary according to individual and contextual characteristics.
9 The aim of this paper was to (1) describe HUT patterns after multidimensional clustering of
10 similar trajectories, (2) assess the proportion of individuals presenting favorable HUTs and
11 (3) identify factors associated with favorable HUTs.

12 **Design:** cohort study

13 **Setting and participants:** A cohort of 103317 people newly diagnosed with ADRS identified
14 in the French health reimbursement system (SNDS) was followed for 5 years with their
15 monthly utilization on 11 healthcare dimensions.

16 **Methods:** For 3 age groups (65-74, 75-84, ≥ 85 yrs), 15 clusters of patients were identified
17 using partitioning around medoids applied to Levenshtein distances. They were qualitatively
18 assessed by pluridisciplinary experts. Individual and contextual determinants of clusters
19 denoting favorable trajectories were identified using mixed random effects multivariable
20 logistic regression models.

21 **Results:** Clusters with favorable HUTs denoting slow, progressive trajectories centered on at-
22 home care, represented approximatively 25% of the patients. Determinants of favorable
23 HUTs were mostly individual (age, female gender, absence of certain comorbidities,

24 circumstances of ADRS identification, lower deprivation). Contextual determinants were also
25 identified, in particular accessibility to nurses and nursing homes. Inter-territories variance
26 was small but significant in all age groups (from 0.9 to 1.8%).

27 **Conclusion and implications:** Favorable HUTs remain the minority and many efforts can still
28 be made to improve HUTs. Qualitative studies could help understanding underlying barriers
29 to favorable HUTs.

INTRODUCTION

Alzheimer's Disease and Related Syndromes (ADRS) is a severe, progressive and inexorable disabling neurodegenerative condition, without current cure¹. An increasing life expectancy has resulted in a rising prevalence worldwide, which constitutes a public health priority²⁻⁴. Guidelines for ADRS management recommend a graduated and individualized care plan, based on multidisciplinary care centered on patient's needs⁵. It aims to (1) preserve and maintain autonomy, as long as possible, through family care, medical and paramedical (including nursing care) home care supports, and (2) prevent complications, unplanned hospitalizations and emergency stays, which are often critical moments^{6,7}. Regular specialist appointments, careful pharmacological and non-pharmacological management, and when necessary, social and nursing support, physiotherapy, and speech therapy can be provided. When dependency becomes incompatible with life at home, several services can be used, such as day care, respite platforms, temporary or permanent housing in nursing homes (NHs) with or without specialized ADRS care. In France, this range of services were progressively rolled-out, notably since the 2008-2012 national Alzheimer plan⁸⁻¹⁰. Underuse or low continuity of care leads to poor outcomes for both patients and caregivers. However, suboptimal management of ADRS symptoms has been reported in various recommended care dimensions, such as specialist visits, drug management, home care¹¹⁻¹⁴. These studies were generally focused on one ADRS healthcare dimension, for limited periods of time, and consequently identify incomplete healthcare utilization and trajectories.

Therefore, we conducted a longitudinal study among individuals newly diagnosed with ADRS to (1) describe 5-year multidimensional healthcare utilization trajectories (HUT), (2) identify

clusters of similar HUTs (3) identify determinants of HUT considered as favorable, including contextual determinants due to geographic variations in health services availability.

METHODS

We conducted a cohort study within the French healthcare data system (Système National des Données de Santé, SNDS¹⁵) which includes all reimbursed health expenditures, information on long-term disease (LTD) registration (providing full coverage of LTD-related expenses), and NH admission dates^{16,17}. The French health insurance system is universal, with a main scheme (>70% of the population) dedicated to salaried workers and various other professional schemes¹⁷. It covers most health expenses and the remaining out-of-pocket charges may be covered by supplementary health insurance (subscribed by 95% of the population).

We used the FRA-DEM cohort (French data protection authority (CNIL) authorization n°1631786-DE-2013-037) that includes all individuals newly diagnosed with ADRS identified in France since 2011 in the SNDS. ADRS was identified through registration with ADRS as a LTD, hospital diagnoses (ICD codes: "F00-F03", "G30", "G31" except "G31.2" and "G318") or ≥ 2 antimentia/ADRS drug (anticholinesterasics or memantine) dispensations^{18–20}. A 5-year window before ADRS identification ruled out individuals already diagnosed with ADRS ('prevalent cases').

For this analysis, individuals with ADRS were those identified in 2012, followed until 31/12/2017, affiliated with the mandatory health insurance, in the main scheme, living in continental France and aged 65 years or older on ADRS identification.

From the month following the index date (1st ADRS identification), we identified monthly patients' use for 11 healthcare dimensions (specifically developed for this study). Each dimension was composed of 2 to 5 categories that reflect an increase in healthcare use (Table 1): 1) ambulatory medical care, 2) ambulatory nursing care, 3) ambulatory allied health professional care, 4) anti-dementia/ADRS drugs use, 5) antipsychotic drugs use, 6) hospitalization for ADRS follow-up (planned), 7) hospitalization for ADRS (unplanned) or behavioral and psychological symptoms of dementia (BPSD), 8) medical specialists, 9) other hospitalizations (unrelated to ADRS), 10) emergency care, and 11) institutionalization in NH. In the 3 first dimensions, health services could have been offered in either ambulatory or in-home setting. The occurrence of at least 1 monthly use was assessed for each category. When a patient used several categories in the same dimension and month, the "most intense" level of use was chosen (e.g. 9.4 for dimension 9). For each dimension and month, the patient could also have no use, be dead or censored. Censoring occurred if the patient left the main scheme, had no recorded medical event for 24 consecutive months or moved out of continental France.

Therefore, each patient had a 59-month 11-dimension HUT. HUTs were clustered in 3 age groups: 65-74 years, 75-84 years and 85 years and older, notably because of expected differences in access rates to some dimensions. 15 HUT clusters were identified within each age group using partitioning around medoids²¹ applied to Levenshtein distances computed dimension-wise on data-driven state-dependent weights (Jupyter Notebook 5.7.8 for Python 3.7.3, Weighted Levenshtein and Pyclustering libraries). Clusters were qualitatively assessed by an expert panel, invited to 4 in-person work sessions. Each work session involved the same 3-4 healthcare providers with expertise in ADRS management (including geriatricians, neurologists, general practitioners (GPs), nurses working in the ambulatory sector, hospitals

or NHs), During a first in-person meeting, the experts received a presentation of the study objectives, instructions and training regarding interpretation of the figures, based on preliminary subsamples constituted of about a quarter of the final sample. 3 work sessions were then held, each assessing 15 clusters from one of the 3 age classes.

Experts were collectively asked to assess each cluster in 3 steps (without the help of the study team): (1) description, (2) ranking, (3) final statement about the favourability of the cluster (yes/no). During step (1), experts were asked to qualify, dimension by dimension, baseline rates of healthcare use, longitudinal use (enhancement and/or continuity of care¹⁴), and the characteristics suggested by the cluster (e.g. BPSD, late diagnosis). If there were no *a priori* criteria set by the experts suggesting favorable, neutral or unfavorable trajectories in each dimension set by the experts before the sessions, rules emerged consensually during data interpretation, considering the patients' perspective (supplementary appendix). During step (2), based on a multidimensional assessment of descriptions made in step 1 and the criteria presented in appendix, experts ordered clusters from worst to best, on a scale of 0 to 10. Assessments were also based, regardless of survival, on i) a histogram of the mean half-yearly use of each category (figures 1A,B,C) and ii) cluster summary statistics including the distribution of gender, age, comorbidities, deprivation index and first ADRS identification criterion. There was no predefined cut-off (such as 5/10) considered as defining an unfavorable HUT, experts secondarily defined which scores were considered to reflect favorable HUT. Discussions were facilitated by AG, AR, VG. The panel collectively debated on the cluster's description, scoring and final classification (favorable or not). Disagreements were resolved during the session, through discussion, including several rounds of discussion when necessary, although this was generally not the case. Thereafter, conclusions for the 45

121 clusters were summarized by the researchers and checked for any inconsistencies across age
122 groups and experts were asked for ultimate validation.

123 Clusters where more than 90% of patients had died during the first year were removed
124 because experts were unable to adequately assess their trajectory. The experts' assessment
125 was also uncertain for some clusters (in particular when HUTs suggested a questionable
126 ADRS diagnosis based on the patterns of ADRS identification criteria and flat trajectories).
127 We removed uncertain clusters in a sensitivity analysis.

128 Individual and contextual determinants of favorable HUTs (supplementary table 1) were
129 identified using mixed random effects multilevel multivariable logistic regression models, by
130 age groups. Individual variables were age, gender, comorbidities measured in 2012 through
131 multi-source algorithms based on healthcare use and LTD registration²², and two variables
132 related to ADRS: ADRS identification during an urgent hospital stay, and being registered
133 with ADRS as a LTD during the first year. Some variables were measured at the municipality
134 level (considered as individual variables because of the very small number of patients in
135 most municipalities): living in a rural area, deprivation index of the town of residence²³, local
136 potential accessibility (LPA) to GPs and nurses²⁴, travel time to (i) nearest emergency
137 department (ED), (ii) visiting nursing services, (iii) NH, (iv) NH providing daycare, (v) NH
138 providing temporary housing or respite platforms, (vi) NH providing specialized ADRS units.
139 Other contextual variables were measured at the département's level (94 'départements' in
140 continental France): number of beds in hospitalization sectors (surgery and medicine,
141 rehabilitation, psychiatry, long-term care), number of permanent and temporary NH beds,
142 number of spots for daycare and specialized ADRS care in NHs. Individual and contextual
143 variables were introduced in a forward stepwise selection using Akaike Information Criterion

(AIC). Non-significant variables ($\alpha=0.05$) were removed from the final model, controlling for confounding. Linearity assumptions for continuous determinants and residual normality were verified. Intra and inter-department variances were estimated. Analyses were conducted using STATA 14.2 (College Station, TX: StataCorp LP).

RESULTS

103 317 patients were identified (11.3% aged 65-74 years, 41.2% aged 75-84 and 47.5% aged 85 years or older). 66.2% were female and 55.9% identified as having ADRS through hospital stays, 30.6% registration with LTD system and 25.5% through medication (25.1% had at least two of these criteria). 55.4% had died over the 5-year period.

Five ($n=21134$) of the 45 clusters were removed from the experts' assessment because >90% died during the 1st year (Figures 1A,B,C). Experts rated 12 clusters as suggesting favorable HUTs: 3 of the 14 remaining clusters in the 65-74 years (24.4%), 4 of the 13 (23.4%) in the 75-84 age group and 5 of the 13 (28.2%) in the oldest group. For example, cluster n°207 was considered favorable due to the rate of ambulatory medical care and medical specialist use (sustained over time); the increasing use of ambulatory nursing care, speech therapy/physiotherapy, and ADRS drugs; the slowly progressive and limited rate of institutionalization in NH; the sustained very limited use of antipsychotics, unplanned hospitalization for ADRS/BPSD, and ED visits. Table 2 compares the use of each dimension during the first 12 months of follow-up between favorable and unfavorable HUTs clusters. Patients in favorable HUT clusters had a higher use of GP, specialists, nurses, speech therapy and ADRS drugs than in other clusters. For speech therapy and ADRS drugs the difference was particularly notable in younger patients. Patients in favorable clusters were less frequently hospitalized overall, especially for emergency stays and via emergency

hospitalizations (7.2, 10.1, 10.2) and were younger than patients in other clusters. However, patients in favorable clusters were more frequently hospitalized for ADRS or BPSD without any emergency (7.1 and 6.3). Finally, institutionalization within the first 12 months was less frequent in favorable clusters.

Table 3 shows possible determinants of favorable HUTs. Analyses of determinants for clusters with favorable HUTs were conducted among 80372 (98.3%) patients with no missing data on contextual variables (Table 4). The share of Inter-département variance in total variance was small but statistically significant in all age groups (about 1.8% for the 2 younger groups, 0.9% for the oldest). The effect of age varied across age groups: being older was associated with a higher probability of favorable HUTs in the youngest group, but with a lower probability in the two older groups. For all age groups, female gender, being registered with ADRS as a LTD and higher LPA to nurses were associated with favorable HUTs. On the opposite, patients with ADRS identified during an emergency hospitalization had significantly fewer favorable HUTs. Overall, comorbidities (with variations across age groups) were associated with a lower probability of favorable HUTs. Patients in the two older age groups living in more disadvantaged municipalities had a lower likelihood of favorable HUT. Only among the 65-74 year old, living in a rural area was associated with favorable HUTs. In the older groups, other contextual variables were associated with favorable HUTs: being far from a NH and close to an emergency department. Finally, 3 variables were only associated with favorable HUTs in one of the 2 older groups: being close to a NH offering temporary housing and respite platforms, living in a département with many hospital beds in medicine and surgery, or with few long-term care hospital beds.

Experts identified 7 uncertain clusters, all except one of which were considered as unfavorable (Figures 1). These clusters generally presented flat trajectories, low levels of ADRS drugs and ambulatory care. A sensitivity analysis excluding them yielded stable results (supplementary Table 2).

DISCUSSION

Our study has 3 main findings. First, various patterns of HUTs were observed among age groups (some in all age groups, others specific to one age group), and approximately 25% of the individuals able to undergo expert assessment presented favorable HUT. Second, determinants of favorable HUTs revealed the predominant role of individual factors over the healthcare offer. Last, determinants of favorable HUTs differed according to age group.

Approximately **25% of the population presented favorable HUTs**, with relatively similar proportions across age groups. This is disappointing in France, where ADRS medical healthcare is fully reimbursed through LTD, and massive investments were made in training, early diagnosis, and dedicated structures countrywide^{25–27}. Favorable trajectories showed progressive institutionalization, mostly after several years, suggesting early diagnosis and planning for at-home medical, paramedical and social care, in line with criteria raised by experts, such as i) use of specialized care (e.g. visits to ADRS specialists, use of ADRS drugs that were still recommended at the time), particularly in younger individuals, ii) sustained or enhanced use of recommended care that can be linked to ADRS, such as nursing care, physical therapy, speech therapy, ii) limited or decreasing use of antipsychotics over time iv) sustained use of outpatient care or hospitalization unrelated to ADRS, v) planned ADRS-related hospitalizations.

Unfavorable HUTs revealed various patterns, in different proportions across age groups. Several clusters showed high mortality, sometimes suggesting the burden of comorbidities, but also the possible role of late diagnosis and a previous erratic trajectory, particularly among the youngest. Other clusters revealed early institutionalization, suggesting high level of dependency, poor informal care support, or possibly a late diagnosis. Other clusters showed high use of emergency care without concomitant comorbidities, or high use of antipsychotics. Finally, clusters showing low healthcare use and little change over time suggested several underlying profiles: error in diagnosis, slow progression, patient's refusal of healthcare, or caregiver denial. The proportion of individuals experiencing unfavorable HUT, and the amount of unfavorable patterns in our study raise concerns about their potential deleterious effects, ranging from unnecessary burden for individuals, to increasing healthcare costs²⁸. Iatrogeny has been associated with avoidable care^{29–31}. Conversely, aging at home without the right resources and context conditions in place is deleterious³². Therefore, policies favoring integrated care aiming to promote aging in place have emerged³³, but our results suggests a room for improvement.

Several factors were associated with favorable HUTs in all or 2/3 age groups. **Women** were more likely to favorable HUTs, in accordance with the literature showing healthier lifestyle, more regular medical visits, better adherence to prevention programs and care, more supportive care and more favorable health outcomes than men^{34,35}. **The effect of age varied according to age groups**. Among 65-74 year-olds, being younger was associated with lower favorable HUTs, maybe because of barriers to dedicated pathways and structures, which may be more suitable for older individuals. Among > 75 year-olds, being older was associated with less favorable HUTs. ADRS care provided by healthcare professionals may be increasingly suboptimal with increasing age, because of ADRS portrayal and fatalism^{36,37}.

236 Among the 75 and older, increased **deprivation** was associated, with a gradient, with less
237 favorable HUTs, in accordance with literature, and despite universal coverage for healthcare
238 (but not social care) for ADRS. Deprivation may reflect several barriers³⁸: financial,
239 perception of the convenience of healthcare, low empowerment, low health literacy, and
240 cultural portrayal of aging or ADRS^{39,40}. **The absence of several comorbidities** was associated
241 with a higher probability of favorable HUT. Overall, a low comorbidity burden may be
242 associated with fewer events that could deteriorate ADRS HUTs such as fewer ED visits. Life-
243 threatening diseases inducing short life expectancy may explain ADRS care neglect (e.g.
244 active cancer). Some diseases can specifically affect ADRS care such as cardiac rhythms
245 disorders that prevent the use of cholinesterase inhibitors, while others may introduce
246 competitive demands. Psychiatric disorders and addiction may alter adherence to care but
247 are also stigmatized, resulting in a lower chance of accessing ADRS dedicated structures and
248 care⁴¹. The role of comorbidities diminished in older groups where their frequency increases.

249 Two factors of early ADRS trajectories were associated with HUTs. Hospital **admission via**
250 **the ED at the index date** decreased the chance of favorable HUTs, suggesting that ADRS is
251 identified during ADRS complication or a concomitant disease. It evokes a major break in
252 ADRS illness pathway, suggesting a delayed diagnosis and previous erratic trajectories. As
253 expected, **ADRS registered as LTD in the year following the index date** increased the chance
254 of favorable HUTs, since it usually implies an individualized care plan, reassessed yearly,
255 coordinated by GP.

256 **Only 2 contextual determinants were consistently associated with favorable HUTs:**
257 **département of residence and ambulatory nurse LPA.** The département is the relevant
258 geographical level to study regulation and policies for elderly care services. Départements
259 are in charge of various elderly management care networks such as a service focusing on

integrated care for dependent elderly, with case management for complex cases. Easy access to ambulatory care nurses may facilitate visits by nurse and therefore prevent ADRS complications. This highlights nurses' role in counseling⁴². The availability and/or proximity of other health resource were not associated with favorable HUT in every age groups, which is consistent with the literature reporting that the lack of availability of services was not a major impediment to their use⁴³. Except for the youngest group, living in rural area was not associated with favorable HUTs, in line with previous research⁴⁴. However, among 1 or 2 of the 2 oldest groups, our results suggest an effect of healthcare availability on HUT: an increase in travel time to NHs with temporary housing or respite platforms, to emergency services, and a few short-stay hospital beds were associated with a lower chance of favorable HUTs. This could suggest restriction to specialized ADRS healthcare. Living in an environment with many long-term care beds and NH in close proximity was associated with less favorable HUTs. This might be explained by the fact that the experts tended to consider trajectories in which patients stayed at home as more favorable. Unfortunately, we were unable to determine whether longer home management was appropriate.

This study presents several limitations. The firsts concern a possible selection bias. To ensure data quality, our analysis was restricted to the main health insurance scheme (>70 % of the French population in this age group in 2018). 2% of individuals were excluded from the multilevel analysis because of missing data, however multiple imputation sensitivity analyses retrieved very similar results (data not shown). Administrative data can only provide information on diseases identified or managed by the healthcare system. Therefore, we may not fully or accurately capture all ADRS individuals, especially since ADRS is known to be underdiagnosed^{45,46} and subject to coding variability. However, our results were robust in sensitivity analysis excluding uncertain clusters. Besides, the index date does not coincide

with the diagnosis date, nor with first symptoms, due to frequent late diagnosis, but studying people newly diagnosed with ADRS reflect the spectrum of ADRS stages at identification by the healthcare system. Second, though a very rich database, the SNDS does not provide data on all healthcare services dedicated to ADRS, such as social care, memory centers or mobile ADRS teams, due to the financing system of these structures. Institutionalization data are not exhaustive and their quality has improved over our study period. Also, the SNDS does not provide data on other potential determinants of HCU trajectories such as education level, lifestyle, ADRS etiology, severity, cognitive and functional impairments, BPSD, informal caregiver's availability and characteristics. Assigning a HUT cluster as being "favorable" or not did not account for the individual context of the individuals. Last, the most original feature of our study was the multidimensional and integrated outcome evaluating HUTs. However, this outcome is limited by the fact that distances used for clustering were computed dimension-wise and synchronization was lost between events occurring simultaneously on multiple dimensions. The qualitative integration of multiple factors in qualifying a cluster as having favorable HUT was not based on a formal method such as the Delphi consensus.

Despite these limitations, this recent population-based nationwide study, conducted on an exhaustive cohort of people newly diagnosed with ADRS, allowed us to examine long-term trajectories in multiple healthcare use dimensions with limited attrition. Its large sample size allowed multilevel analyses, with stable results in sensitivity analyses.

CONCLUSION AND IMPLICATIONS

Our work provides useful data on ADRS care practices and determinants of favorable trajectories that remain the minority. Many efforts to improve HUTs are still needed and our

307 results offer insight at the individual and contextual levels to inform ADRS care planning.

308 Further qualitative studies could help understanding underlying barriers to favorable HUTs.

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Bibliography

1. Winblad B, Amouyel P, Andrieu S, et al. Defeating Alzheimer's disease and other dementias: a priority for European science and society. *Lancet Neurol.* 2016;15(5):455-532. doi:10.1016/S1474-4422(16)00062-4
2. World Health Organization, Alzheimer's Disease International. *Dementia : A Public Health Priority*; 2012. Accessed June 12, 2020. https://www.who.int/mental_health/publications/dementia_report_2012/en/
3. GBD 2016 Dementia Collaborators. Global, regional, and national burden of Alzheimer's disease and other dementias, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol.* 2019;18(1):88-106. doi:10.1016/S1474-4422(18)30403-4
4. Alzheimer's Disease International. *World Alzheimer Report 2015 : The Global Impact of Dementia*. Accessed June 12, 2020. <https://www.alz.co.uk/research/WorldAlzheimerReport2015.pdf>
5. Livingston G, Sommerlad A, Orgeta V, et al. Dementia prevention, intervention, and care. *Lancet.* 2017;390(10113):2673-2734. doi:10.1016/S0140-6736(17)31363-6
6. Feast AR, White N, Candy B, Kupeli N, Sampson EL. The effectiveness of interventions to improve the care and management of people with dementia in general hospitals: A systematic review. *Int J Geriatr Psychiatry.* 2020;35(5):463-488. doi:10.1002/gps.5280
7. Clanet M. *Quel Parcours Pour Les Personnes Atteintes de La Maladie d'Alzheimer ?*; 2017. Accessed June 12, 2020. https://solidarites-sante.gouv.fr/IMG/pdf/rapport_pr_michel_clanetdf.pdf
8. French Minister of Health. *French Alzheimer Plans (2001-2005, 2004-2008, 2008-2012)*. Accessed June 15, 2020. [https://www.alzheimer-europe.org/Policy/National-Dementia-Strategies/France/Nov-2014-France-launches-Neurodegenerative-diseases-plan/\(language\)/eng-GB](https://www.alzheimer-europe.org/Policy/National-Dementia-Strategies/France/Nov-2014-France-launches-Neurodegenerative-diseases-plan/(language)/eng-GB)
9. French Minister for Social Affairs, Health and Women's Rights. *Neurodegenerative Diseases Plan 2014-2019*. Accessed June 15, 2020. https://solidarites-sante.gouv.fr/IMG/pdf/french_neurodegenerativediseasesplan2014_2019-2.pdf
10. Saidlitz P, Sourdet S, Voisin T, Vellas B. Management of behavioural symptoms of dementia in a specialized unit care. *Psychogeriatrics.* 2017;17(2):81-88. doi:10.1111/psyg.12193
11. LaMantia MA, Stump TE, Messina FC, Miller DK, Callahan CM. Emergency Department Use Among Older Adults With Dementia. *Alzheimer Dis Assoc Disord.* 2016;30(1):35-40. doi:10.1097/WAD.0000000000000118
12. Gardette V, Lapeyre-Mestre M, Piau A, et al. A 2-year prospective cohort study of antidementia drug non-persistence in mild-to-moderate Alzheimer's disease in Europe :

- predictors of discontinuation and switch in the ICTUS study. *CNS Drugs*. 2014;28(2):157-170. doi:10.1007/s40263-013-0133-3
13. Weber SR, Pirraglia PA, Kunik ME. Use of services by community-dwelling patients with dementia: a systematic review. *Am J Alzheimers Dis Other Dement*. 2011;26(3):195-204. doi:10.1177/1533317510392564
 14. Amjad H, Carmichael D, Austin AM, Chang C-H, Bynum JPW. Continuity of Care and Health Care Utilization in Older Adults With Dementia in Fee-for-Service Medicare. *JAMA Intern Med*. 2016;176(9):1371-1378. doi:10.1001/jamainternmed.2016.3553
 15. Système National de Données de Santé. Accessed June 12, 2020. <https://www.snds.gouv.fr/SNDS/Accueil>
 16. Tuppin P, Rudant J, Constantinou P, et al. Value of a national administrative database to guide public decisions: From the système national d'information interrégimes de l'Assurance Maladie (SNIIRAM) to the système national des données de santé (SNDS) in France. *Rev Epidemiol Sante Publique*. 2017;65 Suppl 4:S149-S167. doi:10.1016/j.respe.2017.05.004
 17. Bezin J, Duong M, Lassalle R, et al. The national healthcare system claims databases in France, SNIIRAM and EGB: Powerful tools for pharmacoepidemiology. *Pharmacoepidemiol Drug Saf*. 2017;26(8):954-962. doi:10.1002/pds.4233
 18. Gombault-Datzenko E, Gallini A, Carcaillon-Bentata L, et al. Alzheimer's disease and related syndromes and hospitalization: a nationwide 5-year longitudinal study. *Eur J Neurol*. Published online April 13, 2020. doi:10.1111/ene.14256
 19. Poncet M, Gardette V, Couret A, Renoux A, Lapeyre-Mestre M, Gallini A. Benzodiazepine exposure in subjects with incident Alzheimer's disease and related syndromes in France: a longitudinal study 2011-2017. *Int Clin Psychopharmacol*. Published online April 21, 2020. doi:10.1097/YIC.0000000000000312
 20. Couret A, Gallini A, Poncet M, Renoux A, Lapeyre-Mestre M, Gardette V. Benzodiazepine Dispensing to Persons With Dementia in France, 2011-2016: A Nationwide Study. *J Am Med Dir Assoc*. Published online April 13, 2020. doi:10.1016/j.jamda.2020.02.019
 21. Kaufman L, Rousseeuw PJ. Clustering by means of Medoids. In: *Statistical Data Analysis Based on the L1-Norm and Related Methods*. Dodge Y. North-Holland; 1987:405-416.
 22. Caisse Nationale d'Assurance Maladie. *Méthodologie Médicale de La Cartographie Des Pathologies et Des Dépenses, Version G6 (Années 2012 à 2017)*.; 2019. Accessed June 12, 2020. https://www.ameli.fr/fileadmin/user_upload/documents/Methodologie_medicale_cartographie.pdf
 23. Rey G, Jouglu E, Fouillet A, Hémon D. Ecological association between a deprivation index and mortality in France over the period 1997 - 2001: variations with spatial scale,

degree of urbanicity, age, gender and cause of death. *BMC Public Health*. 2009;9:33. doi:10.1186/1471-2458-9-33

24. Lucas-Gabrielli V, Nestrigue C, Coldefy M. *Analyse de Sensibilité de l'Accessibilité Potentielle Localisée (APL)*. IRDES; 2016. Accessed June 12, 2020. <https://www.irdes.fr/recherche/documents-de-travail/070-analyse-de-sensibilite-de-l-accessibilite-potentielle-localisee-apl.pdf>
25. Spinney L. Alzheimer's disease funding and the French health system. *Lancet Neurol*. 2008;7(1):26-27. doi:10.1016/S1474-4422(07)70315-0
26. Robert PH. The French National Alzheimer disease plan 2008-2012. *Int J Geriatr Psychiatry*. 2010;25(9):900-901. doi:10.1002/gps.2593
27. Pimouguet C, Bassi V, Somme D, Lavallart B, Helmer C, Dartigues JF. The 2008-2012 French Alzheimer plan: a unique opportunity for improving integrated care for dementia. *J Alzheimers Dis*. 2013;34(1):307-314. doi:10.3233/JAD-121648
28. Bernabei R, Landi F, Gambassi G, et al. Randomised trial of impact of model of integrated care and case management for older people living in the community. *BMJ*. 1998;316(7141):1348-1351. doi:10.1136/bmj.316.7141.1348
29. Gruneir A. "Avoidable" emergency department transfers from long-term care homes: a brief review. *Healthc Q*. 2013;16(2):13-15.
30. Lemoyne SE, Herbots HH, De Blick D, Remmen R, Monsieurs KG, Van Bogaert P. Appropriateness of transferring nursing home residents to emergency departments: a systematic review. *BMC Geriatr*. 2019;19(1):17. doi:10.1186/s12877-019-1028-z
31. Sources of Potentially Avoidable Emergency Department Visits. *Healthc Q*. 2014;17(4):82.
32. Golant SM. *Aging in the Right Place*. Health Professions Press, Incorporated; 2015.
33. WHO | Integrated Care for Older People. WHO. Accessed January 18, 2021. <http://www.who.int/ageing/health-systems/icope/en/>
34. Forbes DA, Jansen SL, Markle-Reid M, et al. Gender differences in use and availability of home and community-based services for people with dementia. *Can J Nurs Res*. 2008;40(1):39-59.
35. Hankivsky O. Women's health, men's health, and gender and health: implications of intersectionality. *Soc Sci Med*. 2012;74(11):1712-1720. doi:10.1016/j.socscimed.2011.11.029
36. Lahjibi-Paulet H, Dauffy Alain A, Minard A, Gaxatte C, Saint-Jean O, Somme D. Attitudes toward Alzheimer's disease: a qualitative study of the role played by social representation on a convenient sample of French general practitioners. *Aging Clin Exp Res*. 2012;24(4):384-390. doi:10.1007/BF03325270

37. Moore V, Cahill S. Diagnosis and disclosure of dementia--a comparative qualitative study of Irish and Swedish General Practitioners. *Aging Ment Health*. 2013;17(1):77-84. doi:10.1080/13607863.2012.692763
38. Ford JA, Wong G, Jones AP, Steel N. Access to primary care for socioeconomically disadvantaged older people in rural areas: a realist review. *BMJ Open*. 2016;6(5):e010652. doi:10.1136/bmjopen-2015-010652
39. Cooper C, Tandy AR, Balamurali TBS, Livingston G. A systematic review and meta-analysis of ethnic differences in use of dementia treatment, care, and research. *Am J Geriatr Psychiatry*. 2010;18(3):193-203. doi:10.1097/JGP.0b013e3181bf9caf
40. Kenning C, Daker-White G, Blakemore A, Panagioti M, Waheed W. Barriers and facilitators in accessing dementia care by ethnic minority groups: a meta-synthesis of qualitative studies. *BMC Psychiatry*. 2017;17(1):316. doi:10.1186/s12888-017-1474-0
41. Gronholm PC, Thornicroft G, Laurens KR, Evans-Lacko S. Mental health-related stigma and pathways to care for people at risk of psychotic disorders or experiencing first-episode psychosis: a systematic review. *Psychol Med*. 2017;47(11):1867-1879. doi:10.1017/S0033291717000344
42. Jennings LA, Tan Z, Wenger NS, et al. Quality of Care Provided by a Comprehensive Dementia Care Comanagement Program. *J Am Geriatr Soc*. 2016;64(8):1724-1730. doi:10.1111/jgs.14251
43. Brodaty H, Thomson C, Thompson C, Fine M. Why caregivers of people with dementia and memory loss don't use services. *Int J Geriatr Psychiatry*. 2005;20(6):537-546. doi:10.1002/gps.1322
44. Koller D, Eisele M, Kaduszkiewicz H, et al. Ambulatory health services utilization in patients with dementia - Is there an urban-rural difference? *Int J Health Geogr*. 2010;9:59. doi:10.1186/1476-072X-9-59
45. Connolly A, Gaehl E, Martin H, Morris J, Purandare N. Underdiagnosis of dementia in primary care: variations in the observed prevalence and comparisons to the expected prevalence. *Aging Ment Health*. 2011;15(8):978-984. doi:10.1080/13607863.2011.596805
46. Amjad H, Roth DL, Sheehan OC, Lyketsos CG, Wolff JL, Samus QM. Underdiagnosis of Dementia: an Observational Study of Patterns in Diagnosis and Awareness in US Older Adults. *J Gen Intern Med*. 2018;33(7):1131-1138. doi:10.1007/s11606-018-4377-y

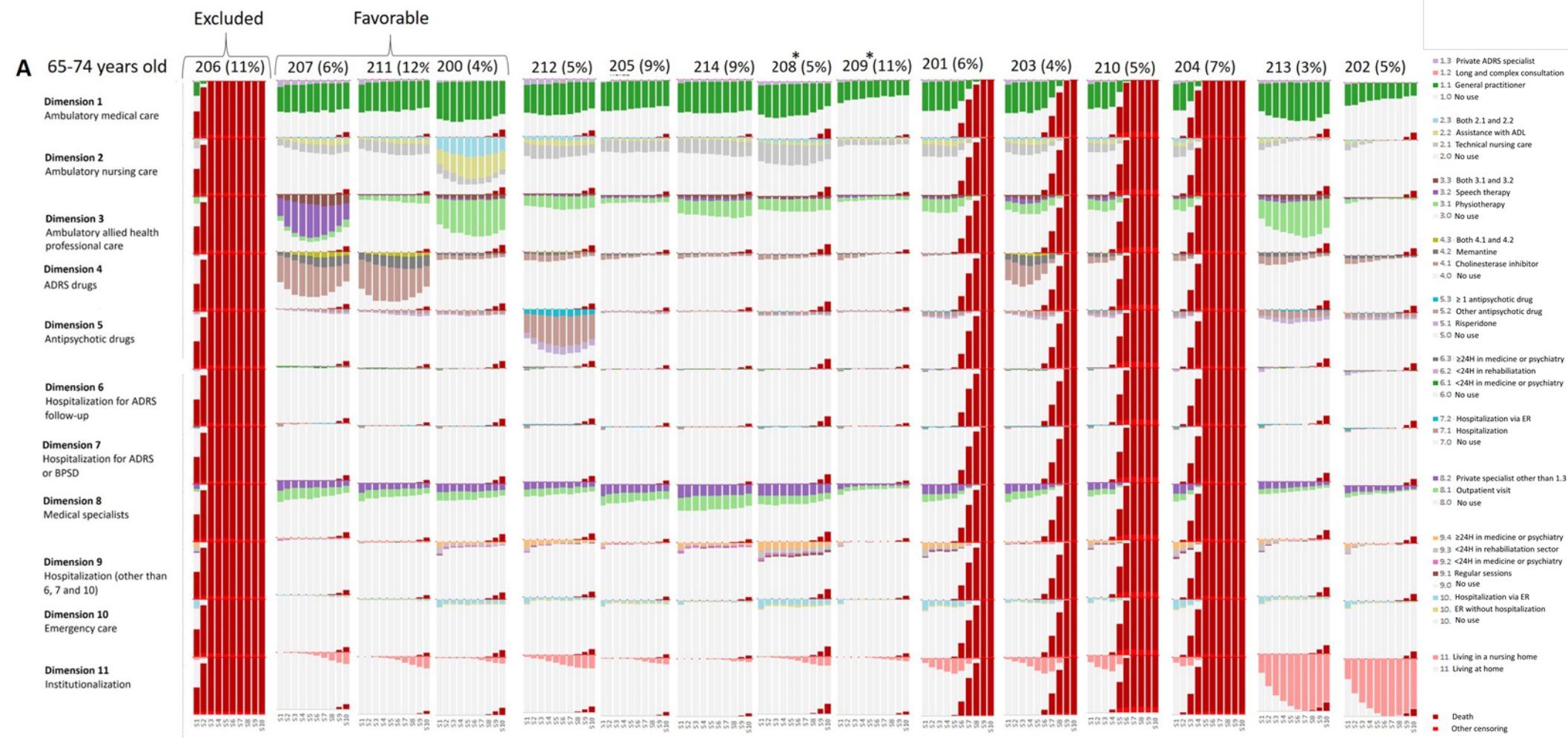
Table 1: Dimensions of care measured each month in the database

Table 2: Use of each healthcare dimension during the first 12 months following ADRS identification in clusters with trajectories favorable to the patients and other clusters by age groups

Table 3: Individual and contextual characteristics of patients in clusters with trajectories favorable to the patients and other clusters by age groups

Table 4: Multivariable analyses of factors associated with belonging to a cluster of trajectories favorable to the patients (stratified by age groups) N=80,372

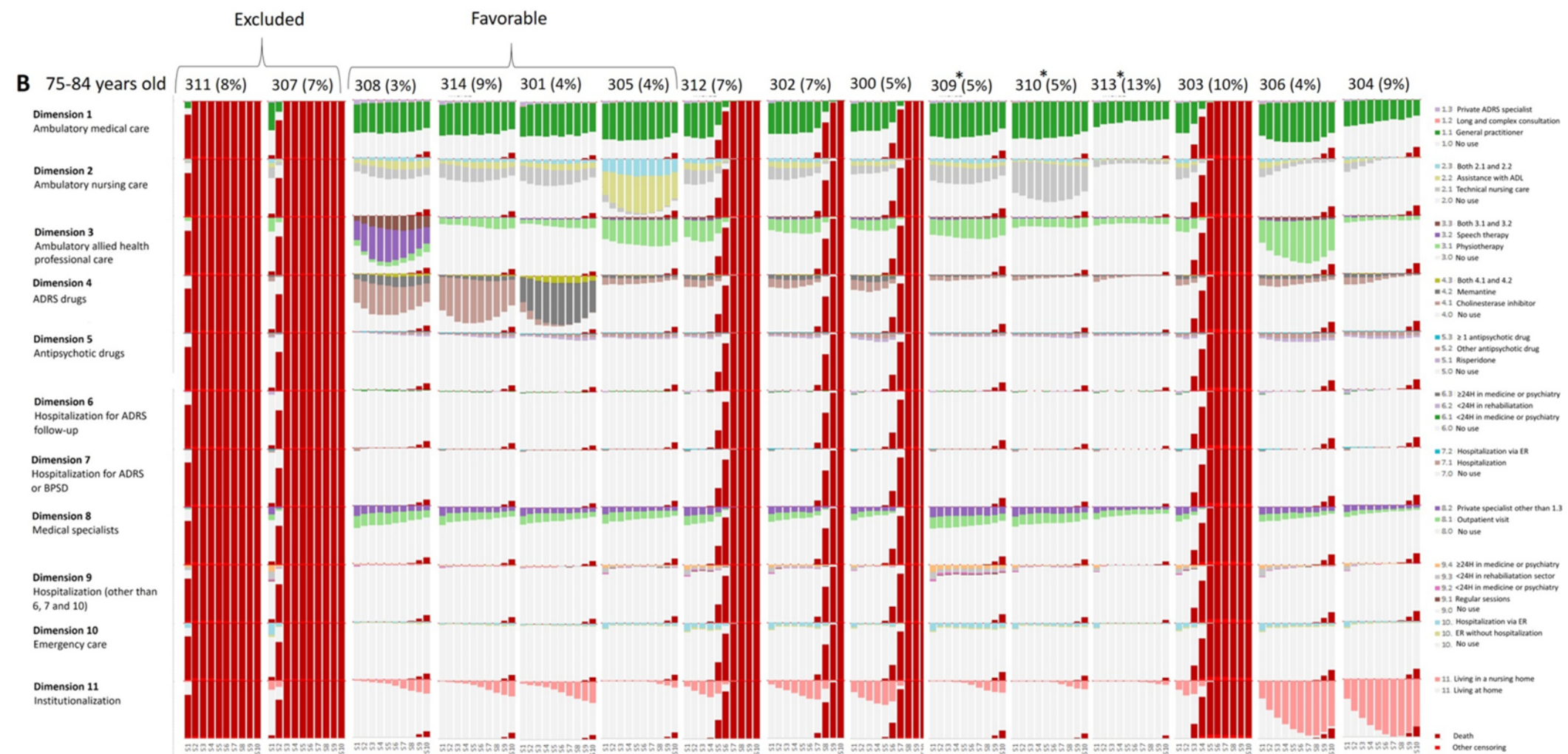
Figure 1A : Classification of clusters for 65-74 years



This figure shows the healthcare utilization trajectories (HUT) of the 15 clusters (x00 to x14, represented in the columns) identified in the 65-74 age class for the 11 different dimensions (represented in rows). The proportion indicated beside each cluster number refers to the proportion of subjects in the age class belonging to this cluster (for example, 11% of subjects in the 65-74 age group belong to cluster no. 206). Clusters are presented in the following order from left to right: excluded clusters, favorable clusters, and other clusters. For each dimension within each cluster, the stacked bar chart represents (1) on the x-axis, the number of semesters (S1 to S10) elapsed since the index date (i.e. ADRS identification), and (2) on the y-axis, the mean monthly proportion, during the semester in question, of patients using each category (color-coded as per the legend) of healthcare at least once a month. When a patient used several categories in the same dimension and month, only the “most intense” level of use was represented (e.g. in dimension 9, the use of category 9.3 was represented only if there was no use of 9.4). Within each dimension, the categories are presented in the same order as in the legend, from bottom to top, with the ‘no use’ category (dimension x.0, in light gray) always shown at the bottom of the stacked bar .

The * represents uncertain clusters according to the experts, which were excluded in the sensitivity analysis .

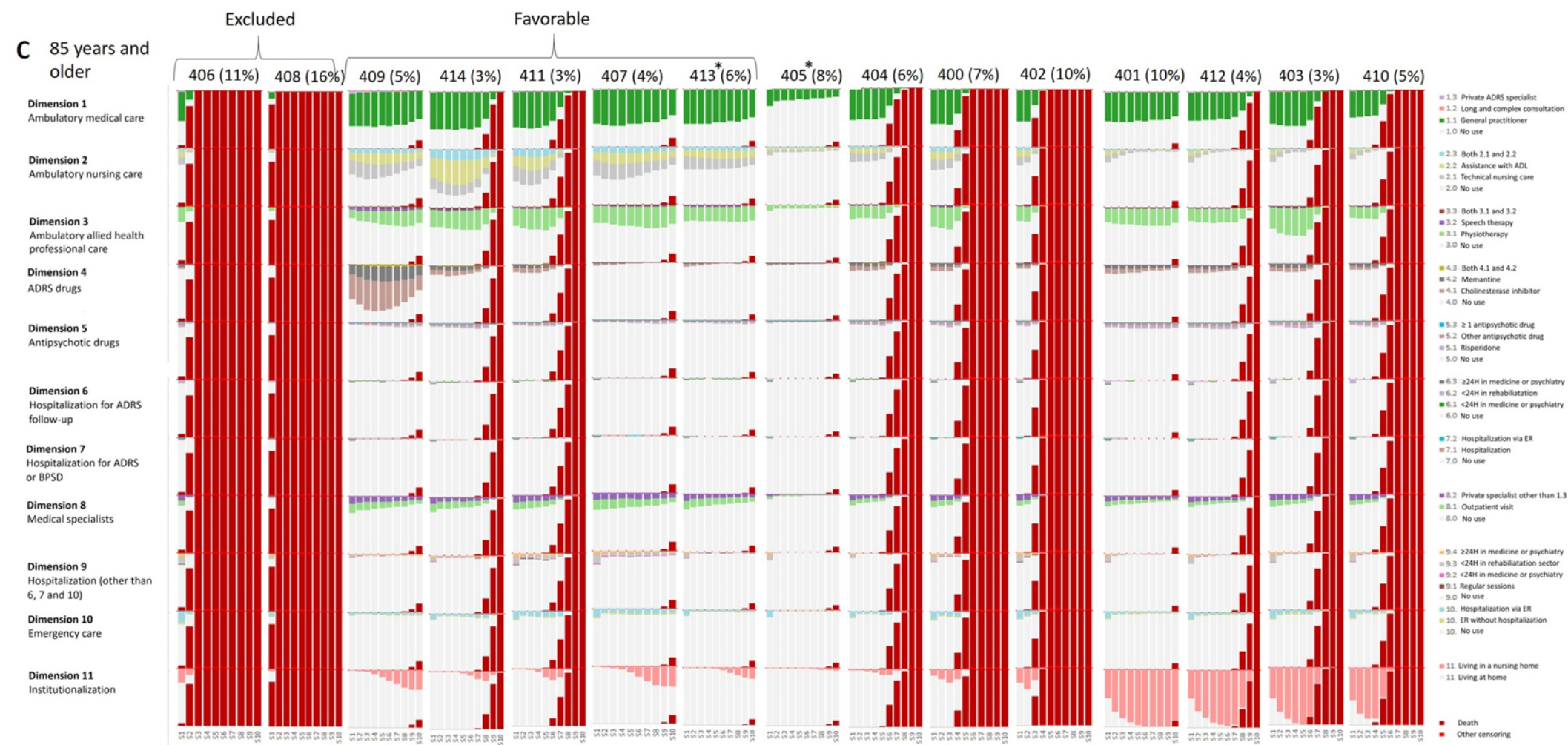
Abbreviations: ADRS: Alzheimer’s disease and related syndromes, BPSD: behavioral and psychological symptoms of dementia, ER: emergency room



This figure shows the healthcare utilization trajectories (HUT) of the 15 clusters (x00 to x14, represented in the columns) identified in the 75-84 age class for the 11 different dimensions (represented in rows). For further details, see Figure 1A.

The * represents uncertain clusters according to the experts, which were excluded in the sensitivity analysis .

Abbreviations: ADRS: Alzheimer's disease and related syndromes, BPSD: behavioral and psychological symptoms of dementia, ER: emergency room



This figure shows the healthcare utilization trajectories (HUT) of the 15 clusters (x00 to x14, represented in the columns) identified in the 65-74 age class for the 11 different dimensions (represented in rows). For further details, see Figure 1A.

The * represents uncertain clusters according to the experts, which were excluded in the sensitivity analysis .

Abbreviations: ADRS: Alzheimer's disease and related syndromes, BPSD: behavioral and psychological symptoms of dementia, ER: emergency room

Table 1: Dimensions of care measured each month in the database

1	Ambulatory medical care	1.0	No use
		1.1	Consulting a general practitioner
		1.2	“Long and complex” consultation with a general practitioner
		1.3	Consulting a private ADRS specialist (neurologist, psychiatrist, geriatrician)
2	Ambulatory nursing care	2.0	No use
		2.1	Technical nursing care (e.g. drug administration, ...)
		2.2	Assistance with ADL (e.g. toileting, bathing etc.)
		2.3	Both 2.1 and 2.2
3	Ambulatory allied health professional care	3.0	No use
		3.1	Physiotherapy
		3.2	Speech therapy
		3.3	Both 3.1 and 3.2
4	ADRS drugs	4.0	No use
		4.1	Cholinesterase inhibitor (donepezil, rivastigmine or galantamine)
		4.2	Memantine
		4.3	Both 4.1 and 4.2
5	Antipsychotic drugs	5.0	No use
		5.1	Risperidone
		5.2	Another antipsychotic drug
		5.3	More than one antipsychotic drug
6	Hospitalization for ADRS follow-up	6.0	No use
		6.1	Less than 24 hours in medicine or psychiatry
		6.2	More than 24 hours in rehabilitation
		6.3	More than 24 hours in medicine or psychiatry
7	Hospitalization for ADRS or BPSD	7.0	No use
		7.1	Hospitalization in medicine or psychiatry
		7.2	Hospitalization in medicine or psychiatry via the emergency room
8	Medical specialists	8.0	No use
		8.1	Outpatient visit
		8.2	Consulting a private medical specialist other than 1.3
9	Hospitalizations (other than 6, 7 and 10)	9.0	No use
		9.1	Regular sessions (dialysis, chemotherapy, transfusion, hyperbaric chamber)
		9.2	Less than 24 hours in medicine or psychiatry (other than 6.1 or 7)
		9.3	More than 24 hours in rehabilitation (other than 6.2)
		9.4	More than 24 hours in medicine or psychiatry (other than 6.3 or 7)
10	Emergency	10.0	No use
		10.1	Emergency room without hospitalization
		10.2	Hospitalization in medicine or psychiatry via the emergency room (other than 7.2)
11	Institutionalization	11.0	Living at home
		11.1	Living in a nursing home

Abbreviations: ADL: activities of daily living, ADRS: Alzheimer’s disease and related syndromes, BPSD: behavioral and psychological symptoms of dementia

For each month and dimension, patients may have at least one use or no use or be dead or censored. The occurrence of at least 1 monthly use was assessed for each category. When a patient used several categories in the same dimension and month, the “most intense” level of use was chosen (e.g. 9.4 for dimension 9).

Table 2: Use of each healthcare dimension during the first 12 months following ADRS identification in clusters with trajectories favorable to the patients and other clusters by age groups (number and frequencies of individuals using the service at least once)

		Total*		65-74 years old				75-84 years old				85 years or older			
		N=103,317		Favorable N=2,529		Other N=7,816		Favorable N=8,400		Other N=27,424		Favorable N=10,168		Other N=25,846	
		N	%	N	%	N	%	N	%	N	%	N	%	N	%
Dimension 1: ambulatory medical care															
1.3	Consulted a private ADRS specialist	15,314	(14.8)	964	(38.1)	1,886	(24.1)	2,625	(31.3)	4,798	(17.5)	1,455	(14.3)	2,275	(8.8)
1.2	"Long and complex" consultation	696	(0.7)	15	(0.6)	40	(0.5)	59	(0.7)	212	(0.8)	79	(0.8)	206	(0.8)
1.1	Consulted a general practitioner	92327	(89.4)	2,490	(98.5)	7,293	(93.3)	8,307	(98.9)	25,837	(94.2)	10,018	(98.5)	22,998	(89.0)
Dimension 2: ambulatory nursing care															
2.2 or 2.3	Use of technical nursing care	23,019	(22.3)	483	(19.1)	1,098	(14.0)	2,619	(31.2)	5,395	(19.7)	3,744	(36.8)	5,587	(21.6)
2.1 or 2.3	Use of assistance with ADL	53,417	(51.7)	1,452	(57.4)	4,399	(56.3)	5,712	(68.0)	16,121	(58.8)	7,168	(70.5)	11,092	(42.9)
Dimension 3: ambulatory allied health professional care															
3.2 or 3.3	Use of speech therapy	7,731	(7.5)	645	(25.5)	875	(11.2)	1,438	(17.1)	2,113	(7.7)	780	(7.7)	1,264	(4.9)
3.1 or 3.3	Use of physical therapy	44,328	(42.9)	872	(34.5)	3,121	(39.9)	3,035	(36.1)	11,986	(43.7)	5,280	(51.9)	12,070	(46.7)
Dimension 4: ADRS drugs															
4.2	Use of memantine	12,295	(11.9)	500	(19.8)	745	(9.5)	2,111	(25.1)	3,508	(12.8)	1,487	(14.6)	2,803	(10.8)
4.1 or 4.2 or 4.3	Use of ADRS drugs	31,454	(30.4)	2,044	(80.8)	2,142	(27.4)	6,692	(79.7)	8,785	(32.0)	3,838	(37.7)	5,629	(21.8)
Dimension 5: antipsychotic drugs															
5.1 or 5.2 or 5.3	Use of antipsychotic drugs	19,224	(18.6)	267	(10.6)	1,893	(24.2)	948	(11.3)	5,612	(20.5)	1,326	(13.0)	5,540	(21.4)
Dimension 6: hospitalization for ADRS follow-up															
6.3	Hospitalized for ADRS follow-up ≥ 24 hours in medicine or psychiatry	3,427	(3.3)	174	(6.9)	312	(4.0)	497	(5.9)	1,100	(4.0)	469	(4.6)	666	(2.6)
6.2	Hospitalized for ADRS follow-up in rehabilitation	11,687	(11.3)	55	(2.2)	627	(8.0)	337	(4.0)	3,219	(11.7)	743	(7.3)	3,991	(15.4)
6.1	Hospitalized for ADRS follow-up < 24 hours in medicine or psychiatry	1,512	(1.5)	32	(1.3)	253	(3.2)	58	(0.7)	490	(1.8)	66	(0.6)	326	(1.3)
Dimension 7: hospitalization for ADRS or BPSD															
7.2	Emergency hospitalization for ADRS or BPSD	10,956	(10.6)	97	(3.8)	850	(10.9)	423	(5.0)	3,156	(11.5)	851	(8.4)	3,248	(12.6)
7.1	Hospitalized for ADRS or BPSD	15,261	(14.8)	625	(24.7)	1,543	(19.7)	1,752	(20.9)	4,735	(17.3)	1,669	(16.4)	3,143	(12.2)
Dimension 8: medical specialists															
8.2	Consultations with other private medical specialists	52,593	(50.9)	1,683	(66.5)	5,129	(65.6)	5,311	(63.2)	16,368	(59.7)	5,802	(57.1)	12,157	(47.0)

		Total*		65-74 years old				75-84 years old				85 years or older			
		N=103,317		Favorable N=2,529		Other N=7,816		Favorable N=8,400		Other N=27,424		Favorable N=10,168		Other N=25,846	
		N	%	N	%	N	%	N	%	N	%	N	%	N	%
8.1	Outpatient visits to medical specialists	54,568	(52.8)	1,966	(77.7)	5,012	(64.1)	6,312	(75.1)	16,819	(61.3)	6,902	(67.9)	11,850	(45.8)
Dimension 9: other hospitalizations															
9.4	Hospitalizations ≥24 hours in medicine or psychiatry	29,072	(28.1)	468	(18.5)	2,963	(37.9)	1,431	(17.0)	8,350	(30.4)	2,412	(23.7)	6,286	(24.3)
9.3	Hospitalizations ≥24 hours in rehabilitation	29,791	(28.8)	234	(9.3)	1,899	(24.3)	1,010	(12.0)	7,880	(28.7)	3,089	(30.4)	8,342	(32.3)
9.2	Hospitalizations < 24h	10,972	(10.6)	385	(15.2)	1,498	(19.2)	1,113	(13.3)	3,799	(13.9)	1,172	(11.5)	1,751	(6.8)
9.1	Regular hospital sessions (dialysis, chemotherapy, etc.)	1,622	(1.6)	17	(0.7)	242	(3.1)	44	(0.5)	481	(1.8)	84	(0.8)	276	(1.1)
Dimension 10: emergency															
10.2	Hospitalization via the ER (other than 7.2)	57,495	(55.6)	471	(18.6)	3,666	(46.9)	1,992	(23.7)	14,274	(52.0)	5,149	(50.6)	15,806	(61.2)
10.1	ER without hospitalization	20,733	(20.1)	352	(13.9)	1,704	(21.8)	1,196	(14.2)	6,038	(22.0)	2,069	(20.3)	5,758	(22.3)
Dimension 11: institutionalization															
11.1	Living in a nursing home	24,628	(23.8)	30	(1.2)	1,118	(14.3)	281	(3.3)	6,475	(23.6)	277	(2.7)	11,697	(45.3)

*including clusters where >90% died during the 1st year (and removed from experts' assessment)

Abbreviations: ADL: activities of daily living, ADRS: Alzheimer's disease and related syndromes, BPSD: behavioral and psychiatric symptoms of dementia, ER: emergency room, NH: nursing home

Table 3: Individual and contextual characteristics of patients in clusters with trajectories favorable to the patients and other clusters by age groups

	Total	65-74 years old		75-84 years old		85 years or older	
		Favorable	Other	Favorable	Other	Favorable	Other
	N=80,372	N=2,479	N=7,580	N=8,241	N=26,844	N=9,986	N=25,242
Variables measured at the individual or municipality level							
Mean age (SD)	82.9 (7.0)	70.8 (2.7)	70.4 (2.9)	79.9 (2.8)	80.3 (2.7)	88.1 (2.8)	89.5 (3.5)
Female N (%)	54,900 (68.3)	1,500 (60.5)	3,864 (51.0)	5,698 (69.1)	17,029 (63.4)	7,603 (76.1)	19,206 (76.1)
ADRS identification is concomitant with an emergency hospital stay, N (%)	31,113 (38.7)	259 (10.4)	2,707 (35.7)	1,145 (13.9)	10,594 (39.5)	3,761 (37.7)	12,647 (50.1)
Registered with LTD within 12 months of ADRS identification, N (%)	30,977 (38.5)	1,584 (63.9)	2,288 (30.2)	5,223 (63.4)	9,362 (34.9)	4,011 (40.2)	8,509 (33.7)
Cardiac rhythm disorders, N (%)	19,896 (24.8)	209 (8.4)	1,168 (15.4)	1,123 (13.6)	6,694 (24.9)	2,828 (28.3)	7,874 (31.2)
Coronary disease, N (%)	13,550 (16.9)	244 (9.8)	1,101 (14.5)	990 (12.0)	4,678 (17.4)	1,736 (17.4)	4,801 (19.0)
Stroke, N (%)	12,095 (15.0)	240 (9.7)	1,341 (17.7)	687 (8.3)	4,590 (17.1)	1,292 (12.9)	3,945 (15.6)
Heart failure, N (%)	11,067 (13.8)	77 (3.1)	627 (8.3)	421 (5.1)	3357 (12.5)	1504 (15.1)	5081 (20.1)
Diabetes, N (%)	15388 (19.1)	510 (20.6)	1,990 (26.3)	1,486 (18.0)	6,208 (23.1)	1,538 (15.4)	3,656 (14.5)
Active cancer, N (%)	5,496 (6.8)	93 (3.8)	589 (7.8)	385 (4.7)	2,082 (7.8)	633 (6.3)	1,714 (6.8)
Psychotic disorders, N (%)	2,037 (2.5)	46 (1.9)	542 (7.2)	92 (1.1)	814 (3.0)	118 (1.2)	425 (1.7)
Addictive disorders, N (%)	921 (1.1)	43 (1.7)	356 (4.7)	47 (0.6)	360 (1.3)	31 (0.3)	84 (0.3)
Neurotic, mood and other psychiatric disorders, N (%)	17,973 (22.4)	471 (19.0)	2,215 (29.2)	1,343 (16.3)	6,694 (24.9)	1,956 (19.6)	5,294 (21.0)
Parkinson’s disease, N (%)	7,025 (8.7)	246 (9.9)	967 (12.8)	664 (8.1)	2,875 (10.7)	615 (6.2)	1,658 (6.6)
Chronic respiratory diseases, N (%)	10,059 (12.5)	218 (8.8)	1,124 (14.8)	748 (9.1)	3,698 (13.8)	1,204 (12.1)	3,067 (12.2)
Rheumatoid arthritis, ankylosing spondylitis and related disorders, N (%)	1,446 (1.8)	30 (1.2)	122 (1.6)	152 (1.8)	571 (2.1)	152 (1.5)	419 (1.7)
Liver and pancreas diseases, N (%)	2,221 (2.8)	63 (2.5)	457 (6.0)	132 (1.6)	890 (3.3)	187 (1.9)	492 (1.9)
Multiple chronic diseases or other, N (%)	10,775 (13.4)	211 (8.5)	1,165 (15.4)	734 (8.9)	3,532 (13.2)	1,478 (14.8)	3,655 (14.5)
Deprivation index: 1st quintile (most favored), N (%)	15,628 (19.4)	433 (17.5)	1,337 (17.6)	1,558 (18.9)	4,888 (18.2)	2,233 (22.4)	5,179 (20.5)
Deprivation index: 2nd quintile, N (%)	15,126 (18.8)	514 (20.7)	1,320 (17.4)	1,699 (20.6)	4,740 (17.7)	2,006 (20.1)	4,847 (19.2)
Deprivation index: 3rd quintile, N (%)	15,882 (19.8)	492 (19.8)	1,454 (19.2)	1,727 (21.0)	5,339 (19.9)	1,982 (19.8)	4,888 (19.4)
Deprivation index: 4th quintile, N (%)	16,775 (20.9)	497 (20.0)	1,683 (22.2)	1,667 (20.2)	5,802 (21.6)	1,936 (19.4)	5,190 (20.6)
Deprivation index: 5th quintile (most deprived), N (%)	16,961 (21.1)	543 (21.9)	1,786 (23.6)	1,590 (19.3)	6,075 (22.6)	1,829 (18.3)	5,138 (20.3)
Rural area, N (%)	12,773 (15.9)	467 (18.8)	1,230 (16.2)	1,271 (15.4)	4,375 (16.3)	1,422 (14.2)	4,008 (15.9)
Local potential accessibility to general practitioners*, mean (SD)	73.1 (24.9)	72.0 (24.5)	72.4 (25.2)	74.0 (24.4)	72.9 (25.1)	73.0 (24.3)	73.4 (25.0)
Local potential accessibility to nurses*, mean (SD)	98.9 (58.0)	103.7 (65.4)	97.2 (59.3)	108.9 (64.3)	95.8 (55.0)	102.7 (60.8)	97.3 (56.0)

	Total	65-74 years old		75-84 years old		85 years or older	
		Favorable	Other	Favorable	Other	Favorable	Other
	N=80,372	N=2,479	N=7,580	N=8,241	N=26,844	N=9,986	N=25,242
Lives in a city with a nursing home, N (%)	62,391 (77.6)	1,749 (70.6)	5,665 (74.7)	6,121 (74.3)	20,645 (76.9)	7,847 (78.6)	20,364 (80.7)
If not, travel time to nearest nursing home (min)	[3.0-	[3.0-	[3.1-	[3.0-	[2.9-	[2.8-	[3.0-
median [IQR]	4.6 6.6]	4.6 6.5]	4.7 6.8]	4.7 6.6]	4.6 6.6]	4.5 6.5]	4.7 6.7]
Lives in a city with NH with specialized ADRS care, N (%)	46,272 (57.6)	1,323 (53.4)	4,228 (55.8)	4,614 (56.0)	15,277 (56.9)	5,837 (58.4)	14,993 (59.4)
If not, travel time to nearest NH with specialized ADRS care (min) median [IQR]	[3.1- 5.3 8.7]	[3.2- 5.3 8.7]	[3.1- 5.2 8.4]	[3.2- 5.3 8.4]	[3.1- 5.3 8.8]	[3.1- 5.2 8.2]	[3.1- 5.4 8.9]
Lives in a city with NH with temporary housing or respite care platforms, N (%)	45,311 (56.4)	1,267 (51.1)	4,188 (55.3)	4,493 (54.5)	14,904 (55.5)	5,808 (58.2)	14,651 (58.0)
If not, travel time to nearest NH with temporary housing or respite platforms (min), median [IQR]	[3.3- 5.8 9.4]	[3.3- 5.6 9.0]	[3.4- 5.7 9.3]	[3.3- 5.6 8.9]	[3.3- 5.8 9.4]	[3.3- 5.6 9.2]	[3.4- 5.9 9.7]
Lives in a city with NH with daycare, N (%)	35,992 (44.8)	1,006 (40.6)	3,372 (44.5)	3,666 (44.5)	11,856 (45.3)	4,625 (46.3)	11,467 (45.4)
If not, travel time to nearest NH with daycare (min) median [IQR]	[3.7- 6.7 11.4]	[3.8- 6.5 10.5]	[3.5- 6.4 11.2]	[3.8- 6.6 10.8]	[3.7- 6.8 11.4]	[3.5- 6.3 10.9]	[3.7- 6.9 11.7]
Lives in a city with visiting nurse services, N (%)	42,600 (53.0)	1,194 (48.2)	4,007 (52.9)	4,161 (50.5)	14,058 (52.4)	5,509 (55.2)	13,671 (54.2)
If not, travel time to nearest visiting nurse services (min), median [IQR]	[3.8- 6.3 9.6]	[4.0- 6.3 9.4]	[3.8- 6.1 9.5]	[3.9- 6.1 9.2]	[3.8- 6.3 9.7]	[3.8- 6.1 9.4]	[3.9- 6.4 9.8]
Lives in a city with emergency department, N (%)	29,162 (36.3)	823 (33.2)	2,832 (37.4)	2,951 (35.8)	9,548 (35.6)	3,790 (38.0)	9,218 (36.5)
If not, travel time to nearest emergency department (min) median [IQR]	[4.3- 8.7 15.3]	[4.6- 8.7 14.8]	[4.2- 8.4 15.1]	[4.5- 8.5 14.6]	[4.4- 9.0 15.6]	[3.9- 8.1 14.6]	[4.3- 9.0 15.7]
Variables measured at the contextual level (department)							
Medical and surgical hospital beds**, mean (SD)	3.7 (0.9)	3.7 (0.8)	3.7 (0.9)	3.7 (0.8)	3.7 (0.9)	3.8 (0.9)	3.7 (0.9)
Rehabilitation hospital beds**, mean (SD)	1.0 (0.3)	1.0 (0.3)	1.0 (0.3)	1.0 (0.3)	1.0 (0.3)	1.0 (0.3)	1.0 (0.3)
Long-term care hospital beds**, mean (SD)	0.5 (0.2)	0.5 (0.2)	0.5 (0.2)	0.5 (0.2)	0.5 (0.2)	0.5 (0.2)	0.5 (0.2)
Psychiatric hospital beds**, mean (SD)	2.6 (0.7)	2.6 (0.7)	2.6 (0.7)	2.7 (0.7)	2.6 (0.7)	2.6 (0.7)	2.6 (0.7)
Beds in nursing homes***, mean (SD)	42.1 (10.1)	42.0 (9.4)	41.7 (10.1)	42.1 (9.5)	42.3 (10.2)	41.3 (10.2)	42.3 (10.1)
Daycare spots available in NH***, mean (SD)	1.0 (0.4)	1.0 (0.4)	1.0 (0.4)	1.0 (0.3)	1.0 (0.4)	1.0 (0.4)	1.0 (0.4)
Beds for temporary housing in NH***, mean (SD)	0.9 (0.3)	0.9 (0.3)	0.9 (0.3)	0.9 (0.3)	0.9 (0.3)	0.9 (0.3)	0.9 (0.3)
Specialized ADRS care beds in NH***, mean (SD)	3.8 (2.2)	3.9 (2.1)	3.8 (2.1)	3.8 (2.2)	3.9 (2.2)	3.7 (2.2)	3.8 (2.2)
Spots in visiting nurse services***, mean (SD)	10.0 (2.0)	9.9 (2.0)	10.1 (2.1)	9.9 (2.0)	10.1 (2.0)	10.0 (2.1)	10.0 (2.0)

* Higher figures indicate better accessibility to professionals.

**per 1,000 inhabitants in the department of residence

***per 1,000 inhabitants aged 65 years or older in the department of residence

Abbreviations: ADRS: Alzheimer's disease and related syndromes, IQR: interquartile range, NH: nursing home, SD: standard deviation

Table 4: Multivariable analyses of factors associated with belonging to a cluster of trajectories favorable to the patients (stratified by age groups)
N=80,372

	65-74 years old			75-84 years old			85 years and older		
	OR	95% CI	p	OR	95% CI	p	OR	95% CI	p
Variables measured at the individual or municipality level									
Age	1.03	1.01-1.05	0.001	0.95	0.94-0.96	<10 ⁻⁴	0.87	0.87-0.88	<10 ⁻⁴
Female	1.36	1.23-1.50	<10 ⁻⁴	1.24	1.17-1.32	<10 ⁻⁴	1.14	1.08-1.21	<10 ⁻⁴
ADRS identification is concomitant with an emergency hospital stay	0.38	0.32-0.44	<10 ⁻⁴	0.42	0.39-0.45	<10 ⁻⁴	0.69	0.65-0.72	<10 ⁻⁴
Registered with LTD within 12 months of ADRS identification	2.65	2.38-2.94	<10 ⁻⁴	2.10	1.98-2.23	<10 ⁻⁴	1.08	1.02-1.14	0.008
Cardiac rhythm disorders	0.82	0.69-0.97	0.023	0.76	0.70-0.82	<10 ⁻⁴	--		
Stroke	--		--	0.72	0.66-0.79	<10 ⁻⁴	0.85	0.79-0.91	<10 ⁻⁴
Heart failure	0.71	0.54-0.92	0.011	0.65	0.58-0.73	<10 ⁻⁴	0.80	0.75-0.85	<10 ⁻⁴
Diabetes	--		--	0.92	0.86-0.98	0.016	--		
Active cancer	0.57	0.45-0.72	<10 ⁻⁴	0.66	0.58-0.74	<10 ⁻⁴	0.86	0.78-0.95	0.004
Psychotic disorders	0.42	0.30-0.58	<10 ⁻⁴	0.58	0.46-0.72	<10 ⁻⁴	0.72	0.58-0.90	0.003
Addictive disorders	0.64	0.45-0.89	0.009	0.64	0.46-0.88	0.006	--		
Neurotic, mood and other psychiatric disorders	0.74	0.66-0.84	<10 ⁻⁴	0.72	0.67-0.77	<10 ⁻⁴	--		
Parkinson's disease	--		--				0.87	0.79-0.96	0.007
Chronic respiratory diseases	0.76	0.64-0.89	0.001	0.80	0.73-0.87	<10 ⁻⁴	--		
Liver and pancreas diseases	0.73	0.55-0.97	0.031	0.70	0.57-0.85	<10 ⁻⁴	--		
Multiple chronic diseases or other	0.74	0.63-0.87	<10 ⁻⁴	0.82	0.75-0.90	<10 ⁻⁴	1.08	1.01-1.16	0.028
Deprivation index: 1st quintile (most favored)				Ref		<10 ⁻⁴	Ref		0.006
Deprivation index: 2nd quintile	--			0.99	0.90-1.09		0.97	0.89-1.05	
Deprivation index: 3rd quintile	--			0.87	0.79-0.96		0.98	0.90-1.06	
Deprivation index: 4th quintile	--			0.81	0.73-0.89		0.88	0.81-0.97	
Deprivation index: 5th quintile (most deprived)	--			0.76	0.68-0.84		0.82	0.75-0.90	
Rural area	1.21	1.06-1.38	0.005	--			--		
Local potential accessibility to nurses	1.00	1.00-1.00	0.002	1.00	1.00-1.00	<10 ⁻⁴	1.00	1.00-1.00	<10 ⁻⁴
Travel time to nearest nursing home	--			1.04	1.03-1.05	<10 ⁻⁴	1.02	1.01-1.03	<10 ⁻⁴
Travel time to nearest NH with temporary housing or respite platforms	--			0.99	0.98-1.00	0.032	--		
Travel time to nearest emergency department	--			0.99	0.99-1.00	0.001	0.99	0.99-0.99	<10 ⁻⁴
Variables measured at the contextual level (department)									
Medical and surgical hospital beds	--			--			1.05	1.01-1.09	0.021

	65-74 years old			75-84 years old			85 years and older		
	OR	95%CI	<i>p</i>	OR	95%CI	<i>p</i>	OR	95%CI	<i>p</i>
Long-term care hospital beds	--			--			0.81	0.69-0.94	0.008

Analyses are controlled for living in a nursing home with an internal pharmacy and living in a nursing home with a global budget payment system during follow-up

Abbreviations: ADRS: Alzheimer’s disease and related syndromes, CI: confidence interval, LTD: long-term disease, NH: nursing home, OR: odds ratio, p: p-value