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► **To cite this version:**

Philippe de Souto Barreto, Emmanuel Gonzalez-Bautista, Heike Bischoff-Ferrari, Vitor Pelegrim de Oliveira, Renato Gorga Bandeira de Mello, et al.. Real-life intrinsic capacity screening data from the ICOPE-Care program. *Nature Aging*, 2024, 4 (9), pp.1279-1289. <10.1038/s43587-024-00684-2>. <hal-04938534>

HAL Id: hal-04938534

<https://hal.science/hal-04938534v1>

Submitted on 20 Feb 2025

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Real-life intrinsic capacity screening data from the ICOPE Care program

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Abstract

The Integrated Care for Older People (ICOPE) program is a health-care pathway which uses a screening test for intrinsic capacity (IC) as its entry point. Yet, real-life data informing on how IC domains cluster and change over time, as well as their clinical utility, are lacking. Using primary health-care screening data from > 20,000 French adults ≥ 60 years, this study identified four clusters of IC impairment: “Low impairment” (most prevalent), “Cognition+Locomotion+Hearing+Vision”, “All IC impaired”, and “Psychology+Vitality+Vision”. Compared to “Low impairment” people, those in the other clusters had higher likelihood of having frailty and limitations in both activities of daily living (ADL) and instrumental ADL (IADL) with the strongest associations being obtained for “All IC impaired”. This study found that the ICOPE screening might be a useful tool for patient risk stratification in clinical practice, with the higher the number of IC domains impaired at screening the higher the probability of functional declines.

Main text

Introduction

The Integrated Care for Older People (ICOPE) is a healthcare pathway program developed by the World Health Organization (WHO) in collaboration with experts worldwide. ICOPE adopts a care model that focuses on optimizing intrinsic capacity (IC – all of an individual's physical and mental capacities) and functional ability (the ability to do what people have reason to value) as the key for promoting healthy aging(1–4). This represents a significant change in the approach to care of older adults since it focuses on maintaining function and preventing care dependency rather than responding to and managing individual disease presentations.

The ICOPE model is composed of five steps: Step1 involves screening for potential IC impairment; Step2, in-depth assessment of IC and looking for causes of confirmed IC impairments; Step3, development of a person-centered, individualized care plan; Step4, referral and monitoring of the care plan; Step5, engaging community and support to caregivers. Previous studies have shown the validity of the IC structure(5–7) and suggested six operational domains (i.e., locomotion, cognition, psychology, hearing, vision, and vitality). While other research has investigated elements of ICOPE implementation(8,9), to the best of our knowledge, only the French ICOPE Care program(10,11) has been implementing ICOPE embedded in the real-life of the health-care system, including reimbursement experimentation funded by the French Ministry of Health and Prevention. Furthermore, no study has investigated how the domains of IC overlap (ie, clusters of IC domains) and the natural history of IC decline using real-life data. A better understanding of the natural history of IC impairments may inform the development of timely strategies for the prevention and early treatment of functional declines before the onset of severe disability. Moreover, the extent to which IC clusters and declining trajectories are associated with adverse health events, including frailty and limitations in activities of daily living (ADL) and instrumental ADL (IADL), is still unknown.

The primary objective of this study was to describe IC domain impairments and their most frequent clusters as measured by the ICOPE Step1 (screening tool) using real-life data from users of the French healthcare system. The secondary objective was to examine the cross-sectional associations of the IC clusters with frailty, IADL, and ADL performance. In addition, the changes of IC domain impairments and IC clusters over time were explored as well as the associations of baseline clusters with longitudinal changes in frailty, IADL, and ADL. We hypothesized that the prevalence of IC impairments would increase with age, and that the higher the number of impaired IC domains in the clusters the higher the probability of having frailty, and IADL and ADL limitations.

Results

24,825 of the 27,720 individuals registered in the ICOPE Care cohort between January 2020 and February 2023 had complete screening data (no missing values) for all the six IC domains: locomotion, cognition, vitality, psychology, hearing, and vision. Among them, 21,642 individuals (mean age 76.7 ± 8.9 years; 62.4% women) had received a healthcare professional assessment of the ICOPE Step1 screening, while the other 3,183 people (mean age 70.9 ± 7.3 years; 58.1% women) had completed a self-assessment. Although our analysis focuses on the ICOPE screening performed by healthcare professionals, data on self-screening are also reported. Table 1 shows the prevalence of impaired IC domains at baseline screening per age-group and sex for individuals receiving professional assessment and those doing self-assessment separately. The highest prevalence of impaired IC domains detected on screening were for vision, cognition, and hearing domains; the lowest prevalence was for vitality. Women had a slightly higher prevalence of impaired IC on screening than men in most IC domains (in particular, for the psychology domain), and the prevalence of impaired IC domains increased with age.

Clusters of IC domains at baseline

The latent class analysis (LCA) that better fit the data generated by healthcare professional screening identified four impairment clusters: C1 “Low impairment” – people in C1 had low probability of having impairments in all IC domains (except for Vision, for which a moderate probability of impairment was found); C2 “Cog+Loc+Hea+Vis” – high probability of having impairments in Cognition, Locomotion, Hearing, and Vision; C3 “All IC impaired” – high probabilities of having impairments in all the six IC domains; and C4 “Psy+Vit+Vis” – high probability of having impairment in Psychology, Vitality, and Vision (and a moderate probability of having Locomotion and Cognition impairments). A high frequency of people ≥ 80 years-old belonged to C2 and C3 (clusters with more IC impairments), whereas those < 80 years were mainly in C1: the frequency of people ≥ 80 years belonging to C1, C2, C3, and C4 were 22.9%, 34.6%, 32%, and 10.5%, respectively; the figures for those < 80 were 56.7%, 19.2%, 10.1%, and 14%, respectively. Table 2 shows the four clusters, the sample per cluster, and the conditional probabilities of having impairment in each IC domain when belonging to a cluster. Supplementary Table 3 provides the results of the LCA analysis for people undertaking self-screening (three clusters identified: “All IC impaired”; “Low impairment”; and “Psy+Vit+Hea+Vis”).

Clusters obtained from observed overlap impairments across IC domains are shown in Supplementary Tables 1 (healthcare professional screening) and 2 (self-screening). The only two clusters with a prevalence $> 5\%$ were those of only “Vision impairment” and “No IC impairment”. The majority of the most prevalent clusters had at least one sensory domain impairment (vision and/or hearing).

Cross-sectional associations of IC with frailty / IADL / ADL

In the subset of individuals receiving the ICOPE Step2 in-depth assessments, a baseline frailty score was available for 1,710 subjects (21.8% robust; 44% pre-frail; 34.2% frail); an IADL assessment for 1571 (30.3% had limitations on IADL (score < 100%)); and an ADL assessment for 1,905 individuals (34% had limitations on ADL (score < 6)). The cross-sectional associations of the four IC clusters (from LCA analysis) with frailty, ADL, and IADL disability are shown in Table 4. Logit models adjusted for age, sex, body weight, and number of co-morbidities showed that, compared to people in C1 “Low impairment”, those in any of the other three clusters had a higher likelihood of being frail and disabled in both ADL and IADL. For all the outcomes, the magnitude of the associations was the strongest in people belonging to the cluster C3 “All IC impaired”. Linear regressions on ADL and IADL limitations found similar findings.

In addition, the probability of being frail and of having limitations in ADL and IADL were the highest in the cluster C3 “All IC impaired” and was the lowest in C1 “Low impairment”. The probabilities for C1, C2, C3, and C4 were, respectively: 14%, 29%, 64%, and 37% for frailty; 20%, 36%, 52%, and 33% for ADL; 9%, 34%, 57%, and 18% for IADL.

Evolution of IC domain impairments and IC clusters

Among people receiving professional assessment, the number of subjects with two ICOPE Step1 screenings varied across IC domains, from 1,281 (for Hearing) to 4,765 (for Psychology and Vision); the mean interval between the two Step1 screenings was 183 days (SD = 64). For self-assessment, the number of people with two ICOPE Step1 assessments (interval 158 ± 43 days) was 598 for all the six domains. Table 5 displays impaired IC domains' incidence, reversibility, and persistence on screening between baseline and first follow-up of ICOPE Step1. For professional assessment, the highest incidence and persistence levels were obtained for Vision, while the lowest were observed for Vitality and Psychology (these two latter IC domains had the highest reversibility rates). Cognition, Locomotion, and Hearing had incidence rates nearing 1 out of 4 individuals and very high persistence rates (particularly for Locomotion). Except for Vision and Hearing, the incidence and, in most cases, persistence levels were higher in people ≥ 80 years-old than in those 60-79 years. Compared to professional assessments, self-assessments showed higher levels of reversibility for all IC domains, except Psychology.

Using the data of the two Step1 professional-based screenings, complete data on all six domains of IC were available for 1190 individuals. The conditional probability of belonging to one of the four IC clusters at follow-up (C-FU1 “Low impairment”; C-FU2 “All IC impaired”; C-FU3 “Only Vision”; C-FU4 “Cog+Loc+Hea+Vis”), as a function of the baseline IC cluster are shown in Figure 1 and Table 6. Individuals with baseline C1 “Low impairment” had high probability to become impaired “Only Vision” (63%) or to remain “Low impairment” at follow-up. The highest probability for individuals in

baseline C2“Cog+Loc+Vis+Hea” was found to remain in this same cluster at follow-up (47%), whereas those in baseline C3“All IC impaired” had the highest probability of becoming “Cog+Loc+Vis+Hea” (45%), and people in baseline C4“Psy+Vit+Vis” became preferentially “Only Vision” (54%).

Baseline IC and longitudinal changes in frailty/ IADL / ADL

In the subset of individuals receiving the ICOPE Step2 in-depth assessments twice (mean follow-up 206 ± 107 days), the incidence/worsening of outcomes was available for 198 subjects for frailty (27.3% frailty worsening; 11.6% frailty incidence); 334 for IADL (17.7% worsened IADL); and 380 for ADL (17.1% ADL worsening). The C3“All IC impaired” (OR 5.72; 95%CI 1.32, 24.73; $p=0.02$) and C4“Psy+Vit+Vis” (OR 3.99; 95%CI 1.01, 15.7; $p=0.048$) clusters were associated with incident frailty. Only the IC cluster C3“All IC impaired” was associated with ADL worsening (OR 3.89; 95%CI 1.70, 8.93; $p=0.001$) and nearly associated (OR 2.43; 95%CI 0.98, 6.02; $p=0.055$) with IADL worsening (see Table 7).

Discussion

This study examined the prevalence and clusters of IC screening impairments in an older adult population of real-life users of the healthcare system. LCA modeling of data from more than 20,000 users of primary care services defined four clusters (professional IC assessments) according to IC domain impairments on screening: C1“Low impairment”, C2“Cog+Loc+Hea+Vis”, C3“All IC impaired”, and C4“Psy+Vit+Vis”. Compared to people in the “Low impairment” cluster, those in any of the other IC impairment clusters had higher likelihood of having frailty and limitations in both ADL and IADL; the strongest associations were obtained for the “All IC impaired” cluster. The most prevalent IC cluster was the C1“Low impairment” group, suggesting that a fraction of the older adult population (about 7% according to observed data at baseline) had no impairment in any capacity. This cluster was mainly composed of people < 80 year-old (nearly 80% of the cluster), whereas the clusters with the highest numbers of IC domain impairments (clusters C2 and C3) were more prevalent in people ≥ 80 , reflecting the increasing prevalence of impairment with age for almost all IC domains.

Among all the IC domains, vision impairment had the highest prevalence, incidence, and persistence rates. Furthermore, people in all clusters had high probabilities of having vision impairment (for the “Low impairment” cluster the probability was moderate, ie, 57%). Vision is a strong contributor for healthy aging and has already been found to be associated to other IC domains, such as hearing and cognitive function(12–15) as well as to IADL(12,16–18), frailty(19) and mortality(17,20,21). At the same time, vision was the only IC domain in which the prevalence did not increase with increasing age, raising questions on whether the way it is operationalized in the ICOPE Step1 is accurate enough to screen individuals with potential vision loss. Indeed, most older adult have “difficulties in seeing far,

reading, eye diseases or currently under medical treatment (e.g., diabetes, high blood pressure)” – the question of the ICOPE Step1 – since a large majority of people 60 or older have, for example, presbyopia(22). Since the screening question for vision impairment does not state if the participant should account or not for the use of corrective devices, it may lead to confusion when responding to it. Therefore, to what extent vision impairment plays a central role on the natural history of IC declines deserves further investigations.

Besides impairment on vision, impairment on cognition had the highest prevalence and incidence rates, while impairments on locomotion had the highest persistence over time. Cognition and locomotion were often grouped together, with about 24% of the population having concomitant impairments in these IC domains (Supplementary Table 2); their incidence and persistence were higher in people 80 or older, compared to those 60-79 years. Furthermore, cluster transition analysis showed that people belonging to baseline clusters with high probabilities of impairment on cognition and locomotion (ie, C2“Cog+Loc+Hea+Vis” and C3“*All IC impaired*”) mainly belonged to a cluster characterized by impairment in these same IC domains at follow-up (C-FU4“Cog+Loc+Hea+Vis”). Taken together, these findings suggest that the combination of impairment cognition-locomotion is a phenotype difficult to revert, and this is still more true after the age of 80. Indeed, a recent study by Lee et al. (23) found that a multidomain lifestyle intervention (exercise and cognitive training, diet education, and chronic conditions’ management) was more effective for improving measures of cognitive function and frailty in people with only one impairment on either cognition or mobility rather than in those with impairments on both. The associations of cognitive function and mobility with adverse functional outcomes and care dependency are largely reported in the literature(24–26). Several constructs have been created to take into account the combined adverse effects of impairments in cognitive and physical functions, such as cognitive frailty(27–29), motoric cognitive risk syndrome(30), and Physio-Cognitive Decline Syndrome(31,32). The present study extends the literature by assessing the concomitant effects of cognitive and mobility declines using simple screening tests designed to be broadly used within a public health perspective in a real-world population of healthcare users.

Cluster analysis found hearing loss has often been grouped with cognition and locomotion (almost 15% of the population had these three IC domains impaired – see Supplementary Table 2). Hearing loss had high persistence rates, but its incidence did not differ between people 60-79 and those ≥ 80 . The literature is rich on the associations between hearing loss and cognitive function(33–35), associations that might be bidirectional(36). For the hearing-locomotion associations, although the literature is more sparse, some evidence shows that hearing impairment is associated with mobility limitations(37,38). These associations might be partly mediated by cognitive function, since they are stronger in people with lower cognitive capacity(39), highlighting the complexity of the sensory-cognitive-motor functions.

Psychology and vitality impairments were often expressed together. Cluster transition analysis highlighted the reversible characteristic of both vitality and psychology, since people belonging to baseline clusters with high probabilities of impairment on psychology and vitality (ie, C3“All IC impaired” and C4“Psy+Vit+Vis”) mainly belonged to a cluster characterized by the absence of impairment in these IC domains at follow-up (C-FU4“Cog+Loc+Hea+Vis” and C-FU3“Only Vision”). Although there is a large body of evidence showing that depressive symptoms and appetite loss/anorexia of aging are closely related(40–46), it remains unclear why these clinical conditions were largely reversible over time in our study. Even though this deserves further investigations, it is possible that the subjective nature of the questions defining psychology and vitality impairment contributes to the low stability of the responses over time. Indeed, these questions screen, but do not diagnose, depression or malnutrition, conditions that once established are more difficult to revert. It is also possible, since this is a real-life population, that people detected with declines in IC received healthcare interventions (eg, psychotherapy, nutritional counseling or supplementation) that were effective in reducing depressive symptoms and appetite/weight loss. Furthermore, we can not exclude a selection bias, where people in worse health, for whom clinical phenotypes are more difficult to revert, having greater lost to follow-up.

Overall, the findings in participants who undertook screening by self-assessment were consistent with the findings obtained by professional assessment. Although three instead of four clusters better fitted self-screening data, as for professional assessment, the cluster “Low impairment” was the most prevalent. Given its high prevalence and persistence, psychology appears to play an important role among people undertaking self-screening, which is corroborated by the fact psychology was a strong contributor (highest conditional probability) for the self-screening cluster “Psy+Vit+Hea+Vis”. In contrast, locomotion impairments had lower importance in self-screening (low incidence and high reversibility rates). One explanation for these differences may be, at least partly, related to age differences since locomotion impairment occurs more frequently in late ages, being less common in people in their early 70’s (mean age of participants doing self-assessment); in contrast, depressive symptoms occur at all ages, including in young older adults(47,48). An alternative explanation is that older individuals who feel depressed are more prone to undertake a self-assessment of ICOPE, while health professionals are more prone to assess their older patients when they observe a mobility problem. Further investigations are needed to better understand the differences between professional screening and self-screening for IC domain impairment and their changes over time.

Regarding changes in IC over time, self-screening showed high reversibility rates for most IC domains. Although lack of stability over time in IC self-assessment impairments is a potential explanation for that finding, it is also possible that the older adults undertaking self-assessment are more

resilient than those receiving a professional assessment. Indeed, they are younger and probably have more resources to fight against stressors and revert from an IC impairment.

The findings of this study support the utility of the ICOPE screening tool for risk stratification in clinical care and highlights the importance of having an integrated care approach for older adults, as emphasized by the ICOPE healthcare pathway. Indeed, all the clusters with impaired IC domains were associated with a higher likelihood of frailty, ADL and IADL limitations, even after adjusting for the number of comorbidities. The “All IC impaired” cluster had the strongest cross-sectional associations with these clinical outcomes and was the only cluster longitudinally associated with incident frailty and worsening ADL. Previous research from our team(49) and others(50) has shown that IC impairment using the ICOPE screening tool or modified versions of this tool was associated with clinical outcomes, such as frailty. This is an important finding since investigations around IC and ICOPE are increasing exponentially, and potential issues related to conceptual and measurement models may arise(51). Furthermore, we showed that impairment on screening in almost all IC domains is more prevalent and had higher incidence and persistence rates in individuals ≥ 80 years than in those aged 60-79, suggesting a reduction in resilience in the oldest people (potentially reflecting low responsiveness to interventions). Identifying the determinants of loss of resilience at cellular and molecular levels might pave the route to developing preventive, innovative and timely strategies (such as gerotherapeutics(52)) before a reduced level of resilience trigger the onset of disabilities.

This study has a number of strengths. It is the first large-scale investigation examining clusters of IC domains and how IC domains and clusters evolve and we used a real-life sample of older adults’ users of primary healthcare services evaluated through the ICOPE healthcare pathway. Nevertheless, some limitations are worth mentioning: IC clusters were obtained using a screening tool, with an inherent risk of bias related to both false positives and false negatives for IC domain impairments. Another potential limitation related to a screening tool is that the screening measurements may not fully capture all the facets of IC domains; for example, chair rise might not be fully capturing locomotion (although it is an easy assessment that is a precursor of locomotor capacity). However, in the real-life of health-care systems such a screening tool is more likely to be systematically used by overstretched primary care providers than time-consuming (although more accurate) full-length scales and tests. Furthermore, only a small fraction of people undertook Step 2 assessments and had usable follow-up data; this limited the longitudinal analyses and the findings regarding the associations of IC impairment on screening with incident clinical outcomes and the natural history of IC changes over time. For the same reason of limited data availability on Step 2, we were not able to examine the differences in clinical events between individuals included in this study and those excluded; therefore, an eventual sample selection bias cannot be excluded. Furthermore, this is a real-life population and the patients may have adopted healthy strategies after their first ICOPE evaluation, which may have influenced the findings of

longitudinal analysis. It is important to bear in mind our study sample comprises care-seeking people; therefore, our findings should be taken with caution when comparing to a general population of older adults. Finally, further investigations on the self-screening should be encouraged. Indeed, to the best of our knowledge, only one preliminary study examined the agreement between self-screening and care professional screening (both screenings performed in the same day)(53), showing good agreements for psychology, vitality, and locomotion, moderate agreements for vision and hearing, and weak agreement for cognition in people 60 and older (n=34). Future studies should endeavor in well-delineating the most appropriate measurements for self-screening across all the domains of IC. Moreover, in our study, individuals self-screened hearing loss through a self-reported question. Although this is a simple assessment, other options exist, such as the automated app-based digit-in-noise test(54); such a test has numerous advantages since it is an objective measure that leverages technology, and probably provides more accurate data for self-screening. To what extent such an objective test performs better for screening for hearing loss compared to the Whisper test also deserves to be examined since it can lead to a standardization of screening regardless the assessment mode at screening (care professional or self-assessment).

Clinical implications and conclusions

In this community-based sample of care-seeking older adults, we showed that younger individuals (60-79 years) had lower prevalence of IC impairments on screening than older adults (≥ 80 years), who also had higher incident and persistent impairments. This suggests, on one hand, that screening for IC impairment should be performed more often in people ≥ 80 ; for example, people 80 years or older might be screened every four months (it is currently recommended in this French ICOPE Care implementation to screen for IC impairments every six months for older adults of any age(10)). On the other hand, older adults less than 80 years-old can revert from IC impairments more easily than those ≥ 80 ; interventions to improve IC have a higher potential to be effective in the former than in the latter. Vision was the most prevalent and incident IC impairment. Cognition and locomotion impairments on screening were persistent conditions, suggesting the concomitant presence of these IC impairments may require increased attention from care professionals since it may drive a cascade of functional decline(55). Patients with cognition and locomotion impairments on screening may benefit from a fast-track pathway for progressing in priority through ICOPE Step2 (in-depth assessments and search for causes of IC impairment) and Step3 (personalized care plan) in order to slow down or even reverse functional declines. Furthermore, the cognition-locomotion combination often co-occurs alongside sensory declines. The clusters and concomitant occurrence of IC positive screenings highlight the importance of having an integrated approach to the care of older people. Future studies examining the whole ICOPE healthcare pathway (from Step 1 to Step 5) must investigate how the different IC clusters respond to the healthcare providers' real-life interventions.

Methods

This study complies with all relevant ethical regulations. The database used in this study is hosted under a secure hosting supplier, in compliance with the General Data Protection Regulation (RGPD)(56) and The French National Commission for Computing and Liberties (CNIL registration number 247169284s), approved in 2017 (N / Ref: MMS / OSS / NDT171027).

ICOPE Care cohort

Details on the ICOPE care cohort, which is composed of primary healthcare users in France (in particular from the South-West region Occitania), have been published elsewhere(10,11). ICOPE Step 1 (screening) are performed by healthcare professionals, in particular nurses, general practitioners, pharmacists, and physical therapists in the context of routine consultations or through self-assessment by the older adults themselves. The data on ICOPE Step1 are collected using the ICOPE Monitor mobile app or the ICOPEBOT on-line conversational robot(11). After accessing the information notice and consent form, participants consent to data storage and monitoring by checking on the digital tools(10) the box indicating that the data collected will be stored in a secured database under the responsibility of the Toulouse University Hospital and that they can be used for research purposes; this box can also be checked by the healthcare professional after receiving the oral consent of the participants. The digital checking of this box was considered as providing informed consent. Results from both the healthcare professional assessment and self-assessment feed a secure database that generates an alert in the case of a positive screening (potential impairment in IC).

Upon reception of an alert, the healthcare provider/team in charge of the patient's follow-up may decide to perform the ICOPE Step 2, in which an in-depth IC assessment is performed (in order to confirm the IC impairment) as well as clinical assessments, such as frailty, IADL, and ADL.

Study population

Users of primary care services, aged 60 years and older who underwent ICOPE screening between January 2020 (start of the program) and the end of February 2023 (data extraction date) were included. At baseline, 24,825 individuals (n=21,642 assessed by a healthcare professional; n=3,183 undertaking self-assessment) met the eligibility criteria and had complete screening data for all the six IC domains (ie, locomotion, cognition, vitality, psychology, hearing, and vision). No statistical methods were used to pre-determine sample sizes but our sample sizes are larger than those reported in previous publications(50,57).

A subpopulation of individuals receiving the ICOPE Step2 (sample size varying from 1,571 to 1,905 according to the outcome) was operationalized.

For investigations on the overtime changes of IC domains and clusters, participants were included if they had undergone two ICOPE Step1 screenings (baseline and follow-up) within an interval comprised between 90 and 365 days (period chosen to capture significant functional changes and allowing to achieve a reasonable sample size). The sample size varied according to IC domain from 1,281 to 4,765 (n=1190 people had complete data on the six IC domains at both Step1 baseline and follow-up).

A subpopulation of individuals having been assessed twice through the ICOPE Step2 in-depth evaluations was used to study the associations of baseline IC clusters with changes in frailty, ADL or IADL (sample size varied from 198 to 380 according to the clinical outcome).

Extended Data Figure 1 provides a flowchart with the study samples used in the different analysis.

ICOPE Step1 – screening for IC impairment

IC impairments on screening (referred hereafter as “IC impairments”) were operationalized as follows:

Cognition. Participants are asked to repeat and remember three words (eg, flag, flower, door) and to provide the entire date today. Then, they are asked to recall the three words. An impairment is defined as one or more mistakes in the three-word recall or time orientation (day of week, day of month, month, year).

Locomotion. From a sitting position, participants must raise from a chair, arms crossed on the chest, five times as fast as possible; the chronometer (embedded into the data collection tools) is stopped once the participant complete the 5th chair rise. Then, either the healthcare professional or the participant (in self-assessment) responded to the question: “Was the individual able to complete the five repetitions in 14 seconds or less?” Responding “No” to the question was considered a locomotion impairment.

Vitality. A vitality impairment is defined if the person answers Yes to any the following binary (yes/no) items: weight loss (3kg in the last three months) or appetite loss.

Vision. Impairment is defined when answering Yes to the question: "Do you have any problems with your eyes: difficulties in seeing far, reading, eye diseases, or currently under medical treatment (e.g., diabetes, high blood pressure)?"

Hearing. Healthcare professionals perform the whisper test: behind the person, the professional whispers four words at both the left and right ears (with the person closing off the opposite ear by pressing on the tragus). Hearing impairment is ascertained if the participant fails to repeat at least three words in at least one of the ears. For self-assessment, an impairment is ascertained if the person responds Yes to the question: have you perceived or has a person close to you (family or friend) indicated you have had a reduction in your hearing capacity in the past four months.

Psychology. A positive screening is defined if the person answers Yes to any of the binary (yes/no) items: “Over the past two weeks, have you been bothered by: feeling down, depressed, or hopeless? Little interest or pleasure in doing things?”

Other clinical measures

Frailty was measured by the Fried frailty phenotype(58): weight loss (self-reported involuntary loss of at least 4.5 kg or 5% weight loss during the last year), slowness (4-meter walking speed stratified by height and sex), low physical activity (self-reported), weakness (low dominant handgrip strength stratified by sex and BMI) and exhaustion (self-reported with the question “During the last week everything I did represented an effort”). Participants meeting ≥ 3 criteria were classified as frail; 1 or 2 criteria, pre-frail; no criterion, robust.

IADL were measured according to Lawton’s scale(59), testing the ability (yes/no) to perform the following activities: use the phone, do the groceries, cook, do housekeeping, do laundry, use transportation, handle own medication, and manage finances. The total IADL score varied from 0 to 100%, with higher scores indicating better performance (% score was adopted because the number of applicable IADL may vary since some activities did not apply to some participants: for example, men sometimes declared to have never tried to cook or do laundry, in which case the maximum number of applicable IADL would be 6 or 7. People capable of executing all applicable IADL received a score of 100%). A binary IADL variable was created by grouping participants with 100% scores *versus* others (< 100%).

ADL were measured according to Katz’s scale(60) by testing the ability to perform alone the following activities: showering, getting dressed, using the toilet, displacing inside a room, continence, and self-feeding. Each activity was coded as “need help to do = 0”, “do alone with limitation = 0.5”, and “do alone without limitation = 1”. Scores vary from 0 to 6; higher is better. A binary ADL variable was created by grouping fully independent participants (ADL score = 6) *versus* others (scores < 6).

Statistical Analysis

We describe below the cross-sectional and longitudinal analyses separately. All analyses were performed with Stata (StataCorp LLC, College Station, Texas, USA) version 17; statistical significance was set at $p < 0.05$.

Cross-sectional analysis

Descriptive baseline statistics

For the prevalence of IC impairment per domain, we used standard descriptive statistics (absolute numbers and percentage) stratified by age-group (60-69, 70-79, 80-89, 90-99, ≥ 100 year-old), sex, and mode of Step1 screening (by a professional or self-screening).

Clusters of IC domain impairments at baseline

We applied the latent class analyses (LCA) to ICOPE Step1 to find groups of people with a similar combination of IC domain impairments. The latent classes consider the frequency and the number of IC domains affected. Participants allocated to a latent class have the same average probability of being impaired in the IC domains. We modeled the baseline and follow-up data separately to explore the composition and the optimal number of classes cross-sectionally. We obtained Bayesian and Akaike information criteria (BIC and AIC) as the goodness of fit statistics for models with two, three, four, and five latent classes (Extended Data Figure 2). We opted for the model with four latent classes for the professional assessment and three for the self-assessment based on the physio-clinical correlation and the model diagnostics.

The clusters created from the observed co-occurrence of IC domain impairments at baseline were provided as a secondary approach, with each individual belonging to only one cluster (Supplementary Tables 2 (healthcare professional screening) and 3 (self-screening)).

Cross-sectional associations of IC clusters with frailty, ADL, and IADL

In the subset of the population with an ICOPE Step2 assessment, the cross-sectional associations of the clusters obtained in the LCA (Step1 performed by healthcare professional) with frailty, and IADL and ADL performance were analyzed; analyses were adjusted for age, sex, self-reported weight and number of comorbidities.

For frailty, an ordered logit regression model was run. The proportional odds assumption was checked using the approximate likelihood-ratio test of proportionality of odds across response categories (omodel logit in Stata) and the Brant test. For ADL and IADL, we ran linear regression models (continuous variables) and binary logit models (binary variables) separately for each outcome. For all

outcomes, we obtained from the logit models the marginal probabilities of being frail or disabled on ADL or IADL at baseline, given the membership to a given cluster.

Longitudinal analyses

Incidence, reversibility, and persistence of IC domain impairment

In individuals with two Step1 over time, we investigated the changes in IC domain impairments over time by describing the incidence, reversibility, and persistence of impairments on screening for each IC domain. We defined *Incidence* as the percentage of people with a new IC impairment among those without the impairment at baseline; *Reversibility* as the percentage of those without the IC impairment at follow-up among those with the IC domain impaired at baseline; *Persistence* as the percentage of people with an IC impairment at follow-up among those who were already impaired at baseline.

IC Cluster temporal transition

The LCA model estimated the latent classes using the follow-up Step1 data. Then, the transition probabilities for transitioning from a baseline to a follow-up cluster were obtained from an age- and sex-adjusted multinomial logistic model within the population with complete data for both time points (Step1 at both baseline and follow-up).

Association of IC clusters at baseline with incidence/worsening in frailty, ADL, and IADL

We finally explored the longitudinal associations of IC clusters with the incidence and worsening of frailty as well as the further deterioration of IADL and ADL disability using logit models adjusted for age, sex, and weight. Worsening outcomes reflected clinically meaningful changes (e.g., going from robust to prefrail or frail, or from prefrail to frail; decreasing at least 0.5 points in ADL; and IADL decrease equivalent to being limited in one activity). Incidence and worsening analyses were restricted to people with professional assessments.

Data Availability

The data reported in this manuscript (text, tables, figures and the supplementary material) will be shared in de-identified form owing to privacy protections. Request for de-identified data and a data dictionary will be evaluated by the ICOPE Care data-sharing committee, which can be contacted at the following address: tavassoli.n@chu-toulouse.fr. Data will be made available for investigators upon request for a pre-identified scientific purpose developed in a research proposal with sound methodology, subject to the approval of the appropriate ICOPE Care committee; a data use agreement must also to be signed. Given the nature of the ICOPE Care program (on-going, real-life data from healthcare services), the authors are unable to make the dataset publicly accessible at this time. In addition, according to the ICOPE Care policy, all analyses using ICOPE Care data (including the present study) must be evaluated and approved by the committee after submission of a comprehensive analysis proposal. Therefore, for researchers interested in accessing the data used for the current study, the same evaluation procedure must be followed.

Code Availability

The codes supporting the findings of this study are available upon reasonable request from the corresponding author. All analyses were performed using programming languages in the Stata package software.

Acknowledgements

We thank all the health-care professionals who participated in the ICOPE Care program; the members of the Gerontopole of Toulouse especially those of the “Regional Team for Ageing and Prevention of Dependency” (Isabelle Carrié, Justine de Kerimel, Christine Lafont, Céline Mathieu, Fanny Paris, Delphine Pennetier, Brune Rieunier, Alessia Robert-Millocco) and the “ICOPE remote monitoring platform” (Véronique Bezombes, Pascale Baby, Laure Bouchon, Marie Christine Cazes, Florence Da Costa, Nadia Moussa, Magali Poly, Charlene Seguela, Lay-Nien Sephan, Catherine Takeda); all the members of the Occitanie Territorial Teams of Ageing and Prevention of Dependency; and the project leaders of National Experimentation - Article 51 (Mutualité Française PACA, DAC Sante landes, Inter-CPTS Haut-Rhin, CPTS Haute-Corrèze, Périgueux University Hospital, Filiaris Sud, Civic Hospitals of Lyon, CPTS Grand Sud Réunion, InterURPS Pay de la Loire, CPTS Cerebellum, DAC 17, DAC 46, Clinique des Augustines, Brest University Hospital, Mutualité Française Bretagne).

The ICOPE-Care program was supported by grants from the Occitania Regional Health Agency (Region Occitanie and Pyrénées-Méditerranée; reference number 1901175), the European Regional Development Fund; project number MP0022856) and The Interreg Program V-A Spain-France-Andorra (European Union) in the context of the APTITUDE project (reference EFA232/16). This work was performed into the context of the IHU HealthAge, which has benefited from funding by the Agence Nationale de la Recherche under the France 2030 program (reference number: ANR-23-IAHU-0011). The funders had no role in study design, data collection and analysis, decision to publish or preparation of the manuscript

Author Contribution Statement

PSB, EGB, MESM, and BV contributed to the study design. PSB, EGB, MESM, and BV supervised the study. NT, CB, and EGB contributed to data collection and/or verification. EGB analyzed the data. PSB, EGB, HBF, VPO, RGBM, CB, NT, JRB, YR, MESM, and BV contributed to data interpretation. PSB wrote the first version of the manuscript. All authors revised the manuscript with important intellectual content. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication

Competing Interests Statement

PSB declares to have received research grant and consultancy fees from Pfizer

BV is the founder president of IHU HealthAge, Toulouse University Hospital, and an investigator in clinical trials sponsored by several industry partner (IHU, CRC, and Inspire geroscience platforms).

All the other authors declare no conflicts of interest

Tables

Table 1. Prevalence of ICOPE Step1 IC impairment on screening per age-decade and sex at baseline in people with complete data for locomotion, cognition, psychology and vitality.

		IC impairment on screening, n(%)					
Professional assessments							
Age	Sex (n)	Cognition	Locomotion	Vitality	Psychology	Vision	Hearing
60-69	Men (2,012)	677(33.65)	308(15.31)	253(12.57)	458(22.76)	1,286(63.92)	582(28.93)
	Women (3,188)	931(29.20)	550(17.25)	428(13.43)	1,151(36.1)	2,052(64.37)	692(21.71)
	Total (5,200)	1,608(30.92)	858(16.50)	681(13.10)	1,609(30.94)	3,338(64.19)	1,274(24.50)
70-79	Men (3,004)	1,560(51.93)	843(28.06)	560(18.64)	955(31.79)	1,916(63.78)	1,406(46.80)
	Women (4,972)	2,060(41.43)	1,481(29.79)	949(19.09)	2,126(42.76)	3,283(66.03)	1,734(34.88)
	Total (7,976)	3,620(45.39)	2,324(29.14)	1,509(18.92)	3,081(38.63)	5,199(65.18)	3,140(39.37)
80-89	Men (2,523)	1,699(67.34)	1,227(48.63)	682(27.03)	991(39.28)	1,617(64.09)	1,645(65.20)
	Women (4,201)	2,516(59.89)	2,290(54.51)	1,208(28.76)	2,094(49.85)	2,835(67.48)	2,261(53.82)
	Total (6,724)	4,215(62.69)	3,517(52.31)	1,890(28.11)	3,085(45.88)	4,452(66.21)	3,906(58.09)
90-99	Men (575)	440(76.52)	401(69.74)	200(34.78)	251(43.65)	370(64.35)	427(74.26)
	Women (1,121)	864(77.07)	828(73.86)	440(39.25)	586(52.27)	766(68.33)	768(68.51)
	Total (1,696)	1,304(76.89)	1,229(72.46)	640(37.74)	837(49.35)	1,136(66.98)	1,195(70.46)
>100	Men (17)	13(76.47)	10(58.82)	9(52.94)	9(52.94)	15(88.24)	10(58.82)
	Women (29)	27(93.10)	25(86.21)	10(34.48)	17(58.62)	23(79.31)	18(62.07)
	Total (46)	40(86.96)	35(76.09)	19(41.30)	26(56.52)	38(82.61)	28(60.87)
All	Men (8,131)	4,389(53.98)	2,789(34.30)	1,704(20.96)	2,664(32.76)	5,204(64.00)	4,070(50.06)
All	Women (13,511)	6,398(47.35)	5,174(38.29)	3,035(22.46)	5,974(44.22)	8,959(66.31)	5,473(40.51)
All	Total (21,642)	10,787(49.84)	7,963(36.79)	4,739(21.90)	8,638(39.91)	14,163(65.44)	9,543(44.09)
Self-assessments							
Age	Sex (n)	Cognition	Locomotion	Vitality	Psychology	Vision	Hearing
60-69	Men (545)	161(29.54)	70(12.84)	34(6.24)	120(22.02)	289(53.03)	170(31.19)
	Women (954)	282(29.56)	152(15.93)	59(6.18)	321(33.65)	560(58.70)	280(29.35)
	Total (1,499)	443(29.55)	222(14.81)	93(6.20)	441(29.42)	849(56.64)	450(30.02)
70-79	Men (591)	272(46.02)	117(19.80)	53(8.97)	154(26.06)	312(52.79)	243(41.12)
	Women (677)	294(43.43)	137(20.24)	53(7.83)	225(33.23)	408(60.27)	233(34.42)

	Total (1,268)	566(44.64)	254(20.03)	106(8.36)	379(29.89)	720(56.78)	476(37.54)
80-89	Men (177)	108(61.02)	47(26.55)	25(14.12)	51(28.81)	104(58.76)	69(39.98)
	Women (189)	102(53.97)	70(37.04)	42(22.22)	88(46.56)	117(61.90)	87(46.03)
	Total (366)	210(57.38)	117(31.97)	67(18.31)	139(37.98)	221(60.38)	156(42.62)
90-99	Men (19)	14(73.68)	16(84.21)	4(21.05)	7(36.84)	13(68.42)	12(63.16)
	Women (31)	21(67.74)	18(58.06)	9(29.03)	16(51.61)	15(48.39)	17(54.84)
	Total (50)	35(70.00)	34(68.00)	13(26.00)	23(46.00)	28(56.00)	29(58.00)
All	Men (1,332)	555(41.67)	250(18.77)	116(8.71)	332(24.92)	718(53.90)	494(37.09)
All	Women (1,851)	699(37.76)	377(20.37)	163(8.81)	650(35.12)	1,100(59.43)	617(33.33)
All	Total (3,183)	1,254(39.40)	627(19.70)	279(8.77)	982(30.85)	1,818(57.12)	1,111(34.90)

Table 2. Clusters from latent class analysis using healthcare professional screening, and the conditional probabilities (%) of impairment in each IC domain when belonging to a cluster.*

IC domain impairment	Conditional probability of having IC domain impairment (%)			
	C1 “Low impairment” (n=9,419)	C2 “Cog+Loc+Hea+Vis” (n=5,454)	C3 “All IC impaired” (n=4,035)	C4 “Psy+Vit+Vis” (n=2,734)
Cognition	24	66	84	42
Locomotion	11	45	79	36
Vitality	6	14	58	35
Hearing	57	68	70	73
Vision	25	61	66	30
Psychology	16	26	76	86

*The labels of the clusters were defined based on the comparison of the conditional probabilities with the prevalence of impairment per IC domain: when the conditional probability was higher than the observed prevalence for a given IC domain, such a domain appears in the label of the cluster (numbers in bold in the table).

Table 3. Clusters from latent class analysis, and the conditional probabilities of impairment in each IC domain given the belonging to a cluster for the self-screening.*

IC domain impairment	Conditional probability of having IC domain impairment (%)		
	SC1 “All IC impaired” (n=604)	SC2 “Low impairment” (n=1928)	SC3 “Psy+Vit+Hea+Vis” (n=651)
Cognition	70.2	28.8	36.2
Locomotion	43.1	10.6	17.9
Vitality	21.7	2.6	18.1
Hearing	65.4	51.2	68.2
Vision	58.9	21.2	39.5
Psychology	44.3	6.2	86.7

*The labels of the clusters were defined based on the comparison of the conditional probabilities with the prevalence of impairment per IC domain: when the conditional probability was higher than the observed prevalence for a given IC domain, such a domain appears in the label of the cluster (numbers in bold in the table).

Table 4. Cross-sectional, age-, sex-, weight- and comorbidity-adjusted associations of the four baseline IC clusters with frailty, and ADL and IADL performance.*

IC Clusters	Frailty ordinal; n=1,710 ^a			ADL continuous; n=1,905 ^b			ADL binary; n=1,905 ^c			IADL continuous; n=1,571 ^b			IADL binary; n=1571 ^c		
	OR	95% CI	p	Coeff	95% CI	P	OR	95% CI	p	Coeff	95% CI	P	OR	95% CI	p
C1 "Low impairment" (Reference)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
C2 "Cog+Loc+Hea+Vis"	2.57	1.98, 3.33	<.001	-0.16	-0.25, -0.07	.001	2.24	1.69, 2.96	<.001	-10.1	-12.9, -7.28	<.001	4.90	3.39, 7.07	<.001
C3 "All IC impaired"	11.1	8.2, 15.1	<.001	-0.60	-0.70, -0.50	<.001	4.44	3.3, 5.96	<.001	-23.9	-26.9, -20.8	<.001	12.6	8.51, 18.6	<.001
C4 "Psy+Vit+Vis"	3.76	2.8, 5.05	<.001	-0.07	-0.18, 0.03	.15	1.98	1.44, 2.71	<.001	-0.66	-3.85, 2.52	.68	2.05	1.31, 3.21	.002

*All analyses were two-sided and adjusted for age, sex, self-reported weight and number of comorbidities. For frailty, an ordered logit regression model was run. For ADL and IADL, both linear regression models (continuous variables) and binary logit models were run.

^aFrailty with three categories (robust, pre-frail, frail) has been analyzed using ordered logit model. "Robust" was used as the reference category.

^bContinuous ADL and IADL were analyzed using multiple linear regression, with higher scores indicating higher function.

^cBinary ADL and IADL were analyzed using binary logistic regression, fully independent (reference) vs. any limitation.

Table 5. Incidence, reversibility and persistence of ICOPE Step1 impairment on screening of IC domains over time.

	Cognition	Locomotion	Vitality	Psychology	Hearing	Vision
Professional assessment (all ages)						
Population <i>at risk</i> of Incidence, n	2577	1314	3895	32976	657	1269
Population <i>at risk</i> of Reversibility/Persistence, n	2137	812	856	1789	624	3496
Incidence	661 (25.6%)	300 (22.8%)	352 (9%)	338 (11.4%)	149 (22.7%)	707 (55.7%)
Reversibility	855 (40%)	195 (24%)	635 (74.2%)	946 (52.9%)	189 (30.3%)	457 (13.1%)
Persistence	1282 (60%)	617 (76%)	221 (25.8%)	843 (47.1%)	435 (69.7%)	3039 (86.9%)
Professional assessment (60-79 years-old)						
Population <i>at risk</i> of Incidence, n	1769	872	2485	1886	390	761
Population <i>at risk</i> of Reversibility/Persistence, n	1104	309	407	1011	254	2137
Incidence	389 (22%)	177 (20.3%)	186 (7.5%)	186 (9.9%)	88 (22.6%)	425 (55.8%)
Reversibility	554 (50.2%)	105 (34%)	303 (74.4%)	567 (56.1%)	90 (35.4%)	287 (13.4%)
Persistence	550 (49.8%)	204 (66%)	104 (25.6%)	444 (43.9%)	164 (64.6%)	1850 (86.6%)
Professional assessment (\geq 80 years-old)						
Population <i>at risk</i> of Incidence, n	808	442	1410	1090	267	508

Population <i>at risk</i> of Reversibility/Persistence, n	1033	503	449	778	370	1359
Incidence	272 (33.7%)	123 (27.8%)	166 (11.8%)	152 (13.9%)	61 (22.8%)	282 (55.5%)
Reversibility	301 (29.1%)	90 (17.9%)	332 (73.9%)	379 (48.7%)	99 (26.8%)	170 (12.5%)
Persistence	732 (70.9%)	413 (82.1%)	117 (26.1%)	399 (51.3%)	271 (73.2%)	1189 (87.5%)
Self-assessment						
Population <i>at risk</i> of Incidence, n	376	511	570	443	408	251
Population <i>at risk</i> of Reversibility/Persistence, n	222	87	28	155	190	347
Incidence	144 (38.3%)	58 (11.3%)	33 (5.8%)	65 (14.7%)	46 (11.3%)	41 (16.3%)
Reversibility	109 (49.1%)	55 (63.2%)	22 (78.6%)	64 (41.3%)	96 (50.5%)	138 (39.8%)
Persistence	113 (50.9%)	32 (36.8%)	6 (21.4%)	91 (58.7%)	94 (49.5%)	209 (60.2%)

Incidence – people with impaired screening at follow-up among people without impairment on screening at baseline

Reversibility – people without impaired screening at follow-up among those who had impaired screening at baseline

Persistence – people with impairment on screening at follow-up among people with impaired screening at baseline

Table 6. Conditional probabilities of belonging to a follow-up intrinsic capacity cluster as a function of the membership to a baseline cluster.

Transition probabilities with IC (age- and sex-adjusted)				
	Conditional probability (%)	p-value	95% CI	
Baseline C1 "Low impairment"				
Follow-up C-FU1 "Low impairment"	17	<.001	13	21
Follow-up C-FU2 "All IC impaired"	3	.001	1	4
Follow-up C-FU3 "Only Vision"	63	<.001	58	68
Follow-up C-FU4 " Cog+Loc+Hea+Vis"	18	<.001	14	22
Baseline C2 "Cog+Loc+Hea+Vis"				
Follow-up C-FU1 "Low impairment"	3	.001	1	5
Follow-up C-FU2 "All IC impaired"	10	<.001	7	13
Follow-up C-FU3 "Only Vision"	40	<.001	34	45
Follow-up C-FU4 " Cog+Loc+Hea+Vis"	47	<.001	42	53
Baseline C3 "All IC impaired"				
Follow-up C-FU1 "Low impairment"	1	.08	0	3
Follow-up C-FU2 "All IC impaired"	26	<.001	20	31
Follow-up C-FU3 "Only Vision"	28	<.001	22	34
Follow-up C-FU4 " Cog+Loc+Hea+Vis"	45	<.001	39	52
Baseline C4 "Psy+Vit+Vis"				
Follow-up C-FU1 "Low impairment"	6	.002	2	10
Follow-up C-FU2 "All IC impaired"	16	<.001	10	22
Follow-up C-FU3 "Only Vision"	54	<.001	46	62
Follow-up C-FU4 " Cog+Loc+Hea+Vis"	24	<.001	17	31

Table 7. Longitudinal age-, sex-, weight and comorbidity-adjusted associations of the four IC baseline clusters with frailty (incidence and worsening), and ADL and IADL worsening over time for participants with two Step2 in-depth assessments (apart from each other in average 206 ± 107 days)^a

IC Clusters	Frailty incidence (n=198)			Frailty worsening (continuous; n=198)			ADL worsening; n=380)			IADL worsening (n=334)		
	OR	95% CI	P	OR	95% CI	P	OR	95% CI	p	OR	95% CI	P
C1 "Low impairment" (Reference)	-	-	-	-	-	-	-	-	-	-	-	-
C2 "Cog+Loc+Hea+Vis"	2.23	0.66, 7.54	.20	1.17	0.55, 2.52	.68	1.62	0.69, 3.78	.26	2.02	0.85, 4.79	.11
C3 "All IC impaired"	5.73	1.32, 24.7	.02	1.58	0.51, 4.90	.43	3.89	1.70, 8.93	.001	2.43	0.98, 6.02	.055
C4 "Psy+Vit+Vis"	3.99	1.01, 15.7	.048	1.56	0.63, 3.87	.33	1.92	0.71, 5.23	.20	0.69	0.17, 2.82	.60

^aAll analyses were two-sided logit models adjusted for age, sex, and self-reported weight.

Figure Legend/Captions

Figure 1. Age-and-sex adjusted conditional probabilities for the transition of IC clusters between baseline and follow-up.

Figure 1 Legend.

Study sample with two consecutive professional screenings $n = 1,190$. Numbers in colored rectangles are the transition probabilities. The most likely transition is marked with a bold arrow. Transition probabilities were obtained from an age- and sex-adjusted multinomial logistic model. For clarity, transition probabilities $< 20\%$ are not shown.

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