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Screening for intrinsic capacity impairments as markers of increased risk of frailty and disability in the context of integrated care for older people: Secondary analysis of MAPT

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Abstract

Aim: This longitudinal secondary analysis of the Multidomain Alzheimer Preventive Trial (MAPT) aimed to test whether the Integrated Care for Older People (ICOPE) Step 1 screening tool is able to identify people at risk of developing frailty and disability in basic (ADL) and instrumental (IADL) activities of daily living among community-dwelling older adults.

Participants and setting: Seven hundred and fifty-nine (n=759) non-demented participants of the MAPT aged 70-89 years were assessed in memory clinics in France between 2008 and 2013.

Methods: We measured six intrinsic capacity (IC) impairments, adapted from the ICOPE screening tool. We used Cox models to estimate the adjusted hazard ratios of incident frailty and IADL/ADL disability. Incident frailty was defined by Fried's phenotype, and incident disability was measured according to Lawton and Katz for IADLs and ADLs. **Results:** Limited mobility (HR= 2.97, 95%CI= 1.85-4.76), depressive symptoms (HR= 2.07, 95%CI= 1.03-4.19), and visual impairment (HR= 1.70, 95%CI 1.01-2.86) were associated with a higher incidence of frailty over 5 years. Each additional IC condition demonstrated a positive association with a higher risk of incident frailty, IADL, ADL disability, with risk increased by 47%, 27%, and 23% over 5 years, respectively. **Conclusion:** Screening for IC impairments identifies older adults at higher risk of incident frailty and incident IADL/ADL disability. It is relevant to screen for these impairments together because the risk of frailty and disability increases with each additional one.

ClinicalTrials.gov identifier: NCT00672685

Keywords

Functional performance, intrinsic capacity, frailty, disability, screening

1. Background

The Integrated Care for Older People (ICOPE) approach, launched by the World Health Organisation (WHO), provides a function and person-centered model to adapt health systems for population aging. The main goal of the ICOPE strategy is to maintain optimal functional levels in older adults and avoid or delay care dependency as much as possible[1]. Intrinsic capacity (IC), a crucial element to promote healthy aging, is the composite of an individual's physical and mental capacities. To identify people at risk for care dependency, the ICOPE health care pathway starts by screening for impairments in five IC domains (ICOPE Step 1): cognitive decline, limited mobility, malnutrition, visual impairment, hearing loss, and depressive symptoms [1–3]. These IC impairments do not represent clinical diagnoses, rather, they may be attributable to underlying health conditions. The screening results will trigger the next steps in the ICOPE healthcare pathway (i.e., in-depth assessments, looking for the causes of IC decline, establishing the care plan). The added value of this screening is its balance between comprehensiveness and feasibility. It can be applied in a few minutes by health workers, trained community agents, or, in some cases, by the older adults themselves. [1,4]

The ICOPE approach and the IC framework are supposed to identify people at-risk for care dependency. To the best of our knowledge, there are no reports of a screening tool for IC

impairments to detect people at higher risk of events in the disabling cascade (frailty/disability). [2,3,5]. The ICOPE screening is easy-to-use (i.e., composed of a few simple questions and one test) and not time-consuming. The ICOPE screening tool's main goal is to identify IC impairments, and to act as a trigger for more comprehensive assessment where IC losses are identified. It is essential to investigate if the ICOPE screening can detect people at high risk for clinically meaningful adverse health events[4,6]. The ICOPE screening tool tested in this study and the ICOPE clinical pathways are expected to help the health systems transition to a function- and person-centered care approach.

Therefore, our study aims to evaluate the ICOPE screening tool's ability to identify people at risk of developing frailty and disability in basic (ADL) and instrumental (IADL) activities of daily living among community-dwelling older adults.

2. Methods

This study uses longitudinal data of the Multidomain Alzheimer Preventive Trial (MAPT). The detailed methodology of MAPT has been described elsewhere[7,8]. In summary, MAPT was a randomized controlled trial (RCT) testing the effect of a multidomain intervention (nutritional counseling, physical exercise, and cognitive stimulation) with and without supplementation of omega-3 polyunsaturated fatty acids (PUFA) versus usual care on the prevention of cognitive decline among community-dwelling adults aged 70 years and older recruited in memory clinics in France. The Ethical Committee (CPP SOOM II) based in Toulouse approved the study (ClinicalTrials.gov identifier: NCT00672685). All participants signed a consent form before study assessments. After a three-year-long RTC period, MAPT continued as an observational study for an additional 2 years.

2.1 Participants

MAPT inclusion criteria were meeting at least one of a) spontaneous memory complaints expressed to their physician, b) limitation in one instrumental activity of daily living (IADL), or c) slow gait speed (≤ 0.8 m/s). Exclusion criteria comprised: a) participants with a Mini-Mental State Examination (MMSE) score < 24 , b) diagnosis of dementia, c) limitation for one or more basic activities of daily living (ADLs), and d) those taking PUFA supplements at baseline.

Of the 1,679 participants enrolled, 759 had complete information for the IC domains since they received a preventive consultation as part of the multidomain intervention. A physician assessed their hearing and vision. The differences in sample size across the three tested outcomes are accounted for in Fig S1.

2.2 IC domains assessment – Step 1 (screening)

Using a retrospective approach, we operationalized an IC screening tool similar to the ICOPE Step 1, based on the detection of IC impairments. We follow the exact definition of the ICOPE Step 1 tool [1] for three domains: cognition (time and space orientation plus word recall), locomotion (perform five chair rises within 14 seconds), and vitality/nutrition (self-reported weight loss or appetite loss). Due to data availability, we had to adapt the operationalization of *vision*: answering "yes" to any of: "Even if wearing glasses, do you have visual problems to a) distinguish the faces of people in the same room? b) move indoors/outdoors? c) other activities (reading a paper, watching television)?"; *hearing*: answering "sometimes" or "yes" to the question "Do you have difficulty hearing when someone speaks in a whisper?" (HHSE-S[9,10]); *psychological function*: answering "yes" to the item 2 of Geriatric Depression Scale (GDS-15) "Have you dropped many of your activities and interests?", or responding "no" to the item 7 of

the GDS-15 "Do you feel happy most of the time?" [11]. Three experts (one geriatrician, one general practitioner, and one researcher in clinical gerontology) judged these GDS items as the closest ones to the ICOPE screening [1]. The resulting set of items was called "MAPT Step 1" (Supplementary Table 1).

Besides, we calculated a "total score" by adding the number of IC impairments found by the MAPT Step 1 (score range 0-6, higher is worst) (Table 1).

2.3 Incident frailty

Participants were assessed for frailty at baseline and 6, 12, 24, 36, 48, and 60 months of follow-up. We used the phenotype criteria of frailty proposed by L. Fried and cols.[12]: reported unintentional weight loss, slowness, low physical activity, weakness, and exhaustion. Participants who met ≥ 3 criteria were classified as frail, with one or two criteria, pre-frail, and otherwise, robust. We excluded participants frail at baseline.

2.4 Incident disability

Disability for IADL was assessed according to Lawton[13] (baseline, 36, 48, and 60 months from follow-up). IADLs included were: use the phone, do the grocery, cooking, housekeeping, laundry, use of means of transportation, handle own medication and manage finances. Incident disability for IADLs was defined if the participant had an increase in the number of IADLs during follow-up, compared to the baseline status. We defined incident IADL disability whenever participants developed disability for a new IADL, regardless the baseline number of IADLs affected. ADL disability was assessed according to Katz[14] at baseline and 48 and 60 months of follow-up. ADLs included were: showering, getting dressed, using the toilet, displacing inside a

room, continence, and self-feeding. Incident ADL disability was registered if the participant reported needing help or being care dependant for at least one of the ADLs.

2.5 Statistical Analysis

Besides descriptive statistics, we used Cox's proportional hazards models for non-recurrent events to estimate the hazard ratios for frailty, IADL, and ADL disability incidence. For each outcome, we ran one separate model testing each condition of interest. (Model 1), another mutually adjusted model including the six IC impairments simultaneously to detect which were the strongest predictors (Model 2), and one model with the "total score" to see if the risk increased with each additional condition (Model 3). We adjusted the frailty models for pre-frail/robust baseline status and the IADL models for baseline IADL to account for different baseline risks. All models were adjusted for age, sex, level of education, MAPT group (multidomain intervention, multidomain intervention + omega 3 supplementation), and multimorbidity (defined as self-reporting 2 or more of COPD/asthma, stroke, active cancer, ischemic heart disease, diabetes, hypertension or heart failure). The proportionality assumption was confirmed by plotting the cumulative risk function against the analysis time and verifying that the predictor-time interactions were not statistically significant at $\alpha=0.05$. We estimated the predictive ability of models 2 and 3 using Harrell's C ($C > 0.5$ and close to 1.0 indicate higher discrimination[15]). We compared the characteristics of the participants lost to follow-up, looking for any differences that could impact our modeling of the outcomes (t-test or c2 as appropriate). Receiver operator characteristic (ROC) analyses were performed *vis à vis* the three outcomes of interest. Data were analyzed using STATA 14®.

3. Results

The baseline characteristics and sample size are described in Table 1 and Supplementary Figure 1, respectively. Briefly, the baseline frailty status of participants with complete data on frailty and IC domains was: robust 56.5% (n=409), pre-frail 40.3% (n= 292) and frail 3.2% (n=23).

On average, participants lost to follow-up had a significantly higher number of deficits in IC domains, were older, and had a worst physical performance (chair-rise test) than the ones retained (data not shown). However, obtaining the adjusted Kaplan- Meier curves helped us rule out the impact of informative censoring on our results [16] (Figures 1 and S2). We decided not to perform a competing risk approach because we observed a mean follow-up period of 4.8 years and low cumulative mortality (n=14, 1.8% of the study sample).

In model 1, we found an association of limited mobility, depressive symptoms, and visual impairment with an increased risk of frailty. Model 2 showed that limited mobility imposed a three-fold risk, depressive symptoms a two-fold risk, and visual impairment a 70% higher risk of incident frailty over five years, after adjusting for covariates and the other five IC impairments. Each additional condition associated with IC declines increased the risk of becoming frail by 47% (model 3).

Each additional condition increased the risk of incident IADL disability in the next five years by 27% (model 3). Limited mobility and depressive symptoms (marginally, $p=0.055$) increased the risk of incident ADL disability (model 1). Each additional IC condition increased the risk of becoming disabled for ADLs by 23% (Table 2). All models showed a good predictive ability based on the Harrell C statistic ($0.70 < C < 0.83$) [15]. Cut points for the ICOPE sum score were ≥ 3 for incident frailty and incident ADL disability and ≥ 2 for incident IADL, according to Youden's index [17]. (Supplementary Table 3).

4. Discussion

Our adapted version of the ICOPE screening tool (MAPT Step 1) demonstrated a noteworthy ability to identify older adults at higher risk of incident frailty and disability at a five-year follow-up among the MAPT study participants. Participants screened with limited mobility, depressive symptoms, or visual impairment had a higher risk of developing frailty. Limited mobility and depressive symptoms (to a lesser extent) were also associated with incident ADL disability. Furthermore, each additional domain impairment identified by the screening tool increased the risk of incident frailty by 47% and of incident disability and by 27% (IADL) and 23% (ADL)

The studies reporting the association between IC domains and functional outcomes have not used a screening tool [3,5]. Our findings suggest that using a screening tool to detect impairments in IC might help the primary care providers to identify older adults at higher risk of frailty and disability, for example, those who had limited mobility, visual impairment, and depressive symptoms. Thus, primary care providers can follow at-risk individuals more closely as part of an integrated care plan. Adopting a pro-active screening approach might foster early interventions, even if the older adults do not expressly complain about impairment in the IC domains.

Chaudhry and cols. showed that an increasing number of geriatric impairments (corresponding to some of the IC domains) was associated with a higher risk of ADL and mobility disability [18]. Also, locomotion and psychological domains play a role in the multisystem dysregulation underlying frailty and disability [19–21]. Low physical performance leads to mobility difficulty and disability [22–24]. Mobility impairments can cause or result from low levels of physical activity and sarcopenia, which are hallmarks of frailty[20,25,26].

Recently, Swenor and cols. have reported that older adults with objectively measured vision impairment are more likely to progress to frailty than their counterparts due to its direct and indirect effects on physical functioning[27]. On the other hand, exhaustion might explain the overlapping of the psychological domain and the disability cascade. Exhaustion is an indicator of poor endurance within the frailty phenotype [12]. In parallel, studies recognize it as a depressive symptom in the psychological domain [12,28].

Cognitive decline, malnutrition, and hearing loss were not significant predictors of frailty or disability in our study. This does not mean these IC domains are not involved in the disabling cascade. Potential explanations are the potential effects of cognitive training in the MAPT study, the exclusion of individuals with a MMSE <24 at baseline and prioritizing sensitivity over specificity to measure the IC domains.

For example, nutritional status is core for preserving function[29] given the influence of diet in functionality, possibly mediated by the gut microbiota[30]. A very low prevalence of malnutrition among MAPT participants (6.6%)[31] might hinder the detection of a significant association of malnutrition with our outcomes of interest. On the other hand, hearing and vision provide peripheral inputs to the central nervous system to allow interaction with the environment. Screening for vision and hearing impairments is helpful because there are quick and relatively cheap interventions to improve the sensory domain, resulting in a delay of cognitive impairment[32,33].

Our study has several strengths: this is the first study to use a screening tool adapted from the ICOPE Step 1[1] to identify older adults at higher risk of functional decline; longitudinal design with a reasonably long follow-up period; the use of clinical outcomes relevant from the geriatric standpoint. Limitations in our study include the following: reduction of the sample size due to

incomplete data on IC domains and losses to follow-up; this is a secondary analysis using data from a clinical trial, in which all participants received advice on exercise and nutrition and cognitive training[34] however, we adjusted for the intervention group in the multivariable analysis.

4.1 Conclusion

Screening for IC declines using a simple-to-use tool like the ICOPE Step 1 is useful to identify community-dwelling older adults at higher risk of functional decline (incident frailty and incident IADL/ ADL disability) even after adjustments for comorbidity and personal characteristics. Limited mobility, vision impairment, and depressive symptoms were the strongest predictors of adverse health outcomes. Each additional decline in the IC screening significantly increased the risk of adverse functional outcomes. Therefore, screening for IC impairments is a time-effective strategy with important clinical implications for identifying older adults at higher risk of adverse health outcomes who would benefit from a comprehensive assessment.

Contributors

Emmanuel González-Bautista contributed to conception and design, analysis and interpretation of data, statistics and manuscript writing.

Philippe de Souto Barreto contributed to conception and design, analysis and interpretation of data, statistics and manuscript writing.

Sandrine Andrieu contributed to conception and design, analysis and interpretation of data.

Yves Rolland contributed to conception and design, analysis and interpretation of data.

Bruno Vellas contributed to conception and design, analysis and interpretation of data.
All authors provided valuable intellectual input, reviewed the manuscript and approved the version to be published.

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Conflict of interest

The authors declare that they have no conflict of interest.

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Ethical approval

The Ethical Committee (CPP SOOM II) based in Toulouse approved the MAPT study. All participants signed a consent form before study assessments.

Provenance and peer review

This article was not commissioned and was externally peer reviewed.

Research data (data sharing and collaboration)

There are no linked research data sets for this paper. Data will be made available on request.

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Table 1. Description of the population according to incident frailty, IADL and ADL disability in MAPT participants over 5 years.

n(%) or mean (SD)	Total		Incident frailty				Incident IADL disability				Incident ADL disability			
	n=759		No=591		Yes=83		No=524 ^a		Yes=91		No=398		Yes=70	
Age	75.2	(4.3)	74.8	(4.1)	78	(4.6)*	74.7	(4.0)	77.2	(4.9)*	74.3	(4.0)	76.2	(4.2)*
Sex (female)	483	(63.6)	372	(87.5)	53	(12.5)	342	(87.2)	50	(12.8)	251	(81.5)	57	(18.5)*
Education														
Less than primary	31	(4.1)	20	(3.4)	8	(9.6)*	23	(4.4)	2	(2.2)	14	(3.6)	4	(5.8)
Primary	122	(16.2)	85	(14.5)	17	(20.5)	72	(13.9)	22	(24.4)	52	(13.2)	8	(11.6)
Secondary	271	(36.1)	219	(37.4)	21	(25.3)	194	(37.4)	30	(33.3)	141	(35.9)	27	(39.1)
High-school	111	(14.8)	88	(15.0)	12	(14.5)	69	(13.3)	15	(16.7)	54	(13.7)	12	(17.4)
Graduate or higher	216	(28.8)	174	(29.7)	25	(30.1)	161	(31.0)	21	(23.3)	132	(33.6)	18	(26.1)
Multimorbidity^c (yes)	128	(16.9)	90	(15.2)	20	(24.1)*	75	(14.3)	29	(31.9)*	57	(14.3)	14	(20.0)
Frailty														
Robust	409	(56.5)	373	(94.9)	20	(5.1)*	312	(92.0)	27	(8.0)*	242	(89.6)	28	(10.4)*
Pre-frail	292	(40.3)	218	(77.6)	63	(22.4)	178	(76.7)	54	(23.3)	129	(78.2)	36	(21.8)
Frail	23	(3.2)	^b	^b	^b	^b	9	(52.9)	8	(47.1)	9	(69.2)	4	(30.8)
Intrinsic capacity impairments														
Cognitive decline	396	(52.2)	301	(86.0)	49	(14.0)	257	(82.1)	56	(17.9)*	201	(87.0)	30	(13.0)
Limited mobility	146	(20.2)	84	(71.2)	34	(28.8)*	82	(75.9)	26	(24.1)*	59	(74.7)	20	(25.3)*
Malnutrition	50	(6.6)	35	(85.4)	6	(14.6)	32	(82.1)	7	(17.9)	23	(79.3)	6	(20.7)
Visual impairment	137	(18.1)	90	(77.6)	26	(22.4)*	79	(79.0)	21	(21.0)	57	(79.2)	15	(20.8)
Hearing loss	426	(56.2)	332	(87.4)	48	(12.6)	282	(82.5)	60	(17.5)*	218	(84.5)	40	(15.5)
Depressive symptoms	296	(39.0)	216	(83.1)	44	(16.9)*	183	(81.0)	43	(19.0)*	129	(81.1)	30	(18.9)
IC impairment sum score														
0	81	(10.7)	69	(93.2)	5	(6.8)*	67	(93.1)	5	(6.9)*	50	(86.2)	8	(13.8)*
1	210	(27.7)	179	(93.2)	13	(6.8)	168	(92.8)	13	(7.2)	124	(85.5)	21	(14.5)
2	248	(32.7)	199	(90.0)	22	(10.0)	167	(83.9)	32	(16.1)	136	(91.3)	13	(8.7)
3	149	(19.6)	103	(81.1)	24	(18.9)	80	(72.7)	30	(27.3)	63	(76.8)	19	(23.2)
4	58	(7.6)	34	(66.7)	17	(33.3)	37	(80.4)	9	(19.6)	23	(74.2)	8	(25.8)
5	12	(1.6)	6	(75.0)	2	(25.0)	5	(71.4)	2	(28.6)	2	(66.7)	1	(33.3)
6	1	(0.1)	1	(100.0)	0	(0.0)	524	(85.2)	91	(14.8)	398	(85.0)	70	(15.0)

Abbreviations: MAPT= Multidomain Alzheimer Preventive Trial; IADLs= instrumental activities of daily living; ADL= basic activities of daily living

^a We included the participants with any number of IADL at baseline for consistency with the population in the models

^b Excluded because they already had the event of interest at baseline

^c Self-reporting 2 or more of COPD/asthma, stroke, active cancer, ischemic heart disease, diabetes, hypertension, or heart failure

* Bivariate t-test for continuous or χ^2 for categorical variables, p-value <0.05

Table 2. Adjusted hazard ratios for the Cox's models linking intrinsic capacity declines and incident frailty and Disability during a five years follow-up among MAPT participants.

	Hazard ratio	CI 95%	p value	Hazard ratio	CI 95%	p value
Frailty (n=674)			Model 1 ^a	Model 2 ^a		
Depressive symptoms	1.88	1.20 - 2.92	0.005	2.07	(1.03 - 4.19)	0.042
Cognitive decline	1.12	0.71 - 1.76	0.620	1.38	(0.70 - 2.74)	0.345
Limited mobility	2.80	1.76 - 4.44	<0.001	2.97	(1.85 - 4.74)	0.000
Malnutrition	1.45	0.63 - 3.35	0.365	0.97	(0.41 - 2.32)	0.954
Visual impairment	1.95	1.20 - 3.17	0.007	1.70	(1.01 - 2.86)	0.044
Hearing loss	0.92	0.58 - 1.43	0.701	0.81	(0.52 - 1.31)	0.430
			Model 3			
Total IC score	1.47	(1.22 - 1.78)	0.000			
IADL disability (n=615)			Model 1	Model 2 ^b		
Depressive symptoms	1.47	(0.96 - 2.23)	0.071	1.47	(0.94 - 2.27)	0.089
Cognitive decline	1.19	(0.76 - 1.85)	0.431	1.25	(0.78 - 2.00)	0.347
Limited mobility	1.39	(0.85 - 2.30)	0.193	1.42	(0.86 - 2.35)	0.169
Malnutrition	1.05	(0.49 - 2.29)	0.888	0.75	(0.30 - 1.86)	0.533
Visual impairment	1.45	(0.88 - 2.38)	0.140	1.25	(0.73 - 2.12)	0.408
Hearing loss	1.30	(0.83 - 2.02)	0.250	1.25	(0.78 - 1.98)	0.356
			Model 3			
Total IC score	1.27	(1.06 - 1.53)	0.010			
ADL disability (n= 468)			Model 1	Model 2		
Depressive symptoms	1.60	(0.98 - 2.53)	0.055	1.60	(0.98 - 2.64)	0.060
Cognitive decline	0.73	(0.45 - 1.18)	0.199	0.72	(0.44 - 1.18)	0.202
Limited mobility	1.92	(1.12 - 3.30)	0.021	1.82	(1.06 - 3.15)	0.029
Malnutrition	1.36	(0.59 - 3.17)	0.464	1.22	(0.52 - 2.91)	0.643
Visual impairment	1.49	(0.84 - 2.64)	0.177	1.40	(0.78 - 2.52)	0.301
Hearing loss	1.14	(0.70 - 1.84)	0.597	1.14	(0.70 - 1.87)	0.595
			Model 3			
Total IC score	1.23	(1.00 - 1.52)	0.051			

All models were adjusted for age, sex, education, MAPT group and multimorbidity. Model 1 shows the HR for the intrinsic capacity declines assessed separately. Model 2 shows HR for intrinsic capacity declines mutually-adjusted. Model 3 shows the HR according to the IC sum score.

Abbreviations: CI= confidence interval; MAPT= Multidomain Alzheimer Preventive Trial; MI=multidomain intervention; IADLs= instrumental activities of daily living; ADL= basic activities of daily living.

^aAdjusted for baseline frailty status.

^bAdjusted for baseline IADL disability.

Figure1. Kaplan-Meier failure function for incident frailty in each of the intrinsic capacity domains, adjusted for standardized baseline covariates in MAPT participants during a five-year follow-up.

Failure functions for incident frailty were estimated adjusting for standardized baseline covariates: age, sex, education and MAPT group. The y axis represents the Kaplan-Meier failure function for the outcome in each measured time point.

Supplementary Table 1. Comparison of the operationalization of IC impairments between the ICOPE handbook and the definitions applied in MAPT study.

ICOPE handbook[1]		MAPT study	
Item	Condition	Item	Condition
Cognitive decline			
Orientation in time and space: What is the full date today? Where are you now (home, clinic, etc.)?	Wrong to either question or does not know	The same as ICOPE ^a	
Remember three words. Recalls the three words?	Cannot recall all the three words	The same as ICOPE ^a	
Limited mobility			
Chair rise test: Did the person complete five chair rises within 14 seconds?	No	The same as ICOPE	
Malnutrition			
Weight loss: have you unintentionally lost more than 3 kg over the last three months?	Yes	The same as ICOPE	
Appetite loss: have you experienced a loss of appetite?	Yes	The same as ICOPE	
Visual impairment			
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)?	Yes	Even wearing glasses, do you have visual problems to a) distinguish the faces of people in the same room? b) move indoors/outdoors? c) other activities (reading a paper, watching television)	Yes to any question
Hearing loss			
Hears whispers (whisper test) or screening audiometry result is 35dB or less or passes the automated app-based digits-in-noise test	Fail	"Do you have difficulty hearing when someone speaks in a whisper?" (item 3 of HHIE-S)	If "sometimes" or "yes" ^b
Depressive symptoms			
Over the past two weeks, have you been bothered by a) feeling down, depressed or hopeless?	Yes	Do you feel happy most of the time? (item 7 of GDS-15)	No
b) little interest or pleasure in doing things?	Yes	Have you dropped many of your activities and interests? (item 2 of the GDS-15)	Yes

^aParticipants were explicitly asked for each of the items in the time and spatial orientation, and not only an open-ended question. The participant was recorded as with cognitive decline if he/she was wrong to tell the date (number and name of the day, month, year), or wrong to tell the name of the hospital, the level of the building, department and region.

^b We used item number 3 of the HHIE-S because of its similarity with the whisper test.

Supplementary Table 2. Frailty criteria and cut points used in the MAPT study in accordance with Fried and cols.[12]

Participant scores 1 point if:

Weight loss	self-reported loss of >4.5 kg involuntarily during the previous year			
Fatigue	answer to the following questions was "often (3-4 days)" or " most part of the time": During the previous week, how many days did I feel like a) everything I did was an effort b) I could not get going			
Low grip strength	Men		Women	
	IMC (kg/m ²)	Force (kg)	IMC (kg/m ²)	Force (kg)
	IMC ≤ 24	≤29	IMC ≤ 23	≤17
	24.1 ≤ IMC ≤ 26	≤30	23.1 ≤ IMC ≤ 26	≤17.3
	26.1 ≤ IMC ≤ 28	≤30	26.1 ≤ IMC ≤ 29	≤18
	IMC >28	≤32	IMC >29	≤21
Slow gait speed	Men		Women	
	height (cm)	speed	height (cm)	speed
	≤ 173	<0.65 m/s	≤ 159	<0.65 m/s
	> 173	<0.76 m/s	> 159	<0.76 m/s
Low physical activity	kcal= [time (min) x frequency during the last 2 weeks / 2] x coefficient of the activity			
	Men		Women	
	< 383 kcal		< 270 kcal	

0 frailty criteria = robust

1-2 frailty criteria = pre-frail

3-5 frailty criteria = frail

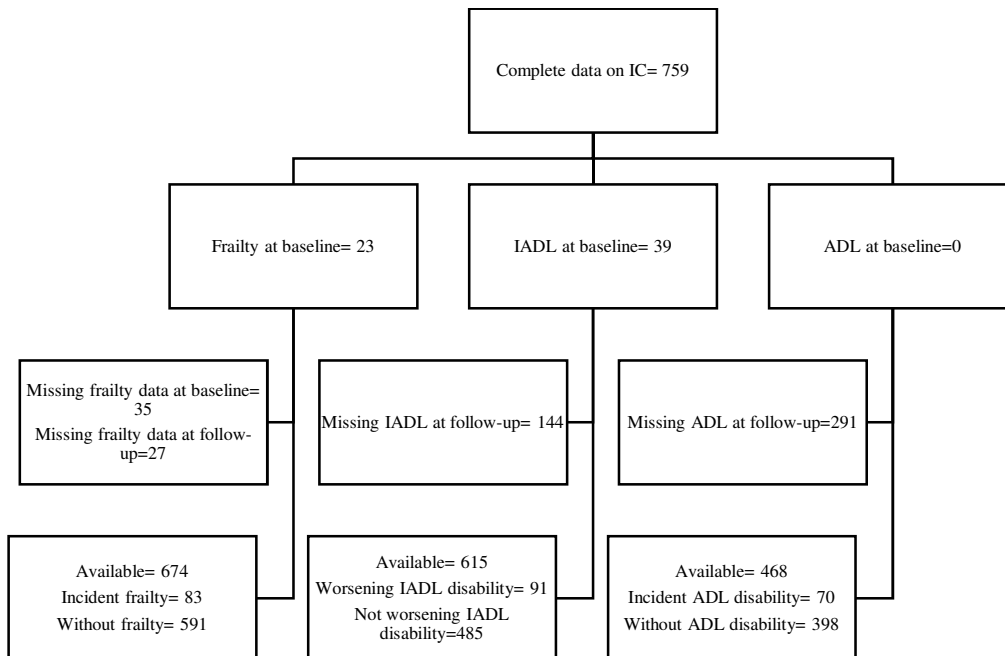
Supplementary table 3. Cut points for the ICOPE Step 1 sum score obtained by the Youden index and their parameters for physical function outcomes

Incident Outcome	Cut-off	Sens	95% CI ^a	Spec	95% CI ^a	AUC	95% CI ^a	HR ^b	95% CI ^b
Frailty	≥3	0.52	(0.37 - 0.67)	0.76	(0.62 - 0.89)	0.67	(0.60 - 0.73)	3.0	1.90 4.60
IADL	≥2	0.8	(0.50 - 1.00)	0.45	(0.15 - 0.75)	0.65	(0.60 - 0.71)	2.5	1.46 4.14
ADL	≥3	0.4	(0.26 - 0.54)	0.78	(0.61 - 0.95)	0.56	(0.48 - 0.64)	2.0	1.22 3.32

^aObtained by 1,000 bootstrap repetitions

^bCox hazard ratio for those who are at or above the cut point adjusted by age, sex, education, MAPT group and multimorbidity

Supplementary Figure S1. Flow diagram of the study sample



Supplementary Figure S2. Kaplan-Meier failure function for incident IADL and ADL disability in each of the intrinsic capacity domains, adjusted for standardized baseline covariates in MAPT participants during a five-year follow-up.

Failure functions for incident frailty were estimated adjusting for standardized baseline covariates: age, sex, education and MAPT group. The y axis represents the Kaplan-Meier failure function for the outcome in each measured time point.

