SPECIAL ARTICLE

IMPLEMENTATION OF THE INTEGRATED CARE OF OLDER PEOPLE (ICOPE) APP AND ICOPE MONITOR IN PRIMARY CARE: A STUDY PROTOCOL

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Abstract: *Introduction:* The World Health Organization (WHO) has recently launched the term "intrinsic capacity", defined as "the composite of all the physical and mental capacities of an individual". Intrinsic capacity has a positive value towards healthy aging, and is constructed by five domains: cognition, vitality/nutrition, sensory, psychology, and mobility. ICOPE App and ICOPE Monitor are applications for the assessment (screening) of intrinsic capacity. *Hypothesis:* Intrinsic capacity assessed by the ICOPE Apps at baseline could be associated with the incidence of frailty, functional decline, and health outcomes during 1-year follow-up. *Objectives:* To assess the association between intrinsic capacity measured by the ICOPE Apps at baseline and the incidence of frailty in community-dwelling older adults during 1-year follow-up. Secondarily, to assess the association of intrinsic capacity and functional decline, mortality, pre-frailty, falls, institutionalization, and quality of life. *Methods:* Protocol for a cohort study of community-dwelling adults ≥65-year-old, with no other exclusion criteria than the inability to use the Apps or communicate by telephone/video-call for any reason (cognitive or limited access to telephone/video-call) OR being considered frail at baseline (defined as having a Rockwood's clinical frailty scale, CFS score ≥4). Intrinsic capacity measured by the ICOPE Apps and CFS will be assessed at baseline, 4-, 8- and 12-month follow-up by telephone/video-call. Assuming a prevalence of frailty of 10.7%, and incidence of 13% (alpha-risk=0.05), 400 participants at 12-month end-point (relative precision=0.10) and 600 participants at baseline will be required. *Results:* Associations among the decrease in intrinsic capacity and higher risk of frailty, functional decline, and health adverse outcomes during 1-year follow-up are expected. *Conclusions:* ICOPE Apps might identify individuals at higher risk of frailty, functional decline, and health adverse outcomes. The implementation of the ICOPE Apps into clinical practice might help to deliver efficient person-centered care-plans, and benefit the healthcare systems.

Key words: ICOPE; Intrinsic capacity; App; Functional decline; Older people; Study protocol.

Introduction

The World Health Organization aims at promoting initiatives focused on the preservation of individuals' physical and mental capacities to achieve older ages in a good health status (healthy aging, defined as "the process of developing and maintaining the functional ability that enables well-being") (1). Intrinsic capacity is a new term launched in the WHO in the plan of action 2016-2020 (1). The operational definition of "intrinsic capacity" is "the composite of all the physical and mental capacities of an individual" and is constructed by 5 domains: locomotion, vitality, sensory (vision and hearing), cognition, and psychological domain (2). Intrinsic capacity has a positive value, is focused on function, and switches the viewpoint from a negative paradigm of ageing (diseases, disability, frailty, etc.) towards the positive focus of a "healthy aging" (2,3).

The Integrated Care for Older People (ICOPE) program was launched by the WHO n. Global strategy and action plan on ageing and health in 2016 (4) and is focused on individuals' comprehensive assessment and potential interventions on the 5 domains of intrinsic capacity (5, 6). In a second step, the strategy the WHO is aimed on providing evidence about trajectories of life (Normograms for Healthy Ageing Standards). The WHO plan of action scheduled for 2020-2030 would provide the continuity of this line of research (https://www.who.int/ageing/en/). The WHO guidelines on community-level interventions in integrated care have been recently launched, aimed at "Redesigning care for older people to preserve physical and mental capacity", and involve the comprehensive assessment of the domains of intrinsic capacity (5, 6).

Two new technologies for the assessment of intrinsic capacity are available and capable to screen for individual's intrinsic capacity (7, 8): The ICOPE application (App) has

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been developed by WHO and the ICOPE Monitor, has been developed as part of the INSPIRE program, an initiative from the Gérontopôle of Toulouse, which is a WHO Collaborating Center, in collaboration with the WHO and several partners from Toulouse (7, 8). The two Apps are already available free-of-charge in Apple or Android Store.

Frailty, defined as a "syndrome characterized by a clinical state in which there is an increase in an individual's vulnerability for developing an increased dependency and/or mortality when exposed to a stressor" (9), is also a construct of several domains (10, 11). Despite frailty is a different construct, it would be expected that a decrease in intrinsic capacity, measured by the Apps is associated to the occurrence of frailty and functional decline, but these associations remain unexplored (3).

We hypothesize that intrinsic capacity, assessed by the ICOPE App and ICOPE Monitor at baseline, could identify individuals at higher risk of developing frailty, functional decline, and health adverse outcomes during 1-year follow-up. If these hypotheses are confirmed, ICOPE Apps could be incorporated into clinical practice in community-dwelling older people.

Objectives: Our primary objective is to assess the relationship between intrinsic capacity assessed with the ICOPE Apps (ICOPE App and ICOPE Monitor) at baseline and the incidence of frailty in community-dwelling older adults during 1-year follow up. Secondarily, to assess the association between intrinsic capacity measured by the ICOPE App and the ICOPE Monitor at baseline and the risk of functional decline, mortality, incidence of pre-frailty, falls, institutionalization, and loss of quality of life in this population during 1-year follow-up will be assessed.

Methods

Design

Protocol for a prospective cohort study, designed to determine the incidence of frailty in community-dwelling older people during 1-year follow-up. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement (12) will be followed. Subjects who volunteer and meet eligibility criteria will be consecutively included.

Settings

The study will be conducted in Liège, a city located in the French-speaking region of Belgium. Volunteers will be recruited from 1) the Geriatric Department of the university hospital, 2) Outpatient clinics of primary care, and 3) Local press, television, and radio advertisements. In the first two options, the clinicians in the Geriatrics or primary care department that collaborate with the study, would identify a potential candidate and send an electronic mail with contact details to the personal from the study. In the third option,

volunteers will receive instructions to proactively contact by telephone or electronic mail (e-mail) with the personal from the study. After receiving the e-mails, a telephone or video-call between the volunteer and the personal from the study will be scheduled in a maximum of 1 week. During the first interview, subjects will be assessed for eligibility, receive detailed information about the study, and sign electronically the informed consent by drawing their own signature in the screen of the mobile and forwarding it as an image. A printed copy of the informed consent with the signature in paper will be sent to volunteers' homes by post mail afterward. Technical assistance in downloading the two Apps, signing the informed consent, the baseline assessment, and schedule next follow-up will be given during the first interview. The 4-, 8-, and 12-month follow-up will be conducted in a similar way. The Geriatric and primary care Department count with the technical devices and facilities to conduct the proposed test, and the Apps are free-of-charge (Apple /Android Store https://www.youtube.com/watch?v=gLva4ReV9KA). Data will be analysed at the Research Unit in Biostatistics, Public Health Department, University of Liege, Belgium. Table 1 summarizes study settings, variables, and timeline of the study.

Population

Prospective cohort study of community-dwelling adults ≥65-year-old living at home, with no other exclusion criteria than the inability to use the ICOPE Apps or communicate by telephone/video-call for any reason (cognitive or limited access to technologies like telephone/video-call) OR being considered frail at baseline (defined as having a Rockwood's clinical frailty scale, CFS score ≥4).

Intrinsic capacity assessment: Will be administered with the two Apps, the ICOPE App and the ICOPE Monitor.

ICOPE App: The screening by ICOPE App includes polar questions (yes/no) about the 5 domains of intrinsic capacity. Two results are possible: positive (probable decrease in intrinsic capacity) or negative (intrinsic capacity not decreased), as a total binary result of the 5 domains together. The App includes possibility to record the summary of the screening, download it in pdf, or send it by mail.

ICOPE Monitor: For the moment, ICOPE Monitor is equipped with ICOPE Step 1 (i.e. screening tool). ICOPE Monitor includes identification and informed consent of both the professional and the participant, detailed intrinsic capacity assessment of the 5 domains and reports the results obtained in each one of the 5 domains separately afterwards. The results obtained in the 5 domains are provided as a checklist: two results are possible for each one of the 5 domains: "right" or "wrong" in each domain. Updated advice for each domain and a link for further information is also provided. The App automatically schedules the date for the next 4-month follow-up and sends the informed consent by mail to the volunteer.

The results in the two Apps provide different approaches to IC. First, a global binary decision (IC decline or not) is directly

Table 1
Variables, study settings, and timeline

	Baseline		4-month follow-up	8-month follow-up	12-month follow-up (end-point)
Study settings	Geriatrics Department, General practitioners' outpatient clinics	Telephone/video-call assessment	Telephone/video-call assessment	Telephone/video-call assessment	Telephone/video-call assessment [a]
OUTCOME VARIABLES					
Primary outcome: Incidence of frailty by Rockwood's Clinical Frailty Scale (CFS)	-	x	x	x	x
Secondary outcome measures:		x	x	x	x
- Functional decline (Chair Stand Test OR loss of ≥20 points of Barthel index)	-	x	x	x	x
- Death (date)	-	x	x	x	x
- Pre-frailty in CFS	-	x	x	x	x
- Falls (number and date)	-	x	x	x	x
- Institutionalization (date)	-	x	x	x	x
- Quality of life (EuroQol)	-	x	x	x	x
Intrinsic capacity assessment (screening)					
ICOPE App	-	x	x	x	x
ICOPE Monitor	-	x	x	x	x
Functional status					
Instrumental activities of daily living (Lawton index)	-	x	x	x	x
Basic activities of daily living (Barthel index)	-	x	x	x	x
Clinical and demographic variables	-	x	x	x	x
Technological, Economical, Legal, Operational, Schedule (TELOS)-feasibility score	-	x	-	-	x
Identification of possible candidates, volunteers' information	x	-	-	-	-
Volunteers' information, sign electronically the informed consent, and consent form collection	-	x	-	-	-

a. Statistical analysis will be conducted at the Research Unit in Biostatistics, Public Health Department, University of Liege, Belgium; The sign "x" means test or probe performed and registered; the sign "-"means test not performed.

provided by the ICOPE App (IC decline or not). Second, a binary decision of each one of the 5 domains per separate is provided directly by the ICOPE Monitor (each domain decreased or not); third, the binary decision obtained in the 5-domains could be combined as a score which might be just a count of IC declines, e.g. if we have 3 domains with decline among the 5 domains, the score would be 3/5. For purpose of this analysis, the second approach, a binary decision of each one of the 5 domains per separate provided directly by the ICOPE will be selected; the other two options would be studied as part of further secondary analysis.

Outcome measures

Primary outcome measure: Incidence of frailty assessed by Rockwood's clinical frailty scale (CFS) will be assessed at baseline, 4-, 8- and 12-month follow-up by telephone/video-call. An score <4 will indicate robustness, 4-6 pre-frailty status, and ≥ 6 frailty (10). Secondary outcome measures: Incidence of functional decline (assessed by Chair stand test (14,15) and the loss of ≥20 points in Barthel index (16,17), death (date), incidence of pre-frailty (assessed by CFS) (10), falls (number and date), institutionalization (date), and quality of life (EuroQol) (18) will be assessed at 4-, 8-, and 12-month follow-up by a telephone/video-call with the volunteer or a contact person.

Functional decline: Incidence of functional decline will

Table 2
Sample size calculation according to the prevalence and expected incidence of frailty

| Precision (Δ) | 95% Confidence Interval | Prevalence of 10.7% | | Incidence 13% with α = 0.05 | |
		Number of subjects	Relative precision (ε)	Number of subjects	
1%	9.7% - 11.7%	3671	0.05	1537	
2%	8.7% - 12.7%	918	0.06	1068	
3%	7.7% - 13.7%	408	0.07	785	
4%	6.7% - 14.7%	229	0.08	601	
5%	5.7% - 15.7%	147	0.09	475	
6%	4.7% - 16.7%	102	0.10	385	
7%	3.7% - 17.7%	75	0.12	267	
8%	2.7% - 18.7%	57	0.14	197	
9%	1.7% - 19.7%	45	0.20	97	
10%	0.7% - 20.7%	37	0.30	43	

be defined as 1) The loss of the capacity to raise from a chair within 14 seconds, measured by the chair stand test in the ICOPE Monitor (Chair stand test) (14, 15); or 2) The loss of at least one activity of daily living, defined as loss of ≥20 points in Barthel index (16, 17), administered by phone (19) at baseline, 4-, 8- and 12-month follow-up (16, 17, 19, 20).

Death: Date of death will be recorded, reported by the contact person if the participant did not respond to the scheduled follow-up visit at 4-, 8-, and 12-month follow-up.

Pre-frailty: Incidence of pre-frailty will be assessed by CFS at baseline, 4-, 8- and 12-month follow-up by telephone/video-call. An score <4 will indicate robustness, 4-6 pre-frailty status, and ≥6 frailty (10).

Falls (number and date) will be recorded by the volunteers on a personal dairy book.

Institutionalization: Date of institutionalization will be reported by the contact person if the participant did not respond to the scheduled follow-up.

Quality of life will be measured by self-reported EuroQol (ranging from 0 -the worst possible health status- to 1 -the best possible health status-) (18) by telephone/video-call at baseline, 4-, 8-, and 12-month follow-up.

Covariate data collection: Demographic and clinical data will be collected during the telephone/video calls and used as covariates. Instrumental activities of daily living (IADL) (maximum score 8 points) will be recorded using the Lawton scale (21). The ratio of the total score obtained / total score of the applicable items will be used to avoid any discrimination based on usual housework distribution among couple as in Gillain et al., 2017. E.g. if one of the members of a couple does not usually perform an activity, that item will not account for that individual, then, the total score of the applicable items will be 7 instead of 8 (22).

Feasibility of the ICOPE App and ICOPE Monitor: Feasibility will be defined as "the state or degree of being easily or conveniently done" and explored by the Technological, Economical, Legal, Operational, Schedule (TELOS)-feasibility score, which assesses the potential of implementation of new systems, and considers them feasible if TELOS-feasibility score ≥3) (23). It will be administered to the geriatric and primary care practitioners who collaborate with the study.

Sample size calculation

Sample size has been calculated in terms of the ICOPE study primary objective: to identify incidence of frailty in community-dwelling older patients. Table 2 shows the sample size calculation determined by a power calculation based on the width of the confidence interval for a proportion and on the estimation of an incidence rate (24). Assuming a prevalence of frailty of 10.7% (25), an incidence of 13% (26) with an alpha risk of 0.05, we estimated that 400 participants at the 12-month end-point of the study would be necessary to meet a degree of certainness regarding the incidence (relative precision of 0.10) meaning a sample of 600 volunteers at baseline should be cover a potential large dropout regarding the characteristics of this study (observational, 1-year follow-up, potential frail people, unknown adherence rate to the follow-up).

Statistical plan

Descriptive analysis will be performed for each variable of the study. Qualitative variables will be described by absolute numbers and relative frequencies (%). Quantitative variables will be summarized by the use of means and standard deviation (SD) for symmetrical distribution or median and the interquartile deviation for asymmetrical distributions. Normality of variables will be checked graphically with histograms and quantile-quantile plots, and tested by the Shapiro-Wilk test. A transformation of the data might be performed, if needed.

The evolution of intrinsic capacity during the 1-year follow-

up will be analyzed by Generalized Linear Mixte Model (GLMM). These models will be also used to study the evolution of outcomes measured every 4 months and the impact of covariates on these evolutions. Kaplan-Meier methods will be use to represent graphically the notion of time occurrence of frailty and mortality (4-month follow-up time will be used as notion of time).

For the outcomes with a precise date of event (frailty, mortality, falls, institutionalization), their association with intrinsic capacity will be analyzed by a joint model for longitudinal and time-to-event data (27); the same analysis might be performed for other variables of interest, if required. Indeed, on one hand, we want to analyze the evolution over time of covariates and on the other hand the effect of these covariates on the outcome. Multiple imputations methods would be applied to deal with missing data. The data will be processed using SAS 9.4 (©SAS Institute Inc., Cary, NC, USA) and R (version 3.5) (R Core Team) software packages. The level of statistical significance will be set as $\alpha = 5\%$ ($p < 0.05$).

Ethics

National and International research Ethics guidelines will be followed, including the 1964 Declaration of Helsinki and its further amendments, and the Committee on Publication Ethics (COPE) guidelines (28)(29). Data will be treated according to the law of data protection in Belgium and the Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data (30). The approval of the Ethics Committee (Comité d'Ethique Hospitalo-Facultaire Universitaire de Liège) will be obtained. Written and oral information will be provided and informed consent will be signed electronically by all participants. The study has been registered at www.clinicaltrials.gov (NCT04413877 on June 2, 2020).

Discussion

Our study will determine the associations among decrease in intrinsic capacity and the incidence of frailty, functional decline, and occurrence of health adverse outcomes in community-dwelling older people during 1-year follow-up. If these associations are observed in the study, the measurement of intrinsic capacity by new technologies would be ready to be implemented in clinical practice.

Several aspects of the study should be highlighted. First, it will include intrinsic capacity assessment (2). Indeed, even if the association of intrinsic capacity with mortality, functional decline, and falls was recently shown in older people in nursing homes (31), there is still very few data in community-dwelling population. The rationale to select intrinsic capacity, instead of using other syndromes or diseases, for example, sarcopenia, malnutrition, or dementia, is due to the multidimensional characteristics of older people, which require a global assessment. A single point of view might not be complete enough to take complex decisions in clinical practice.

Second, the study will provide evidence about the relationship between intrinsic capacity and frailty, which is a different multidimensional construct. Wide differences among frailty and intrinsic capacity have been pointed out, i.e. frailty is driven by deficits, while intrinsic capacity is driven by reserves; frailty is an approach towards treatment usually measured in clinical settings, while intrinsic capacity is an approach focused on function maintenance in the community setting; frailty has wide evidence about its prognosis capacity, while intrinsic capacity is quite new. It would be expected that intrinsic capacity, measured by the Apps is associated to the incidence of frailty, but this association remains unexplored and requires further studies (3).

Three different approaches of IC will be explored, in order to provide novel insight about how to deal with IC as variable, which is still an uncharted territory; for purpose of analysis, the approach that uses a binary decision of each one of the 5 domains per separate provided directly by the ICOPE will be selected, as it is effortless, obtained directly by the ICOPE Monitor, and provide insight to deliver potential therapeutic interventions. The other two options would be studied as part of further secondary analysis.

Mortality has been selected as clinically meaningful outcome of the study, as recommended by the Common data elements (CDE) and core outcome measures (COMs) in Frailty research consensus (32) and the Physical Frailty: ICFSR International Clinical Practice Guidelines for Identification and Management (33). Frailty has shown association with 2-fold higher all-cause mortality (HR 2.17, 95%CI 1.90-2.48) (34), including infectious diseases (HR 1.79, 95%CI 1.03-3.11) (34). Sample size calculation was based on a prevalence of frailty of 10.7% (25) and incidence 13%, (26)(35). Despite lower incidence rates (3.9%, 8%)(35–37), have been shown in other large cohorts, the highest one was selected for our sample size calculation to ensure the detection of frailty (11). Providing data about the relationship between intrinsic capacity and frailty will pave the path towards the change in the negative paradigm of aging, and a person-centred model focused on enhancing the 5 domains towards healthy aging (3).

Third, our study will include the use of new technologies by older people, which is an emerging field with promising results. Several projects on the use of technologies to support health status of older people are currently ongoing, e.g. the J48 supervised machine learning algorithm is identifies future fallers among otherwise healthy, independent older adults (38); eMIND is a randomized controlled trial that includes web-based multidomain interventions (39); and the ALLEGRO living lab is an experimental hospital-based room for the testing of devices by frail hospitalized older people (40). The International Network of Agencies for Health Technology Assessment (INAHTA) provides high quality evidence about new technologies to help health care suppliers and policy

makers in their decisions. The Belgian Health Care Knowledge Centre (KCE) has recently joined the INAHTA in 2020 (41), which might be promising for this line of research.

Finally, some limitations related to the cohort design should be acknowledged. The inclusion of healthy community-dwelling older volunteers will be considered as a selection bias, as it has been previously reported in other cohorts of community-dwelling older people (42). The characteristics of voluntary older participants (motivation, involvement in self-care management, etc.) might differ from those who refused to get involved in a research study. Moreover, volunteers who are able to use online resources might be relatively younger at baseline, and their health status might be better than the population of the same age.

In summary, this study will apply the "Action-research philosophy" (43) to bridge the gap between research and clinical practice. It will provide evidence to implement the ICOPE App and ICOPE Monitor, deliver efficient person-centered care-plans, and benefit older adults, professionals, and the healthcare systems.

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