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From Survival to Quality of Life: Investigating Frailty and Sarcopenia in Older People

Céline Demonceau

Thesis submitted in fulfilment of the requirements for the degree of Doctor of Philosophy (PhD) in Public Health

2025

University of Liège - Faculty of medicine - Research Unit of Public Health, Epidemiology, and Health Economics

PUBLIC HEALTH
EPIDEMIOLOGY AND
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PUBLIC HEALTH EPIDEMIOLOGY AND HEALTH ECONOMICS

Acknowledgements

"Not all those who wander are lost."

J.R.R. Tolkien

If I have learned anything over the past few years, it is that completing a PhD is not an end in itself. What truly matters is the journey you take to get there. This path, sometimes clear, sometimes uncertain, has shaped me far beyond what I expected.

Along the way, I have had the chance to meet people who have guided, supported and inspired me. I would like to express my sincere thanks to all of them.

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This thesis is the result of years of work, but above all, it is the trace of a path and I am grateful to each of you who walked part of it with me.

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Summary

The recent growing number of older adults has profoundly transformed the demographic landscape, raising new challenges to public health systems worldwide. As populations age, chronic and geriatric conditions become more prevalent, and sarcopenia and frailty have emerged as significant conditions due to their high prevalence and association with adverse outcomes. While these conditions appear to be partly preventable, evidence on their impact on long-term mortality and on outcomes related to Coronavirus Disease 2019 (COVID-19) outcomes remains scarce in nursing home (NH) residents. Furthermore, despite its importance in ageing research, health-related quality of life (HRQoL) in community-dwelling older adults is often assessed using generic tools, which are not sensitive enough to capture the specific impact of sarcopenia.

This thesis was designed to address these gaps through two complementary approaches. The first chapter investigates the associations between sarcopenia, frailty and critical health outcomes, including 8-year mortality, COVID-19 incidence and severity and changes in HRQoL. This chapter uses two longitudinal cohorts developed at the Research Unit in Public Health, Epidemiology and Health Economics, University of Liège: SENIOR, involving NH residents, and SarcoPhAge, involving community-dwelling older adults since 2013. The second chapter focuses on strengthening the psychometric robustness of the Sarcopenia and Quality of Life questionnaire (SarQoL), the only disease-specific questionnaire developed to evaluate quality of life in people with sarcopenia. Together, these two perspectives aim to provide new evidence to better characterise these conditions and support the use of valid, sensitive tools to inform prevention strategies and clinical care for ageing populations.

The main results arising from the five investigations conducted across both chapters of this thesis are summarized below.

- **COVID-19 incidence and severity (SENIOR cohort, n=75):** 56% of residents contracted COVID-19 during the first waves, with no significant associations between frailty (OR=0.96, 95%CI: 0.65–1.42), nutritional status (OR=1.15, 95%CI: 0.92–1.45), grip strength (OR=1.00, p=0.92) and COVID-19 incidence or severity.
- **Eight-year mortality risk (SENIOR cohort, n=533):** Median survival was 4.0 years (IQR: 1.9–6.9). Higher Short Physical Performance Battery (SPPB) scores were

significantly and independently associated with lower risk of 8-year mortality (HR=0.93 (0.90–0.97)).

- **Changes in health-related quality of life and sarcopenia components (SarcoPhAge cohort, n=333):** Over 4 years, increases in physical performance, grip strength and muscle mass were each independently associated with increased HRQoL, as measured with SarQoL.
- **Content validity of SarQoL:** Interviews with 17 patients and 11 experts confirmed the relevance, comprehensiveness and comprehensibility of the questionnaire confirming that SarQoL adequately captures the HRQoL experienced by individuals with sarcopenia
- **Psychometric properties of SarQoL (meta-analysis, 25 studies, n=4,585):** SarQoL showed strong psychometric properties, with high internal consistency, test-retest reliability and construct validity. Its responsiveness to meaningful changes in HRQoL was also confirmed.

Three main contributions can be derived from these results. First, the SPPB emerges as a key indicator of functional capacity, associated with both mortality risk and HRQoL. This underlines the importance of systematically assessing physical performance in order to anticipate and prevent decline. Second, this thesis consolidates the evidence supporting SarQoL as a robust, disease-specific instrument to assess HRQoL in sarcopenic individuals. By demonstrating strong psychometric properties and complementing objective measures such as the SPPB, SarQoL provides valuable patient-centered insights that generic tools often fail to capture. Third, it suggests that research on successful ageing should consider outcomes beyond traditional clinical measures to better capture the patient perspective. Approaches promoting self-management and autonomy, potentially supported by digital health tools, may help translate improvements in physical performance and HRQoL into sustained benefits for older adults.

While these findings provide new insights, this thesis has certain limitations, including its focus on Belgian cohorts, modest sample sizes for some analyses, and limited exploration of environmental and social determinants of ageing. Future research should aim to replicate these results in larger and more heterogeneous populations and clarify how SPPB scores can be best interpreted and used to support early detection of functional decline and timely intervention. In this context, future studies should also consider using the disease-specific SarQoL questionnaire

in clinical and research settings to better capture patient-reported outcomes and improve the evaluation of preventive and therapeutic strategies.

This doctoral thesis contributes to advancing knowledge on the associations between frailty, sarcopenia and key health outcomes in older adults, and strengthens the evidence supporting the psychometric robustness of SarQoL. Throughout the thesis, the SPPB emerges as a key indicator of mortality and HRQoL, complementing SarQoL to provide a fuller picture of functional decline, illustrating how ageing research can evolve towards a more comprehensive approach that considers both clinical outcomes and lived experience. More broadly, this thesis contributes to the reflection on how to define and assess successful ageing, highlighting the importance of integrating both clinical outcomes and patient-reported measures to capture the lived experience of older adults.

Résumé

L'augmentation récente du nombre de personnes âgées a profondément transformé le paysage démographique, posant de nouveaux défis aux systèmes de santé publique à travers le monde. Dans ce contexte de vieillissement des populations, les maladies chroniques et les conditions gériatriques deviennent plus fréquentes, et la sarcopénie ainsi que la fragilité se sont imposées comme des problématiques majeures en raison de leur forte prévalence et de leur association avec des issues de santé défavorables. Bien que ces conditions semblent en partie évitables, les données concernant leur impact sur la mortalité à long terme et sur les conséquences liées à la COVID-19 restent limitées chez les résidents en maison de repos. Par ailleurs, malgré l'importance croissante accordée à la qualité de vie liée à la santé (QVLS) dans la recherche sur le vieillissement, son évaluation chez les personnes âgées vivant à domicile repose souvent sur des outils génériques, qui peuvent être insuffisamment sensibles pour saisir l'impact spécifique de la sarcopénie.

Cette thèse a été conçue pour combler ces lacunes au travers de deux approches complémentaires. Le premier chapitre étudie les associations entre sarcopénie, fragilité et des enjeux de santé majeurs, incluant la mortalité à 8 ans, l'incidence et la sévérité de la COVID-19 ainsi que les changements de QVLS. Ce chapitre s'appuie sur deux cohortes longitudinales développées au sein de l'Unité de Recherche en Santé Publique, Épidémiologie et Économie de la Santé de l'Université de Liège : SENIOR, comprenant des résidents en maisons de repos, et SarcoPhAge, incluant des personnes âgées vivant dans la communauté depuis 2013. Le second chapitre vise à renforcer la robustesse psychométrique du SarQoL, unique questionnaire spécifique développé pour évaluer la qualité de vie des personnes atteintes de sarcopénie. Ensemble, ces deux perspectives visent à fournir de nouvelles données permettant une meilleure caractérisation de ces conditions et à soutenir l'utilisation d'outils valides et sensibles pour éclairer les stratégies de prévention et les pratiques cliniques destinées aux populations vieillissantes.

Les principaux résultats issus des cinq investigations menées dans le cadre de cette thèse sont résumés ci-dessous :

- **Incidence et sévérité de la COVID-19 (cohorte SENIOR, n=75)** : 56 % des résidents de maisons de repos ont contracté la COVID-19 durant les premières vagues, aucune association significative n'a été observée entre la fragilité (OR=0,96 ; IC95 % : 0,65–

1,42), l'état nutritionnel (OR=1,15 ; IC95 % : 0,92–1,45), la force de préhension (OR=1,00 ; p=0,92) et l'incidence ou la sévérité de la COVID-19.

- **Risque de mortalité à 8 ans (cohorte SENIOR, n=533)** : la survie médiane était de 4,0 ans (IQR : 1,9–6,9). Des scores plus élevés au Short Physical Performance Battery (SPPB) étaient significativement et indépendamment associés à un risque réduit de mortalité à 8 ans (HR=0,93 (0,90–0,97)).
- **Évolution de la qualité de vie liée à la santé et des composantes de la sarcopénie (cohorte SarcoPhAge, n=333)** : sur une période de 4 ans, les augmentations de la performance physique, de la force de préhension et de la masse musculaire étaient chacune indépendamment associées à une amélioration de la QVLS, mesurée avec le SarQoL.
- **Validité de contenu du SarQoL** : les entretiens menés auprès de 17 patients et 11 experts ont confirmé la pertinence, l'exhaustivité et la compréhensibilité du questionnaire, attestant qu'il saisit adéquatement l'expérience de QVLS des personnes atteintes de sarcopénie.
- **Propriétés psychométriques du SarQoL (méta-analyse, 25 études, n=4 585)** : le SarQoL a montré de solides propriétés psychométriques, avec une excellente consistance interne, une fiabilité test-retest élevée et une validité de construit confirmée. Sa réactivité aux changements significatifs de la QVLS a également été démontrée.

Trois contributions principales découlent de ces résultats. Premièrement, le SPPB émerge comme un indicateur clé de la capacité fonctionnelle, associé à la fois au risque de mortalité et à la QVLS. Ceci souligne l'importance d'évaluer systématiquement la performance physique afin d'anticiper et de prévenir le déclin fonctionnel. Deuxièmement, cette thèse consolide les preuves en faveur du SarQoL comme instrument spécifique à la sarcopénie, valide et robuste pour évaluer la QVLS. En démontrant ses propriétés psychométriques solides et en complétant les mesures objectives telles que le SPPB, le SarQoL apporte une perspective centrée sur le patient que les outils génériques ne parviennent souvent pas à capter. Troisièmement, ces résultats suggèrent que la recherche sur le vieillissement en bonne santé devrait aller au-delà des mesures cliniques traditionnelles afin de mieux refléter la perspective des patients. Des approches favorisant l'autonomisation et l'autonomie, potentiellement soutenues par les outils numériques de santé, pourraient contribuer à transformer les améliorations de la performance physique et de la QVLS en bénéfices durables pour les personnes âgées.

Bien que cette thèse apporte de nouvelles connaissances, certaines limites doivent être soulignées, notamment sa portée sur des cohortes belges, la taille modeste de certains échantillons et la faible prise en compte des déterminants environnementaux et sociaux du vieillissement. De futures recherches devraient viser à reproduire ces résultats dans des populations plus larges et hétérogènes et à clarifier la manière dont les scores du SPPB peuvent être interprétés et utilisés pour soutenir la détection précoce du déclin fonctionnel et une intervention en temps opportun. Dans ce contexte, de futurs travaux devraient également envisager l'utilisation du questionnaire spécifique SarQoL dans les milieux cliniques et de recherche afin de mieux recueillir les résultats rapportés par les patients et d'améliorer l'évaluation des stratégies préventives et thérapeutiques.

Cette thèse doctorale contribue à l'avancement des connaissances sur les associations entre fragilité, sarcopénie et principaux enjeux de santé chez les personnes âgées, et renforce les preuves soutenant la robustesse psychométrique du SarQoL. Tout au long de la thèse, le SPPB se distingue comme un indicateur clé de mortalité et de QVLS, venant compléter le SarQoL pour fournir une vision plus complète du déclin fonctionnel, illustrant l'évolution possible de la recherche sur le vieillissement vers une approche plus globale, tenant compte à la fois des résultats cliniques et de l'expérience vécue des personnes âgées.

List of abbreviations

ADL	Activities of daily living
IADL	Instrumental activities of daily living
BMI	Body mass index
CGA	Comprehensive geriatric assessment
CI	Confidence interval
COSMIN	COnsensus-based Standards for the selection of health Measurement INstruments
DEXA	Dual-energy X-ray absorptiometry
EQ-5D	EuroQuol-5D
EWGSOP	European Working Group on Sarcopenia in Older People
HR	Hazard ratio
HRQoL	Health-Related Quality of Life
MMSE	Mini-Mental State Examination
MNA	Mini Nutritional Assessment
NH	Nursing home
OR	Odds ratio
PROM	Patient Reported Outcome Measure
QoL	Quality of life
SarQoL	Sarcopenia & Quality of Life
SarcoPhAge	Sarcopenia and Physical Impairment with Advancing Age
SD	Standard deviation
SE	Standard error
SF-36	36-Item Short Form Health Survey
SENIOR	Sample of Elderly Nursing home Individuals: an Observational Research
SPPB	Short Physical Performance Battery
WHO	World Health Organization

INTRODUCTION

Introduction

1. Global context

Over the past decades, the considerable increase in life expectancy has profoundly transformed the demographic structure of our societies. While this represents a major public health achievement, it also presents unprecedented challenges. A society is considered as an 'ageing society' when the proportion of individuals aged 65 and over exceeds 7% of the total population. It becomes an 'aged society' when this proportion reaches 14% and a 'hyperaged society' when it exceeds 20% [1]. This demographic shift reflects not only the increasing proportion of older adults but also the steady rise in life expectancy, with more people than ever before living beyond the age of 80 years [2]. By 2050, it is expected that one in five people worldwide will be aged 65 or over, with proportions approaching 25% in Belgium and 30% across Europe, far exceeding the threshold for a hyperaged society [2-4]. This rapid demographic change raises significant challenges for public health, calling for strategies to ensure additional years are accompanied by preserved functional capacity, maintained autonomy and good quality of life (QoL). Indeed, health is no longer defined solely by the absence of disease, but also by the ability to maintain independence, social participation and quality of life throughout the life course, a concept that is particularly relevant in older age [5].

One of the most direct consequences of this ageing trend is the growing burden of chronic diseases, such as diabetes, neurodegenerative diseases and musculoskeletal disorders [6]. In parallel, sarcopenia and frailty have emerged as two key geriatric conditions due to their high prevalence and clinical consequences. Sarcopenia is defined by the European Working Group on Sarcopenia in Older People (EWGSOP) as a decrease in muscle strength and mass, the severity of which is measured by physical performance [7], while frailty, according to Fried's phenotype, includes broader components such as exhaustion, weight loss, reduced activity and slow gait speed [8]. Both conditions are common in ageing populations, with prevalence estimates ranging from 10% to 27% for sarcopenia and from 7% to 24% for frailty depending on the definitions used [9, 10]. They have been associated with poorer QoL and increased risk of functional decline, falls, hospitalization and mortality [11-13], emphasizing their substantial public health impact and the need for early identification and prevention. The impact of the Coronavirus Disease 2019 (COVID-19) pandemic on older adults has further highlighted these concerns, revealing that older individuals with frailty and sarcopenia are more susceptible to severe forms of the disease, including an increased risk of mortality [14, 15]. However,

investigations in nursing home (NH) residents were scarce, as clinical data required to investigate these potential associations were difficult to obtain, primarily due to the severe restrictions on access to residents during this period.

Beyond their clinical consequences, sarcopenia and frailty are increasingly recognized as conditions influenced by modifiable biological and lifestyle factors. In a recent editorial, we emphasized the interconnected roles of systemic inflammation, poor nutrition, and reduced physical activity in the development and progression of sarcopenia [16]. Interestingly, these factors are also recognised for their association with the onset and progression of frailty in older people [17-19]. These findings support the idea that sarcopenia and frailty are not inevitable consequences of aging, but conditions that can potentially be prevented or delayed through appropriate interventions.

Nevertheless, several important research gaps remain. In NH residents, few studies have explored which factors are associated with mortality over extended follow-up, despite the need to better understand these associations in this population. During the pandemic, evidence on COVID-19 incidence and severity in NH residents was extremely limited. In addition, in community-dwelling older adults, only a few longitudinal studies have investigated whether changes in sarcopenia, and more specifically in its components (i.e. muscle mass, muscle strength and physical performance), were associated with health-related quality of life (HRQoL) over time, and none has used a disease-specific instrument to address this question. Addressing these gaps constitutes the rationale of the first chapter of this thesis, which examines potential associations between frailty, sarcopenia components and three major adverse outcomes: COVID-19 incidence and severity, 8-year mortality in frail individuals, and HRQoL in sarcopenic individuals using the Sarcopenia and Quality of Life (SarQoL) questionnaire, the only instrument currently available to specifically assess HRQoL in sarcopenic populations [20].

To complement this perspective, the second part of this thesis focuses on the measurement of HRQoL in sarcopenia [21]. This is particularly true for ageing research, where the complexity and heterogeneity of health trajectories necessitate the use of instruments specifically designed for older populations [22, 23]. It is therefore essential to rely on a robust, disease-specific instrument to assess HRQoL in sarcopenic populations. The SarQoL questionnaire, designed specifically for this assessment in sarcopenia, remains the only available tool for this purpose. Despite its growing international use, and its initial construction and validation in 2013 according to recommended procedures for PROMs development, further research is required to

consolidate the scientific evidence supporting its psychometric robustness, in line with updated COnsensus-based Standards for the selection of health status Measurement Instruments (COSMIN) guideline [24, 25]. This objective constitutes the focus of the second chapter of this thesis.

To support this scientific endeavor, the first chapter relies on data from two complementary Belgian longitudinal cohorts developed by the Research Unit in Public Health, Epidemiology and Health Economics at the University of Liège: SarcoPhAge (Sarcopenia and Physical Impairment with Advancing Age) and SENIOR (Sample of Elderly Nursing Home Individuals: an Observational Research). These cohorts offer valuable insights into the health and well-being of older adults living in different settings and provide the empirical basis for investigating associations between frailty, sarcopenia and major health outcomes

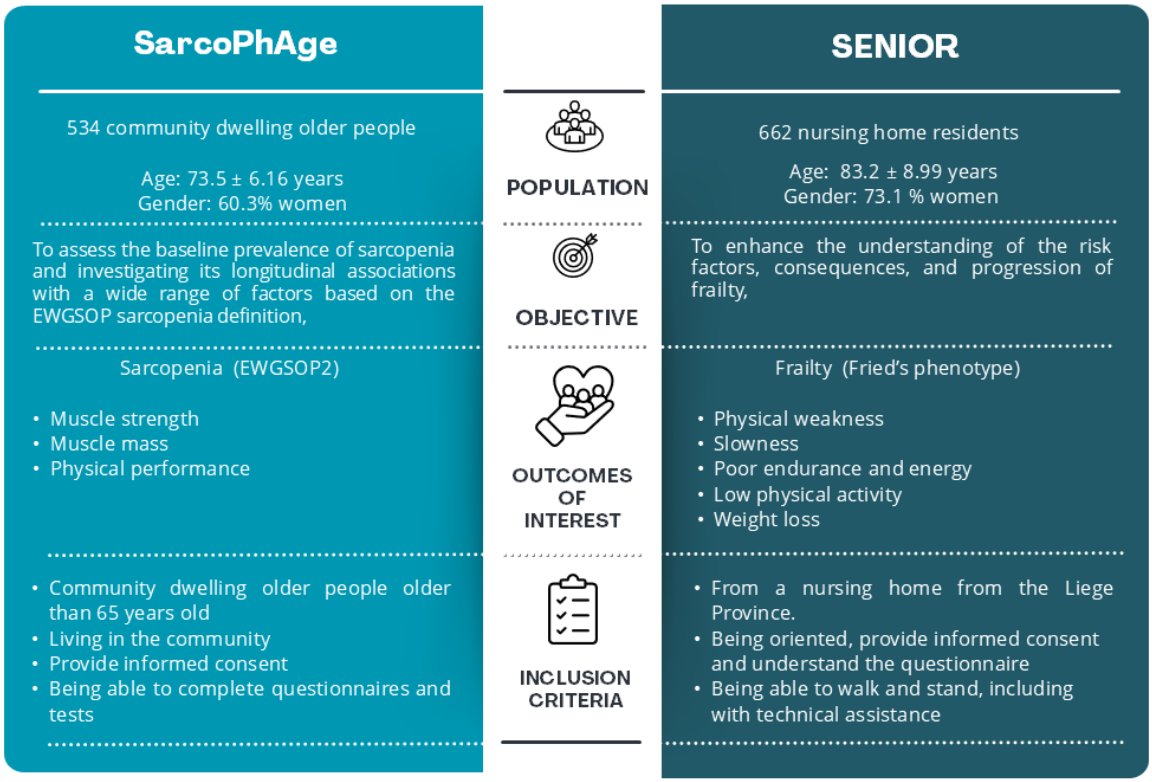
The two chapters of the present thesis are therefore inherently connected and complementary. The first aims to identify factors associated with three major outcomes: COVID-19 incidence and severity, long-term mortality in NH residents, and longitudinal changes in HRQoL in community-dwelling older adults using a disease-specific questionnaire. The second focuses on reinforcing the scientific evidence supporting the SarQoL questionnaire through a qualitative evaluation of its content validity and a systematic review and meta-analysis of its psychometric properties. This order of presentation was deliberately adopted, since the first part provides longitudinal evidence of the adverse outcomes associated with frailty and sarcopenia, while the second addresses the methodological need to consolidate the measurement of HRQoL in sarcopenia, which is increasingly recognised as a major outcome in ageing research and clinical care. Together, the two chapters of this thesis contribute to strengthening the scientific understanding and assessment of adverse health outcomes in older adults with frailty or sarcopenia, providing new longitudinal evidence on key associated factors and consolidating the robustness of SarQoL, the only disease-specific instrument available to evaluate HRQoL in sarcopenic individuals, a core dimension of ‘Healthy Ageing’, defined by the World Health Organization (WHO) as the process of developing and maintaining the functional ability that enables well-being in older age [26].

2. Cohorts

The present doctoral thesis is based on data collected from two complementary longitudinal cohorts developed by the Research Unit in Public Health, Epidemiology and Health Economics at the University of Liège: SarcoPhAge and SENIOR. While these two cohorts have distinct

target populations and initial objectives, they provide complementary perspectives and offer a solid foundation for investigating frailty, sarcopenia, and their consequences in older adults. An overview of their key characteristics is provided in Table 1.

Table 1. Key characteristics of the SarcoPhAge and SENIOR cohorts.



2.1. SarcoPhAge cohort

The SarcoPhAge cohort was initiated in Belgium in 2013. Its aim was to assess the prevalence of sarcopenia and explore its associations with a wide range of socio-demographic, clinical, and physical factors in community-dwelling older adults, using both longitudinal follow-up and cross-sectional comparisons based on the EWGSOP sarcopenia definition [27]. The cohort comprises 534 community-dwelling older adults aged 65 years and over, underwent annual assessments as part of the longitudinal study. The data collected encompasses a broad range of parameters, including notably muscle strength, muscle mass, physical performance, nutritional status, cognitive function and comorbidities. Since its inception, the cohort has been used to explore many areas of research, especially in two fields: the health outcomes related to sarcopenia and the QoL in the sarcopenic population. This cohort has indeed brought new insights to the field sarcopenia not yet explored, notably by highlighting the significant associations between sarcopenia and malnutrition and the association between declines in

muscle health and bone health [27, 28]. Secondly, a major contribution to the field of sarcopenia was the development and validation of the SarQoL questionnaire. This questionnaire is the first patient-related outcome measure (PROM) designed to assess the HRQoL specifically in people with sarcopenia. Acknowledging the limitations of generic HRQoL tools, such as the EuroQuol-5D (EQ-5D) and the 36-Item Short Form Health Survey (SF-36), in capturing the impairments specific to sarcopenia, Beaudart et al. designed the SarQoL to address this gap [29]. The questionnaire comprises 22 questions and 55 items distributed across seven domains: physical and mental health, locomotion, body composition, functionality, activities of daily living, leisure activities and fears (see Appendix 1). It generates both domain-specific scores and a global score ranging from 0 to 100, with higher scores indicating better QoL. SarQoL has demonstrated strong psychometric properties, including good internal consistency, test-retest reliability, construct validity, and responsiveness to change. Since its development, it has been translated and validated in over 35 languages, establishing it as a widely used and culturally adaptable tool for evaluating the impact of sarcopenia on quality of life in clinical and research settings.

The extensive longitudinal data collected within this cohort, notably the accurate measurement of sarcopenia using adapted tools during the follow-up, makes the SarcoPhAge cohort particularly suitable for investigating the longitudinal relationships between changes in sarcopenia components and changes in health-related quality of life, a central focus of the first part of this thesis.

2.2. SENIOR cohort

The SENIOR cohort, which was initiated in 2013, focuses on older adults residing in 28 different nursing homes in the province of Liège, in Belgium. The main objectives of the cohort were to improve the understanding of the risk factors, consequences, and progression of frailty, and to inform potential management strategies for NH residents, a population often underrepresented in research. The cohort includes 662 NH residents, with baseline and annual follow-up data collected [30]. The SENIOR cohort has generated valuable findings notably regarding frailty and nutritional status in NH settings. Notably, investigations conducted in this cohort showed a significant relationship between one frailty component, higher level of physical activity, and health outcomes such as quality of life and functional abilities in NH residents [30]. In addition, this cohort has provided valuable insights into potential strategies to manage frailty, particularly through nutritional support, promotion of physical activity and reduction of polypharmacy [31-33]. Similarly to the SarcoPhAge cohort, one of the key

strengths of this cohort is the extensive longitudinal data collected for 5 years allowing investigations with temporal associations. Another strength is that this cohort is based on a population that is often underrepresented in clinical research, which makes it a unique feature to explore.

This extensive longitudinal dataset, with repeated and detailed assessments of frailty and related factors, combined with the unique opportunity to collect data shortly before the COVID-19 pandemic, makes the SENIOR cohort a particularly valuable resource for investigating how frailty relates to long-term mortality as well as COVID-19 incidence and severity in NH residents, a population that was otherwise difficult to access during the pandemic. This makes it particularly relevant for addressing the objectives of the first part of this thesis

Interestingly, interconnections between sarcopenia and frailty were observed in both cohorts. In the SENIOR cohort, frail participants were at a higher risk of being sarcopenic, while sarcopenic participants were more likely to be frail [34]. Similar associations were also found in the SarcoPhAge cohort with a significantly higher proportion of frail individuals among sarcopenic participants (34.2%) compared to non-sarcopenic participants (12.6%) [35].

3. Objectives of the thesis

This thesis addresses the central question of how sarcopenia, frailty and their components are associated with long-term health outcomes and HRQoL in older adults, as well as how the evidence supporting the measurement of sarcopenia-related QoL can be strengthened.

To address this question, this thesis is structured into two chapters and pursues five specific objectives (see Table 2).

The first chapter explores the prospective associations of clinical characteristics in older adults from the SENIOR and SarcoPhAge cohorts. The first two investigations presented in this chapter aim to improve our understanding of the relationships between frailty, nutritional status, muscle function, and major health outcomes, namely the incidence and severity of COVID-19 and long-term survival in NH residents. The third investigation explores the longitudinal associations between changes in sarcopenia components and changes in HRQoL in community-dwelling older adults. Quantitative approaches were employed in this first chapter, involving various statistical analysis, such as survival analyses, linear regressions and mixed-model regressions. These investigations address the current lack of longitudinal studies that assess frailty, sarcopenia and their impact on survival and QoL.

The second chapter of this thesis focuses on the evaluation of the psychometric properties of the SarQoL questionnaire. While the last study presented in the first chapter investigated the association between sarcopenia components and HRQoL, its proper evaluation requires the use of condition-specific instrument. The SarQoL questionnaire, developed precisely for this purpose, is currently the only tool available for measuring QoL in this specific population. While its initial validation demonstrated good psychometric properties [36], recent international recommendations highlight the need for a more thorough evaluation of its content validity and measurement properties to ensure its suitability for research and clinical practice [24, 37]. The second chapter of the present thesis therefore aims to reinforce the validity and psychometric robustness of the SarQoL. The first investigation evaluates its content validity while the second consists on a systematic review and meta-analysis of all available evidence regarding its measurement properties**.** The investigations of this chapter mixed quantitative and qualitative approaches. The content validity of SarQoL was assessed through interviews with sarcopenic participants and experts in the field of sarcopenia following approval from the Ethics Committee of Liège. The measurement of the psychometric properties was investigated through a systematic review and meta-analysis.

Together, these five articles follow a logical continuum: from exploring the determinants of severe outcomes (COVID-19 and long-term mortality), to investigating longitudinal associations between sarcopenia components and HRQoL, and finally reinforcing the validity of the SarQoL questionnaire, ensuring that future research and clinical practice can rely on accurate, disease-specific measures of HRQoL.

Each objective was addressed through a dedicated investigation, with the resulting studies published or submitted as part of this doctoral thesis, as summarized in Table 2.

Table 2. Summary of the structure of the thesis

CHAPTER 1 *Prospective associations between clinical characteristics and major health outcomes in the SENIOR and SarcoPhAge cohorts*		
Objectives	**Cohort investigated**	**Publications**
To investigate the relationships between frailty, nutritional status, muscle strength and the COVID-19 incidence and severity in nursing home residents	SENIOR	Demonceau C, Buckinx F, Reginster JY, Bruyère O. Investigation of the relationships between frailty, nutritional status and muscle strength and the incidence and severity of COVID-19 among the residents of nursing homes. Results from the SENIOR cohort. Maturitas. 2023 Nov;177:107800.
To identify factors predictive of 8-year survival in nursing homes.	SENIOR	Demonceau C, Buckinx F, Reginster JY, Bruyère O. Assessment of risk factors associated with long-term mortality in nursing homes: result from the SENIOR cohort. Aging Clin Exp Res. 2023 Dec;35(12):2997-3005. doi: 10.1007/s40520-023-02579-5. Epub 2023 Nov 2. PMID: 37917376.
To investigate the association between changes in sarcopenia components and changes in HRQoL over four years using the SarQoL questionnaire	SarcoPhAge	Demonceau C, Beaudart C, Mwamba Mbayo T, Monseur J, Reginster JY, Bruyère O. Longitudinal Associations Between Changes in Muscle Strength, Muscle Mass, and Physical Performance and Health-Related Quality of Life in Older Adults: A Four-Year Analysis from the SarcoPhAge Cohort. *Submitted in European Geriatric Medicine*
CHAPTER 2 *Psychometric robustness of the SarQoL questionnaire*		
Objectives		**Publications**
To enhance the evidence supporting the content validity of the SarQoL questionnaire.		Demonceau C., Voz B., Reginster J.-Y., Bruyère O., Beaudart C. Content validity of SarQoL, a Quality of Life Questionnaire specific to Sarcopenia. Aging Clin Exp Res. 2024 Apr 30;36(1):101. PMCID: PMC11074221.
To provide a quantitative summary of all evidence reported on the reliability, validity, responsiveness and floor/ceiling effects of SarQoL in older adults.		Demonceau C, Brabant C, Shukuru E, Alokail M, Al-Daghri N, Rolland Y, Bautmans I, Bauer JM, Cherubini A, Cruz-Jentoft AJ, Dawson-Hughes B, Fielding RA, Harvey NC, Landi F, Visser M, Duque G, Rizzoli R, Reginster JY, Bruyère O, Beaudart C. Psychometric properties of the SarQoL questionnaire: a systematic review and meta-analysis → *Submitted in Journal of Cachexia Sarcopenia and Muscle*

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RESEARCH SYNTHESIS

CHAPTER 1

Prospective associations between clinical characteristics and major health outcomes in the SENIOR and SarcoPhAge cohorts

Investigation of the relationships between frailty, nutritional status and muscle strength and the incidence and severity of COVID-19 among the residents of nursing homes. Results from the SENIOR cohort.

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Abstract

Few studies have investigated the factors associated with the incidence of COVID-19 in nursing homes. The aim of this study was to investigate the relationships between frailty, nutritional status, muscle strength and the COVID-19 incidence and severity in nursing home residents. Data from the last two years of follow-up of the SENIOR (Sample of Elderly Nursing homes individuals: an Observational Research) cohort were used. A total of 75 participants of the cohort were included, 56 % of whom had COVID-19. After adjustment for covariates, no association was found between frailty, nutritional status or grip strength and the incidence and severity of Covid-19.

Introduction

The COVID-19 pandemic created an extraordinary context in which some populations were quickly identified as being at higher risk to develop severe forms of COVID-19 and/or as having higher mortality rates, such as older people, and in particular nursing home (NH) residents. Frailty, malnutrition and lower muscle strength are common in older people. All these three components have been widely studied in the literature in older people and have been shown to be significantly associated with the COVID-19 incidence and severity [1]. However, few studies have considered the specific case of older people in NHs. During the different waves of the pandemic, NHs closed their doors to outsiders to protect their residents. Data collection in this context was therefore extremely complicated.

The main aim of this study was to investigate the association between frailty, nutritional status, muscle strength and the incidence of COVID-19 in NH residents using data from the SENIOR (Sample of Elderly Nursing Home Individuals: An Observational Research) cohort [2]. Secondary objectives were to assess the association between frailty, nutritional status, muscle strength and COVID-19 severity as well as the impact of 2-year changes in these factors on COVID-19 incidence and severity.

Methods

This study used the data from the last two years of follow-up of the SENIOR cohort (2018 and 2019). Frailty was identified using Fried's criteria, nutritional status was assessed using the Mini Nutritional Assessment Short Form (MNA-SF) and muscle strength was measured using handgrip strength. Retrospective COVID-19 data were obtained from medical records in 2022. Symptom severity, collected in patients' medical records, was categorised as asymptomatic/moderate (i.e., fever, cough, dyspnoea, anosmia, diarrhoea, pneumonia) and severe/death (i. e., oxygen saturation ≤ 94 %, respiratory rate > 30 breaths/min, lung infiltrates > 50 %, need for nasal oxygen, fluid infusion or hospitalisation). Gender, age, number of comorbidities and medications, body mass index (BMI; kg/m^2), cognitive status (MMSE), activities of daily living (Katz), physical abilities (SPPB) and the level of physical activity (Minnesota questionnaire) were collected from the participants' medical records and considered as potential confounding factor. All eligible participants were vaccinated against COVID-19 in accordance with the procedure introduced in Belgium. Therefore, vaccination status was not considered a confounding factor. Univariate regressions, expressed as odds ratio (OR) and its confidence interval (IC95%), were first performed. Significant variables and all variables with a p-value below 0.10 in the univariate analyses were included in logistic regression models, also expressed as odds ratio and confidence interval. All analyses were performed using R Studio version 4.1.2. and a p-value < 0.05 was considered statistically significant.

Results

The initial population of the SENIOR cohort in 2014 consisted of 662 NH residents. Among them, 191 were alive at pandemic onset in 2020. Of these, 2 were lost to follow-up due to a change of NH (1 %) and 83 were not assessed for frailty, malnutrition or low muscle strength in 2018 and/or 2019 (43.4 %). Data were not available for 31 individuals (16.2 %) for the assessment of COVID-19 incidence and for 75 individuals (38.7 %) for the investigation of COVID-19 severity.

A total of 42 residents were diagnosed with COVID-19 at least once (56 %). No significant differences were observed in the characteristics of residents in 2019 between those who contracted COVID-19 (“COVID +”) and those who did not (“COVID −”). Univariate and multivariate regressions showed no association with COVID-19 incidence (Table 1).

Table 1. Association between the residents' characteristics in 2019 and the COVID-19 incidence (n=75)

	Incidence of COVID-19		Univariate			Multivariate *	
	COVID + (n=42)	COVID – (n=33)	OR	IC95%	P-	OR	IC95%
Age, years	86.78 ± 9.99	87.27 ± 9.76	0.99	0.95-1.04	0.83		
Gender, women	31 (73.8)	25 (75.8)	0.90	0.31-2.57	0.85		
Comorbidities per individual	4.10 ± 1.92	3.19 ± 2.76	1.19	0.97-1.47	0.10	1.15	0.92-1.45
Body Mass Index, kg/m^2	28.61 (24.43-33.31)	23.93 (21.30-29.51)	1.08	0.99-1.19	0.08	1.07	0.98-1.17
Number of medications per individual	13.43 ± 4.27	11.15 ± 5.56	1.11	1.00-1.23	0.05	1.07	0.97-1.20
Frailty, /5 points	2 (1.25-3.0)	2 (1.0-3.0)	0.96	0.65-1.42	0.85		
Grip strength, kg	16.8 (12.5-23.1)	15.2 (11.7-27.7)	1.00	1.00-1.00	0.92		
Katz, score /32	15 (10.25-19)	13 (9-16)	1.07	0.97-1.17	0.18		
Mini Mental State Examination,	25 (19-27)	26 (23-28)	0.93	0.84-1.03	0.15		
Mini Nutritional Assessment, /14 points	12 (11-13)	12 (10-13)	1.15	0.92-1.45	0.22		
Short physical Performance Battery,	4 (2-7)	5 (1-7)	0.97	0.85-1.12	0.67		
Minnesota, kcal/day	490 (245-1470)	857.5 (245-1450)	0.99	0.99-1.00	0.96		

*Adjusted on comorbidities, Body Mass Index and number of drugs

In the univariate analyses, no significant association was observed between changes in patients' characteristics between 2018 and 2019 and COVID-19 incidence. However, in the multivariate regression, the MMSE score in 2018, used as a confounding variable, was associated with a decreased risk of contracting COVID-19 as the score increased (OR = 0.87 (0.77–0.98)). Regarding COVID-19 severity, no association was observed between NH resident characteristics in 2019, the changes between 2018 and 2019 and COVID-19 severity. Multivariate regression was not performed because there were no variables with a p-value below 0.10.

Discussion

Our study did not show an association between frailty, poor nutritional status, low muscle strength and COVID-19 incidence and severity in NH residents. To our knowledge, this is the first study to investigate these associations in a population of NH residents.

Our findings are consistent with some of the literature. Indeed, a UK study showed no significant association between frailty and COVID-19 incidence in community-dwelling older people [3]. Similarly, a Belgian study of older people aged over 65 reported no association between nutritional status and COVID-19 incidence [4]. However, our results differ from other studies. In fact, a meta-analysis by Zhang et al. reported a 2-fold higher mortality risk in frail NH residents with COVID-19 compared to non-frail residents [5]. Moreover, Lengelé et al.

reported a 7-fold higher risk of contracting COVID-19 in frail compared to robust older people [4]. Our findings also differ from the study by Kara et al., which observed that individuals with low grip strength had a 3-fold increased risk of developing severe forms of COVID-19 [6]. However, it is difficult to directly compare our results with these studies as they were conducted primarily in community-dwelling older people. Although no floor effect was observed in our sample in terms of activities of daily living in our sample, the NH resident population is specific and has specific characteristics, such as social status and drug consumption that could influence their health status. In addition, some studies, such as the one of Lengelé, rely on self-reported incidence of COVID-19. In cases of asymptomatic or mild forms, participants may not have been tested, which could reduce the true incidence of COVID-19.

This study has some limitations that make it difficult to generalise our findings, in particular a limited sample size, missing data, a specific population that may not be representative of the NH residents, possible misreporting of data on COVID-19 in residents' medical records and the lack of some potentially confounding variables such as the effect of the NH structure.

In this study, the cognitive level in 2018 was associated with COVID-19 incidence. This finding must be considered with great caution as this confounding variable was not associated with COVID-19 incidence in 2019 or with the changes between 2018 and 2019. Furthermore, its clinical relevance is unknown.

In conclusion, the divergent results in the literature underline the need to remain cautious and to continue to consider older people, and particularly NH residents, as a high-risk population for COVID-19 and to continue to implement strategies to protect them.

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Assessment of risk factors associated with long-term mortality in nursing homes: result from the SENIOR cohort

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Abstract

Background Previous studies on risk factors for death in nursing homes have focused on short-term observation and limited number risk factors.

Aims This study aims to identify factors predictive of 8-year survival in nursing homes.

Methods The study used the baseline measurements from the SENIOR cohort collected in 2013–2014. Data included clinical assessments (i.e., body composition, nutritional status, physical performance, level of dependence and cognition, frailty phenotype) as well as demographic information, number of medications and medical history. Mortality data were collected annually for 8 years. Univariate analyses were initially performed to assess potential predictive factors, followed by a Cox regression model using stepwise selection.

Results Of the 662 participants enrolled in the cohort, 58 (8.8%) were not further assessed due to the withdrawal of 2 nursing homes and 71 (10.7%) had no mortality data available (i.e., relocation, refusal to continue the study). Among the 533 patients included, 111 (20.8%) were still alive in 2022. Median survival time was 4 years (1.93–6.94). Multivariate regression showed that younger age (HR=1.04 (1.03–1.06)), higher body mass index (HR=0.96 (0.94–0.98)), higher score on the Mini-Mental State-Examination (HR=0.97 (0.94–0.99)) and higher score on the Short Physical Performance Battery (HR=0.93 (0.90–0.97)) were protective factors against mortality.

Conclusions This study highlights that certain modifiable factors related to physical or mental health contribute to increased survival in nursing homes. Because of its ability to improve physical performance and partly cognitive function, promoting physical activity in nursing homes appears to be a public health priority.

Introduction

The world is witnessing a shift in the population pyramid, with the number of people over the age of 65 steadily increasing. According to the World Health Organisation (WHO), the number of people aged over 80 is expected to triple by 2050 [1]. The aging process can be accompanied by functional decline, reflected in a loss of mobility, cognitive impairment, dependency in daily living and contributors to old age [2]. At a certain stage, the impact of the decline on older people living in the community may lead to their placement in adapted structures such as nursing homes (NHs) [3]. The current context of an ageing population, combined with medical progress but also the development of age-related chronic pathologies and functional decline is likely to have a significant impact on the need for more beds in NHs in most developed countries in the coming years [4].

The care provided by NHs aims to meet the needs of this specific population. Indeed, they have some particularities compared to the community-dwelling older people. For example, NH residents have been shown to be older, more dependent and have more comorbidities than other older people [5, 6]. In addition, older adults living in NHs tend to have lower life expectancy and higher mortality rates than community-dwelling older people [5]. A study conducted in the UK showed that the risk of dying within a year was 4 times higher for NH residents than for other senior of the same age [7]. In fact, in addition to mortality risk factors such as smoking, chronic disease and physical inactivity [8], prevalent geriatric conditions in NH residents have been associated with poorer short-term survival, such as frailty, low physical performance, low cognitive status and malnutrition [9–12].

Few studies have examined long-term mortality in NHs and they have focused on a limited number of potential risk factors. In the present study, we aimed to use a wide range of data from the SENIOR (Sample of Elderly Nursing Home Individuals: An Observational Research) cohort to identify factors associated with mortality 8 years after cohort entry.

Methods

Study design

This study used baseline data from the Sample of Elderly Nursing Home Individuals: An Observational Research (SENIOR) cohort, which is a prospective longitudinal study, to examine the mortality after 8 years.

Population

A full and detailed description of the SENIOR cohort has been described previously [13]. Concisely, 662 residents were recruited from 28 different NHs in Belgium. All the participants met the inclusion criteria, namely: living in an NH, being mobile with or without walking aids, being able to sign and understand an informed consent form. This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of the Teaching Hospital of the University of Liège (reference 2013/178) with an amendment related to this study in July 2022.

Mortality

The primary outcome of the study was 8-year mortality. All cause mortality was recorded from the residents' medical records in each year of follow-up and retrospectively with an update in 2022. Patients who were considered lost to follow up (i.e., relocated, withdrew from the study) were considered as censoring event in the survival analyses.

Data collection

Data were collected by trained researchers with the active participation of the residents (i.e., physical tests and questionnaires) and from medical records, especially for socio-demographic and anthropometric data.

Frailty

Frailty was assessed according to Fried's phenotype criteria, namely: an unintentional weight loss of 5 kg or≥5% in the previous year by self-report, physical weakness assessed by grip strength, poor endurance and energy assessed by two items of the Centre for Epidemiological Studies Depression Scale, slowness assessed by gait speed and low physical activity level measured by self-reported time spent in physical activity in the previous 7 days based on the Minnesota scale. An individual was defined as frail if three or more criteria were met, as pre-frail if one or two criteria were met and as robust if none of the criteria were met [14].

Body composition

Appendicular lean mass (ALM) was measured using a validated multi-frequency bioelectrical impedance analyser (Biospace Co, Ltd, Korea/Model JMW140). BIA electrodes were placed at 8 points on the body for a multisegmental frequency analysis and the sum of the lean mass of

the arms and legs was used to calculate ALM [15]. The ALM was then divided by the square of the height (ALM/h2) to obtain the appendicular lean mass index (ALMI).

Nutritional status

Nutritional status was assessed using the Mini Nutritional Assessment Short-Form (MNA-SF) which consists of 6 nutritional questions (i.e., weight loss, mobility, acute illness or psychological stress, neuropsychological problem, body mass index) and provides a score between 0 and 14. The score is used to determine nutritional status: normal (12–14), at risk of malnutrition (8–11) or malnutrition (0–7) [16].

Cognitive level

Cognition was assessed using the Mini Mental State Examination (MMSE). This questionnaire consisted of questions to measure cognitive impairment (i.e., repetition of word lists, language use and comprehension, basic motor skills, orientation, concentration, short-term memory, language skills, visuospatial skills and ability to understand and follow instructions). Out of a maximum score of 30 points, a score of 27 or more indicates a normal cognitive status. Below this threshold, mild, moderate and severe cognitive impairment are indicated by scores between 19 and 24, between 10 and 18 and below or equal to 9 [17].

Muscle strength

Muscle performance was assessed by grip strength measured using a hydraulic dynamometer (Seahan Corporation, MSD Europe Bvba, Belgium). Specifically, the participants had to squeeze the dynamometer as hard as possible 3 times in each hand. The highest value was taken as the reference.

Physical performance

Physical performance was first assessed using the Short Physical Performance Battery test (SPPB), a geriatric-validated tool consisting of 3 different tests: balance, gait speed and chair stand. Each of the test is scored separately and then summed to give an overall score. Secondly, physical performance was assessed using the Tinetti test or Performance Oriented Mobility Assessment (POMA) which is designed to assess body balance and gait abnormalities in older people. The test is made up 16 items: 9 assessing balance and 7 assessing gait. Each item is

scored on a scale of 0 to 2, with a maximum score of 28 and lower scores indicating impairment [18].

Level of autonomy and dependence

The ability to perform activities of daily living (ADLs) was assessed using the Katz scale which is based on 6 categories of assessment: bathing, dressing, toileting, transferring, continence and feeding. Scores between 1 and 4 are assigned for each activity category, with higher scores reflecting higher dependence in ADLs [19].

Health related quality of life

The EuroQol-5-Dimension (EQ-5D) questionnaire was used to assess self-reported health state. The dimensions covered by this test are mobility, self-care, usual activities, pain or discomfort and anxiety or depression. Each dimension is scored on 3 levels and converted into a global score ranging from 0 (death) to 1 (perfect health) using an index [20].

Covariates

Sociodemographic and anthropometric data were collected from the participants' medical records at baseline. Based on the literature, some of these data were considered as potential confounding factors: age, sex, level of education, number of medications, number of medical histories, waist circumference and body mass index (BMI) [21–24].

Statistical analysis

Quantitative variables that were normally distributed were expressed as mean and standard deviation (SD), and quantitative variables that were not normally distributed were expressed as median and percentiles (P25-P75). Normality was assessed using the Shapiro–Wilk test, the observation of the Q–Q plot and histogram. The association between patient characteristics and mortality was first examined using the T-Student or Mann–Whitney test and in a bivariate hazard model, expressed as a hazard ratio (HR) and its confidence interval (CI). To retain only those factors most strongly associated with mortality, factors with a p-value < 0.05 were entered into a stepwise proportional hazards model, with variables removed if they did not reach the significant a-level of 0.05. The HR and CI were derived from this model. All analyses were performed with SAS version 9.4 (SAS Institute, Cary, North Carolina).

Results

Of the 622 patients included in the cohort at baseline, 58 were excluded because 2 NHs refused to continue the study. During the different times of follow-up, some participants were lost to follow-up because of relocation (n=41) or refusal to continue the study (n=30) and therefore no survival data were available for them. After considering these losses to follow-up, this study was performed on a final sample of 533 participants from the SENIOR cohort (Fig. 1).

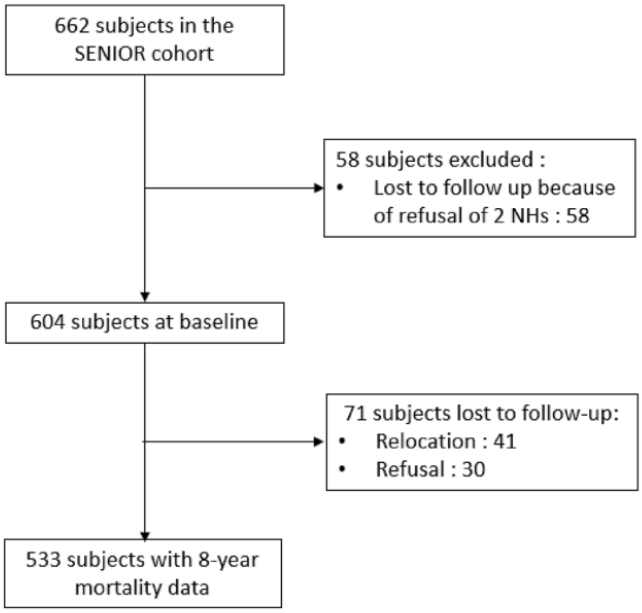

Figure 1. Flowchart of the study

Table 1 shows the characteristics of the participants included in this study. The mean age was 83.4±8.82 years and 86 (73%) were women. The mean number of medications per day was 10.0±4.2 and the mean number of medical histories was 5.6±3.9. Most of the participants had completed secondary education (67.45%). In this sample, 138 (26%) were considered frail and the majority had a normal nutritional status (65%). As shown in the Kaplan–Meier curve (Figure S1 in the supplementary material), median survival time from entry into the cohort to death was 4.0 (1.9–6.9) years.

Table 1. Characteristics of the sample at baseline according to 8-year survival status

			8-year survival status		
		Total	Deceased (n=422)	Alive (n=111)	P-value
Age, years	n=533	83.42 ± 8.82	84.99 ± 7.76	77.50 ± 10.04	**<0.0001**
Gender, women	n=531	391 (73.36%)	305 (72.3%)	86 (77.5%)	0.27
BMI, kg/m^2	n=527	26.13 ± 5.41	25.77 ± 5.58	27.48 ± 4.52	**0.0008**
Medication, number	n=524	10.01 ± 4.23	10.05 ± 4.19	9.87 ± 4.43	0.71
Medical history, number	n=498	5.60 ± 3.89	5 (3-8)	5 (2-7)	0.22
Educational level	n=510				0.44
None or primary education		66 (12.94%)	52 (12.3%)	12 (11.0%)	
Secondary education		344 (67.45%)	268 (63.5%)	76 (68.5%)	
Tertiary education		100 (17.2%)	81 (19.2%)	19 (16.3%)	
Waist circumference, cm	n=519	99.43 ± 14.72	98.70 ± 14.84	102.12 ± 14.02	**0.03**
Grip strength, kg	n=527	18.74 ± 10.27	18.19 ± 9.67	20.79 ± 12.09	**0.04**
ALMI, kg/m^2	n=211	8.9 ± 4.88	8.64 ± 2.92	10.06 ± 9.47	0.20
Fried phenotype	n=531				**0.0002**
Robust		78 (14.69%)	52 (12.4%)	26 (23.4%)	
Prefail		315 (59.32%)	244 (58.1%)	71 (64.0%)	
Frail		138 (25.99%)	124 (29.5%)	14 (12.6%)	
MMSE, /30 points	n=528	24.10 ± 4.58	23.88 ± 4.69	24.90 ± 4.03	**0.03**
MNA	n=524				**0.002**
Normal		341 (65.08%)	255 (61.7%)	86 (77.5%)	
Risk of malnutrition		163 (31.11%)	138 (33.4%)	25 (22.5%)	
Malnutrition		20 (3.82%)	20 (4.8%)	0 (0%)	
SPPB, /12 points	n=527	5.52 ± 3.15	5.14 ± 3.06	6.94 ± 3.07	**<0.0001**
Katz, /30 points	n=522	11.27 ± 3.37	11.59 ± 3.50	10.09 ± 2.47	**<0.0001**
EQ-5D	n=523	0.57 ± 0.23	0.56 ± 0.24	0.62 ± 0.21	**0.01**
Tinetti, /28 points	n=514	22.68 ± 5.66	22.10 ± 5.72	24.83 ± 4.90	**<0.0001**

BMI= Body Mass Index; ALM = Appendicular Lean Mass; MMSE = Mini Mental State Examination; MNA

The results of the univariate Cox regression model are detailed in Table 2. A large proportion of the variables included in the analysis were associated with mortality 8 years after cohort entry. On the one hand, some factors appear to be negatively predictive of mortality, namely, age (HR=1.05 (1.04–1.06)), pre-frail (HR=1.39 (1.03–1.87)) and frail phenotype (HR = 2.16 (1.56–3.00)) compared with robust, risk of malnutrition (HR=1.51 (1.22–1.85)) and malnutrition (HR = 3.26 (2.05–5.18)) compared to normal nutritional status and the Katz score (HR=1.07 (1.04–1.10)). On the other hand, higher BMI (HR =0.96 (0.94–0.98)), higher waist

circumference (HR = 0.99 (0.98–1.00)), higher grip strength (HR=0.98 (0.97–0.99)), higher MMSE score (HR = 0.97 (0.95–0.99)), higher SSPB score (HR=0.90 (0.88–0.93)), higher EQ-5D index (HR=0.50 (0.34–0.76)) and higher Tinetti score (HR=0.95 (0.93–0.97)) were associated with decreased probability of mortality in the cohort.

All significant variables from the univariate regression were entered into the multivariate Cox regression model with stepwise selection. These variables were added to and removed from the model until the model that best explained mortality in the cohort was obtained. The model obtained included 4 variables associated with mortality: age, BMI, MMSE score and SPPB score. Older age was associated with poorer survival, with each additional year increasing the risk of death in the 8 years after the cohort entry by 4%. (HR=1.04 (1.03–1.06)). A one-unit increase in BMI and a one-point increase in MMSE and SPPB scores decreased mortality by reducing the risk of death by 4, 3, and 7%, respectively (HR=0.96 (0.94–0.98), HR=0.97 (0.94–0.99), HR=0.93 (0.90–0.97)).

Table 2. Crude and adjusted Hazard ratio of 8-year mortality

	Crude HR (95% C.I.)	Adjusted HR (95% C.I.)
Age, years	**1.05 (1.04-1.06)**	**1.04 (1.03-1.06)**
Gender, women	0.84 (0.68-1.04)	
BMI, kg/m^2	**0.96 (0.94-0.98)**	**0.96 (0.94-0.98)**
Medication, number	1.01 (0.98-1.03)	
Medical history, number	1.02 (0.99-1.04)	
Educational level		
None or primary education	Ref	
Secondary education	0.85 (0.63-1.14)	
Tertiary education	0.90 (0.64-1.27)	
Waist circumference, cm	**0.99 (0.98-1.00)**	
Grip strength, kg	**0.98 (0.97-0.99)**	
ALMI, kg/m^2	0.97 (0.93-1.02)	
Fried phenotype		
Robust	Ref	
Prefail	**1.39 (1.03-1.87)**	
Frail	**2.16 (1.56-3.00)**	
MMSE, /30 points	**0.97 (0.95-0.99)**	**0.97 (0.94-0.99)**
MNA		
Normal	Ref	
Risk of malnutrition	**1.51 (1.22-1.85)**	
Malnutrition	**3.26 (2.05-5.18)**	
SPPB, /12 points	**0.90 (0.88-0.93)**	**0.93 (0.90-0.97)**
Katz, /30 points	**1.07 (1.04-1.10)**	
EQ-5D	**0.50 (0.34-0.76)**	

Tinetti, /28 points	**0.95 (0.93-0.97)**

HR = Hazard ratio; C.I. = confidence interval; BMI= Body Mass Index; ALM = Appendicular Lean Mass; MMSE = Mini Mental State Examination; MNA = Mini Nutritional Assessment; SPPB = Short Physical Battery Test; EQ-5D = EuroQol- 5 Dimension

Discussion

This study aimed to identify potential factors associated with 8-year mortality in the SENIOR cohort composed of more than 600 NH residents. Our study showed that among the various factors covering different aspects of health, age, BMI, cognitive level and physical performance level were independently associated with mortality in this cohort. Many studies have focused on short-term mortality in NHs and within our SENIOR cohort some short-term associations have been highlighted. In particular, 1-year mortality was associated, notably, with sarcopenia (which includes a component of physical performance) [22], a lower risk of 2-year mortality was associated with higher BMI [25] and higher 3-year mortality was associated with a decline in physical performance [26]. However, the investigation of long-term mortality is a necessary concern to adapt the care of NH residents.

A recent study exploring 9-year mortality in NHs in Poland showed a median survival time of 2.4 years and that 17% of NH residents survived for 8 years or more [27]. In our study, we found a median survival time of 4 years and 20.8% of the participants were still alive after 8 years. The difference in median survival time can be partly explained by the fact that the population included was substantially different; the Polish study focused on NH residents with chronic diseases and a certain level of dependency. As the presence of chronic diseases is associated with mortality, shorter life expectancy could be one way of explaining this difference [28]. Furthermore, due to the inclusion criteria in the SENIOR cohort, in particular mobility, the sample in this study might be in better general health than the Polish sample with a longer life expectancy in the SENIOR cohort.

We highlighted that each year of age increased the mortality by 4% in the cohort. This finding is consistent with the literature where age is a well-known non-modifiable factor decreasing the probability of survival [29]. The association between age and mortality in NH residents reported in other studies varies with hazard ratios between 0.5 and 4% depending on the time of observation.

In our study, a higher BMI was associated with a 4% decrease in 8-year mortality. This finding is consistent with a meta-analysis constituted of more than 19.000 NH residents worldwide, which showed an inverse association between BMI and mortality [30]. At first glance, this

seems paradoxical because in the general population, overweight and obesity are associated with an increased risk of disability and decreased survival [31]. However, in the geriatric population, there is a J-shaped curve for BMI, observable with a protective effect of overweight and obesity [30, 32]. Although on the one hand, a higher BMI is associated with improved survival, on the other hand, obesity can lead to potential negative health effects, especially on comorbidities, disability, physical performance and malnutrition [32]. However, within our cohort, the mean BMI of the participants was 26, which corresponds to an overweight status and a lower risk of adverse outcomes. Few studies have investigated the association between cognition level and mortality in NHs. Our results are in concordance with an observational study that showed a higher number of deaths in NH residents with lower cognitive level after 3 years [33]. A Chinese study also conducted on NHs showed a decreased risk of death within 5 years with higher cognitive level (HR = 0.95 (0.92–0.99)) [12]. These findings are consistent with studies carried out outside NHs, which have shown a robust and significant association between cognitive status and survival. This association could be explained by three possible explanations: cognitive decline is an early indicator of dementia, which can reduce life expectancy; the presence of comorbidities, which can affect both cognition and mortality; and the difficulty of maintaining a healthy diet or physical activity in the presence of cognitive impairment [34]. Finally, we showed that physical performance level was significantly associated with mortality. This finding was also reported in a 5-year survival study conducted in Brazil, where the risk of death was 2.7 times higher in people with low physical performance assessed by the SPPB (HR = 2.77 (1–40,5.50)) [11]. However, an analysis of 1-year mortality using a composite score of the SPPB showed no association with survival [35]. Obviously, the shorter follow-up time may partly explain the different results obtained. Indeed, a meta-analysis conducted by Pavasini et al., regrouping no less than 16.000 older people, showed that an SPPB score below 10 was associated with an increased risk of all-cause mortality [36]. In addition, in the NH resident population, a decline in SPPB score over time has also been shown to be associated with an increased risk of mortality, providing some consistency with the findings of our study [26].

On the other hand, some other factors have been associated with medium-or long-term mortality in NHs in the literature, but not in our study. In the study by Kantoch et al., gender and nutritional status were significantly associated with long-term survival (i.e., 9 years) [27]. In the same vein, Ozturk et. al recently highlighted the association of MNA-SF with mortality up to 7 years [37]. Regarding nutritional status, some differences in our methodology could explain

the different results obtained. In our univariate analysis nutritional status was significantly associated with mortality but not in the stepwise proportional hazards model. In fact, in the case of two highly correlated variables, this statistical method only retains one of them [38]. This is likely to be the case for nutritional status, which has been reported in the literature to be associated with several variables included in our analyses, such as cognitive status and BMI [39, 40]. Surprisingly, our study found no association between gender and survival. It has been known for years that women have a longer life expectancy than men [41]. Logically enough, gender should have been significantly associated with mortality in our study. The rationale we can put forward to explain why this is not the case is the gender distribution within our cohort. In fact, the proportion of women was 73%, which possibly leads to a lower statistical power of this variable. Furthermore, no association between mortality and frailty was highlighted in this study, in contrast to the meta-analysis conducted by Zhang et al. which included 9076 NH residents and in which frailty appeared to be a strong predictor of mortality (HR = 1.88 (1.57, 2.25)) [42]. There are several possible explanations for this difference. Firstly, thirteen of the fourteen studies included in Zhang's meta-analysis had a time span of 2 years or less compared to the follow-up of 8 year of our study. Secondly, it was shown that the ability to discriminate between frail and non-frail patients, as well as the likelihood of negative outcomes such as mortality, varied according to the definition of frailty used [43, 44]. At last, frailty appeared to be significantly associated with mortality in our univariate analysis. It is possible that, in the SENIOR cohort, frailty was a weaker factor associated with mortality as it did not remain significant in the multivariate analysis.

This study has several limitations. First, there is some evidence that changes in health status over time could influence survival, as reported in a Belgian study that used data on physical performance over time to identify evolutionary trajectories that were significantly associated with mortality [26]. However, we have only used baseline data, which is a non-dynamic reflection of the health status of the participants. Second, survival probabilities should not be limited to health elements in old age. In fact, conditions throughout life can have an impact on mortality, as shown by this recent Italian study, which looked at mortality in a cohort of men during a follow-up period of 61 years. It appeared that some factors such as literacy, Mediterranean diet, early maternal death were associated with mortality in the very long term [45]. Unfortunately, we did not have the opportunity to collect these data and, therefore, to include them in this study. Third, several factors could not be included in this analysis. This is particularly the case for preventive factors, such as pneumococcus or influenza vaccinations,

social engagement and depressive disorders which have been associated with mortality in NH residents [46,47,48,49]. Fourth, it is important to consider the fact that some of the mortality data in this study were collected during the COVID-19 pandemic, which severely affected NHs. As in many other countries, excess mortality was reported in Belgium. Up to October 2021, half of all COVID-19 deaths in Belgium involved nursing home residents, representing 7.9% of the nursing home population (out of 162,700 residents) [50]. Then, we did not measure comorbidities with a standardised and validated tool, but as a "medical history" consisting of all the participants' antecedents. Furthermore, our results must be considered cautiously. Indeed, the population included in our cohort in 2013 may no longer correspond to the actual population in NHs. In fact, the living habits of older people have been changing for several years. Particularly in Europe, many aids have been developed to help older people stay at home despite their daily difficulties. This has led to people being admitted to NHs later and in poorer health than before [51]. Finally, due to refusal to continue the study and relocation, we were unable to include data from one-fifth of the patients enrolled at baseline. This significant proportion of missing data may have influenced the results.

On the other hand, this study has some strengths. First, mortality in the SENIOR cohort has been explored at different follow-up times with some consistent results. In particular, a significant association was observed between lower mortality rate and lower BMI, decline in physical performance and age [22, 25, 26]. We can hypothesise that these factors are strong predictors of mortality over time, which reinforces the robustness of the results obtained. Secondly, the cohort consisted of a relatively large sample size which contributes to the robustness of the statistical analyses. Finally, the 8-year period with a large inclusion of health components provided a unique opportunity to observe factors associated with mortality in the long term.

This study has some interesting implications. The first is to encourage further studies to explore the long-term survival in NHs to confirm our findings. The second is to encourage the promotion of physical activity in nursing homes. Indeed, physical activity seems to be a good lever to act on both physical performance and cognitive abilities, in addition to improve, notably, quality of life [52, 53]. The third is to encourage interventional studies to assess the impact of physical activity on the levels of physical performance and cognitive abilities in NH residents.

In conclusion, our study shows that in addition to age, which is a non-modifiable risk factor, certain modifiable factors related to physical or mental health contribute to increased 8-year

survival in NHs. In addition to the assessment and screening with regular follow-up of these factors, the promotion of physical activity in nursing home residents should be a public health priority.

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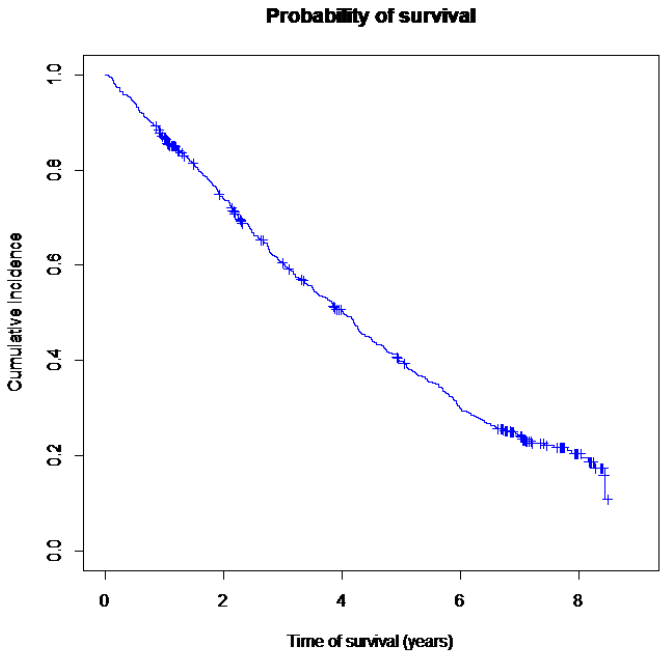
Supplementary material

Figure S1. Probability of survival



Longitudinal Associations Between Changes in Muscle Strength, Muscle Mass, and Physical Performance and Health-Related Quality of Life in Older Adults: A Four-Year Analysis from the SarcoPhAge Cohort

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Abstract

Background Sarcopenia, defined by a decline in muscle strength, muscle mass and physical performance, is associated with poorer health-related quality of life (HRQoL) in older adults. However, longitudinal studies investigating this relationship using sarcopenia-specific HRQoL instruments remain scarce.

Objective To investigate the association between changes in sarcopenia components and changes in HRQoL over four years using the SarQoL questionnaire, a tool specifically designed for individuals with sarcopenia.

Methods This study included 333 community-dwelling older adults from the SarcoPhAge cohort, followed annually for four years. HRQoL was evaluated using the SarQoL questionnaire. Sarcopenia components were measured using a handgrip dynamometer to assess muscle strength, dual-energy X-ray absorptiometry (DEXA) to assess muscle mass and the Short Physical Performance Battery (SPPB) test to assess physical performance. Associations between changes in sarcopenia components and changes in global and domain-specific SarQoL scores were assessed using linear mixed models, with random effects to account for within-subject variation.

Results Over four years, the increases in physical performance ($\beta = 1.04$; $p < .0001$), grip strength ($\beta = 0.195$; $p = .0001$) and muscle mass ($\beta = 2.47$; $p < .0001$) were independently associated with an improvement in the global SarQoL score. Analyses of the seven SarQoL domains yielded consistent findings.

Conclusion The results support the use of the SarQoL questionnaire as a specific and sensitive instrument for monitoring HRQoL in older adults, as it appears responsive to changes in muscle mass, strength and physical performance.

Introduction

In the current context of an ageing global population, there is an increasing need to enhance our comprehension and response to the health challenges associated with ageing [1]. Although increased longevity is frequently considered as a sign of progress, it also raises questions regarding the quality of these additional years of life, particularly in relation to the burden of chronic diseases and age-related syndromes. Quality of life (QoL) is a multidimensional concept encompassing the individual's perception of their physical health, psychological state, level of independence, social interactions and the relationship with key environmental factors [2]. Importantly, QoL is increasingly recognised not only as an outcome, but also as a key component in assessing the impact of chronic diseases and geriatric conditions on daily functioning and well-being [3]. Health-related quality of life (HRQoL) focuses specifically on the impact of health status on QoL [4]. HRQoL is usually assessed using standardised questionnaires belonging to the broader category of patient-reported outcome measures (PROMs). These questionnaires are increasingly used in clinical research to capture the patients' subjective experiences and complement traditional clinical indicators [5].

Sarcopenia is a common geriatric condition, with an estimated prevalence of between 10% and 27% in the population of older adults aged 60 years and over [6]. While there is no universally accepted definition, sarcopenia is commonly characterised by a decline in three core components: muscle strength, muscle mass and physical performance [7-11]. In addition to its physiological consequences, including an increased mortality and hospitalisation [12], sarcopenia is also associated with a significant decline in quality of life [13, 14]. Historically, HRQoL in people with sarcopenia has been assessed using generic tools such as the 36-item Short Form Health Survey (SF-36) or the Euroqol five item questionnaire (EQ-5D) questionnaires. However, these instruments may lack sensitivity to the specific impairments and limitations associated with sarcopenia. In response to this, the Sarcopenia and Quality of life (SarQoL) questionnaire was developed in 2015 as the first PROM specifically designed to assess HRQoL in sarcopenic populations [15]. This validated, self-administered instrument covers multiple domains, including notably physical and mental health, locomotion, functionality and activities of daily living, making it particularly suited to explore the subjective burden of sarcopenia.

Despite the availability of cross-sectional data on the relationship between sarcopenia and HRQoL, longitudinal studies remain limited. Furthermore, existing longitudinal studies have

only used generic HRQoL instruments and have not disaggregated sarcopenia into its core components. Moreover, the majority of these studies have used sarcopenia status at baseline, however it has been demonstrated that sarcopenia, and more specifically, its core components can deteriorate or improve over time [16-18]. The present study aims to address these gaps by investigating whether longitudinal changes in muscle mass, muscle strength and physical performance are associated with longitudinal changes in HRQoL, as measured by a specific-instrument, namely the SarQoL questionnaire, over a four-year period in community-dwelling older adults from the SarcoPhAge cohort.

Methods

Population

This study used data from the SarcoPhAge (Sarcopenia and Physical Impairment with Advancing Age) cohort, which is a prospective observational study that was initiated in 2013. The cohort initially included 534 community-dwelling participants aged 65 years or over, who were followed up for five years. The study design of this cohort has been described in detail elsewhere [19].

The present study used data from five annual follow-up waves (Y1 to Y5). As the SarQoL questionnaire was introduced at Y1, information collected at Y0 was excluded from the analysis. Only participants who completed the SarQoL questionnaire at Y1, defined as the baseline for this study, were considered eligible (n=387, 72.5%). Given the aim to analyse the longitudinal evolution of SarQoL scores, patients with fewer than two visits involving a SarQoL assessment were excluded. This resulted in a final sample size of 333 participants (62.3%) for the longitudinal analysis (Figure 1).

Ethics Statement

This study has been approved by the Ethics Committee of the Teaching Hospital of the University of Liège (reference 2012/277). Written informed consent was obtained from all participants before they were included in the study.

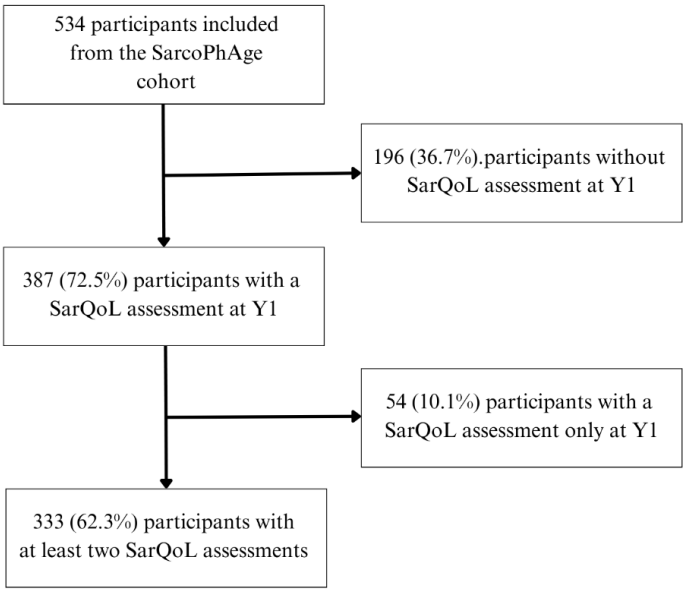

Figure 1. Selection of patients included in the analysis

Health related quality of life

HRQoL was assessed using the SarQoL questionnaire. This validated self-administered questionnaire is specifically designed to measure HRQoL in people with sarcopenia. The questionnaire consists of 22 questions comprising 55 items distributed across seven different domains: physical and mental health, locomotion, body composition, functionality, activities of daily living, leisure activities and fears. Each domain is scored from 0 to 100 and these scores are then converted into a global score, also ranging from 0 to 100 with higher scores indicating higher levels of HRQoL. The SarQoL has demonstrated good psychometric properties, content validity and responsiveness [20-22].

Components of sarcopenia

Sarcopenia was assessed according to the criteria proposed by the EGWSOP definition, with each component considered separately in this study [8].

- Muscle strength was measured using a hydraulic hand dynamometer (Saehan Corporation, Korea or MSD Europe Bvba, Belgium). Participants pressed the dynamometer three times with each hand, and the highest value was taken as the reference [23].
- Muscle mass was measured using dual-energy X-ray absorptiometry (DEXA; Hologic Discovery A, USA), with daily calibration to ensure accuracy. Skeletal

muscle mass index (SMI) was calculated by dividing appendicular lean mass by height squared (kg/m²).

- Physical performance was assessed using the Short Physical Performance Battery (SPPB) test, which includes a balance test, a walking speed test and a chair-stand test [24].

Covariates

In addition to the HRQoL and sarcopenia components, additional data were systematically collected from all participants at each annual follow-up visit. Some of these were considered potential confounders due to their reported association with QoL and sarcopenia and were therefore included in our statistical models. The following covariates were therefore included: age, gender, level of education, number of concomitant diseases, number of medications, nutritional status assessed by the Mini Nutritional Assessment (MNA) [25], limitation in activities and functional activities of daily living assessed by the Katz and Lawton scales [26, 27], cognitive function evaluated using the Mini Mental State Examination (MMSE)[28], depressive symptoms assessed by the Geriatric Depression Scale (GDS) [29] and level of activity measured using the Minnesota scale [30].

Statistical analysis

Qualitative variables were summarised using frequency tables, while quantitative variables were expressed as median and interquartile range (Q1-Q3). The normality of the distribution was assessed using histograms, Q-Q plots and the Shapiro-Wilk test. All the variables were considered longitudinally (i.e. changes between the different follow-up times), except for age, gender and education, which were only considered at baseline. Linear mixed effects models for longitudinal data were used to examine factors associated with HRQoL in participants. A random effect was included in each model to account for within-subject variation due to repeated individual measurements over time. The model was adjusted for baseline characteristics and identified potential confounders. To account for the difference in Lawton score between men and women, the interaction between gender and Lawton score was included in the model. Model results are reported as coefficients (β), standard errors (SE) and p-values. As certain variables (i.e. MMSE, MNA and GDS) were not available at the third visit (Y3), the data corresponding to this wave were not included in the model. The same approach was followed for each of the seven SarQoL domains. All available observations were included in

the analysis with no imputation of missing data. The confidence level was set at 95% ($p<0.05$) and statistical analyses were performed using R (version 4.2.0), linear mixed models were conducted using nlme R package [31].

Results

Table 1 presents the baseline characteristics of the 333 participants included in this study from the SarcoPhAge cohort. The median age of the participants was 72.6 years (68.7-77.5) and 196 participants (58.9%) were women. The majority had a high level of education (40.2%). The median number of follow-up visits was 4 (3–5). The median body mass index was 26.8 kg/m2

Table 1. Baseline characteristic of the participants (n=333)

	Total (n=333)
Age, years	72.6 [68.7-77.5]
Gender	
Women	196 (58.9%)
Level of education	
Without qualification	5 (1.5%)
Primary school	29 (8.7%)
Lower secondary school	62 (18.6%)
Upper secondary school	99 (29.7%)
Post-secondary education	134 (40.2%)
Doctoral	4 (1.2%)
Visits per participant, number	4.00 [3.00-5.00]
BMI, kg/m^2	26.8 [23.8-30.0]
MMSE, /30 points	29.0 [28.0-30.0]
Katz, /24 points	8.00 [8.00-8.00]
Minnesota, kcal/day	897 [368-1580]
GDS, /15 points	2.00 [1.00-5.00]
Concomitant disease, number	4.00 [3.00-5.00]
Medication, number per day	5.00 [3.00-8.00]
Lawton	
Men, /5 points	5.00 [5.00-5.00]
Women, /8 points	8.00 [8.00-8.00]
Sarcopenia diagnosis, EWGSOP2	12 (3.6%)
Sarcopenia component	
SPPB, /12 points	11.0 [9.00-12.0]
Grip strength, kg	26.0 [20.0-38.0]
SMI, kg/m^2	6.72 [5.90-7.66]

BMI: Body Mass Index; MMSE: Mini Mental State Examination; GDS: Geriatric Depression Scale; SPPB: Short Physical Performance Battery; SMI: Skeletal muscle mass index.

(23.8-30.0) and the MMSE was 29 (28-30). The median Katz scale score was 8 (8-8) while the median score for instrumental activities of daily living, assessed using the Lawton scale, were 5 (5-5) for men and 8(8-8) for women. The median energy expenditure, measured with the Minnesota questionnaire, was 897 kcal/day (368-1580). The median GDS score was 2 (1-5). The median number of concomitant diseases was 4 (3-5) and the median number of medications per day was 5 (3-8). According to the EWGSOP2 criteria, 12 participants (3.6%) were identified as sarcopenic. Regarding its components, component, the median physical performance score measured with the SPPB was 11 (9-12), the median muscle strength assessed by grip strength was 26 kg (20-38) and the median SMI was 6.72 kg/m2 (5.90-7.66).

Results from the adjusted linear mixed effect regression assessing the association between changes in sarcopenia components and changes in the global SarQoL score are shown in Table 2. In this table positive coefficients indicate that an increase in the corresponding sarcopenia component (grip strength, SMI or SPPB score) is associated with an increase in the corresponding SarQoL domain score. Over the 4-year follow-up period, significant and independent associations between increases in HRQoL and sarcopenia components were observed. More specifically, improvements in physical performance, as measured by changes in SPPB scores over time, were significantly associated with increases in the global SarQoL score ($\beta = 1.04$, $p < .0001$). Similarly, improvements in grip strength ($\beta = 0.195$, $p = .0001$), and skeletal muscle mass index ($\beta = 2.47$, $p < .0001$) were independently associated with an increase of HRQoL.

Table 2. Results of the adjusted linear mixed model modelling changes in the global SarQoL score in association with changes with sarcopenia components (N=333)

Variable		Coefficient±SE	P-value
Follow up, days		-0.002±0.0005	***<.0001***
Sarcopenia components			
SPPB		1.04±0.170	***<.0001***
Grip strength, kg		0.195±0.050	***0.0001***
SMI, kg/m²		2.47±0.596	***<.0001***
Gender (ref= men)	Women	1.75±4.46	0.69
Age, years		-0.351±0.096	***0.0003***
Education (ref=none)	Primary school	-0.368±4.68	0.94
	Lower secondary school	0.994±4.50	0.83
	Upper secondary school	1.83±4.44	0.68
	Post-secondary education	2.31±4.42	0.60
	Doctoral	2.33±6.34	0.71
BMI, kg/m^2		-0.845±0.134	***<.0001***
MMSE, /30 points		-0.010±0.135	0.94
Katz scale, /24 points		-0.482±0.218	*0.027*
Lawton (ref=men)	Women	0.115±0.770	0.88
MNA, /12 points		0.364±0.179	*0.043*
Minnesota, kcal/week		0.0003±0.0001	***0.0022***
GDS, /15points		-1.10±0.099	***<.0001***
Concomitant disease, number		-0.771±0.184	***<.0001***
Medication, number		-0.332±0.094	***0.0004***

SE: standard error; Model adjusted for baseline characteristics (age, gender, education) and for changes in BMI, cognitive status, functional status, nutritional status, depressive symptoms, concomitant diseases, and the number of medications

As presented in Table 3, after adjustment for potential confounders, improvements in physical performance were significantly associated with increased HRQoL across all seven SarQoL domains (all $p < 0.01$). Improvements in grip strength were also associated with increased HRQoL scores in domain 1 (physical and mental health), domain 4 (functionality) and domain 5 (leisure activities). Finally, increased scores in SMI were significantly associated with higher HRQoL scores in five of the seven SarQoL domains. Although the associations between SMI and domains 6 (fears) and 7 (mobility), as well as between grip strength and domains 2, 3, 6 and 7, did not reach statistical significance, the observed trends remained consistent with those of the global SarQoL scores.

Models adjusted for baseline characteristics (age, gender and level of education) and for longitudinal changes in follow-up time, body mass index, level of cognition, activities of daily living, instrumental activities of daily living, level of activity, nutritional status, depressional symptoms, number of concomitant diseases and medications.

Table 3. Results of the adjusted linear mixed models modelling changes in the seven domains of SarQoL with the sarcopenia components changes (N=333)

	Increase in Grip strength (kg)		**Increase in SMI (kg/m²)**		**Increase in SPPB (points)**	
	Coefficient±SE	P-valeur	Coefficient±SE	P-valeur	Coefficient±SE	P-valeur
Domain 1	0.147±0.067	**0.028**	2.16±0.778	**0.0055**	0.982±0.233	**<.0001**
Domain 2	0.123±0.084	0.14	3.60±0.987	**0.0003**	1.39±0.294	**<.0001**
Domain 3	0.103±0.077	0.18	1.94±0.895	**0.031**	0.986±0.279	**0.0004**
Domain 4	0.171±0.056	**0.0024**	2.46±0.663	**0.0002**	1.43±0.193	**<.0001**
Domain 5	0.341±0.074	**<.0001**	2.86±0.869	**0.0011**	1.09±0.259	**<.0001**
Domain 6	0.102±0.098	0.30	1.65±1.10	0.14	1.75±0.367	**<.0001**
Domain 7	0.045±0.060	0.45	1.62±0.676	**0.017**	0.579±0.220	**0.0086**

Models adjusted for baseline characteristics (age, gender and level of education) and for longitudinal changes in follow-up time, body mass index, level of cognition, activities of daily living, instrumental activities of daily living, level of activity, nutritional status, depressional symptoms, number of concomitant diseases and medications.
Kg: kilograms; SMI: Skeletal Muscle Mass Index; m^2: meter squared; SPPB: Short Physical Performance Battery; SE: standard error.

Discussion

In the present study, we have investigated the association between longitudinal changes in muscle mass, muscle strength and physical performance with the longitudinal changes of HRQoL over a 4-year follow-up period. To our knowledge, this is the first study to explore the three components of sarcopenia in relation to HRQoL, assessed using SarQoL, the only questionnaire specifically designed for individuals with sarcopenia. The study highlighted that increases in muscle mass, muscle strength and physical performance were independently and significantly associated with a higher HRQoL level.

To our knowledge, the only other longitudinal study, using the same statistical analyses as ours, that explored the relationship between HRQoL and sarcopenia components is the study by Trombetti et al [32]. Our findings partially align with those reported in their study. Firstly, contrary to the study by Trombetti et al., a significant association between muscle strength and HRQoL was observed in the present study. This difference could be partially explained by the different methods used to assess muscle strength. Indeed, Trombetti et al. used the lower extremity muscle strength whereas we used grip strength. Furthermore, they assessed HRQoL using the SF-36 questionnaire in a relatively small sample size (N=48), whereas this generic

questionnaire has been reported to be less sensitive than SarQoL in measuring HRQoL [13]. On the other hand, and consistently with our findings, they also reported a significative association between muscle mass and HRQoL (β = 0.102, p=0.046). However, it should be noted that different methods were used to assess muscle mass. Indeed, Trombetti et al. measured muscle mass using computed tomography while DEXA was used in the present study. Finally, the present study showed an association between physical performance and HRQoL. which is in line with Trombetti et al., who demonstrated that increased SPPB scores were associated with a higher HRQoL level over 3 years. These findings are reinforced by a large longitudinal study which, although not directly evaluating the HRQoL, showed a significant association between SPPB scores and mobility impairment, ADL disabilities and IADL disabilities over a period of 12 years [33]. Interestingly, these aspects (i.e., mobility and (I)ADL) are covered by various domains of the SarQoL questionnaire. This conceptual overlap reinforces the robustness of the observed association between physical performance and HRQoL.

One of the key strengths of this study is that it is, to our knowledge, the first study to examine the association between changes in sarcopenia components and HRQoL assessed using the SarQoL instrument. To date, SarQoL is the only sarcopenia-specific questionnaire and offers a more appropriate alternative than generic questionnaires for assessing HRQoL regarding the sarcopenia components in older populations [13]. Additionally, the data regarding HRQoL and sarcopenia components were treated longitudinally, as were all the variables that were introduced in the model (except for age, gender and level of education). This allowed for the capture of intra-individual changes in sarcopenia components and their impact on HRQoL over a period of 4 years, independently of the evolution of other covariates. Another strength lies in the consistency of the observed associations across the seven SarQoL domains. While muscle strength and mass were associated with most of the domains, physical performance was consistently associated with all of them. This multidimensional consistency strengthens the robustness of our findings and underscores the value of domain-specific assessments in capturing the more nuanced aspects of HRQoL. Interestingly, even without applying a threshold-based definition to each sarcopenia component, SarQoL scores appeared sensitive to changes in muscle mass, strength and physical performance. This suggests that SarQoL may capture relevant variations in HRQoL and have a broader utility in older adults experiencing physical decline, beyond those formally diagnosed with sarcopenia. This important finding supports the expanded use of the SarQoL questionnaire in clinical practice and research, particularly in the context of prevention and intervention.

Nevertheless, some limitations must be acknowledged. Firstly, the research was carried out exclusively in Belgium. However, it has been reported that quality of life measures may vary in different cultural or geographical contexts [34]. This could potentially limit the external validity and generalisation of our findings. Therefore, caution should be exercised when extrapolating our findings to populations with different sociocultural contexts. In addition, some potential confounding factors that have been reported as being associated with HRQoL in relation to muscle strength, muscle mass, and physical performance, such as nutritional intake, lifestyle habits and sleep quality [35-37], were not included in this study, as the necessary data was not collected during the SarcoPhAge cohort follow-up. Another potential limitation is the lack of information on any medical or lifestyle interventions that participants may have received during the follow-up period. Indeed, treatments or interventions such as physiotherapy or nutritional support may have affected muscle strength, muscle mass and physical performance, and consequently quality of life [38, 39].

In conclusion, this study highlights that increases in muscle strength, muscle mass and physical performance are each independently associated with higher level of HRQoL over time.

These findings emphasise the importance of regularly monitoring sarcopenia components in older adults to maintain or improve their quality of life. Using a sarcopenia-specific questionnaire, such as SarQoL, appears to be an appropriate and informative approach in this context. Further longitudinal studies using the SarQoL questionnaire are needed to confirm these results in other populations and settings.

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CHAPTER 2

Psychometric robustness of the SarQoL questionnaire

Content validity of SarQoL, a quality of life questionnaire specific to sarcopenia

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Abstract

Background The Sarcopenia & Quality of Life (SarQoL) questionnaire is a patient-reported outcome measure designed for assessing health-related quality of life in individuals with sarcopenia. Despite its wide acceptance in the scientific literature, its content validity has only been partially demonstrated so far.

Aims To enhance the evidence supporting the content validity of the SarQoL questionnaire.

Methods Following COSMIN methodology, semi-structured interviews were conducted with 17 Belgian older adults who met the EWGSOP2 criteria for the diagnosis of sarcopenia and 11 experts in sarcopenia, with clinical or research back ground. Comprehensiveness, relevance and comprehensibility of SarQoL content were assessed through individual transcripts and were qualitatively analyzed thematically according to the seven dimensions of SarQoL.

Results The majority of the concepts elicited during the semi-structured interviews fitted within existing SarQoL dimensions. Importantly, the different domains of SarQoL were consensually considered as relevant by patients and experts. Some new emergent concepts were identified by the participants. While many of them could be considered as enrichments of existing dimensions or sub-concepts, other new concepts (i.e. self-fulfilment, acceptance of the reduced condition, adaptation/ use of strategies, depression) may highlight two potential dimensions not covered by SarQoL, i.e. patient empowerment and depression. Cognitive interviews also highlighted that SarQoL items and instructions were clear and comprehensible.

Conclusions SarQoL, in its current form, demonstrates good evidence of content validity for assessing health-related quality of life in patients with sarcopenia. We do not recommend adding new items or dimensions to SarQoL. Instead, for researchers or clinicians who aim to specifically address self-empowerment or depression of sarcopenic populations, we suggest completing the assessment of quality of life by concurrently using additional validated scales of patient empowerment or depression.

Introduction

Sarcopenia, defined as a progressive decline in muscle mass and muscle strength, the severity of which is determined by physical performance [1], has been widely highlighted in the scientific literature for its impact on health-related quality of life (HRQoL) [2]. In 2013, a HRQoL sarcopenia-specific patient-reported outcome measure (PROM), namely the Sarcopenia & Quality of Life (SarQoL) questionnaire, has been developed. Indeed, while generic tools (e.g. SF-36, EQ-5D) were previously used to measure HRQoL in sarcopenic individuals, specific instruments have been shown to be associated with greater validity, credibility and responsiveness to change at the individual level and are wide spread due to their ability to capture patient experiences that cannot be measured by traditional physiological outcomes [3]. Today, the SarQoL questionnaire, available in more than 30 languages (www.sarqol.org) is the unique available HRQoL specific questionnaire for sarcopenia. Nineteen validation studies performed on SarQoL have consensually confirmed the capacity of SarQoL to detect difference in HRQoL between older people with and without sarcopenia, its reliability and its validity [4].

Although SarQoL is widely accepted and used, one of its psychometric properties, i.e. content validity, is considered as insufficient according to the COSMIN guidelines published in 2018 [5]. The reason is that, since the initial development of the SarQoL questionnaire in 2013, more detailed guidelines and standards have been established for demonstrating PROMs' content validity. Demonstrating the content validity of a PROM requires to generate qualitative evidence that ensures that the questionnaire's framework and items align effectively with the intended measurement concept, population and context of use [6]. The development of SarQoL was based on an exhaustive literature review, experts and sarcopenic patients' interviews, from which a list of 180 potential items was generated. Professionals and sarcopenic patients were then asked to review the list and select the items they considered most relevant to be included in SarQoL. After that, a pre-test of SarQoL was conducted with 21 sarcopenic individuals that confirmed the comprehensibility and comprehensiveness of the tool [5, 7]. Nevertheless, concerning the content validity itself, COSMIN methodology requires to evaluated criteria encompassing 3 major aspects: relevance, comprehensibility and comprehensiveness in patients and experts [5]. To date, only one study has conducted a content validity analysis per se of SarQoL [8]. While the results of this study highlighted an adequate and acceptable content validity, this study was based solely on professionals' opinions without fulfilling all the COSMIN criteria and without any patient involvement, leaving the content validity of SarQoL

not entirely confirmed according to the COSMIN criteria [7].

The current study aimed to fill this gap to provide a complete assessment of content validity of SarQoL by conducting qualitative interviews with experts and patients suffering from sarcopenia.

Methods

This study has been approved by the Ethics Committee of the Teaching Hospital of the University of Liège in June 2023 with an amendment to a previous study protocol (reference 2012/277). Prior to the interviews, all patients provided written informed consent. The specific proto col related to this research is available on Open Science Framework (https://osf.io/6swue/). The COSMIN standard for validating the content validity of a PROM was followed thorough the whole conduct of this research [5].

The SarQoL questionnaire

SarQoL consists of 55 items integrated into 22 questions covering 7 dimensions of HRQoL: physical and mental health (Domain 1 (D1), locomotion (D2), body composition (D3), functionality (D4), activities of daily living (D5), lei sure activities (D6) and fears (D7). Most of these items can be thought of as 3-, 4-, or 5-point Likert items, whereas the remaining are multiple choice questions that permit more than one answers. The questionnaire gives a score for each of these dimensions as well as an overall score out of 100 points. Higher scores reflect better HRQoL.

Participants

Patients

Patients were recruited within the SarcoPhAge (Sarcopenia and Physical Impairment with Advancing Age) cohort [9]. This cohort consists of French-speaking Belgian community-dwelling older adults (65 years and older), followed annually since 2013.

For the assessment of content validity of SarQoL, patients diagnosed with sarcopenia, according to EWGSOP2 criteria, were contacted to be part of the research [1]. Specifically, the sarcopenic patients in this cohort were invited to participate in this study on a step-by-step basis until the data saturation was reached. Efforts were made to recruit participants representing the full spectrum of sarcopenic patients, including those suffering from severe sarcopenia. In line with the COSMIN methodology and based on original studies with similar aims to this study [5, 10, 11], we set an initial sample size of 20 participants as the target sample. However, to ensure

adequacy, concept saturation was examined [5] and interviews were conducted until complete concept saturation was observed.

Experts

Eleven experts with clinical or research experience in the field of sarcopenia were recruited to evaluate the relevance, comprehensiveness, and comprehensibility of SarQoL. The panel consisted of five clinical researchers, one gerontologist, four geriatricians, one intensive care physician and one cardiologist, ensuring a diversity of expertise. Interviews were conducted either in French or English, depending on the language preference of the expert [5].

Qualitative interviews

A semi-structured interview guide (available on the OSF account related to this project https://osf.io/6swue/) was developed based on the ten criteria for good content validity of a PROM recommended by the COSMIN guideline [5] as well as on the interview guide developed by the EORTC Quality of Life Working Group who recently published a study with similar objectives to our study [10]. Two trained researchers team member (CD, CB) conducted face-to-face interviews with participants and experts and recorded them with their consent. All interviews began with an open discussion to allow participants to describe how sarcopenia may affect their HRQoL. This ensures a free and open generation of concepts. Afterward, SarQoL was thoroughly reviewed to explore the relevance of the seven domains to ensure that each domain was explored in detail. The final step of the interview consisted of a structured cognitive debriefing on the comprehensibility and comprehensiveness of each question of SarQoL. Participants were also asked to provide their feedback on their understanding of the instructions and their opinion on the length of the SarQoL questionnaire.

Data analysis

The content validity of SarQoL was assessed through a qualitative analysis of interview data. Audio recordings were integrally transcribed and anonymised. A thematic frame work, based on the seven dimensions originally established in the SarQoL questionnaire, was used as the conceptual framework, using NVivo software. Verbatims of the inter views were categorised into the corresponding framework sections. Any newly identified elements not included in the original SarQoL framework were integrated in the frame work if they met to the criteria of homogeneity, objectivity, exclusivity and relevancy [12]. As recommended by the COSMIN methodology, in addition to involving researchers with experience in the domain of sarcopenia and the con struct of interest, an additional qualitative researcher (BV) with experience of

PROM development, who was not part of the development of the questionnaire, was involved in the analysis to ensure the quality and objectivity of the analysis [5]. To ensure consistency and appropriate interpretation of the thematic framework, a quality control of 10% of the transcriptions was initially analysed independently by two researchers (CD, BV) with subsequent cross-checking to ensure the accuracy of completion. Other transcripts were cross-checked in case of inconsistencies or uncertainties.

Comprehensiveness was determined by eliciting the verbatims of the open discussion to ensure that key concepts or dimensions associated with HRQoL in sarcopenia were covered by SarQoL. A dimension was considered to be elicited if the participants expressed that this dimension impacts HRQoL. Concepts elicited by at least 2 patients or 2 experts were considered in the thematic mapping. The relevance of SarQoL was assessed by going through the questionnaire with participants. For patient's interviews, an item was considered as relevant when participants expressed either a bit difficulties, difficulties or incapacity of performing this item. For experts, relevance of each individual items was measured on a scale ranging from 1-not relevant to 4-very relevant.

The comprehensibility of SarQoL was measured by the comprehensibility of the instructions, the questions and the responses items. For patient's interviews, comprehensibility was considered as good when patients expressed verbal evidence of their comprehension of each question with a relevant answer. Experts, on the other side, were asked to rate their comprehensibility of each item on a scale ranging from 1-not comprehensible to 4-very clear and comprehensible. A cognitive debriefing was then performed to investigate the opinion of participants regarding the length of the questionnaire and the order of questions. It was also asked if participants considered that any items should be deleted from the questionnaire, or if any item could be missing to offer a comprehensive assessment of the impact of sarcopenia on HRQoL

Results

Participants characteristics

A total of 28 interviews (i.e., 17 with patients and 11 with experts) were conducted. Interviews lasted from 10 to 62 min. Data saturation was reached during interviews, indicating that no new dimensions or concepts were introduced to complete the framework during the last interviews with patients. Sarcopenic patients had a mean age of 82 ± 6.4 years and 75.4% of the sample were women. They took a mean of 4.8 ± 2.8 medications per day and had 2.9 ± 3.0 concomitant diseases. All patients (100%) were diagnosed with sarcopenia according to EWGSOP2 criteria

and 23.5% were also severe sarcopenic. Expert panel was composed with five clinical researchers, one gerontologist, four geriatricians, one intensive care physician and one cardiologist. Experts were from Belgium, Spain, France, Germany and Saudi Arabia, 8 were women, and they had a mean professional experience of 9.6 ± 4.8 years with sarcopenia.

Comprehensiveness

Patients

During the 17 interviews where participants discussed their experience of sarcopenia in daily life and the impact of sarcopenia on their HRQoL, six out of the seven dimensions present in the SarQoL questionnaire were spontaneously elicited by at least 2 patients. The thematic mapping showed that 58.9% of the participants mentioned an impact of sarcopenia on their activities of daily living (Domain 5 (D5) of SarQoL), 41.2% on their leisure activities (D6 of SarQoL), 23.5% on their locomotion (D2 of SarQoL), 23.5% on fears (D7 of SarQoL) 17.6% on their physical and mental health (D1 of SarQoL) and 17.6% on their functionality (D4 of). Only the D3, i.e. body composition, was mentioned by one unique patient. In addition, some additional concepts or dimensions emerged during the interviews. While some of them, such as the need for assistance (reported by 23.5% of participants) and the fear of the future (reported by 11.8% of them) were already covered by the existing map ping framework, three other concepts (arbitrarily named), i.e. adaptation and use of strategies (reported by 47.1%), self-fulfillment (reported by 29.4%) and acceptance of the reduced condition (reported by 11.8%) could be considered as distinct from the framework, highlighting one domain not covered by SarQoL, the domain of "patient empowerment".

Experts

Out of the 11 interviews where experts discussed the con sequences of sarcopenia on HRQoL based on their clinical or research experience, 6 out of the 7 dimensions of SarQoL were spontaneously elicited by at least two experts. While the dimension of body composition was not elicited (D3 of SarQoL; 0%), other dimensions, namely, activities of daily living (D5 of SarQoL; 100% of experts), physical and mental health (D1 of SarQoL; 73%), leisure activities (D6; of SarQoL 64%), locomotion (D2 of SarQoL; 45%), functionality (D4 of SarQoL; 45%) and fears (D7 of SarQoL; 27%) were elicited according to the thematic mapping. During the assessment of the comprehensiveness of SarQoL, additional concepts or domains emerged. While some of them could once again be considered as already covered by the thematic framework (i.e. hygiene cares and social isolation, reported by 36% of the experts respectively), two new concepts, namely "depression" (reported by 27% of the experts) and "increased

dependency" (reported by 36% of them), were not covered by the thematic framework of the SarQoL questionnaire. These concepts could be integrated into new dimensions, depression and patient empowerment.

After reviewing the SarQoL questionnaire, experts were asked if they considered that any item could be missing to assess the quality of life in sarcopenic patients. Six experts (i.e., 54.5%) highlighted depression as the only missing item.

A detailed analysis of items/concepts elicited by at least two patients or experts is available in the supplementary material (Table 1).

Relevance

Patients

Patients judged the items of SarQoL, displayed under seven dimensions, as relevant. The relevance of the dimensions ranged from 65% (i.e. fears, leisure activities) to 100% (i.e. activities of daily living, body composition), with a global average of 87 ± 15% (Fig. 1).

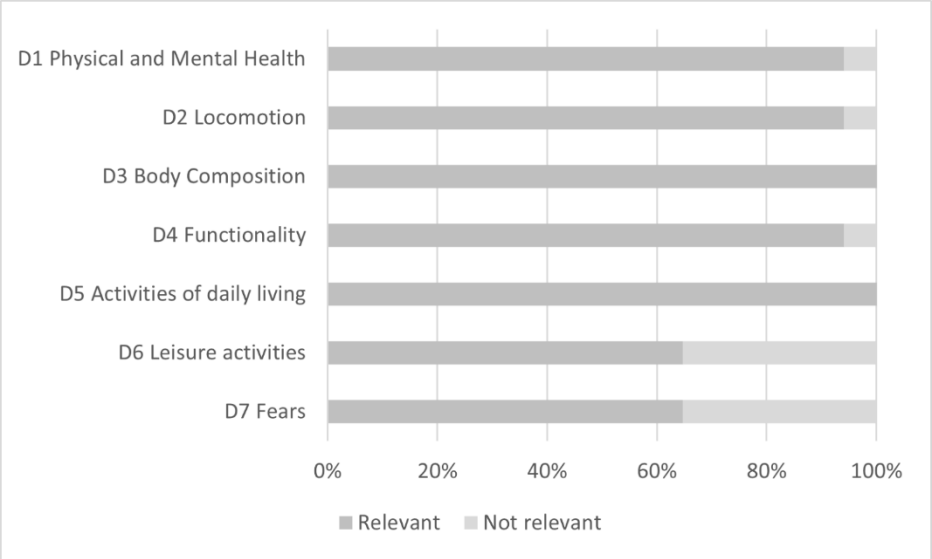

Fig. 1. Proportion of patients reporting SarQoL dimensions as relevant to their experience of sarcopenia (n = 17)

Experts

A detailed analysis of the relevance rating of each item on the questionnaire by the experts is available in the supple mentary material (Table 2). The mean relevance of each dimension ranged from 3.64 for D3 (body composition) to 3.89 for D7 (fears).

Comprehensibility

Patients

All the participants (100%) expressed a clear understanding of the SarQoL questionnaire instructions, providing evidence that instructions are sufficiently clear and appropriate. No participant suggested that the instructions should be rewritten.

Comprehensibility of the different questions was high. Indeed, only two participants (12%) asked for a clarification of one specific term used in the questionnaire (i.e., physical abilities, movement limitations).

All participants reported that it was easy to select responses to the SarQoL questionnaire and all of them indicated that the length of the questionnaire was appropriate and not too long.

Experts

The questionnaire was deemed appropriate by experts, with each question receiving a mean rating between 3.6 and 4. A detailed analysis of the comprehensibility rating of each item by the experts is available in the supplementary material (Table 2).

The length of the questionnaire was judged appropriate by all experts, regardless of their field of activity (clinical or research).

Discussion

The content validity of a PROM is usually considered as the most important psychometric property as it refers to the relevance and understanding of the target population in a specific context [13]. In 2018, new guidance for establishing content validity of PROM have been published by COS MIN [5]. For being considered as sufficient, content validity should include elicitation of concepts by patients and experts via interviews and should also include an assessment of the understanding of the PROM using cognitive debriefing interviews. Although SarQoL has been widely used for 10 years for assessing HRQoL in patients with sarcopenia [4], it is pertinent to evaluate content validity using current recommended methods, ensuring the concepts assessed are important and relevant to patients with sarcopenia today.

The COSMIN guideline required both patient and professional inputs to ensure the content validity of a PROM. Mahmoodi et al. recently performed a content validity analysis with geriatric experts and reported an acceptable and appropriate content validity of SarQoL [8]. However, this study did not fill all the COSMIN criteria for the content validity of a PROM. Indeed, this study, while emphasizing relevance, overlooked the aspects of comprehensive ness and comprehensibility in assessing the content validity of SarQoL, employing a methodology that diverges from COSMIN standards. Therefore, our study should be considered as filling the

gap in content validity assessment of SarQoL, by measuring the content validity in a population of patients with sarcopenia and experts, to be fully adherent to the 2018 COSMIN standard for validating the content validity of a PROM.

This qualitative analysis measured the comprehensive ness, relevance and comprehensibility of SarQoL.

The elicitation of all the dimensions covered by the questionnaire during 17 qualitative interviews with sarcopenic participants and 11 qualitative interviews with experts, using the mapping framework, allowed to confirm the comprehensiveness of the questionnaire. Nevertheless, five new concepts (i.e. higher level of dependance, self-fulfillment, the acceptance of diminished condition, the adaptation or the use of strategies and depression) were elicited by the panel during interviews. 27% of the experts specifically mentioned the concept "higher level of dependence" as relevant. It is important to mention that the development of the original version of SarQoL required the conduct of a systematic literature review, qualitative interviews with five patients and semi-structured interviews with experts. From this, emerged a large list of items (i.e., 180 items), among which, the item "higher level of dependence" was present. However, during the item reduction phase, this item was not rated highly enough to be kept in the final version of SarQoL. Moreover, the concept of "adaptation and use of strategies", as well as the concepts of "personal fulfilment" and "acceptance of the reduced condition", mentioned by patients, can be encompassed in the dimension of "patient empowerment". According to the conceptual framework developed by Bravo et al, patient empowerment is composed of a core set of indicators, including self-efficacy, sense of meaning and coherence about the condition and attitudes and self awareness necessary to influence the health behaviour [14]. Interestingly, the definition of these indicators actually corresponds to the three new concepts elicited during the open discussion [14–16]. Patient empowerment is still an emerging concept in the healthcare literature, with no international consensus on its definition and is generally not included in health-related quality of life questionnaires [17]. The fifth new concept, only elicited by the experts, was the concept of "depression". Once again, this concept was also present in the initial list of items potentially eligible to be included in SarQoL but not rated highly enough during the item reduction phase to be included in the final version of the questionnaire. A recent meta-analysis conducted by Li et al. has highlighted a high prevalence of depression in sarcopenic patients, whatever the criteria used for its diagnosis [18]. This study also highlighted that a multitude of factors could influence the apparition of depression, revealing the difficulty to analyze this aspect in relation with sarcopenia [18]. Expanding the

SarQoL questionnaire to include a single question about depression may not adequately address the complexity of this multifactorial condition, which requires additional space and more specific questions to comprehensively capture its impact. This being taken into account and to achieve the aim of balancing patient burden and maintaining the relevance of the questionnaire for all sarcopenic patients, we do not recommend the introduction of new dimensions or concepts in the SarQoL questionnaire. If deemed relevant, it may be appropriate for researchers or clinicians to use additional validated scales to investigate either the patient empowerment, which can encompass more or less concepts depending on the scale used and the characteristics of the population [19] or the construct of depression, such as the Geriatric Depression scale [20]. It is important here to recall that SarQoL can be used alongside other standalone questionnaires to cover additional concepts important and relevant to specific populations. For example, in 2021, the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) published, in their recommendations for the conduct of clinical trials for drugs aiming at the treatment of sarcopenia, that to obtain a comparison with other trials and a certain generalizability of data, it is possible to combine SarQoL with a generic tool and therefore, obtain a more accurate proxy of treatment efficacy.

Regarding relevance of SarQoL, qualitative interview results indicated that items and the seven dimensions currently covered by SarQoL are relevant.

Finally, the comprehensibility of SarQoL was appropriate, as patients expressed a clear understanding of the questionnaire which was confirmed by an adequate response to the corresponding question. Experts also agreed on the comprehensibility of the formulation of the questions, instructions and proposed answers. Two patients asked for clarification of the words used in the questionnaire, but as this was only reported by two patients for two different words, this very small proportion was not considered to reflect inappropriate wording of the question. In addition, the clear understating of SarQoL is supported by the large body of evidence from translation studies of the SarQoL questionnaire world wide [4]. Indeed, seventeen validation studies reported a high level of comprehensibility of SarQoL items/domains/ instructions/format following cognitive debriefing pre-test. A total of 219 sarcopenic individuals (i.e. 20 participants in the original French version, 25 in the Serbian version, 20 in the Brazilian version, 19 in the Kannada version, 16 in the Lithuanian version, 15 in the Greek version, 14 in the Dutch version and 10 in the Chinese, Polish, Spanish, Taiwanese, Turkish, English, Ukrainian, Cantonese, and Korean versions) confirmed their comprehensibility [21–36] of Sar QoL in its current version.

Although the fact that the COSMIN methodology was strictly followed in this study, some limitations could be highlighted. First, our sample size of patients consisted only of Belgian individuals which may not be representative of all the patients as the SarQoL questionnaire is used world wide. Secondly, the representativeness should be influenced by the qualitative nature of this study. In fact, the results obtained in patients and experts only reflect the views of the participants interviewed and may not be fully representative of the target population. However, the data saturation achieved through data collection and analysis tends to confirm that the study is representative of how the phenomenon of quality of life in sarcopenia is experienced in a Belgian population.

The robust content validity demonstrated by the SarQoL questionnaire is further reinforced by the understanding that a deficiency in content validity can affect various measurement properties of the PROM. Irrelevant items have the potential to reduce the internal consistency, structural validity, and interpretability of the PROM, while the absence of key concepts can compromise validity and responsive ness [5]. Remarkably, so far twenty-four validation studies of SarQoL (i.e. 19 translation/validation studies and 5 studies aiming at assessing specific psychometric proper ties) involving a total of 4807 older individuals all around the world, consistently yielded excellent results across all psychometric properties [4, 37]. This underscores and reinforces the robust evidence supporting the content validity of this study.

Conclusion

In conclusion, the current form of SarQoL provides robust evidence of content validity in evaluating the health-related quality of life in people with sarcopenia. The relevance, the comprehensibility and comprehensiveness of the dimensions and items of the questionnaire have been assessed as adequate patients with sarcopenia and sarcopenia's experts. Taking together, evidence from patients and experts, the current study confirms the content validity of SarQoL according to the COSMIN standard for validating the content validity of a PROM. Additional scales aiming to explore other concepts such as depression or patient empowerment can be used alongside the SarQoL questionnaire if deemed necessary and relevant for a particular study.

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Supplementary materials

Table 1. Frequencies of item and dimensions elicited from patient and expert perspectives.

	Patient elicitation (n, %)	Expert elicitation (n, %)	Already covered in SarQoL + name of domain	Not covered but considered as part of a domain or subdomain	Not covered, considered as a not covered dimension
Dimension 1: Physical and Mental Health	**3 (17.6%)**	**8 (72.7%)**			
Feeling frail		2 (18.1%)	Yes, D1 Physical and Mental Health		
Feeling weak		2 (18.1%)	Yes, D1 Physical and Mental Health		
Feeling tired		3 (27.2%)	Yes, D1 Physical and Mental Health		
D2 Locomotion	**4 (23.5%)**	**5 (45.4%)**			
Limitation in the walking distance	2 (11.8%)	3 (27.2%)	Yes, D2 Locomotion		
Limitation to go out walking		2 (18.1%)	Yes, D2 Locomotion		
Mobilisation skills		3 (27.2%)		Yes, D2 Locomotion	
D3 Body Composition	**1 (5.9%)**	**0 (0%)**			
D4 Functionality	**3 (17.6%)**	**5 (45.4%)**			
Falls		4 (36.3%)	Yes, D4 functionality		
D5 Activities of daily living	**9 (52.9%)**	**11 (100%)**			
Carrying heavy objects		2 (18.1%)	Yes, D5 Activities of daily living		
Doing the housework	2 (11.8%)	4 (36.3%)	Yes, D5 Activities of daily living		
Shopping/groceries		7 (63.6%)	Yes, D5 Activities of daily living		
Undertaking light physical activities		5 (45.4%)	Yes, D5 Activities of daily living		
Getting tired	3 (17.6%)		Yes, D5 Activities of daily living		
Need of assistance	4 (23.5%)			Yes, D5 Activities of daily living	
Hygiene cares		4 (36.3%)		Yes, D5 Activities of daily living	
Cooking		2 (18.1%)		Yes, D5 Activities of daily living	
D6 Leisure activities	**6 (35.3%)**	**7 (63.6%)**			
Sharing time/go out with other people	2 (11.8%)	3 (27.2%)	Yes, D6 Leisure activities		

Doing hobbies	5 (29.4%)	2 (18.1%)	Yes, D6 Leisure activities		
Travelling	3 (17.6%)		Yes, D6 Leisure activities		
Social isolation		4 (36.3%)		Yes, D6 Leisure activities	
D7 Fears	2 (11.8%)				
Fear of falling		3 (27.2%)	Yes, D7 Fears		
Fear of the future	3 (17.6%)			Yes, D7 Fears	
New items not covered by existing dimensions					
Depression	0 (0%)	3 (27.2%)			YES, "depression"
Adaptation and use of strategies	8 (47.0%)				YES, "patient empowerment"
Acceptance of reduced state	2 (11.7%)				YES, "patient empowerment"
Self-fulfillment	5 (29.4%)				YES, "patient empowerment"
Increased dependency		4 (36.3%)			YES, "patient empowerment"

Table 2. Items relevance and comprehension from expert perspective

	Mean and range score of relevance (lowest-highest)	Mean and range score of comprehension(lowest-highest)
Item 1: Reduction of strength in arms	4.0 (4-4)	3.7 (3-4)
Item 2: Reduction of strength in legs	4.0 (4-4)	3.7 (3-4)
Item 3: Reduction of muscle mass	3.4 (2-4)	3.7 (3-4)
Item 4: Reduction of energy	3.7 (3-4)	3.7 (3-4)
Item 5: Reduction of physical capabilities	4.0 (4-4)	3.7 (3-4)
Item 6: Reduction of general flexibility	3.5 (2-4)	3.7 (3-4)
Item 7: Pain in muscles	3.5 (2-4)	3.7 (3-4)
Item 8: Difficulty when undertaking light physical activities	4.0 (4-4)	3.8 (3-4)
Item 9: Get tired when undertaking light physical activities	4.0 (4-4)	3.8 (3-4)
Item 10: Experience pain when undertaking light physical activities	3.7 (2-4)	3.8 (3-4)
Item 11: Difficulty when undertaking moderate physical activities	4.0 (4-4)	3.8 (3-4)

Item 12: Get tired when undertaking moderate physical activities	4.0 (4-4)	3.8 (3-4)
Item 13: Experience pain when undertaking moderate physical activities	3.7 (2-4)	3.8 (3-4)
Item 14: Difficulty when undertaking intense physical activities	4.0 (4-4)	3.8 (3-4)
Item 15: Get tired when undertaking intense physical activities	4.0 (4-4)	3.8 (3-4)
Item 16: Experience pain when undertaking intense physical activities	3.7 (2-4)	3.8 (3-4)
Item 17: Feeling old	3.7 (3-4)	3.6 (1-4)
Item 18: Feeling weakness in muscles	3.8 (3-4)	3.6 (1-4)
Item 19: Feeling physically weak	3.8 (3-4)	3.8 (3-4)
Item 20: Limitation in walking time	4.0 (4-4)	3.8 (3-4)
Item 21: Limitation outings for walking	4.0 (4-4)	3.8 (3-4)
Item 22: Limitation of walking distance	4.0 (4-4)	3.8 (3-4)
Item 23: Limitation of walking speed	3.9 (3-4)	3.8 (3-4)
Item 24: Limitation of length of step	3.6 (2-4)	3.8 (3-4)
Item 25: Feeling tired when walking	4.0 (4-4)	4.0 (4-4)
Item 26: Need to sit down regularly to recover when walking	4.0 (4-4)	4.0 (4-4)
Item 27: Difficulty crossing roads quickly enough	3.8 (2-4)	4.0 (4-4)
Item 28: Difficulties with uneven surfaces	3.8 (2-4)	4.0 (4-4)
Item 29: Problems with balance	3.8 (3-4)	4.0 (4-4)
Item 30: Falls	3.9 (3-4)	3.7 (2-4)
Item 31: Modification of physical appearance	3.6 (2-4)	4.0 (4-4)
Item 32: Loss of muscle mass	3.6 (3-4)	3.9 (3-4)
Item 33: Feeling frail	3.7 (2-4)	3.6 (2-4)
Item 34: Climbing a flight of stairs	4.0 (4-4)	3.7 (2-4)

Item 35: Climbing several flights of stairs	3.9 (3-4)	3.7 (2-4)
Item 36: Going up one or several steps without holding on to the banister	3.8 (3-4)	3.7 (2-4)
Item 37: Squatting or kneeling	3.9 (3-4)	3.7 (2-4)
Item 38: Stooping or leaning down to pick up an object off the floor	3.8 (2-4)	3.7 (2-4)
Item 39: Getting up from the floor without holding on to anything	4.0 (4-4)	3.7 (2-4)
Item 40: Getting out of a low chair without armrests	4.0 (4-4)	3.7 (2-4)
Item 41: Moving from a sitting position to a standing position?	3.8 (2-4)	3.7 (2-4)
Item 42: Carrying heavy object	4.0 (4-4)	3.7 (2-4)
Item 43: Opening a bottle or a jar	3.9 (3-4)	3.7 (2-4)
Item 44: Using public transport	3.5 (2-4)	3.7 (2-4)
Item 45: Getting in or out of a car	3.9 (3-4)	3.7 (2-4)
Item 46: Shopping	3.8 (3-4)	3.7 (2-4)
Item 47: Doing the housework	3.9 (3-4)	3.7 (2-4)
Item 48: Limitation of movement	3.9 (3-4)	3.6 (1-4)
Item 49: Fear of pain	3.9 (3-4)	3.9 (3-4)
Item 50: Fear to not be able	3.9 (3-4)	3.9 (3-4)
Item 51: Fear of feeling tired	3.9 (3-4)	3.9 (3-4)
Item 52: Fear of falling	3.9 (3-4)	3.9 (3-4)
Item 53: Limitation of sex life	3.8 (3-4)	3.6 (1-4)
Item 54: Modification in physical activities/sports	3.8 (3-4)	4.0 (4-4)
Item 55: Modification in leisure activities	3.9 (3-4)	3.8 (2-4)

Psychometric properties of the SarQoL questionnaire: a systematic review and meta-analysis

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Abstract

Background The Sarcopenia and Quality of Life (SarQoL) questionnaire is recognized as the only disease-specific patient-reported outcome measure (PROM) for assessing sarcopenia-related HRQoL. This systematic review and meta-analysis aimed to provide a quantitative summary of all evidence reported on the reliability, validity, responsiveness and floor/ceiling effects of SarQoL in older adults.

Methods Following PRISMA-COSMIN guidelines, a systematic search for studies evaluating psychometric properties of SarQoL (i.e., reliability, validity, responsiveness and floor and ceiling effect) in older people was conducted on MEDLINE (via OVID), PsycINFO, Scopus and EMBASE. Studies published between 2013 and November 2024 using a consensual definition of sarcopenia were included. Study selection and data extraction were made by two independent reviewers. A random-effects model meta-analysis was applied. PROSPERO registration: CRD42024546880.

Results From 411 studies identified by the search strategy, 25 fulfilled the inclusion criteria, including 4585 community-dwelling individuals of which 1311 were diagnosed as sarcopenic. SarQoL demonstrated high reliability (pooled Cronbach's alpha values consistently exceeding 0.80), and excellent test-retest reliability (pooled ICC = 0.98). Construct validity was confirmed with strong convergent correlations (pooled $r > 0.54$) with related dimensions of generic SF-36 and EQ-5D, and weaker divergent correlations (pooled $r < 0.47$). Responsiveness, evaluated in two studies using different methodologies, supported the ability of SarQoL to detect meaningful changes in HRQoL. The certainty of evidence was rated as high for reliability, validity and responsiveness.

Conclusion This meta-analysis consolidates a decade of evidence and confirms the strong psychometric properties of SarQoL, with high level of evidence.

Introduction

Sarcopenia is a common geriatric condition characterized by a loss of muscle mass and strength, the severity of which is reflected by poor physical performance [1]. A recent meta-analysis estimated the prevalence of sarcopenia to be between 10 and 16% among older adults, recognising this condition as a major public health concern [2]. Indeed, numerous studies have highlighted the detrimental impact of sarcopenia on falls, fractures, hospitalisation, mortality, and health-related quality of life (HRQoL) [2]. Beyond its well-documented physical and functional consequences, sarcopenia has also been associated with significant decline in health-related quality of life (HRQoL), notably through its impact on autonomy, mobility, and overall functioning [3]. In this regard, recent international recommendations, including those of the working group if the Global Leadership Initiative in Sarcopenia (GLIS), underscore the importance of considering HRQoL as a key outcome in both clinical assessment and research protocols targeting sarcopenia [4].

HRQoL, defined by the World Health Organization (WHO) as the way individuals view themselves, their place in life, their cultural and value systems, and how these align with their aspirations, concerns, perspectives, and personal standards [5], is considered a complex and multidimensional concept that can be challenging to define and measure accurately [6]. In this context, patient-reported outcome measures (PROMs) are valuable tools to capture the subjective aspects of health, especially in the context of specific diseases [7]. Until 2013, only generic tools were available to assess HRQoL in individuals with sarcopenia. To address this gap, the Sarcopenia and Quality of Life (SarQoL) questionnaire was developed to provide a disease-specific measure of HRQoL [8].

This validated questionnaire consists of 22 questions across seven dimensions that capture critical aspects of life affected by sarcopenia, including physical and mental health, locomotion, body composition, functionality, activities of daily living, leisure activities and fears. It provides a composite score out of 100, providing a comprehensive and holistic reflection of HRQoL [9]. Since its development, SarQoL has gained widespread recognition as the only disease-specific tool for assessing HRQoL in sarcopenia, with translations available in more than 30 languages worldwide (available at: https://sarqol.org/en/sarqol_form). A recent meta-analysis has highlighted the superior discriminatory power of SarQoL to assess HRQoL in sarcopenic individuals compared to generic tools such as SF-36 or EQ-5D questionnaires, underscoring its relevance in clinical and research settings for the sarcopenic population [10].

Given the increasing use of the SarQoL questionnaire in both research and clinical settings, it is essential to ensure that its psychometric properties, including its reliability, validity and responsiveness, are rigorously evaluated in order to confirm its relevance for measuring QoL in older adults with sarcopenia. While many individual studies have reported on these properties, pooling the available evidence within a single statistical model allows for a more comprehensive understanding of the overall performance of the instrument.

PROMs, such as SarQoL, require robust psychometric evaluation to ensure that they accurately reflect HRQoL in people with sarcopenia. According to COSMIN guidance, these evaluations encompass key psychometric properties, such as reliability, validity and responsiveness [11]. While numerous individual studies have reported strong evidence supporting these properties since the initial validation of SarQoL [9], the absence of a comprehensive quantitative synthesis limits the ability to confirm these findings across different populations and settings. Although a recent review of the literature on the psychometric properties of SarQoL provided valuable insights [12], it did not include a meta-analysis to quantitatively synthesise the findings. In addition, since the publication of this review, new evidence on the psychometric properties of SarQoL has emerged, such as a recent publication reporting the content validity of the SarQoL questionnaire, has been published [13]. This evolving body of research provides a robust basis for the first meta-analytic approach to consolidate the existing evidence on the psychometric properties of SarQoL, using a COSMIN-based categorisation of these properties, and incorporating the most recent level of evidence available in the field. This enables a more comprehensive and generalizable assessment of the reliability, validity and responsiveness of SarQoL in older adults.

Methods

Study selection

A protocol has been developed and registered on PROSPERO (CRD42024546880). The objective of this systematic review and meta-analysis was to provide a comprehensive synthesis of the psychometric properties of the SarQoL questionnaire, including its reliability, construct and content validity, responsiveness and the presence of floor or ceiling effects. Specifically, the present study aimed to summarize the available evidence quantitatively, using meta-analytical methods, assess its methodological quality and apply the GRADE approach to evaluate the certainty of the evidence. The 2024 updated PRISMA-COSMIN for Outcome

Measurement Instruments was followed for all steps of this research [14]. The completed relevant checklist can be found in Appendix S1.

Search strategy and selection criteria

Systematic searches on MEDLINE (via OVID platform), PsycINFO, Scopus and EMBASE databases were conducted on 1st March 2024 to identify studies reporting on the psychometric properties of SarQoL, with an update performed in December 2024. The search strategy (Appendix S2) aimed to identify original studies published in English between November 2013 (i.e. the date of SarQoL development) and December 2024. In addition, manual searches of the references of relevant papers were undertaken to identify potential additional references. As the research team included experts in the field of sarcopenia and the development of SarQoL, we used their expertise to minimise the risk of missing relevant studies.

References from both electronic and manual searches have been imported into Covidence software [15]. Two independent reviewers have assessed the eligibility of all identified articles based on the defined inclusion criteria listed in Table 1. The screening was first based on the title and abstract, followed by a second screening based on the full text. A third reviewer was consulted in case of disagreement. Each screening step has been reported and presented in a PRISMA flowchart.

Data from relevant studies have been extracted by two reviewers and recorded in an Excel spreadsheet. The following information has been extracted in a standardised form: article information (e.g., author names, correspondence email, study title, year of publication, continent, country), population characteristics (e.g., age, gender, sarcopenia diagnosis), outcomes (reliability, validity and responsiveness and floor/ceiling effect), funding and conflicts of interest.

Table 1. Inclusion criteria

Participants	Sarcopenic individuals aged 60 years or older (mean or median age of the sample) living in the community or in assisted living facilities are eligible for inclusion.
Sarcopenia definition	The diagnosis of sarcopenia should include at least two biomarkers: lean mass or muscle mass in combination with either muscle strength or physical function using a consensual definition of sarcopenia (e.g. EWGSOP1, EWGSOP2, AWGS, etc.).
Outcome	Only studies reporting the following properties of SarQoL were included Reliability: - Internal validity measured by Cronbach's/Omega's alpha. - Test-retest reliability measured by Intraclass Correlation Coefficients (ICC). - Measurement error measured by the standard error of measurement (SEM), Validity: - Convergent/divergent validity measured by Spearman's/Pearson's correlations - Content validity through relevance, comprehensiveness and comprehensibility Responsiveness: - By distribution or anchor-based methods. Floor and ceiling effects.
Study design	Observational studies (i.e. cross-sectional or longitudinal) providing original data.
Language	English [16]

Quality appraisal

The quality of the studies was assessed using the COSMIN risk of bias checklist This tool rates each measurement property from very good to inadequate according to predefined criteria and the presence of methodological flaws. Two reviewers independently assessed the risk of bias (RoB) for each psychometric property of each study using the COSMIN recommendations [7]. Disagreements were resolved by consensus or by a third reviewer.

Psychometric properties

According to the COSMIN taxonomy, SarQoL has been assessed according to 3 quality domains (i.e., reliability, validity and responsiveness), each including one or more measurement properties [17].

Reliability

Reliability corresponds to the extent to which the patient's score has not changed during a specified period of time under the same test administration conditions [17].

The reliability of SarQoL was assessed using three different measurement properties: internal consistency, test-retest reliability and measurement error.

Internal consistency, which is an estimate of item homogeneity, is measured using the Cronbach alpha coefficient and a value greater than 0.7 is recommended to be considered adequate [18].

In addition, the impact of each domain on reliability can be tested by correlating each domain score with the global SarQoL score using Spearman or Pearson correlation. A correlation above 0.81 is considered as excellent, between 0.61 and 0.80 as very good, between 0.41 and 0.60 as good, between 0.21 and 0.4 as acceptable and finally, less than 0.20 as insufficient [19].
Test-retest reliability corresponds to the correlation of the questionnaire scores, when it is administered over a period of time measured by an intraclass coefficient correlation (ICC) between the scores (global and for each domain). An ICC greater than 0.7 is recommended to be considered adequate reliability [20].
Finally, measurement error, defined as the variation in the patient's score due to systematic and random error rather than changes in the construct being measured, is reported using standard error of measurement (SEM) or smallest detectable change (SDC) [17].

Validity

Validity is defined as the extent to which a questionnaire measures the construct it is intended to measure. Two measurement properties were used to assess the validity of SarQoL: construct validity and content validity [17].
Based on COSMIN recommendations, the construct validity of SarQoL was assessed using a priori hypotheses regarding two other generic questionnaires sometimes used to measure HRQoL: the Short-Form-36 (SF-36) and the EuroQoL 5-Dimension (EQ-5D) questionnaires [21, 22]. Convergent and divergent validity were assessed between SarQoL dimensions and corresponding dimensions using Spearman or Pearson correlations to determine the effectiveness of SarQoL in accurately measuring the intended construct [17].
Content validity refers to the extent to which the content of an instrument accurately reflects the construct being measured. According to the COSMIN methodology, three aspects should be examined to assess the content validity in patients and experts: relevance, comprehensiveness and comprehensibility [23].

Responsiveness

Responsiveness is the ability of a PROMs to capture change, to detect clinically important changes in the measured construct over time, including small changes, and can be compared as longitudinal validity [20]. Responsiveness can be measured using several methods, such as the effect size (ES) of a receiver operator characteristic (ROC) curve [24].

In addition to reliability, validity and responsiveness, we have also considered floor and ceiling effects as quality criteria for SarQoL. However, they are not considered psychometric properties in the COSMIN taxonomy. Floor or ceiling effects are present when more than 15% of respondents score at the lowest or highest possible level [20].

Certainty assessment

The certainty of the evidence for reliability, validity and responsiveness was assessed using the modified GRADE (Grading of Recommendations, Assessment, Development and Evaluation) approach [25]. This approach enables the quality of evidence for each property to be graded, starting at a high level of certainty and potentially downgraded to moderate, low or very low certainty based on 4 factors: (1) risk of bias (reflected in the quality appraisal according to the COSMIN criteria), (2) inconsistency (substantial unexplained heterogeneity with I2>50%), (3) imprecision (sample size of the pooled estimate < 100) and (4) indirectness (evidence from populations, interventions or outcomes that differ from those relevant to this review) [25].

Data analysis

A meta-analysis was conducted to assess the psychometric properties of reliability, validity and responsiveness in studies using SarQoL and a random effects model was applied given the expected heterogeneity between the studies (e.g., diagnosis of sarcopenia, characteristics of population). A two-sided p-value of 0.05 or less was considered statistically significant for all findings, except for heterogeneity, which was considered significant if the p-value was less than 0.1 [10]. R version 4.4.0 was used for all statistical analyses with the packages meta and tidyverse [26, 27]. Psychometric properties, which were reported in only one study, were reported in narrative form.

For the purpose of this study, the internal consistency results of one study, expressed as below a certain level, were considered as the level defined to be calculated in the meta-analysis (e.g., r<0.81 was considered as r=0.81). In addition, when results were reported for the total population of a study first and the sarcopenic population specifically then, the latter was considered before the total population.

To pool the estimates of the intraclass correlation coefficient (ICC), Cronbach's alpha and the correlation coefficients for reliability and construct validity, we applied Fisher's Z-transformation, using an approximate variance determined by the sample size ($z = 0.5 \times \ln((1 + r)/(1 - r))$; $Var(z) = 1/(N - 3)$).

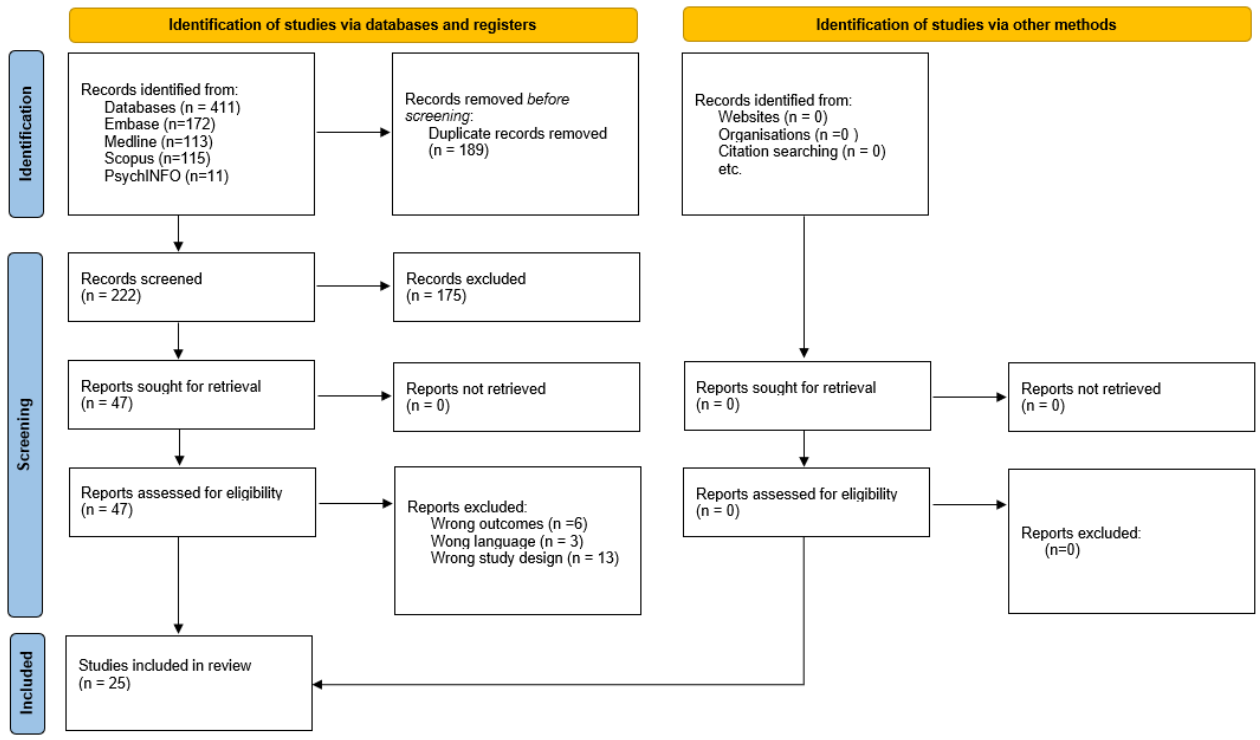
Heterogeneity was assessed using Cochran's Q test and Tau2 was used to measure between-study variance. The I^2 statistic was used to quantify heterogeneity, with values of 25%, 50%, and 75% representing low, moderate and substantial heterogeneity, respectively [28]. In case of significant heterogeneity, subgroup analyses were performed according to sarcopenia diagnosis, age of participants (>75 years or <75 years), continent, study population (total or sarcopenic population), RoB assessment, type of correlation (Spearman's or Pearson's) and, in the specific case of test-retest reliability, stability of health status and time interval between the two administrations of the questionnaire. In addition, leave-one-out analyses were performed to assess the robustness of the results by removing one study at a time [29]. Asymmetry for publication bias was assessed using funnel plots and Egger's regression asymmetry test [30]. In case of publication bias, the Trim and Fill method was applied to evaluate the influence of potential missing studies on the pooled effect size [31].

Results

Study selection

The systematic electronic searches identified 411 potentially eligible studies. After removing duplicates, 222 references were initially screened for titles and abstracts, and 47 of these were screened based on their full text. Finally, 25 references met our inclusion criteria and were included in this systematic review (Figure 1).

Figure 1. Flowchart of the identification and selection of studies



Study characteristics

The articles included were published between 2017 and 2024, and the data was combined from 4585 patients, of which 1311 were sarcopenic. Most studies were conducted in Europe (64%) and used the EWGSOP criteria to diagnose sarcopenia (76%). The characteristics of all included studies are reported in Table 2.

Table 2. Study characteristics

First author's name, year	**Continent**	**Sarcopenia definition** ***(tools used to assess sarcopenia)***	**Participants** ***(sample size, age, sex ratio)***	**Number of participants with sarcopenia (%)**	**Type of population**	**Psychometric properties measured**
Alekna, 2019 [32]	Europe	EWGSOP2 Muscle strength: handgrip strength Lean mass: DXA Physical performance: SPPB	Sample size: 176, Age: 78.2 (74.1-82.6), Women: 59.7%	58 (33%)	Community dwelling older adults	Internal consistency Construct validity Test-retest reliability Floor and ceiling effect
Ariane, 2024 [51]	Asia	AWGS muscle strength: grip strength lean mass: BIA Physical performance: 6-m walk test	Sample size: 176, Age: NR, Women: 61.0%	29 (49.1%)	Community dwelling older adults	Internal consistency Construct validity Test-retest reliability Floor and ceiling effect
Beaudart, 2017 [9]	Europe	EWGSOP1: muscle strength: handgrip strength lean mass: DXA Physical performance: SPPB	Sample size: 296, Age: 73.3 (68.9–78.6), Women: 57.1%	43 (14.5%)	Community dwelling older adults	Internal consistency Construct validity Test-retest reliability Floor and ceiling effect
Beaudart, 2017 [33]	Europe	EWGSOP1: muscle strength: handgrip strength lean mass: DXA Physical performance: gait speed	Sample size: 297, Age: 79.5 ± 2.62, Women: 46.1%	14 (4.7%) *Proportion of patients with low muscle function*	Community dwelling older adults	Internal consistency Construct validity Test-retest reliability Floor and ceiling effect
Demonceau, 2024 [54]	Europe	EWGSOP2: muscle strength: handgrip strength lean mass: DXA Physical performance: SPPB	Sample size: 17, Age: 82±6.4, Women: 75.4%, + 11 Experts	17 (100%)	Community dwelling older adults Experts: 1 gerontologist, 4 geriatricians, 1 intensive care physician, 1 cardiologist	Content validty
de Souza Orlandi, 2023 [34]	South America	EWGSOP2: muscle strength: handgrip strength lean mass: DXA Physical performance: gait speed	Sample size: 221, Age: NR, Women: 68.3%	55 (25%)	Community dwelling older adults	Internal consistency Construct validity Test-retest reliability Floor and ceiling effect

Erdogan, 2021 [35]	Europe [1]	EWGSOP2: muscle strength: handgrip strength lean mass: BIA Physical performance: gait speed	Sample size: 100, Age: 74.7 ± 6.1, Women: 71%	5 (5%) *Proportion of sarcopenic patients with modified cut-off*	Community dwelling older adults	Internal consistency Construct validity Test-retest reliability Floor and ceiling effect
Fabrega-Cuadros, 2020 [36]	Europe	EWGSOP2: muscle strength: handgrip strength lean mass: BIA Physical performance: not assessed	Sample size: 252, Age: 74.00 (70.0-78.0), Women: 82.54%	66 (26%)	Community dwelling older adults	Internal consistency Construct validity Test-retest reliability Floor and ceiling effect
Gasparik, 2017 [37]	Europe	EWGSOP1 muscle strength: handgrip strength muscle mass: Lee Equation Physical performance: gait speed	Sample size: 100, Age: 72 (67–79), Women: 69%	13 (13%) *Proportion of sarcopenic patients with modified cut-off*	NR	Internal consistency Construct validity Floor and ceiling effect
Geerinck, 2018 [55]	Europe	EWGSOP1: muscle strength: handgrip strength lean mass: DXA Physical performance: SPPB	Sample size: 42, Age: 72.90 (68.85–78.81), Women: 59.5%	42 (100%)	Community dwelling older adults	Responsiveness
Geerinck, 2018 [38]	Europe	EWGSOP1: muscle strength: handgrip strength lean mass: BIA Physical performance: gait speed	Sample size: 92, Age: 82 (73-85), Women: 43.5%	30 (32.6%)	Community dwelling older adults	Internal consistency Construct validity Test-retest reliability Floor and ceiling effect
Geerinck, 2019 [53]	Multicenter *(Belgium, Lithuania, UK, Brazil, Poland, Spain, Czech republic, Greece)*	EWGSOP/FNIH: muscle strength: handgrip strength lean mass: Lee equation -BIA - DXA Physical performance: gait speed - SPPB	Sample size: 278, Age: 77.67 ± 7.64, Women: 61.5%	278 (100%)	Community dwelling older adults	Measurement error
Geerinck, 2022 [39]	Europe	EWGSOP2: muscle strength: handgrip strength lean mass: BIA Physical performance: gait speed - 5-STS	Sample size: 70, Age: 80 (68.5-82.5), Women: 77.1%	30 (43%) *participants with low grip strength*	Community dwelling older adults, nursing home residents	Internal consistency Construct validity Floor and ceiling effect
Konstantynowicz, 2018 [40]	Europe	EWGSOP1: muscle strength: handgrip strength muscle mass: Lee equation Physical performance: /	Sample size: 106, Age: 73.3± 5.94, Women: 65.1%	60 (56.6%)	Community dwelling older adults	Internal consistency Construct validity Test-retest reliability Floor and ceiling effect
Kumar, 2023 [56]	Asia	AWGS: muscle strength: handgrip strength lean mass: BIA Physical performance: 5-STS	Sample size: 114, Age: NR, Women: 40.3%	45 (39.5%)	Community dwelling older adults	Internal consistency Test-retest reliability Floor and ceiling effect

Le, 2021 [42]	Asia	AWGS muscle strength: handgrip strength muscle mass: Lee equation Physical performance: gait speed	Sample size: 159, Age: NR, Women: 46.5%	51 (32%)	Community dwelling older adults	Internal consistency Construct validity Test-retest reliability Floor and ceiling effect
Lee, 2023 [43]	Asia	AWGS: muscle strength: handgrip strength lean mass: BIA Physical performance: FTSTS - 6MWT - SPPB	Sample size: 100, Age: 65-74: 48 (48%) - 75-84: 37 (37%)- 85+: 15 (15%), Women: 72 (72%)	50 (50%)	Community dwelling older adults	Internal consistency Construct validity Test-retest reliability Floor and ceiling effect
Mahmoodi, 2023 [44]	Asia	AWGS: muscle strength: handgrip strength lean mass: BIA Physical performance: Gait speed	Sample size: 128, Age: 74.78 ± 5.05, Women: 41.4%	88 (69%)	Community dwelling older adults	Internal consistency Construct validity Test-retest reliability Floor and ceiling effect
Martini, 2024 [52]	Europe	EWGSOP2: muscle strength: grip strength lean mass: DXA Physical performance: NR	Sample size: 185, Age: 79.8 ± 6.1, Women: 76.2%	51 (27.7%)	Community dwelling older adults	Internal consistency Construct validity Test-retest reliability Floor and ceiling effect
Matijević, 2020 [57]	Europe	EWGSOP2: muscle strength: handgrip strength lean mass: DXA Physical performance: gait speed	Sample size: 699, Age: 70 (67–74), Women: 72.7%	12 (2%)	Community dwelling older adults	Internal consistency Construct validity Floor and ceiling effect
Montero-Errasquín, 2022 [46]	Europe	EWGSOP1 - FNIH: muscle strength: handgrip strength lean mass: DXA Physical performance: SPPB *(only for EWGSOP1 definition)*	Sample size: 86, Age: 77.6 ± 5.3 (70-91), Women: 80.2%	16 (18.5%) *according to EWGSOP definition* 13 (15.1%) *according to FNIH definition*	Community dwelling older adults (but 1 participant in nursing home)	Internal consistency Construct validity Test-retest reliability Floor and ceiling effect
Tsekoura, 2020 [47]	Europe	EWGSOP1: muscle strength: handgrip strength lean mass: BIA Physical performance: gait speed	Sample size: 176, Age: 71.19 ± 7.95, Women: 77.27%	50 (28.5%)	Community dwelling older adults	Internal consistency Construct validity Test-retest reliability Floor and ceiling effect Responsiveness
Witham, 2022 [48]	Europe	EWGSOP2: muscle strength: handgrip strength lean mass: BIA Physical performance: SPPB	Sample size: 147, Age: 77.6 ± 7.3, Women: 49%	147 (100%)	Community dwelling older adults	Internal consistency Responsiveness
Yoo, 2021 [49]	Asia	EWGSOP2: muscle strength: handgrip strength lean mass: BIA Physical performance: /	Sample size: 450, Age: 73.9±6.57, Women: 87.7%	53 (12%)	Community dwelling older adults	Internal consistency Construct validity Test-retest reliability

						Floor and ceiling effect
Yu, 2023 [50]	Asia	AWGS: muscle strength: handgrip strength lean mass: BIA Physical performance: gait speed	Sample size: 118, Age: NR, Women: 71.2%	58 (49%)	Community dwelling older adults	Internal consistency Construct validity Test-retest reliability Floor and ceiling effect

5-STS/ *FTSTS: Five Times Sit To Stand Test; 6MWT: Six-Minute Walk Test; AWGS: Asian Working Group on Sarcopenia; BIA: bioelectrical impedance analysis, DXA: dual energy X-ray absorptiometry; EWGSOP: European Working Group on Sarcopenia in Older People; FNIH: Foundation for the National Institutes of Health Biomarkers Consortium Sarcopenia Project; NR: not reported; SPPB: Short Physical Performance Battery test.*

[1] Turkey was considered a European country because the Erdogan study used the EWGSOP2 definition of sarcopenia.

Quality appraisal

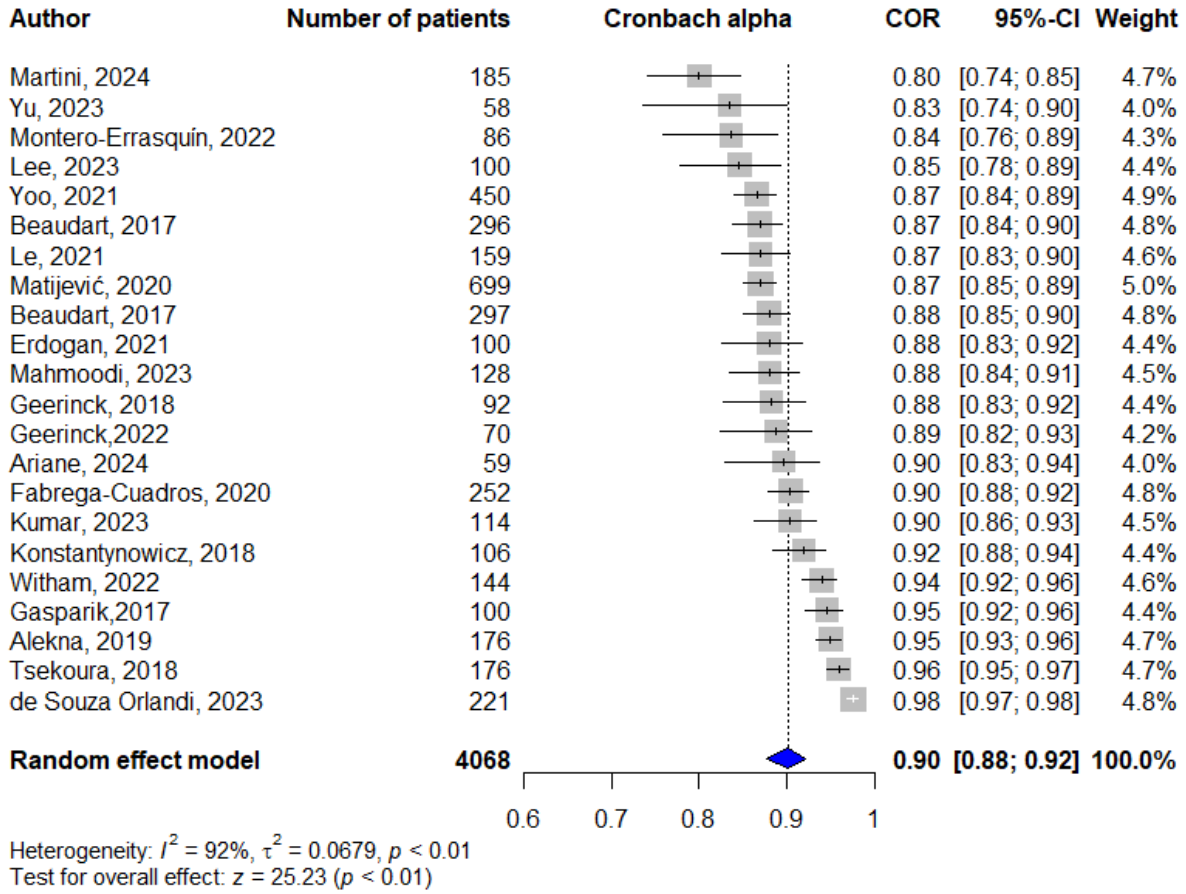
The assessment of the quality of the psychometric properties obtained from the 25 included studies is presented in Supplementary file (Table S1). Among the 22 studies that assessed 'internal consistency' and 'hypothesis testing for construct validity', all were rated as very good for these properties according to the COSMIN criteria [9, 32-52]. The quality of test-retest reliability varied between doubtful [34-36, 49, 50, 52], adequate [41] and very good [9, 32, 33, 38, 40, 42-44, 46-48, 51, 53] and the quality of the content validity was rated as inadequate in one study [44] and very good in the second [54] assessing this property.

Reliability

1.1.Internal consistency – Cronbach alpha

A total of 22 studies assessed the internal consistency of SarQoL global score [9, 32-52]. As shown in Figure 2, the pooled Cronbach's alpha was estimated at 0.90 (95% CI: 0.88; 0.92), demonstrating high reliability despite substantial heterogeneity (I2=92%, Q-test p-value <0.01). As shown in Table 3, the number of studies assessing each SarQoL dimension ranged from 7 to 11, representing 773 to 1610 patients. For these individual dimensions, Cronbach's alpha ranged from 0.89 (95% CI: 0.85; 0.92) for dimension 2 'locomotion' and dimension 4 'functionality' to 0.82 (95% CI: 0.67; 0.90) for dimension 3 'body composition', indicating high internal consistency. Significant heterogeneity was observed across all dimensions, with I2 values ranging from 79% to 97% (Q-test p-values <0.01).

Figure 2. Forest plot of the internal consistency measured with Cronbach's alpha (global SarQoL score)



Subgroup analyses (Appendix, Table S2) showed that the geographic area when the study was performed influenced the internal consistency of the SarQoL global score. More specifically, in Asian countries the pooled Cronbach's alpha of the global score was 0.87 (IC 95%: 0.86; 0.89, I2=0%) compared with 0.90 (IC95%: 0.88; 0.93, I2=90%) in European countries (difference between subgroups p<0.01). Subgroup analyses based on population type (total population versus sarcopenic population) and RoB assessment were not performed, as only one study reported Cronbach's alpha specifically in sarcopenic patients [50] and because the quality assessment of internal consistency was rated as 'very good' in all included studies.

The leave-one-out analysis did not identify any individual study as having a significant impact

on the estimated effect size and examination of the funnel plots and the results of Egger's tests did not reflect potential publication bias.

Table 3. Meta-analysis– Internal consistency – Cronbach's alpha (random effect model)

	No. studies	No. patients	Cronbach a (95% CI)	I^2	P-value for heterogeneity
Dimension 1	9	1213	0.85 (0.80; 0.89)	86%	<0.0001
Dimension 2	9	1017	0.89 (0.85; 0.92)	89%	<0.0001
Dimension 3	8	917	0.82 (0.67; 0.90)	97%	<0.0001
Dimension 4	8	917	0.89 (0.85; 0.92)	79%	<0.0001
Dimension 5	9	1214	0.87 (0.83; 0.90)	86%	<0.0001
Dimension 6	11	1610	0.85 (0.75; 0.91)	97%	<0.0001
Dimension 7	7	773	0.85 (0.73; 0.92)	95%	<0.0001

CI: confidence interval
Dimension 1: Physical and mental health; dimension 2: Locomotion; dimension 3: Body composition; dimension 4: Functionality; dimension 5: Activities of daily living; dimension 6: Leisure activities; dimension 7: Fears.

1.1. *Internal consistency – Correlation between each dimension and the SarQoL global score*

A total of 21 studies assessed the correlation between the different dimensions and the global score of SarQoL [9, 32-37, 39, 40, 42-44, 46-52, 56, 57], including between 3837 and 3907 patients. The pooled correlations, reported in Table 4, ranged from 0.47 (95% CI: 0.41; 0.54) for dimension 6 'leisure activities' to 0.91 (95% CI: 0.89; 0.923) for dimension 4 'functionality'.

Table 4 Meta-analysis– Internal consistency – Correlation between each dimension and SarQoL global score (random effect model)

	No. studies	No. patients	Correlation (95% CI)	I^2	P-value for heterogeneity
Dimension 1	20	3837	0.84 (0.82;0.86)	78%	<0.0001
Dimension 2	20	3837	0.86 (0.83;0.89)	96%	<0.0001
Dimension 3	20	3837	0.69 (0.63;0.73)	88%	<0.0001
Dimension 4	21	3907	0.91 (0.89;0.93)	87%	<0.0001
Dimension 5	20	3837	0.90 (0.87;0.92)	90%	<0.0001
Dimension 6	20	3837	0.47 (0.41;0.54)	83%	<0.0001
Dimension 7	21	3907	0.58 (0.51;0.63)	84%	<0.0001

CI: confidence interval
Dimension 1: Physical and mental health; dimension 2: Locomotion; dimension 3: Body composition; dimension 4: Functionality; dimension 5: Activities of daily living; dimension 6: Leisure activities; dimension 7: Fears.

The models were associated with significant heterogeneity across all dimensions, with I2 values ranging from 78% to 96% (Q-test p-values <0.0001). No significant differences were observed in the subgroup analyses (Appendix, Table S3). The leave-one-out analysis did not identify any individual study as having a significant impact on the estimated effect size and examination of the funnel plots and the results of Egger's tests did not reflect potential publication bias for all dimensions.

1.2. *Test-retest reliability*

Test-retest reliability, measured using the intraclass coefficient (ICC), was assessed in 17 studies for the global score, dimension 1 'physical and mental health' and dimension 6 'leisure activities', regrouping between 1087 and 1095 patients, and in 16 studies for the other dimensions, regrouping 1017 patients. The interval between the two test administrations was 3 days in 1 study, 2 weeks in 13 studies and not reported in 3 studies.

The pooled ICC was 0.98 (95% CI: 0.96-0.99) for the global score, 0.94 (95% CI: 0.90; 0.97) for dimension 1 'physical and mental health', 0.96 (95% CI: 0.93; 0.98) for dimension 2 'locomotion', 0.93 (95% CI: 0.86; 0.97) for dimension 3 'body composition', 0.97 (95% CI: 0.94; 0.98) for dimension 4 'functionality', 0.96 (95% CI: 0.93; 0.97) for dimension 5 'activities of daily living', 1 (95% CI: 1.00; 1.00) for dimensions 6 'leisure activities' and 7 'fears' (Table 5).

Table 5. Meta-analysis– Internal consistency – Test-retest reliability (random effect model)

	No. studies	**No. patients**	**ICC (95% CI)**	**I^2**	**P-value for heterogeneity**
Global score	17	1087	0.98 (0.96;0.98)	93%	<0.0001
Dimension 1	17	1095	0.94 (0.90;0.97)	96%	<0.0001
Dimension 2	16	1017	0.96 (0.93;0.98)	95%	<0.0001
Dimension 3	16	1017	0.93 (0.86;0.97)	97%	<0.0001
Dimension 4	16	1017	0.97 (0.94;0.98)	93%	<0.0001
Dimension 5	16	1017	0.96 (0.93;0.97)	94%	<0.0001
Dimension 6	17	1095	1 (1.00;1.00)	88%	<0.0001
Dimension 7	16	1017	1 (1.00;1.00)	93%	<0.0001

ICC: intra class coefficient, CI: confidence interval
Dimension 1: Physical and mental health; dimension 2: Locomotion; dimension 3: Body composition; dimension 4: Functionality; dimension 5: Activities of daily living; dimension 6: Leisure activities; dimension 7: Fears.

Subgroup analyses (Appendix, Table S4) did not show a significant difference for the global SarQoL score. The leave-one-out analysis did not identify any individual study as having a significant impact on the estimated effect size and the examination of the funnel plots and the results of Egger's tests did not reflect potential publication bias for the global score and all the dimensions of SarQoL.

1.3.*Measurement error*

Geerinck et al. reported the measurement error of SarQoL using the data from 9 different cohorts including 278 sarcopenic participants. Firstly, they reported an SEM of 2.65 points reflecting that there is 68% confidence that the true score of a sarcopenic patient is between -2.65 and +2.65 (out of 100) of the total SarQoL score obtained.

Secondly, by assessing the SDC, they highlighted that an individual change of at least 7.35

points out of 100 of the global SarQoL score needs to be observed to reflect that a true change has indeed occurred.

1.4. Construct validity

Convergent validity

Seventeen studies [9, 32-39, 42, 44, 45, 47, 49-51] assessed the convergent validity of the SarQoL global score with, at least one domain of the SF-36 questionnaire. Six hypotheses were developed regarding the dimensions of the SF-36 and confirmed the convergent validity with the SarQoL global score: bodily pain (k=13, r=0.53(95% IC: 0.45; 0.61)), physical functioning (k=16, r=0.79 (95% IC: 0.72; 0.83)), limitation physical problem (k=15, r=0.60(95% IC: 0.53; 0.66)), general health (k=15, r=0.58(95% IC: 0.53; 0.63)), vitality (k=17, r=0.62(95% IC: 0.53; 0.69)) and physical component score (k=3, r=0.75(95% IC: 0.50; 0.89)) (Table 6).

Table 6. Meta-analysis– Validity – Convergent/Divergent validity

	No. studies	No. patients	Correlation (95% CI)	I^2	P-value for heterogeneity
Convergent validity					
SF-36					
Bodily pain	13	1320	0.53 (0.45; 0.61)	75%	<0.01
Physical functioning	16	2373	0.79 (0.72; 0.83)	89%	<0.01
Limitation physical problem	15	2085	0.60 (0.53; 0.66)	78%	<0.01
General health	15	1676	0.58 (0.53; 0.63)	46%	0.02
Vitality	17	2434	0.62 (0.53; 0.69)	87%	<0.01
Physical component score	3	294	0.75 (0.50; 0.89)	93%	<0.01
Limitation emotional problem[1]	1	58	0.45 (0.21; 0.63)	-	-
Mental health [1]	1	58	0.62 (0.43; 0.46)	-	-
Mental component score [1]	1	106	0.62 (NR)	-	-
EQ-5D					
Utility score	13	2356	0.61 (0.53; 0.68)	79%	<0.01
Mobility	18	1939	-0.53 (-0.67; -0.36)	90%	<0.01
Usual activity	18	1939	-0.51 (-0.65; -0.32)	91%	<0.01
VAS	6	405	0.58 (0.41; 0.71)	79%	<0.01
Pain/Discomfort [1]	1	58	-0.47 (-0.65; -0.24)	-	-
Self-care	2	79	0.04 (-0.88; 0.89)	96%	<0.01
Anxiety/Depression[1]	1	58	-0.62 (-0.76; -0.43)	-	-
Divergent validity					
SF-36					
Mental health	11	1687	0.43 (0.21; 0.60)	94%	<0.01
Social functioning	10	625	0.41 (0.24 ; 0.55)	79%	<0.01
Limitation emotional problem	11	1324	0.40 (0.31 ; 0.48)	57%	0.009
Mental component score	2	188	0.30 (0.16 ; 0.42)	0%	0.83
Limitation physical problem [1]	1	50	0.41 (0.18-0.63)	-	-
EQ-5D					
Self-care	13	2016	-0.43 (-0.58 ; -0.25)	92%	<0.01
Pain/Discomfort	15	1644	-0.30 (-0.47 ; -0.11)	90%	<0.01
Anxiety/Depression	15	2046	-0.22 (-0.33 ; -0.10)	78%	<0.01

CI: confidence interval; NR: not reported, SF-36: 36-Item Short Form Survey, EQ-5D: EuroQol 5-dimension, VAS: Visual analogic scale

[1] No meta-analysis performed because of the insufficient number of studies.

High level of heterogeneity was found across these 6 dimensions (I2 between 46% and 93 %). Subgroup analyses (Appendix, Table S5) showed that population type influenced the SarQoL

global score for the SF-36 'bodily pain' dimension and age category for the SF-36 'role physical' dimension. The leave-one-out analysis did not identify any individual study substantially impacting the effect size. However, the omission of the study of Yoo et al. [49], contributed more to reducing heterogeneity. In fact, omitting this study reduced the I2 for the dimension of 'bodily pain' from 75% to 28% and for the dimension 'role physical' from 79% to 56%. Examination of the funnel plot and the results of Egger's test for the 'bodily pain' dimension (p=0.001) suggested potential publication bias. The Trim and Fill method was applied and identified 7 potential missing studies, which adjusted the pooled correlation to 0.64 (95%IC: 0.55; 0.72) instead of 0.54 (95%IC: 0.45; 0.61).

In addition, 3 other dimensions of the SF-36 questionnaire were assessed quantitatively but not included in a meta-analysis due to insufficient studies (k=1). Yu et al. have reported positive correlations between SarQoL and 'emotional role functioning' (r=0.45 (95% IC: 0.21-0.64)), 'mental health' (r=0.62 (95% IC: 0.42-0.76)) [50] and Konstantynowicz et al. reported a very good correlation of SarQoL with the 'mental component score' (r=0.62 (p<0.001)) [40]. Five dimensions of the EQ-5D questionnaire were explored to test hypotheses of convergent validity and pooled in meta-analyses showing positive and negative correlations with the global SarQoL score: utility score (k=13, r=0.61 (95% IC: 0.53; 0.68)), mobility (k=18, r=-0.53(95% IC: -0.67; -0.36)), usual activity (k=18, r=-0.51(95% IC: -0.65; -0.32)), visual analogic scale (k=6, r=0.58(95% IC: 0.41; 0.71)) and self-care (k=2, r=0.04(95%IC: -0.88; 0.89)) (Table 6). Significant heterogeneity was observed for these dimensions (Table 6). Subgroup analyses (Appendix, Table S5) did not detect significant differences between subgroups, except for the continent of the study for the EQ-5D 'usual activity' dimension, where the pooled correlation was higher for studies conducted in Asia and Europe (-0.48 (IC95%: -0.74; -0.08), -0.49 (IC95%: -0.68; -0.25) respectively) compared to the study conducted in America (-0.72 (IC95%: -0.68; -0.65)). The leave-one-out analysis did not identify any individual study having a significant impact on the effect size.

In addition to these findings, Yoo et al. have reported 'good' and 'very good' correlations between the 'pain and discomfort' and 'anxiety and depression' EQ-5D dimensions and the SarQoL global score. Erdogan et al. have also reported a negative correlation between the 'self-care' dimension of the EQ-5D and the SarQoL global score (r=-0.59, p-value<0.001).

Divergent validity

Four dimensions of the SF-36 were explored to test the hypotheses of divergent validity and showed good correlations with SarQoL global score (Table 6): mental health (k=11, r=0.43(95%

IC: 0.21; 0.60)), social functioning (k=10, r=0.41, (95% IC: 0.24; .55)), limitation emotional problem (k=11, r=0.40, (95% IC 0.31; 0.48)) and mental component score (k=2, r=0.30 (95% IC: 0.16; 0.42). In addition, a good correlation of SarQoL global score with the dimension of 'limitation physical problem' was reported by Tsekoura et al. (r=0.41, p<0.001) [42].

Finally, three dimensions of the EQ-5D questionnaire were explored to test the hypotheses of divergent validity and showed a negative correlation with the total score of SarQoL: self-care (k=13, r=--0.43 (95% IC: -0.58; -0.25)), pain/discomfort (k=15, r=--0.30 (95% IC: -0.47; -0.11) and anxiety/depression (k=15, r=--0.22 (95% IC: -0.33; -0.10)).

Significant heterogeneity was observed for all SF-36 and EQ-5D dimensions, except for the mental component score (I^2=0%, p=0.83). Subgroup analyses (Appendix, Table S5) showed a significant difference for the EQ-5D 'mental health' dimension based on the continent of study (subgroup difference tests, p=0.04,). A higher correlation was observed for studies conducted in Europe (r=0.55 (95% IC: 0.33; 0.72)) compared to studies conducted in Asia (r=0.16 (95% IC: -0.17; 0.46)) The leave-one-out analysis showed that no study had a substantial impact on the overall effect sizes for divergent validity. In addition, examination of the funnel plots and Egger's tests showed no publication bias for the SF-36 and EQ-5D dimensions examined for divergent validity.

1.5.*Content validity*

Two studies have reported on the content validity of SarQoL [44, 54]. Mahmoodi et al. focused on measured content validity of the tool based on expert opinion only and reported acceptable and appropriate content validity. However, the quality assessment of this study was rated as inadequate according to the COSMIN criteria due to the lack of assessment of comprehensiveness, comprehensibility and patient assessment. In contrast, Demonceau et al. assessed content validity with patient and expert perspectives and found an adequate relevance, comprehensiveness and comprehensibility of SarQoL. The quality of this study was rated as very good according to the COSMIN criteria.

Responsiveness

Two studies have assessed the responsiveness of SarQoL. The first, conducted by Geerinck et al. in 42 sarcopenic patients, showed good responsiveness to the questionnaire with over 75% of hypotheses confirmed. The magnitude of change, expressed as the standardized mean difference, was significantly (p?) higher for the SarQoL total score than for the SF-36 and EQ-5D [55]. In a second study, Witham et al. assessed responsiveness in 147 participants with

probable sarcopenia. They reported a weak correlation between SarQoL scores at baseline and after 6 months of follow-up (r =0.27, p =0.03). This study also highlighted that SarQoL is more sensitive to improvements than deteriorations, with sample sizes of 25-100 needed to detect clinically significant changes of 0.074 points [48].

Floor and ceiling effect

Floor and ceiling effects were assessed in 20 studies [9, 32, 33, 35, 37-40, 42-44, 46, 47, 49-52, 58] and none of these effects were observed.

Certainty of evidence

Using the GRADE assessment, the certainty of evidence for reliability, validity and responsiveness was rated as high. Although substantial heterogeneity was observed for some psychometric properties, all effect estimates fell within the same interpretative range and pointed in the same direction. According to GRADE guidance, such variability, in the absence of opposing results or clinically divergent conclusions, does not justify downgrading for inconsistency. The observed heterogeneity is likely due to contextual differences (e.g., population or questionnaire application) rather than contradictory findings, as supported by the consistent direction of results across all studies [59].

Discussion

This systematic review and meta-analysis aimed to report the psychometric properties of SarQoL including reliability, validity, responsiveness and the presence of floor and ceiling effect. A total of 25 published studies were included, providing a comprehensive synthesis of its performance across different populations and settings.

The strong reliability of SarQoL was first demonstrated by robust internal consistency measured by Cronbach's alpha and Spearman's/Pearson's correlations. The pooled Cronbach's alpha values, which assess item homogeneity, were consistently above 0.80 for the global and dimension scores, exceeding the threshold of 0.70 to be considered adequate [18]. Subgroup analyses suggested that the SarQoL questionnaire may be slightly more tailored to European populations, as reflected by the higher pooled Cronbach's alpha observed in studies conducted in Europe. However, the excellent internal consistency (and absence of heterogeneity, probably due to a lower number of studies included in the model) demonstrated in the Asian continent also highlights the robust adaptability of the questionnaire across different cultural and geographical contexts, further supporting its applicability in international settings. Then, the

correlations between the SarQoL global score and the individual dimensions (ranging from 0.48 to 0.91), further validated the consistency of the questionnaire. In addition, the test-retest reliability, reflected by the excellent ICC obtained of 0.98 for the global SarQoL score, underlined the ability of the questionnaire to provide stable results over time. Finally, the measurement error, reported in a single multicentre study [53], suggests that SarQoL is a reliable instrument. Indeed, this study highlighted that observed scores deviating from 2.65 points from the theoretical 'true score' and a smallest detectable change of 7.35 points was identified as the minimum change required to reflect a true difference in HRQoL in sarcopenic individuals. The authors have concluded that SarQoL has equivalent, if not superior, reliability to the SF-36 questionnaire. Although only one study was included for this property, it consisted of 9 multicentre studies with a large and heterogeneous sample, giving good representativeness of measurement error, and we consider this sufficient to strengthen the other evidence for considering the reliability of SarQoL to be adequate.

The validity of SarQoL was first assessed using construct validity. Strong convergent correlations ($r > 0.51$) were observed with the SarQoL global score and related dimensions of the SF-36 and EQ-5D questionnaires, in addition to weaker correlations between the global SarQoL score and unrelated dimensions ($r < 0.43$) of the SF-36 and EQ-5D questionnaires, reflecting divergent validity. Interestingly, subgroup analyses for convergent validity showed significant differences for some dimensions, particularly according to type of population and age category. These differences were reflected in slightly lower correlations for individuals diagnosed with sarcopenia compared to the total population (individuals with and without sarcopenia), and higher correlations for people older than 75 years compared with those younger than 75 years. These differences may reflect that HRQoL in individuals with sarcopenia is perceived primarily in relation to physical and functional limitations, reducing the overlap between SarQoL and the more general SF-36 questionnaire. On the other hand, they may also be due to the fact that older people experience more severe sarcopenia and more severe effects of sarcopenia, which are more in line with SarQoL and strengthen the correlations, while younger people, in better overall health, perceive less impact of sarcopenia on HRQoL, leading to weaker correlations [60]. Some other dimensions were investigated but not pooled in meta-analysis because they were reported in only one study. These dimensions are difficult to interpret because, for example, they related to convergent validity, although most studies used the same dimensions to assess divergent validity. In addition, one study reported that no correlation was found between SarQoL and some SF-36 and 5Q-5D dimensions, such as bodily

pain', 'vitality' and EQ-VAS. This finding can be partly explained by the small sample size (n=39) in this study [51]. Finally, an examination of the funnel plot and the results of Egger's test for the 'bodily pain' dimension (p=0.001) suggested potential publication bias. This dimension of the SF-36 questionnaire may be subject to publication bias because pain is often not considered as specific to sarcopenia compared with more specific dimensions related to functionality or mobility [61]. Variability in pain perception, comorbidities and population differences can also influence the results. However, the Trim and Fill method showed the inclusion of potentially missing studies, but did not significantly change the pooled estimate initially obtained and, therefore, did not affect the robustness of our results. Secondly, the validity of SarQoL was assessed through content validity. Since the creation of SarQoL, new guidelines for adequate content validity have been published, requiring an updated assessment [23]. In this context, two recent studies have specifically investigated this psychometric property. The study by Mahmoodi et al. concluded that the content validity of the questionnaire was adequate, but this study did not follow the updated COSMIN methodology, and we therefore rated the quality of this study as inadequate. Conversely, Demonceau et al. assessed the content validity and concluded that the questionnaire had adequate content validity with patients and experts. We rated this study as very good quality, as it met all the updated COSMIN criteria.

Although the responsiveness of SarQoL was only assessed in two studies, the results support an adequate level of responsiveness in which we are confident, particularly as the studies used two different methodological approaches. Nevertheless, it would be valuable for future research to further explore and strengthen the evidence for this psychometric property, especially in interventional studies. Moreover, the clinically relevant responsiveness threshold of SarQoL remains to be defined.

Finally, our analysis revealed the absence of floor and ceiling effects, indicating that SarQoL provides an adequate range of response options. This is an important finding, as it demonstrated the ability of the questionnaire to differentiate well between individuals with different levels of HRQoL. The absence of extreme values also improves its sensitivity and confirms the ability of SarQoL to accurately reflect the comprehensive spectrum of sarcopenia-related HRQoL [23].

According to the GRADE approach, the certainty of evidence for reliability, validity, and responsiveness was rated as 'high.' This high level of confidence is mainly justified by the fact that the unexplained heterogeneity does not affect the overall estimates or the direction of the

results. In addition, the consistency of the findings across studies supports the robustness of the evidence, making a conservative approach to downgrading unnecessary in this context.

Strengths and limitations

The key strength of this meta-analysis lies in the fact that it is the first time that a quantitative approach has been used to assess the SarQoL psychometric properties including a large sample of data from diverse geographic and cultural contexts, which underscores the wide applicability of SarQoL. Furthermore, by adhering to the COSMIN guidelines, this study ensures methodological rigor in evaluating the reliability, validity and responsiveness of SarQoL. Finally, the use of a meta-analytic approach including subgroup and sensitive analyses, reinforces the robustness of our findings.

However, this meta-analysis is not without limitations. First, a large heterogeneity was observed across the various analyses, the causes of which remain largely unexplained. This could indicate inherent variations between the population or the application of the questionnaire. It is however important to consider that the statistical test I2 may be subject to bias in small meta-analysis, particularly with higher value when using random effect model [62]. In addition, for some properties, such as internal consistency, although large heterogeneity was found, it could be argued that this does not affect the robustness of the results, as Cronbach's alpha remains above the recommended threshold with an extremely precise confidence interval. The observed heterogeneity can largely be attributed to the high precision of the studies, as the narrow 95% confidence intervals limit the chances of overlap. However, despite this heterogeneity, all results point in the same direction, demonstrating the consistency of the findings and strengthening the overall validity of the conclusions.

The majority of the included studies focus on community-dwelling older adults with limited information on other specific patient settings. Further studies in different healthcare contexts, especially among individuals with severe sarcopenia or comorbidities, would help to strengthen our findings in these specific contexts, where the impact of sarcopenia on HRQoL may differ significantly.

Since multimorbidity is common in older individuals, another limitation of this study, also reported by Martinez-Fernandez et al., is the potential impact of comorbidities on the patients' conditions and, more specifically, their functional capacity, which could influence their answers to the questionnaire [2, 12]. While these factors may affect the absolute scores obtained, they are not expected to impact the measurement properties of the questionnaire itself. This review

focused on the evaluation of these properties, rather than on the interpretation of SarQoL scores as clinical outcomes.

Conclusion

The SarQoL questionnaire is the only disease-specific PROM designed to assess HRQoL in people with sarcopenia. This meta-analysis consolidates a decade of evidence and confirms the strong psychometric properties of SarQoL. The reliability, validity and responsiveness of SarQoL, supported by a high level of certainty according to the GRADE approach, reflect robust evidence. Furthermore, the absence of floor and ceiling effects underscores the ability of the questionnaire to capture a wide range of HRQoL variation, reinforcing its clinical utility.

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Supplementary material

S.1. The new PRISMA-COSMIN for Outcome Measurement Instrument

Section and Topic	#	Checklist item*	Location
TITLE			
Title	1	Identify the report as a systematic review and include as applicable the following (in any order): outcome domain of interest, population of interest, name/type of OMIs of interest, and measurement properties of interest.	1
ABSTRACT			
OPEN SCIENCE			
Funding[b]	2.2	Specify the primary source of funding for the review.	NA
Registration	2.3	Provide the register name and registration number.	NA
BACKGROUND			
Objectives	2.4	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	1
METHODS			
Eligibility criteria	2.5	Specify the inclusion and exclusion criteria for the review.	1
Information sources	2.6	Specify the information sources (e.g., databases, registers) used to identify studies and the date when each was last searched.	1
Risk of bias	2.7	Specify the methods used to assess risk of bias in the included studies.	1
Measurement properties	2.8	Specify the methods used to rate the results of a measurement property.	1
Synthesis methods	2.9	Specify the methods used to present and synthesize results.	1
RESULTS			
Included studies	2.10	Give the total number of included OMIs and study reports.	1
Synthesis of results	2.11	Present the syntheses of results of OMIs, indicating the certainty of the evidence.	1
DISCUSSION			
Limitations of evidence	2.12	Provide a brief summary of the limitations of the evidence included in the review (e.g., study risk of bias, inconsistency, and imprecision).	1
Interpretation	2.13	Provide a general interpretation of the results and important implications.	1
PLAIN LANGUAGE SUMMARY			
Plain language summary	3	If allowed by the journal, provide a plain language summary with background information and key findings.	C
OPEN SCIENCE			
Registration and protocol	4a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	4
	4b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	4

Section and Topic	#	Checklist Item[a]	Location
	4c	Describe and explain any amendments to information provided at registration or in the protocol.	4
Support	5	Describe sources of financial or non-financial support for the review, and the role of the funders in the review.	29
Competing interests	6	Declare any competing interests of review authors.	29
Availability of data, code, and other materials	7	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	29
INTRODUCTION			
Rationale	8	Describe the rationale for the review in the context of existing knowledge.	3
Objectives	9	Provide an explicit statement of the objective(s) or question(s) the review addresses and include as applicable the following (in any order): outcome domain of interest, population of interest, name/type of OMIs of interest, and measurement properties of interest.	4
METHODS			
Followed guidelines	10	Specify, with references, the methodology and/or guidelines used to conduct the systematic review.	4
Eligibility criteria	11	Specify the inclusion and exclusion criteria for the review.	5
Information sources	12	Specify all databases, registers, preprint servers, websites, organizations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	4
Search strategy	13	Present the full search strategies for all databases, registers, and websites, including any filters and limits used.	Appendix2
Selection process	14	Specify the methods used to decide whether a study met the inclusion criteria of the review, e.g., including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools/AI used in the process.	4
Data collection process	15	Specify the methods used to collect data from reports, e.g., including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools/AI used in the process.	4
Data items	16	List and define which data were extracted (e.g., characteristics of study populations and OMIs, measurement properties' results, and aspects of feasibility and interpretability). Describe methods used to deal with any missing or unclear information.	5
Study risk of bias assessment	17	Specify the methods used to assess risk of bias in the included studies, e.g., including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools/AI used in the process.	5
Measurement properties	18	Specify the methods used to rate the results of a measurement property for each individual study and for the summarized or pooled results, e.g., including how many reviewers rated each study and whether they worked independently.	6
Synthesis methods	19a	Describe the processes used to decide which studies were eligible for each synthesis.	5
	19b	Describe any methods used to synthesize results.	7
	19c	If applicable, describe any methods used to explore possible causes of inconsistency among study results (e.g., subgroup analysis).	7
	19d	If applicable, describe any sensitivity analyses conducted to assess robustness of the synthesized results.	7

Section and Topic	#	Checklist Item*	Location
Certainty assessment	20	Describe any methods used to assess certainty (or confidence) in the body of evidence.	11
Formulating recommendations	21	If appropriate, describe any methods used to formulate recommendations regarding the suitability of OMIs for a particular use.	-
RESULTS			
Study selection	22a	Describe the results of the search and selection process, from the number of records identified in the search to the number of study reports included in the review, ideally using a flow diagram. If applicable, also report the final number of OMIs included and the number of study reports relevant to each OMI. [T]	9
	22b	Cite study reports that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	9
OMI characteristics	23a	Present characteristics of each included OMI, with appropriate references. [T]	5-7
	23b	If applicable, present interpretability aspects for each included OMI. [T]	NA
	23c	If applicable, present feasibility aspects for each included OMI. [T]	NA
Study characteristics	24	Cite each included study report evaluating one or more measurement properties and present its characteristics. [T]	12-16
Risk of bias in studies	25	Present assessments of risk of bias for each included study. [T]	17
Results of individual studies	26	For all measurement properties, present for each study: (a) the reported result and (b) the rating against quality criteria, ideally using structured tables or plots. [T]	NA
Results of syntheses	27a	Present results of all syntheses conducted. For each measurement property of an OMI, present: (a) the summarized or pooled result and (b) the overall rating against quality criteria. [T]	10-25
	27b	If applicable, present results of all investigations of possible causes of inconsistency among study results.	10-25
	27c	If applicable, present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	10-25
Certainty of evidence	28	Present assessments of certainty (or confidence) in the body of evidence for each measurement property of an OMI assessed. [T]	25
Recommendations	29	If appropriate, make recommendations for suitable OMIs for a particular use.	NA
DISCUSSION			
Discussion	30a	Provide a general interpretation of the results in the context of other evidence.	25-28
	30b	Discuss any limitations of the evidence included in the review.	28
	30c	Discuss any limitations of the review processes used.	28
	30d	Discuss implications of the results for practice, policy, and future research.	28

S2. Search strategy (Medline via Ovid, Scopus, EMBASE and PsycINFO)

Database: Ovid MEDLINE(R) ALL <1946 to February 27, 2024>
Search Strategy:

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1 sarqol.ti,ab,kf.

2 "sarcopenia quality of life".ti,ab,kf.

3 "sarcopenia and quality of life".ti,ab,kf.

4 "sarcopenia & quality of life".ti,ab,kf.

5 or/1-4
****

(TITLE-ABS-KEY (sarqol)) OR (TITLE-ABS-KEY
("sarcopenia and quality of life")) OR (TITLE-ABS-KEY ("sarcopenia quality of life"))
OR (TITLE-ABS-KEY ("sarcopenia & quality of life"))

EMBASE
.....

#5. #1 OR #2 OR #3 OR #4 172 28 Feb 2024

#4. 'sarcopenia & quality of life':ti,ab 65 28 Feb 2024

#3. 'sarcopenia and quality of life':ti,ab 41 28 Feb 2024

#2. 'sarcopenia quality of life':ti,ab 65 28 Feb 2024

#1. sarqol:ti,ab,kw 136 28 Feb 2024

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PSYCHINFO

Database: APA PsycInfo <1806 to February Week 4 2024>
Search Strategy:
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1 sarqol.ti,ab.

2 "sarcopenia quality of life".ti,ab.

3 "sarcopenia and quality of life".ti,ab.

4 "sarcopenia & quality of life".ti,ab.

5 or/1-4

Table S1. Methodological quality assessment according to the COSMIN checklist

	Content Validity	Internal consistency	Reliability (test-retest)	Hypotheses testing for construct validity	Measurement error
Alekna, 2019 [27]	NR	V	V	V	NR
Ariane, 2024 [46]	NR	V	V	V	NR
Beaudart, 2017 [8]	NR	V	V	V	NR
Beaudart, 2017 [28]	NR	V	V	V	NR
Demonceau, 2024 [49]	V	NR	NR	NR	NR
de Souza Orlandi, 2023 [29]	NR	V	D	V	NR
Erdogan, 2021 [30]	NR	V	D	V	NR
Fabrega-Cuadros, 2020 [31]	NR	V	D	V	NR
Gasparik, 2017 [32]	NR	V	NR	V	NR
Geerinck, 2018 [50]	NR	NR	NR	NR	V
Geerinck, 2018 [33]	NR	V	V	V	NR
Geerinck, 2019 [48]	NR	NR	V	NR	V
Geerinck, 2022 [34]	NR	V	NR	V	NR
Konstantynowicz, 2018 [35]	NR	V	V	V	NR
Kumar, 2023 [51]	NR	V	A	V	NR
Le, 2021 [37]	NR	V	V	V	NR
Lee, 2023 [38]	NR	V	V	V	NR
Mahmoodi, 2023 [39]	I	V	V	V	NR
Martini, 2024 [47]	NR	V	D	V	NR
Matijević, 2020 [53]	NR	V	NR	V	NR
Montero-Errasquin 2022 [41]	NR	V	V	V	NR
Tsekoura, 2020 [42]	NR	V	V	V	NR
Witham, 2022 [43]	NR	V	V	V	NR
Yoo, 2021 [44]	NR	V	D	V	NR
Yu, 2023 [45]	NR	V	D	V	NR
V: very good; A: adequate; D: doubtful; I: inadequate; NR: not reported.					

Table S2. Subgroups analysis – Internal consistency – Cronbach a

	No. studies	No. patients	Cronbach a (95% CI)	I^2	P for heterogeneity	P for subgroup differences
Global SarQoL score						
Sarcopenia Diagnosis						0.38
AWGS	6	618	0.88 (0.86; 0.89)	6%		
EWGSOP1	8	1297	0.91 (0.88; 0.94)	90%		
EWGSOP2	8	2153	0.91 (0.85; 0.94)	96%	<0.0001	
Age category[1]						0.49
< 75 years	11	1798	0.92 (0.88; 0.94)	94%	<0.0001	
≥75 years	8	1816	0.90 (0.87; 0.92)	87%	<0.0001	
Continent						**<0.01**
Asia	7	1068	0.87 (0.86; 0.89)	0%	0.41	
America	1	221	0.98 (0.97; 0.98)	/		
Europe	14	2779	0.90 (0.88; 0.93)	90%	<0.0001	

CI: confidence interval,
[1] 3 studies removed (Le, Lee, Ariane) because they did not report the age of total population of the study.

Table S3. Subgroups analysis – Internal consistency – Correlation between each dimension and the SarQoL global score.

	No. studies	No. patients	Cronbach a (95% CI)	I^2	P for heterogeneity	P for subgroup differences
Dimension 1						
Sarcopenia Diagnosis						0.67
AWGS	6	549	0.86 (0.81-0.89)	66%	0.01	
EWGSOP1	7	1205	0.83 (0.78-0.87)	81%	<0.01	
EWGSOP2	7	2083	0.85 (0.81-0.88)	80%	<0.01	
Population						0.67
Total population	18	3734	0.85 (0.82-0.87)	81%	<0.01	
Sarcopenic population	2	103	0.83 (0.76-0.88)	0%	0.44	
Age category [1]						0.52
< 75 years	9	2151	0.83 (0.80-0.87)	81%	<0.01	
≥75 years	8	1368	0.85 (0.81-0.88)	76%	<0.01	
Continent						0.05
Asia	7	999	0.86 (0.83-0.89)	65%	0.02	
America	1	221	0.79 (0.74-0.84)	/		
Europe	12	2617	0.84 (0.81-0.87)	81%	<0.01	
Correlation type [2]						0.71
Spearman	8	1368	0.85 (0.81-0.89)	85%	<0.01	
Pearson	7	1276	0.84 (0.79-0.88)	80%	<0.01	

Methods						0.70
Matrice	3	996	0.85 (0.83-0.87)	0%	0.52	
Per domain	17	2841	0.84 (0.82-0.87)	81%	<0.01	
Dimension 2						
Sarcopenia Diagnosis						0.71
AWGS	6	549	0.88 (0.82-0.92)	88%	<0.01	
EWGSOP1	7	1205	0.85 (0.78-0.90)	92%	<0.01	
EWGSOP2	7	2083	0.86 (0.79-0.91)	98%	<0.01	
Population						0.38
Total population	18	3734	0.87 (0.83-0.90)	96%	<0.01	
Sarcopenic population	2	103	0.84 (0.77-0.89)	0%	0.51	
Age category [1]						0.42
< 75 years	9	2151	0.84 (0.76-0.89)	97%		
≥75 years	8	1368	0.87 (0.84-0.89)	59%		
Continent						0.06
Asia	7	999	0.89 (0.83-0.92)	86%	<0.01	
America	1	221	0.91 (0.88-0.93)	/		
Europe	12	2617	0.85 (0.79-0.89)	96%	<0.01	
Correlation type [2]						0.20
Spearman	8	1368	0.89 (0.86-0.92)	85%	<0.01	
Pearson	7	1276	0.85 (0.78-0.90)	92%	<0.01	
Methods						
Matrice	3	996	0.77 (0.55-0.90)	98%	<0.01	
Per domain	17	2841	0.88 (0.85-0.90)	89%	<0.01	
Dimension 3						
Sarcopenia Diagnosis						0.31
AWGS	6	549	0.71 (0.60-0.79)	**82%**	<0.01	
EWGSOP1	7	1206	0.63 (0.53-0.71)	82%	<0.01	
EWGSOP2	7	2083	0.72 (0.63-0.78)	91%	<0.01	
Population						0.17
Total population	18	3734	0.69 (0.64-0.74)	89%	<0.01	
Sarcopenic population	2	103	0.60 (0.46-0.71)	0%	0.75	
Age category [1]						0.49
< 75 years	9	2151	0.66 (0.56-0.74)	92%	<0.01	
≥75 years	8	1369	0.70 (0.62-0.76)	82%	<0.01	
Continent						0.36
Asia	7	999	0.73 (0.63-0.80)	85%	<0.01	
America	1	221	0.65 (0.56-0.72)	/		
Europe	12	2617	0.66 (0.59-0.72)	86%	<0.01	
Correlation type [2]						0.55
Spearman	8	1368	0.71 (0.61-0.78)	90%	<0.01	

Pearson	7	1276	0.66 (0.54-0.76)	93%	<0.01	
Methods						0.96
Matrice	3	996	0.69 (0.65-0.72)	22%	0.28	
Per domain	17	2841	0.69 (0.63-0.74)	90%	<0.01	
Dimension 4						
Sarcopenia Diagnosis						0.07
AWGS	6	549	0.91 (0.87-0.94)	83%	<0.01	
EWGSOP1	7	1205	0.88 (0.83-0.91)	88%	<0.01	
EWGSOP2	8	2153	0.92 (0.91-0.94)	84%	<0.01	
Population						0.08
Total population	19	3804	0.91 (0.89-0.93)	88%	<0.01	
Sarcopenic population	2	103	0.87 (0.81-0.91)	0%	0.95	
Age category [1]						0.19
< 75 years	9	2151	0.89 (0.86-0.92)	87%	<0.01	
≥75 years	9	1438	0.92 (0.89-0.94)	85%	<0.01	
Continent						0.73
Asia	7	999	0.91 (0.88-0.93)	84%	<0.01	
America	1	221	0.92 (0.90-0.94)	/		
Europe	13	2687	0.91 (0.88-0.93)	90%	<0.01	
Correlation type [3]						0.06
Spearman	8	1368	0.92 (0.90-0.95)	91%	<0.01	
Pearson	7	1276	0.88 (0.85-0.91)	85%	<0.01	
Methods						0.43
Matrice	3	996	0.92 (0.89-0.94)	73%	0.02	
Per domain	18	2911	0.91 (0.88-0.92)	89%	<0.01	
Dimension 5						
Sarcopenia Diagnosis						0.37
AWGS	6	549	0.89 (0.84-0.93)	87%	<0.01	
EWGSOP1	7	1205	0.88 (0.82-0.93)	94%	<0.01	
EWGSOP2	7	2083	0.92 (0.89-0.93)	80%	<0.01	
Population						0.17
Total population	18	3734	0.90 (0.88-0.92)	91%	<0.01	
Sarcopenic population	2	103	0.87 (0.81-0.91)	0%		
Age category [1]						0.63
< 75 years	9	2151	0.89 (0.85-0.92)	91%	<0.01	
≥75 years	8	1368	0.90 (0.86-0.93)	91%	<0.01	
Continent						0.45
Asia	7	999	0.90 (0.86-0.93)	86%	<0.01	
America	1	221	0.92 (0.89-0.94)	/		
Europe	12	2617	0.90 (0.86-0.92)	92%	<0.01	
Correlation type [2]						0.17

Spearman	8	1368	0.92 (0.90-0.94)	82%	<0.01	
Pearson	7	1276	0.89 (0.82-0.93)	94%	<0.01	
Methods						0.61
Matrice	3	996	0.91 (0.89-0.92)	36%	0.21	
Per domain	17	2841	0.90 (0.87-0.92)	91%	<0.01	
Dimension 6						
Sarcopenia Diagnosis						0.86
AWGS	6	549	0.48 (0.33-0.60)	79%	<0.01	
EWGSOP1	7	1205	0.50 (0.42-0.56)	58%	<0.01	
EWGSOP2	7	2083	0.45 (0.30-0.58)	91%	<0.01	
Population						0.80
Total population	18	3734	0.48 (0.41-0.54)	84%	<0.01	
Sarcopenic population	2	103	0.44 (0.09-0.69)	72%	0.06	
Age category [1]						0.67
< 75 years	9	2151	0.44 (0.37-0.51)	69%	<0.01	
≥75 years	8	1368	0.48 (0.33-0.60)	90%	<0.01	
Continent						0.50
Asia	7	999	0.45 (0.32-0.57)	82%	<0.01	
America	1	221	0.54 (0.44-0.63)	/		
Europe	12	2617	0.48 (0.39-0.56)	84%	<0.01;	
Correlation type [2]						0.18
Spearman	8	1368	0.53 (0.40-0.64)	89%	<0.01	
Pearson	7	1276	0.43 (0.35-0.51)	68%	<0.01	
Methods						0.68
Matrice	3	996	0.45 (0.28-0.59)	81%	<0.01	
Per domain	17	2841	0.48 (0.40-0.55)	84%	<0.01	
Dimension 7						
Sarcopenia Diagnosis						0.91
AWGS	6	549	0.58 (0.50-0.65)	65%	<0.01	
EWGSOP1	7	1205	0.56 (0.44-0.66)	82%	<0.01	
EWGSOP2	8	2153	0.59 (0.47-0.70)	91%	<0.01	
Population						0.81
Total population	19	3804	0.58 (0.52-0.64)	86%	<0.01	
Sarcopenic population	2	103	0.60 (0.45-0.71)	0%	0.53	
Age category [1]						0.08
< 75 years	9	2151	0.62 (0.58-0.66)	45%	0.10	
≥75 years	9	1438	0.51 (0.36-0.63)	89%	<0.01	
Continent						0.89
Asia	7	999	0.59 (0.51-0.67)	67%	<0.01	
America	1	221	0.60 (0.51-0.68)	/		
Europe	13	2687	0.57 (0.47-0.65)	89%	<0.01	

Correlation type [3]						0.67
Spearman	8	1368	0.62 (0.50-0.71)	90%	<0.01	
Pearson	7	1276	0.58 (0.47-0.68)	83%	<0.01	
Methods						0.56
Matrice	3	996	0.60 (0.56-0.64)	0%	0.85	
Per domain	18	2911	0.58 (0.50-0.64)	87%	<0.01	

[1] 2 studies removed (Le, Lee) because they did not report the age of total population of the study.
[2] 4 studies removed (*Mahmoodi, Matijevic, Montero-Errasquin, de Souza Orlandi) because they did not report the type of correlation.*
[3] 5 studies removed (*Mahmoodi, Matijevic, Montero-Errasquin, de Souza Orlandi, Geerinck) because they did not report the type of correlation.*

Table S4. Subgroups analysis – Test retest -Intraclass coefficient

	No. studies	**No. patients**	**ICC (95% IC)**	**I^2**	**P for heterogeneity**	**P for subgroup differences**
Global score						
Sarcopenia Diagnosis						0.69
AWGS	6	287	0.98 (0.93; 0.99)	97%	<0.0001	
EWGSOP1	5	299	0.97 (0.93; 0.98)	84%	<0.0001	
EWGSOP2	6	501	0.98 (0.97; 0.98)	71%	0.004	
Population [1]						0.47
Total population	3	475	0.96 (0.95; 0.97)	45%	<0.0001	
Sarcopenic population	14	622	0.95 (0.90; 0.98)	97%	<0.0001	
Age category [2]						0.81
< 75 years	10	789	0.96 (0.90; 0.98)	97%	<0.0001	
≥ 75 years	6	269	0.95 (0.91; 0.98)	86%	<0.0001	
Continent						0.19
Asia	7	340	0.98 (0.94; 0.99)	96%	<0.0001	
America	1	221	0.98 (0.98; 0.99)	-	-	
Europe	9	526	0.97 (0.96; 0.99)	81%	<.0.0001	
Quality of the study						0.62
Very good	10	557	0.98 (0.96; 0.99)	94%	<0.0001	
Adequate	1	25	0.97 (0.93; 0.99)	-		
Doubtful	6	505	0.97 (0.93; 0.99)	94%	<0.0001	
Time interval						0.14
2-week interval	13	685	0.98 (0.97; 0.99)	92%	<0.0001	
3-day interval	1	70	0.96 (0.94; 0.98)	-	-	
Not specified	3	332	0.96 (0.81; 0.99)	97%	<0.0001	
Patient stable						0.57
Yes	12	695	0.98 (0.96; 0.99)	93%	<0.0001	
Not specified	5	392	0.97 (0.91; 0.99)	95%	<0.0001	

[1] 1 study removed (Geerinck, 2019) because they did not report the population of the study
[2] 2 studies removed (Ariane, Lee) because they did not report the age of the participants

Table S5. Subgroups analysis – Validity – Convergent validity SF-36/5Q-5D
Subgroup analyses based on the quality appraisal of the studies was not performed as they all were rated as 'very good' for construct validity

	No. studies	No. patients	Cronbach a (95% CI)	I^2	P for heterogeneity	P for subgroup differences
SF-36						
Bodily pain						
Sarcopenia Diagnosis						**0.56**
AWGS	4	218	0.46 (0.27; 0.61)	54%	0.09	
EWGSOP1	5	295	0.54 (0.45; 0.62)	0%	0.84	
EWGSOP2	4	807	0.58 (0.41; 0.71)	87%	<0.01	
Population						**0.03**
Total population	5	920	0.61 (0.51; 0.69)	77%	<0.01	
Sarcopenic population	8	400	0.46 (0.36; 0.56)	26%	0.22	
Age category						0.24
< 75 years	5	845	0.60 (0.47; 0.70)	81%	<0.01	
≥75 years	7	424	0.51 (0.44; 0.58)	0%	0.86	
Continent						0.23
Asia	5	668	0.54 (0.34; 0.69)	87%	<0.01	
America	1	221	0.61 (0.52; 0.68)	-	-	
Europe	7	431	0.51 (0.43; 0.58)	0%	0.67	
Correlation type [1]						0.86
Spearman	6	967	0.54 (0.39; 0.66)	86%	<0.01	
Pearson	5	263	0.53 (0.43; 0.61)	0%	0.42	
Physical functioning						
Sarcopenia Diagnosis						0.79
AWGS	3	159	0.80 (0.73; 0.85)	0%	0.77	
EWGSOP1	6	591	0.80 (0.68; 0.89)	94%	<0.01	
EWGSOP2	7	1623	0.77 (0.67; 0.84)	85%	<0.01	
Population						0.87
Total population	7	1915	0.79 (0.70; 0.85)	94%	<0.01	
Sarcopenic population	9	458	0.78 (0.68; 0.85)	80%	<0.01	
Age category						0.87
< 75 years	6	1775	0.79 (0.68; 0.97)	95%	<0.01	
≥ 75 years	10	598	0.78 (0.70; 0.84)	77%	<0.01	
Continent						0.08
Asia	4	609	0.81 (0.77; 0.83)	0%	0.76	

America	1	221	0.85 (0.81; 0.88)	-	-	
Europe	11	1543	0.77 (0.67; 0.84)	91%	<0.01	
Correlation type [2]						0.28
Spearman	9	1338	0.76 (0.66; 0.84)	93%	<0.01	
Pearson	4	246	0.82 (0.75; 0.88)	55%	0.09	
Role physical						
Sarcopenia Diagnosis						0.89
AWGS	4	217	0.60 (0.38; 0.75)	78%	<0.01	
EWGSOP1	4	245	0.58 (0.48; 0.66)	0%	0.65	
EWGSOP2	7	221	0.61 (0.50; 0.69)	86%	<0.01	
Population						0.63
Total population	6	1619	0.62 (0.52; 0.70)	86%	<0.01	
Sarcopenic population	9	466	0.58 (0.47; 0.68)	63%	<0.01	
Age category						**<0.01**
< 75 years	5	1487	0.67 (0.58; 0.74)	85%	<0.01	
≥ 75 years	9	547	0.51 (0.44; 0.58)	6%	0.04	
Continent						0.65
Asia	5	667	0.64 (0.47; 0.77)	87%	<0.01	
America	1	221	0.56 (0.53; 0.67)	-	-	
Europe	9	1197	0.58 (0.52; 0.64)	36%	0.13	
Correlation type [2]						0.47
Spearman	9	1134	062 (0.53; 0.70)	83%	<0.01	
Pearson	3	162	0.54 (0.28; 0.72)	71%	0.03	
General health						
Sarcopenia Diagnosis						0.37
AWGS	4	219	0.62 (0.49; 0.73)	41%	0.16	
EWGSOP1	6	591	0.60 (0.51; 0.68)	48%	0.09	
EWGSOP2	5	866	0.54 (0.46; 0.61)	47%	0.11	
Population						0.84
Total population	6	1216	0.57 (0.50; 0.64)	61%	0.02	
Sarcopenic population	9	460	0.59 (0.50; 0.66)	39%	0.11	
Age category						0.21
< 75 years	6	1134	0.61 (0.53; 0.68)	64%	0.02	
≥ 75 years	9	542	0.54 (0.48; 0.61)	5%	0.39	
Continent						0.21
Asia	5	669	0.61 (0.56; 0.66)	23%	0.27	
America	1	221	0.52 (0.42; 0.61)	-	-	
Europe	9	786	0.56 (0.48; 0.64)	56%	0.02	
Correlation type [1]						0.40
Spearman	7	1230	0.57 (0.51; 0.63)	53%	0.05	
Pearson	6	356	0.62 (0.52; 0.71)	45%	0.10	
Vitality						
Sarcopenia Diagnosis						0.44

AWGS	4	220	0.54 (0.30; 0.71)	73%	0.01	
EWGSOP1	6	591	0.72 (0.58; 0.82)	79%	<0.01	
EWGSOP2	7	1623	0.55 (0.45; 0.64)	90%	<0.01	
Population						0.91
Total population	7	1915	0.61 (0.50; 0.70)	93%	<0.01	
Sarcopenic population	10	519	0.62 (0.47; 0.73)	79%	<0.01	
Age category						0.90
< 75 years	7	1833	0.61 (0.49; 0.71)	93%	<0.01	
≥ 75 years	10	601	0.62 (0.48; 0.73)	79%	<0.01	
Continent						0.13
Asia	5	670	0.49 (0.28; 0.65)	83%	<0.01	
America	1	221	0.57 (0.48; 0.65)	-	-	
Europe	11	1543	0.67 (0.57; 0.74)	74%	<0.01	
Correlation type [2]						0.40
Spearman	7	1230	0.57 (0.51; 0.63)	53%	0.05	
Pearson	6	356	0.62 (0.52; 0.71)	45%	0.10	
Physical component score						
Sarcopenia Diagnosis						**<0.01**
AWGS	2	188	0.65 (0.44; 0.80)	78%	0.03	
EWGSOP1	1	106	0.88 (0.83; 0.92)	-	-	
Population						**0.03**
Total population	2	206	0.82 (0.62; 0.92)	90%	<0.01	
Sarcopenic population	1	88	0.55 (0.39; 0.68)	90%	<0.01	
Age category [3]						**<0.01**
< 75 years	1	106	0.88 (0.83; 0.92)	-	-	
≥ 75 years	1	88	0.55 (0.39: 0.68)	-		
Continent						**<0.01**
Asia	2	188	0.65 (0.44; 0.80)	78%	0.03	
Europe	1	106	0.88 (0.83; 0.92)	-	-	
Correlation type						**0.03**
Spearman	2	206	0.82 (0.62; 0.92)	90%	<0.01	
Pearson	1	88	0.55 (0.39; 0.68)	-	-	
EQ-5D						
Utility score						
Sarcopenia Diagnosis						0.36
AWGS	2	172	0.60 (0.36; 0.77)	74%	<0.01	
EWGSOP1	5	631	0.67 (0.54; 0.77)	86%	<0.01	
EWGSOP2	6	1553	0.56 (0.48; 0.64)	75%	<0.01	
Population						0.30
Total population	8	2065	0.58 (0.49; 0.66)	80%	<0.01	
Sarcopenic population	5	291	0.66 (0.52; 0.77)	73%	<0.01	
Age category						0.95

< 75 years	9	2053	0.61 (0.52; 0.69)	80%	<0.01	
≥75 years	4	303	0.60 (0.43; 0.74)	79%	<0.01	
Continent						0.15
Asia	3	622	0.55 (0.39; 0.67)	69%	0.04	
America	1	221	0.51 (0.41; 0.60)	79%	-	
Europe	9	1513	0.64 (0.54; 0.72)	80%	<0.01	
Correlation type [4]						0.59
Spearman	8	1214	0.61 (0.50; 0.70)	84%	<0.01	
Pearson	3	222	0.66 (0.47; 0.79)	77%	<0.01	
Mobility						
Sarcopenia Diagnosis						0.53
AWGS	6	431	-0.48 (-0.78; -0.02)	90%	0.01	
EWGSOP1	6	591	-0.46 (-0.73; -0.06)	94%	<0.01	
EWGSOP2	6	917	-0.62 (-0.71; -0.51)	85%	<0.01	
Population						0.48
Total population	8	1430	-0.58 (-0.68; -0.47)	88%	<0.01	
Sarcopenic population	10	509	-0.48 (-0.76; -0.37)	85%	<0.01	
Age category [6]						0.32
< 75 years	7	1248	-0.43 (-0.66; -0.13)	93%	<0.01	
≥75 years	10	591	-0.60 (-0.74; -0.61)	47%	0.06	
Continent						0.12
Asia	7	881	-0.48 (-0.74; -0.11)	90%	<0.01	
America	1	221	-0.70 (-0.76; -0.62)	-	<0.01	
Europe	10	837	-0.54 (-0.71; -0.32)	91%	<0.01	
Correlation type [5]						0.39
Spearman	12	1504	-0.60 (-0.67; -0.51)	81%	<0.01	
Pearson	3	124	-0.30 (-0.82; 0.49)	96%	<0.01	
Usual activity						
Sarcopenia Diagnosis						0.80
AWGS	6	431	-0.48 (-0.78; 0.01)	92%	<0.01	
EWGSOP1	6	591	-0.46 (-0.76; 0.00)	94%	<0.01	
EWGSOP2	6	917	-0.57 (-0.67; -0.45)	85%	<0.01	
Population						0.43
Total population	8	1430	-0.57 (-0.64; -0.50)	77%	<0.01	
Sarcopenic population	10	509	-0.44 (-0.72; -0.05)	94%	<0.01	
Age category[3]						0.46
< 75 years	7	1248	-0.41 (-0.68; -0.05)	95%	<0.01	
≥75 years	10	591	-0.56 (-0.74; -0.31)	86%	<0.01	
Continent						0.03
Asia	7	881	-0.48 (-0.74; -0.08)	91%	<0.01	
America	1	221	-0.72 (-0.78; -0.65)	-	-	
Europe	10	837	-0.49 (-0.68; -0.25)	90%	<0.01	
Correlation type [5]						0.44

Spearman	12	1504	-0.59 (-0.66; -0.51)	74%	<0.01	
Pearson	3	124	-0.26 (-0.86; 0.66)	96%	<0.01	
VAS						
Sarcopenia Diagnosis						**<0.01**
AWGS	1	20	0.28 (-0.18; 0.65)	-	-	
EWGSOP1	2	198	0.74 (0.67; 0.81)	16%	0.27	
EWGSOP2	3	187	0.48 (0.36; 0.59)	0%	0.48	
Population						**0.01**
Total population	3	268	0.69 (0.55; 0.80)	71%	0.03	
Sarcopenic population	3	137	0.42 (0.27; 0.55)	0%	0.59	
Age category						0.09
< 75 years	1	106	0.71 (0.60; 0.79)	-		
≥75 years	5	299	0.54 (0.33; 0.70)	80%	<0.01	
Continent						0.13
Asian	1	20	0.28 (-0.18; 0.65)	-	-	
Europe	5	385	0.61 (0.44; 0.74)	80%	0.01	
Correlation type [5]						**0.02**
Spearman	3	223	0.55 (0.31; 0.72)	80%	<0.01	
Pearson	1	92	0.78 (0.68; 0.85)	-	-	

[1] 1 study removed (Geerinck 2022) because they did not report the type of correlation used.
[2] 2 studies removed (Geerinck, *Matijevic)* because they did not report the type of correlation used.
[3] 1 study removed (Lee) because they did not report the age of the total population
[4] 2 studies removed (Matijevic, de Souza Orlandi) because they did not report the type of correlation used
[5] 2 studies removed (Geerinck,2022, de Souza Orlandi) because they did not report the type of correlation used
[6] 1 study removed (Lee) because they did not report the age category

Table S6. Subgroups analysis – Validity – Divergent validity SF-36/5Q-5D
Subgroup analyses based on the quality appraisal of the studies was not performed as they all were rated as 'very good' for construct validity

	No. studies	**No. patients**	**Cronbach a (95% CI)**	**I^2**	**P for heterogeneity**	**P for subgroup differences**
SF-36						
Mental health						
Sarcopenia Diagnosis						0.13
AWGS	3	159	0.25 (-0.15; 0.58)	75%	0.02	
EWGSOP1	3	192	0.71 (0.34; 0.89)	92%	<0.01	
EWGSOP2	5	1336	0.31 (0.07; 0.52)	96%	<0.01	
Population						0.19
Total population	4	1311	0.27 (0.00, 0.50)	97%	<0.01	
Sarcopenic population	7	376	0.51 (0.21; 0.72)	88%	<0.01	
Age category						0.48

< 75 years	4	1258	0.54 (0.03; 0.83)	96%	<0.01	
≥75 years	7	429	0.37 (0.18; 0.53)	71%	<0.01	
Continent						0.04
Asia	4	609	0.16 (-0.17; 0.46)	90%	<0.01	
Europe	7	1078	0.55 (0.33; 0.72)	98%	<0.01	
Correlation type [1]						0.05
Spearman	5	710	0.33 (0.09; 0.52)	91%	<0.01	
Pearson	3	188	0.72 (0.38; 0.88)	91%	<0.01	
Social functioning						
Sarcopenia Diagnosis						0.79
AWGS	4	217	0.42 (0.01; 0.71)	90%	<0.01	
EWGSOP1	4	279	0.44 (0.34; 0.53)	15%	0.32	
EWGSOP2	2	129	0.30 (-0.14; 0.65)	85%	0.01	
Population						0.53
Total population	3	24	0.34 (0.10; 0.54)	74%	0.02	
Sarcopenic population	7	376	0.44 (0.22; 0.62)	82%	<0.01	
Age category						0.20
< 75 years	3	167	0.24 (-0.13; 0.55)	83%	<0.01	
≥ 75 years	7	458	0.48 (0.31; 0.61)	74%	<0.01	
Continent						0.90
Asia	4	217	0.42 (0.01: 0.71)	90%	<0.01	
Europe	6	408	0.40 (0.25; 0.52)	61%	0.02	
Correlation type [1]						0.16
Spearman	5	339	0.54 (0.42; 064)	47%	0.11	
Pearson	3	196	0.27 (-0.14; 0.60)	89%	<0.01	
Limitation emotional problem						
Sarcopenia Diagnosis						0.25
AWGS	3	159	0.28 (0.09; 0.45)	25%	0.26	
EWGSOP1	4	279	0.42 (0.23; 0.58)	71%	0.02	
EWGSOP2	4	886	0.45 (0.35; 0.53)	25%	0.26	
Population						0.59
Total population	4	948	0.42 (0.25; 0.57)	70%	<0.01	
Sarcopenic population	7	376	0.37 (0.27; 0.46)	15%	0.32	
Age category						0.07
< 75 years	3	808	0.48 (0.43; 0.53)	0%	0.43	
≥ 75 years	8	516	0.37 (0.24; 0.48)	56%	0.03	
Continent						0.14
Asia	3	159	0.28 (0.09; 0.49)	25%	0.26	
Europe	8	1165	0.43 (0.33; 0.51)	53%	0.04	
Correlation type [2]						0.07
Spearman	6	397	0.44 (0.32; 0.55)	51%	0.07	
Pearson	2	138	0.26 (0.09; 0.41)	0%	0.51	

EQ-5D						
Self-care						
Sarcopenia Diagnosis						0.34
AWGS	4	353	-0.63 (-0.78; -0.42)	84%	<0.01	
EWGSOP1	3	192	-0.23 (-0.73; 0.42)	95%	<0.01	
EWGSOP2	6	1471	-0.36 (-0.52; -0.18)	89%	<0.01	
Population						0.72
Total population	6	1525	-0.39 (-0.52; -0.25)	87%	<.0.01	
Sarcopenic population	7	491	-0.46 (-0.71; -0.10)	93%	<0.01	
Age category [3]						0.08
< 75 years	4	1313	-0.17 (-0.56; 0.27)	95%	<0.01	
≥75 years	8	603	-0.55 (-0.67; -0.39)	81%	<0.01	
Continent						0.25
Asia	5	803	-0.55 (-0.74; -0.27)	95%	<0.01	
Europe	8	1213	-0.35 (-0.55; -0.11)	89%	<0.01	
Correlation type [2]						0.21
Spearman	10	1133	-0.42 (-0.62; -0.18)	93%	<0.01	
Pearson	1	114	-0.58 (-0.69; -0.44)	-	-	
Pain/ Discomfort						
Sarcopenia Diagnosis						**0.81**
AWGS	5	373	-0.23 (-0.37; -0.07)	57%	0.05	
EWGSOP1	5	575	-0.20 (-0.51; 0.15)	90%	<0.01	
EWGSOP2	5	696	-0.50 (-0.74; -0.14)	94%	<0.01	
Population						0.14
Total population	7	1209	-0.43 (-0.64; -0.17)	93%	<0.01	
Sarcopenic population	8	435	-0.17 (-0.41; 0.09)	84%	<0.01	
Age category [3]						0.34
< 75 years	5	969	-0.17 (-0.47; 0.17)	90%	<0.01	
≥75 years	9	575	-0.37 (-0.58; -0.10)	89%	<0.01	
Continent						0.53
Asia	6	823	-0.27 (-0.34; -0.21)	48%	0.09	
Europe	9	821	-0.37 (-0.60; -0.15)	93%	<0.01	
Correlation type [4]						0.87
Spearman	11	1381	-0.24 (-0.38; -0.10)	78%	<0.01	
Pearson	1	114	-0.26 (-0.42; -0.08)	-	-	
Anxiety/Depression						
Sarcopenia Diagnosis						0.81
AWGS	5	373	-0.24 (-0.33; -0.14)	7%	0.36	
EWGSOP1	4	279	-0.10 (-0.52; 0.35)	92%	<0.01	
EWGSOP2	6	1394	-0.26 (-0.36; -0.14)	77%	<0.01	
Population						0.86
Total population	7	1612	-0.22 (-0.31; -0.13)	72%	<0.01	
Sarcopenic population	8	434	-0.20 (-0.43; 0.05)	84%	<0.01	

Age category [3]						0.15
< 75 years	4	1313	-0.01 (-0,39; 0.37)	94%	<0.01	
≥75 years	10	633	-0.30 (-0.37; -0.23)	0%	0.75	
Continent						0.76
Asia	6	823	-0.19 (-0.30; -0.08)	51%	0.07	
Europe	9	1223	-0.22 (-0.40; -0.03)	82%	<0.01	
Correlation type [2]						0.74
Spearman	11	1143	-0.22 (-0.37; -0.06)	80%	<0.01	
Pearson	1	114	-0.18 (-0.35; 0.00)	-	-	

[1] 1 study removed (Geerinck,2022) because they did not report the type of correlation used.
[2] 2 studies removed (Geerinck, *Matijevic)* because they did not report the type of correlation used.
[3] 1 study removed (Lee) because they did not report the age of the total population
[4] 2 studies removed (Geerinck, *Erdogan)* because they did not report the type of correlation used.

DISCUSSION

Discussion

Main findings

The first objective of this thesis was to investigate the prospective evolution of clinical characteristics in older adults from two well-established longitudinal cohorts: SENIOR and SarcoPhAge. To address this objective, three specific investigations were conducted, leading to the following key findings emerging:

- There was no significant relationship between frailty, nutritional status, or muscle strength and the incidence or severity of COVID-19 in nursing home residents.
- Over an eight-year follow-up period better physical performance was independently associated with lower mortality.
- Longitudinal increases in physical performance, grip strength and muscle mass were each independently associated with improvements in health-related quality of life, as measured by the SarQoL questionnaire.

The second objective of this thesis was to provide further evidence of the psychometric robustness of the SarQoL questionnaire. This was addressed through two investigations that assessing its content validity and psychometric properties, respectively. The main findings were the following:

- SarQoL adequately captures the QoL experienced by individuals with sarcopenia. Both patients and experts confirmed the relevance, comprehensiveness and comprehensibility of its items and dimensions, in accordance with COSMIN standards.
- SarQoL showed strong psychometric properties, with high internal consistency, test-retest reliability and construct validity. Its responsiveness to meaningful changes in HRQoL was also supported, reinforcing its utility in clinical and research contexts.

Contributions and implications

SPPB as a core indicator of ageing outcomes

This thesis highlights the central role of physical performance, particularly as assessed by the SPPB, in its longitudinal associations with survival and HRQoL in community dwelling older adults and NH residents. Although direct comparisons between the SENIOR and SarcoPhAge cohorts are complex due to their methodological differences (see Table 1, page 6), our findings consistently emphasise the importance of physical performance in both populations.

The findings of this thesis are largely consistent with previous investigations conducted within the same cohorts, strengthening the role of physical performance, assessed using the SPPB in both cohorts, as a key indicator of ageing outcomes. In SENIOR, a previous study reported that participants with a moderate or fast decline in physical performance had a threefold higher risk of 3-year mortality compared to those with a low decline [1]. Another study from the same cohort showed that frail individuals with lower physical performance reported poorer quality of life [2]. In SarcoPhAge, physical performance was independently associated with mortality. More specifically, a decline in SPPB score over 2 year was highlight to increase the risk of mortality over 5 years (HR = 3.61 (1.23–10.6)) [3]. However, a notable divergence emerged in the context of COVID-19: whereas no significant association was found in our analysis, previous research within SarcoPhAge identified the SPPB score as the only factor significantly associated with increased risk of COVID-19 among frail participants (HR = 5.18 (1.37–19.54)) [4]. This discrepancy may reflect differences in sample characteristics, timing of data collection, or exposure risk during the pandemic. Despite this exception, the overall consistency of findings reinforces the robustness of the associations between physical performance, mortality and quality of life in older adults.

Beyond this internal consistency, these findings are further supported by international literature. Indeed, a meta-analysis involving more than 16,000 older adults showed that SPPB scores below 10 were independently associated with increased risk of all-cause mortality, with a graded relationship as scores decreased [5]. Similar associations have been also observed in the NH population. A Brazilian longitudinal study showed that NH residents with lower SPPB scores had nearly threefold higher 5-year mortality risk (HR = 2.8 (1.7–4.6)), independently of age, comorbidities and cognitive status [6]. Furthermore, low SPPB scores have been consistently associated to poorer HRQoL, as shown in a study conducted in over 400 older adults using the EQ-5D questionnaire [7]. Long-term data from the English Longitudinal Study of Ageing also revealed that a one-point increase in SPPB was associated with a reduced risk of mobility impairment and ADL/IADL disability over a 14-year follow-up period [8], reinforcing the relevance of the SPPB for long-term autonomy and functional ageing.

In addition to the evidence supporting its relevance in the context of ageing, it is also important to consider how the SPPB compares to other physical performance measures commonly used in geriatric assessments. Tools such as gait speed, the Timed Up and Go (TUG) test, the six-minute walk test (6MWT) or the Tinetti test focus on a single domain (e.g. locomotion, balance or endurance). In contrast, the SPPB offers a more multidimensional evaluation by integrating

balance, mobility and strength into a single score [9]. Its feasibility, strong psychometric properties, and demonstrated superiority over other physical performance tests in predicting adverse outcomes and capturing functional health [10, 11] reinforce its value as a reference tool in research and clinical settings, particularly in the context of sarcopenia and frailty [12-14].

However, the relevance of the SPPB extends beyond the assessment of physical function alone. Originally designed to evaluate lower-limb function, SPPB appears to capture a broader physiological dimension. Because it engages multiple physiological systems, it may serve as an indicator of overall physiological reserve [5]. This could explain its strong predictive validity across diverse settings. From this perspective, the SPPB can be interpreted not only as a clinical indicator of the physiological vulnerability involved in ageing process. It may also mediate subjective outcomes, such as HRQoL, through its impact on autonomy, mobility and social participation. The interpretation of SPPB scores, however, must consider the context in which they are applied. In NH residents, where functional decline is often advanced, floor effects may limit its discriminative capacity. In contrast, among community-dwelling older adults, even minor variations may reflect clinically meaningful differences. These nuances support the importance of interpreting SPPB scores not in isolation, but within a broader biopsychosocial framework [15].

In this multidimensional perspective, the concept of intrinsic capacity (IC), as defined by the World Health Organization, provides a relevant theorical and practical framework. IC refers to the composite of all physical and mental capacities of an individual, across five domains: locomotion, vitality, cognition, psychological well-being and sensory function [16]. Within this framework, physical performance, as assessed by the SPPB, offers a practical and sensitive measure of an individual's physiological reserve and relates directly to the locomotion domain as it assesses balance, gait and lower-limb strength [16]. Therefore, it can serve as an operational entry point for the monitoring of intrinsic capacity over time. The findings of the present thesis support this perspective highlighting the robust and consistent associations between SPPB scores and important health outcomes. Rather than being a static indicator of physical function, the SPPB test may reflect a physical reserve that is closely related to an adaptation and resilience capacity in the face of age-related challenges.

In this perspective, identifying low physical performance through screening is only a first step. Indeed, while the SPPB provides a practical and sensitive tool to detect early signs of decline, translating this information into meaningful action requires a broader and structured approach. The Comprehensive Geriatric Assessment (CGA) is a multidimensional and interdisciplinary

diagnostic process designed to evaluate an older person's medical, psychological, functional, and social capacities in order to develop a coordinated care plan [17], which remains the gold standard for holistic evaluation of older adults. Although this thesis did not directly evaluate the integration of the SPPB into the CGA, its findings emphasize the robust associations between physical performance and important ageing outcomes and therefore support the potential utility of the SPPB within the CGA framework, given its feasibility and psychometric robustness [18, 19]. However, variability in the application of the SPPB, such as differences in walking distance, chair height, or instructions, may affect comparability and predictive validity. Therefore, strict adherence to standardized protocols is therefore essential to ensure consistency across settings [18].

Integrating the SPPB into the CGA would offer several advantages. Firstly, it would reinforce the functional assessment component by providing a reproducible and validated measurement. Secondly, it would facilitate the longitudinal monitoring of physical performance, helping to track changes over time and evaluate the impact of interventions. Thirdly, and perhaps most importantly, it would help to identify older adults who could benefit from tailored, function-oriented strategies before more advanced declines emerge.

To support this transition from functional screening to personalized care, several initiatives have demonstrated how SPPB scores can guide the implementation of targeted strategies. Among these, the Vivifrail program provides a relevant example of how SPPB performance assessments can be translated into tailored and multidimensional interventions [20]. This European multicomponent exercise program uses SPPB scores to categorize older adults according their SPPB score, ranging from severe limitation (SPPB ≤ 3) to robust performance (SPPB ≥ 10), in order to prescribe personalized exercise program focusing on strength, balance, endurance and flexibility. The Vivifrail program has been associated with significant improvements in terms of intrinsic capacity, notably in the locomotion domain [21]. In Belgium, a recent study also highlighted improvements not only in SPPB scores but also in molecular biomarkers (miRNAs) following Vivifrail-based training, suggesting systemic benefits beyond functional outcomes [22]. Interestingly, while this program has been originally designed for frail people, its relevance has been also highlighted in sarcopenic and frail NH residents with significant improvements in physical performance after completing the program [23], reinforcing its applicability across a range of functional states and geriatric profiles.

Beyond this example, Vivifrail illustrates a broader set of interventions based on physical activity. Resistance training and multicomponent programs are consistently recognized as

effective strategies to enhance physical performance and support intrinsic capacity, particularly in the domains of locomotion and vitality [14, 15]. However, the implementation of such programs faces several barriers, including low motivation, fear of falling, costs and environmental limitations calling for coordinated public health strategies [16, 17]. For example, low motivation is often linked to a limited awareness of the benefits of physical activity or an absence of personalized guidance. This can be addressed through personalized counselling and setting progressive objectives [24]. Supervised training focused on balance and mobility can help address the fear of falling, especially among individuals with previous falls experience [25]. Financial constraints, including the cost of exercise sessions and transport, as well as lack of reimbursement, particularly affect socioeconomically vulnerable populations. These populations require structural support, such as subsidized access or reimbursable exercise prescriptions [26]. Such prescriptions have been highlighted to significantly improve muscle strength, mass and physical performance [18], supporting their inclusion as part of integrated health interventions. Environmental limitations, including for example insufficient access to safe walking areas or age-friendly infrastructure, require urban planning measures to support active ageing [27]. Addressing these barriers is essential not only to promote adherence but also to ensure equity in access to physical activity interventions across diverse older populations.

While functional improvements remain possible even in later life, prevention remains the most effective and sustainable approach [19, 20]. This calls for a paradigm shift: physical activity should no longer be viewed solely as a therapeutic tool for older adults, but rather as a universal and lifelong health-promoting behavior. Promoting regular physical activity from an early age contributes to preserving functional capacity, delaying the onset of chronic diseases and reducing the burden on healthcare systems [21]. In contrast, interventions initiated only after significant functional decline tend to be less effective and more resource-intensive [21].

Health-Related Quality of Life: the added value of the SarQoL questionnaire

The findings from the two complementary investigations presented in the second chapter of this thesis provide a comprehensive perspective of the measurement properties of SarQoL. To date, SarQoL remains the only condition-specific instrument explicitly designed to assess HRQoL in individuals with sarcopenia. For this reason, it plays a pivotal role in assessing the impact of sarcopenia on QoL in clinical and research settings. These investigations represent the first systematic synthesis of its psychometric properties and the first content validity analysis conducted according the updated 2018 COSMIN guidelines [28]. The convergence of evidence

from the meta-analysis and the qualitative study highlights the multidimensional validity of the instrument and reinforces its relevance.

While SarQoL had already demonstrated satisfactory measurement properties in individual studies [29], no meta-analytic synthesis had been performed until now to formally evaluate the strength and consistency of this evidence. This investigation, conducted as part of this thesis confirmed its internal consistency, test–retest reliability and construct validity across diverse settings and populations, with a high level of evidence according to the GRADE approach. However, it also revealed significant heterogeneity, highlighting the need for more standardized assessment protocols for its psychometric properties. In this meta-analysis, responsiveness supported the ability of SarQoL to detect meaningful change over time. This finding is further supported by a recent meta-analysis comparing the responsiveness of HRQoL instruments, which showed that the SarQoL was more responsive than generic tools such as the EQ-5D and SF-36, reinforcing the value of using a condition-specific instrument in this population [30].

In parallel, the content validity study addressed an unmet assessment by confirming, for the first time, the extent to which the SarQoL captures what matters most to patients following the updated COSMIN guidelines. This investigation showed that the items of SarQoL were considered relevant, comprehensive and comprehensible by both patients and experts. However, some meaningful concepts not currently covered by the questionnaire were elicited, including “patient empowerment” and “depression”. These findings do not undermine the current validity of SarQoL, but rather highlight the multifaceted nature of quality of life in the context of sarcopenia, potentially inviting complementary assessments. In addition to its role in assessing HRQoL, SarQoL questionnaire could also serve as a stratification tool to tailor interventions. Individuals with similar physical parameters may report markedly different levels of limitations in daily life, reduced participation in leisure activities, as well as fears relating to falling and autonomy. SarQoL scores could help to identify subgroups requiring more psychological or social support, even in the absence of significant physical decline. This would support a more personalized and responsive approach to sarcopenia care. This patient-centered stratification is consistent with the broader aim of integrated geriatric care.

In addition to these findings, the investigations of the second chapter of this thesis contribute to the methodological literature on PROMs by combining a meta-analysis of the psychometric properties of the SarQoL with a qualitative assessment of its content validity. Although both approaches are increasingly encouraged, they are still infrequently applied together in PROM validation, particularly in older populations [31]. The recent PRISMA-COSMIN guideline by

Elsman et al. highlights the value of integrating qualitative methods into PROM evaluation and calls for more comprehensive and transparent reporting [31]. In this context, the present thesis offers a modest contribution by illustrating how psychometric properties can be addressed in a coordinated manner to support the robust validation of PROMs in geriatric populations.

From a clinical perspective, SarQoL complements objective measure, such as the SPPB, by capturing the subjective experience of sarcopenia. While SPPB provides essential information on observable functional limitations, SarQoL adds value by addressing emotional, social and daily living impacts that may not be detected through performance-based tools. Together, these instruments offer a more comprehensive assessment of health in older adults, consistent with the person-centered approach advocated by the WHO and aligned with the conceptual framework of IC for healthy ageing. In light of these findings, SarQoL could first serve as a valuable indicator of perceived health trajectories, helping to identify the unmet need and evaluate the impact of preventive strategies. In this context, the inclusion of QoL assessment in the CGA could represent a meaningful evolution. As discussed previously, the CGA remains the gold standard for multidimensional evaluation of older adults, but HRQoL is not systematically included in its core domains [32]. Integrating validated PROMs such as the SarQoL into CGA protocols for sarcopenic patients could enhance the capacity to detect unmet needs and guide more personalized care planning. In addition, such integration would also align with the framework of intrinsic capacity, which focuses on the preservation of physical and mental capacities as essential contributors to healthy ageing. While HRQoL is not formally included as a domain of intrinsic capacity, it can be viewed as a key outcome resulting from the maintenance of those capacities. Secondly, the systematic integration of QoL and more precisely of SarQoL in the context of sarcopenia research and trials protocol appears justified. However, its use in clinical trials remains limited [29] with generic tools such as EQ-5D or SF-36 often preferred due to their widespread recognition, broad applicability across conditions and regulatory recognition [33, 34]. Nevertheless, there is a growing consensus that condition-specific PROMs, such as SarQoL, are more sensitive to change and better reflect the outcomes that matter most to patients [35]. Therefore, the systematic integration of SarQoL into intervention trials targeting sarcopenia should be promoted. This would not only increase measurement precision, but it would also help ensure that improvements in muscle function translate into perceived gains in quality of life.

From a broader perspective, the systematic use of SarQoL contributes to amplifying the voice of sarcopenic individuals in clinical research and care. This aligns with global recommendations

to prioritize patient-reported outcomes in ageing policies and to design health systems that respect the preferences, values and lived experiences of older adults [36]. In this context, SarQoL is not just an evaluation tool, it also promotes equity, inclusion and patient empowerment in the management of age-related conditions.

Empowering older adults through self-management and digital innovation: a complementary pathway to preserve physical function and quality of life

In continuity with the findings presented in this thesis, which highlight the relevance of assessing both objective physical performances as measured by the SPPB in older adults with sarcopenia and frailty and HRQoL using the SarQoL in those with sarcopenia, the question arises as to how such evaluations can be translated into evidence-informed, person-centered interventions. In this perspective, self-management approaches and digital health interventions emerge as promising and complementary strategies to support autonomy, reinforce engagement in health behaviors and monitor function over time.

Although this thesis did not assess digital interventions, several findings provide valuable insight into how such strategies could be improved and implemented. In the longitudinal analyses conducted in the first chapter of this thesis, statistically significant associations were observed between variations in physical performance and changes in HRQoL. While no causal relationship can be inferred, these results suggest that even minor functional changes may have a significant impact, supporting the early identification of individuals at risk**.** Tools such as the SPPB and SarQoL could facilitate the timely development of personalized interventions, particularly if they are integrated into care programs.

In Belgium, initiatives such as the MoveUP digital platform, the first mobile health app in the country to be reimbursed, have demonstrated the feasibility of remotely prescribing and monitoring exercise remotely in older adults. Although MoveUP was initially developed for postoperative rehabilitation, similar platforms are now being adapted for frailty and chronic care management [37, 38]. At the European level, the ProACT project, funded by the Horizon 2020 program, developed a digital health platform to support older adults with multimorbidity in managing their chronic conditions. The system combined wearable devices, a personal health record, tailored feedback, educational content and remote coaching. In a 12-month proof-of-concept study conducted in Belgium and Ireland, participants reported high level of engagement as well as perceived improvements in self-management and health awareness, as revealed through qualitative interviews [39]. While these examples illustrate the potential of digital tools

to support autonomy and continuity of care, it is should be noted that few interventions have been specifically designed or evaluated for sarcopenic or frail populations. Nevertheless, a recent systematic review focusing on e-health interventions in older adults with frailty or sarcopenia, although based on only four studies, reported significant improvements in muscle strength and suggested a positive trend in QoL [40]. These findings support the potential value of digital strategies in frail and sarcopenic populations and highlight the need for more targeted research in this area.

In addition to these structured initiatives, other digital tools are also being explored to support individual self-monitoring and behavior change. Tools such as wearable devices, digital diaries, smartphone applications and telemonitoring platforms have already been used to support the self-monitoring of physical activity and dietary intake. For example, a recent pilot study by Chen et al. showed that older adults who participated in structured, moderated online discussions experienced improvements in health literacy, self-efficacy, and awareness of proactive health behaviors [41]. This demonstrates how digital interventions can foster empowerment when they are designed to be interactive and supportive. This vision aligns with a public health approach that recognizes older adults as active participants in maintaining their functional health, rather than passive recipients of care.

In this evolving context, the development of digital or modular versions of validated instruments such as SarQoL and the SPPB could strengthen their clinical utility and facilitate their integration into routine care. In this context, the SPPB Guide app has been designed to be used on mobile technologies. This application provides standardized instructions, automated timers, and electronic result storage, thereby improving feasibility and consistency [42]. More recently, the MobiSPPB app, based on motion capture technology, demonstrated strong validity and excellent test–retest reliability in a pilot study comparing its automated scoring to expert ratings [43]. These tools make it possible to carry out standardized, remote and repeated assessments of physical function, regardless of the patient's setting. Based on this example, SarQoL could also benefit from digital implementation. A shortened version of the SarQoL, the short form SarQoL (SF-SarQoL), has recently been developed and validated, demonstrating excellent psychometric properties [44]. This format may be more suitable for repeated assessments and integration into mobile applications or telemonitoring platforms. It would also address known barriers to PROM implementation, such as time constraints, paper burden and lack of interoperability with clinical systems. The combination of these tools could facilitate more integrated and person-centered monitoring of function and QoL in older adults.

However, digital exclusion remains a major challenge in promoting equitable access to these innovations. In Belgium, 60% of people over 65 in Wallonia report not feeling capable of using digital health tools. At the European level, only 30% of adults aged 65 and over have basic digital skills. These disparities underscore the need for inclusive design, patient training and structural support to ensure that digitalization does not increase health disparities.

Public funding and institutional support play a key role in the development and implementation of such tools. European initiatives such as ProACT demonstrate how funded pilot projects can bridge the gap between research and practice [39]. The WHO Regional Office for Europe also emphasises the importance of government investment in digital literacy, stakeholder co-creation and reimbursement of validated technologies to support healthy ageing [45].

Together, these elements illustrate the potential of integrating digital health and self-management into geriatric care. This approach is not intended to replace clinical expertise, but rather to empower older adults and promote the adoption of more equitable, responsive and person-centered strategies.

Limits

Although several study-specific limitations have already been addressed, broader methodological limitations of this thesis should be acknowledged.

First, the use of two Belgian cohorts (SarcoPhAge and SENIOR) may limit the external validity of the findings. Indeed, differences in healthcare systems, long-term care infrastructure and social protection across countries and may influence both the determinants and consequences of ageing-related conditions. Additionally, within the Belgian context itself, the participants included may be not fully representative of the national older population. Both cohorts comprised volunteers recruited in relatively stable health conditions, likely more educated and motivated than the general older adult population. This selection process may limit generalizability. Future studies in more diverse settings are warranted to confirm these findings.

Another limitation relates to selection bias as participants had to possess sufficient physical and cognitive capacity to engage in follow-up assessments. This constraint may have led to the underrepresentation of the most vulnerable older adults. Consequently, the observed associations, particularly those relating to sarcopenia components and HRQoL, may underestimate the strength or variability of these relationships in more vulnerable subgroups, where quality of life is likely to be more deeply impacted.

In addition, certain variables of interest were not systematically collected including aspects such as sleep quality, social participation or information on medical or lifestyle interventions during follow-up (e.g. physiotherapy, exercise counselling, nutritional support). The absence of these data precluded adjustment for potentially influential factors, limiting the ability to fully account for confounders. While this reflects the limitations of real-world observational research, it also underscores the need for a more comprehensive approach to data collection in future studies to gain a fuller picture of ageing.

With regard to operational definitions, sarcopenia was defined according to the revised EWGSOP2 criteria, with muscle mass assessed using dual-energy X-ray absorptiometry (DEXA) [46]. While DEXA is considered a reference method and is widely recommended, it does not measure muscle tissue directly but rather lean mass, which also includes non-muscular components such as water and connective tissue. This limitation is particularly relevant in individuals with obesity, where excess adiposity and altered body composition may lead to an overestimation of muscle mass and, consequently, to an underestimation of sarcopenia prevalence [47]. In parallel, frailty was consistently defined in accordance with Fried's physical phenotype [48]. Although this definition is widely used and internationally recognised, it only captures the physical aspect of frailty and does not encompass the broader multidimensional construct included in other definitions. Some of the criteria, such as unintentional weight loss, physical activity and exhaustion, relied on self-reported information, which may have been influenced by cognitive impairment, underreporting or social desirability bias. Taken together, these methodological considerations should be acknowledged as potential sources of bias when interpreting the findings of this thesis.

Another methodological issue concerns the longitudinal modelling approaches. Although most investigations in this thesis were based on prospective cohort data, only one study adopted a fully dynamic longitudinal modelling approach, capturing within-individual change over time. Other studies used baseline measures or change scores over fixed intervals, which are informative but may not fully reflect the complexity of health transitions in later life. Indeed, conditions such as sarcopenia and frailty are dynamic, with individuals moving over time between being at risk, developing the condition, or recovering from it [49, 50]. Future research should focus on dynamic approaches that better reflect the complex and evolving nature of ageing-related condition and the responsiveness of interventions.

Regarding physical performance assessment, the SPPB, although validated and widely recommended, is constrained by ceiling effects that frequently occur in robust older adults. In

these individuals, a large proportion achieve the maximum score, which might mask inter-individual variability and reduces the ability of the test to detect subtle but clinically relevant declines in performance [18]. Some authors have suggested that the use of continuous measures from each subtest, such as walking time in seconds or chair-stand duration, rather than categorised scores could provide greater sensitivity, although this approach remains to be further validated [51]. In addition, complementary assessments such as longer walking tests or the Timed Up and Go have been proposed as useful additions to the SPPB, although the evidence regarding their added value remains limited [13]. Recognising this ceiling effect is essential, as it highlights the risk of underestimating functional decline in healthier populations

Finally, some limitations concern the SarQoL questionnaire itself. While it demonstrated strong psychometric properties and content validity in this thesis, its applicability may be reduced in certain subpopulations or contexts. For example, its use in individuals with significant cognitive impairment remains uncertain, as its comprehensibility and feasibility have not been fully assessed in this group. Moreover, even though the SarQoL has shown good responsiveness to improvement, its ability to detect deterioration remains less well documented. Further longitudinal and interventional studies are needed to confirm its sensitivity across the full spectrum of change experienced by individuals with sarcopenia.

Perspectives

Future research should aim to address the key gaps identified throughout this thesis. These perspectives can be structured according to their expected timeframe, ranging from short to long term.

In the short term, further investigations should focus on individual components of physical performance of the SPPB. While the composite SPPB score is widely used and validated, it encompasses distinct function dimensions, namely balance, gait speed, and lower limb strength, that may differ in their associations with specific outcomes. Disaggregating the predictive value of each subtest could enhance the understanding of which aspects are most sensitive to change and therefore most relevant for use in clinical monitoring or intervention evaluation. Finally, assessing the feasibility, acceptability and content validity of the SarQoL in more vulnerable populations, such as NH residents or frail older adults, could strengthen its applicability in settings where HRQoL is often under-assessed, despite being critically important. In this context, the emerging challenge of sarcopenic obesity deserves particular consideration, as it reflects the coexistence of sarcopenia and excess adiposity, a combination likely to generate

additional QoL consequences beyond those usually captured by sarcopenia alone. Recent findings have shown that the SarQoL questionnaire can discriminate quality of life in individuals with sarcopenic obesity, however further research is required to determine whether its domains fully encompass the specific burden of this phenotype, including aspects such as joint pain, body image or social participation [52]. Addressing this question will be crucial to ensure that the SarQoL remains a comprehensive and sensitive instrument for capturing the QoL consequences of sarcopenia across its different clinical phenotypes.

In the medium term, there is a clear need for long-term longitudinal studies that better reflect the progressive and sometimes reversible nature of ageing-related conditions. Conditions such as sarcopenia and frailty follow dynamic, sometimes reversible trajectories, which cannot be fully captured through baseline or cross-sectional analyses. Future studies should adopt designs and statistical models capable of reflecting the heterogeneity and fluctuation of ageing trajectories. This would allow the identification of clinical thresholds and windows of opportunity for prevention. At the same time, research should explore the integration of PROMs such as SarQoL into existing care pathways. In outpatient geriatric clinics, primary care, or home-based assessments, the routine use of SarQoL could help identify unmet needs and support more individualized care planning. Implementing such approaches will require dedicated training for health professionals, development of user-friendly digital interfaces and consensus on interpretation thresholds to guide decision-making.

In the longer term, more innovative strategies should be developed and evaluated to combine objective and subjective indicators in daily practice. For example, home-based exercise programs supported by telemonitoring and self-administered SarQoL assessments could offer scalable models to promote physical performance and QoL. These models align with broader shifts toward technology-supported, person-centered care and could foster greater autonomy and engagement among older adults. When co-designed with users and supported by policy frameworks, such interventions could contribute to bridging the gap between clinical evaluations and the lived experience of ageing. In this context, evaluating the cost-effectiveness and implementation feasibility of such integrated approaches would also be essential, particularly given the growing demand on healthcare systems to prevent functional decline and maintain autonomy in ageing populations.

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GENERAL CONCLUSION

General conclusion

This doctoral thesis contributes to a better understanding of the health challenges faced by older adults, by investigating how frailty and sarcopenia are associated with major health outcomes, and by evaluating the methodological robustness of the SarQoL questionnaire, a specific tool for assessing quality of life in sarcopenic individuals.

The first chapter explored key health outcomes in two distinct older populations. Within the SENIOR cohort of NH residents, two investigations investigated the determinants of COVID-19 incidence and severity as well as long-term mortality. Meanwhile, data from the SarcoPhAge cohort were used to investigate the relationship between changes in sarcopenia components and changes in HRQoL, as measured by the SarQoL questionnaire. Together, these investigations improve our understanding of the implications of frailty and sarcopenia across different settings and timeframes. They also highlight the value of using condition-specific tools, such as the SarQoL, to capture how changes in muscle function may affect perceived quality of life in sarcopenic individuals.

The second chapter focused on the SarQoL, which remains the only condition-specific instrument available for assessing QoL in people with sarcopenia. Through a systematic review of its measurement properties and a content validity study involving both experts and patients, this thesis strengthens the evidence that SarQoL effectively captures key dimensions of QoL relevant to individuals with sarcopenia, supporting its use in clinical and research settings.

Ultimately, this work reflects the broader ambition conveyed by its title, *from survival to quality of life*, by showing how ageing research on frailty and sarcopenia can evolve from focusing solely on the prediction of adverse events to adopting a more comprehensive approach to ageing. Throughout this thesis, the SPPB emerges as a key indicator of both mortality and quality of life. Alongside the SarQoL, they provide complementary insights into how physical decline and subjective experience interact throughout the ageing process.

More broadly, this thesis is part of a broader reflection on what constitutes successful ageing in the 21st century. It highlights the importance to recognize and address sarcopenia and frailty not as inevitable consequences of ageing, but as modifiable and meaningful targets for action. These conditions are not solely musculoskeletal syndromes; they are major determinants of health trajectories in older adults. By combining functional and subjective indicators, this work modestly contributes to the development of more inclusive and responsive approaches that

recognize that health in older age cannot be reduced to survival alone, but must also consider quality of life and lived experience.

APPENDIX

Appendix1: SarQoL questionnaire

Questionnaire I Time : ±10 min

SarQoL
Sarcopenia and Quality of Life

Quality of life in sarcopenia

This questionnaire asks about sarcopenia, which is a muscle weakness that comes about with ageing. Sarcopenia can affect your daily life. This survey will enable us to find out if the state of your muscles currently affects your quality of life.

Please choose the most appropriate response for each question. The questionnaire should take you approximately 10 minutes to complete.

1. Do you currently feel you have a reduction in:

	A lot	Some	A little	None
The strength in your arms?	☐	☐	☐	☐
The strength in your legs?	☐	☐	☐	☐
Your muscle mass?	☐	☐	☐	☐
Your energy?	☐	☐	☐	☐
Your physical capabilities?	☐	☐	☐	☐
Your general flexibility?	☐	☐	☐	☐

2. Do you have pain in your muscles?

- ☐ Often
- ☐ Sometimes
- ☐ Rarely
- ☐ Never

English version – August 2011 1

SarQoL
Sarcopenia and Quality of Life

3. When undertaking light physical activities (walking slowly, doing the ironing, dusting, washing-up, DIY, watering the garden, etc.), do you:

	Often	Occasionally	Rarely	Never	I do not undertake these types of physical activities
Have difficulty?	☐	☐	☐	☐	☐
Get tired?	☐	☐	☐	☐	☐
Experience pain?	☐	☐	☐	☐	☐

4. When undertaking moderate physical activities (fast walking, cleaning windows, hoovering, washing the car, pulling up weeds in the garden, etc.), do you:

	Often	Occasionally	Rarely	Never	I do not undertake these types of physical activities
Have difficulty?	☐	☐	☐	☐	☐
Get tired?	☐	☐	☐	☐	☐
Experience pain?	☐	☐	☐	☐	☐

5. When undertaking intense physical activities (running, hiking, lifting heavy objects, moving furniture, digging the garden, etc.), do you:

	Often	Occasionally	Rarely	Never	I do not undertake these types of physical activities
Have difficulty?	☐	☐	☐	☐	☐
Get tired?	☐	☐	☐	☐	☐
Experience pain?	☐	☐	☐	☐	☐

6. Do you currently feel old?

- ☐ Yes, very
- ☐ Yes, somewhat
- ☐ Yes, a little
- ☐ No, not at all

SarQoL
Sarcopenia and Quality of Life

7. If yes to question 6, what gives you that impression?
(Choose as many answers as you like)

- ☐ I become unwell easily
- ☐ I take many medications
- ☐ I feel a weakness in my muscles
- ☐ I have problems with my memory
- ☐ I've had to face the death of several people close to me
- ☐ I do not have much energy, I am often tired
- ☐ My eyesight is poor
- ☐ Other:

8. Do you feel physically weak?

- ☐ Yes, completely
- ☐ Yes, somewhat
- ☐ Yes, a little
- ☐ No, not at all

9. Do you feel you are limited in:

	A lot	Some	A little	None
The length of time you can walk for?	☐	☐	☐	☐
How often you go out walking?	☐	☐	☐	☐
The distance you can walk?	☐	☐	☐	☐
The speed at which you can walk?	☐	☐	☐	☐
The length of your steps?	☐	☐	☐	☐

10. When you are walking:

	Often	Occasionally	Rarely	Never	I am unable to walk
Do you feel very tired?	☐	☐	☐	☐	☐
Do you need to sit down regularly to recover?	☐	☐	☐	☐	☐
Do you have difficulty crossing roads quickly enough?	☐	☐	☐	☐	☐
Do you have difficulties with uneven surfaces?	☐	☐	☐	☐	☐

SarQoL
Sarcopenia and Quality of Life

11. Do you have problems with your balance?

- ☐ Often
- ☐ Occasionally
- ☐ Rarely
- ☐ Never

12. How often do you fall?

- ☐ Very often
- ☐ Occasionally
- ☐ Rarely
- ☐ Never

13. Do you think that your physical appearance has changed?

- ☐ Yes, very
- ☐ Yes, somewhat
- ☐ Yes, a little
- ☐ No, not at all

14. If yes to question 13, in what way? (Choose as many answers as you like)

- ☐ Change in your weight (you've put on weight or you've lost weight)
- ☐ Appearance of wrinkles
- ☐ Loss of height
- ☐ Loss of muscle mass
- ☐ Hair loss
- ☐ Getting white or grey hair
- ☐ Other:

15. If yes to question 13, are you upset by this change?

- ☐ Yes, very
- ☐ Yes, somewhat
- ☐ Yes, a little
- ☐ No, not at all

SarQoL
Sarcopenia and Quality of Life

16. Do you feel frail?

- ☐ Very much so
- ☐ A little
- ☐ Not at all

17. Do you currently have difficulty in undertaking any of the following daily activities:

	Unable to do	Great difficulty	A little difficulty	No difficulty	Not applicable
Climbing a flight of stairs?	☐	☐	☐	☐	☐
Climbing several flights of stairs?	☐	☐	☐	☐	☐
Going up one or several steps without holding on to the banister?	☐	☐	☐	☐	☐
Squatting or kneeling?	☐	☐	☐	☐	☐
Stooping or leaning down to pick up an object off the floor?	☐	☐	☐	☐	☐
Getting up from the floor without holding on to anything?	☐	☐	☐	☐	☐
Getting out of a low chair without armrests?	☐	☐	☐	☐	☐
Moving, generally, from a sitting position to a standing position?	☐	☐	☐	☐	☐
Carrying heavy objects (large bags full of shopping, saucepan filled with water, etc.)?	☐	☐	☐	☐	☐
Opening a bottle or a jar?	☐	☐	☐	☐	☐
Using public transport?	☐	☐	☐	☐	☐
Getting in or out of a car?	☐	☐	☐	☐	☐
Doing your shopping?	☐	☐	☐	☐	☐
Doing the housework (making the bed, hoovering, doing the ironing, washing the dishes, etc.)?	☐	☐	☐	☐	☐

SarQoL
Sarcopenia and Quality of Life

18. Does your muscle weakness limit your movement?

- ☐ Yes, a lot
- ☐ Yes, somewhat
- ☐ Yes, a little
- ☐ No, not at all

19. If yes to question 18, for what reasons? (Choose as many answers as you like)

- ☐ Fear of pain
- ☐ Fear that you might not be able to
- ☐ Fear of feeling tired after these activities
- ☐ Fear of falling
- ☐ Other:

20. Does your muscle weakness limit your sex life?

- ☐ I am not sexually active
- ☐ Yes, completely
- ☐ Yes, somewhat
- ☐ Yes, a little
- ☐ No, not at all

21. How has your participation in physical activities/sport changed?

- ☐ Increased
- ☐ Decreased
- ☐ Unchanged
- ☐ I have never participated in physical activities or sports

22. How has your participation in leisure activities (going out to eat, gardening, doing DIY, shooting/fishing, senior citizens clubs, playing bridge, going for a walk, etc.) changed?

- ☐ Increased
- ☐ Decreased
- ☐ Unchanged
- ☐ I have never participated in leisure activities