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MONOGRAPHIC SECTION

Prevalence of frailty at population level in European ADVANTAGE Joint Action Member States: a systematic review and meta-analysis

Rónán O'Caoimh[1], Lucia Galluzzo[2], Ángel Rodríguez-Laso[3], Johan Van der Heyden[4], Anette Hylen Ranhoff[5], Maria Lamprini-Koula[6], Marius Ciutan[7], Luz López Samaniego[8], Laure Carcaillon-Bentata[9], Siobhán Kennelly[1*], Aaron Liew[1] on behalf of Work Package 5 of the Joint Action ADVANTAGE

[1]*Health Service Executive of Ireland (Social Care Division) and National University of Ireland (Discipline of Medicine), Galway, Ireland*
[2]*Dipartimento Malattie Cardiovascolari, Dismetaboliche e Invecchiamento, Istituto Superiore di Sanità, Rome, Italy*
[3]*Fundación para la Investigación Biomédica del Hospital Universitario de Getafe, Getafe, Spain*
[4]*Sciensano, Brussels, Belgium*
[5]*Nasjonalt Folkehelseinstitutt (Norwegian Institute of Public Health), Oslo, Norway*
[6]*Society of Psychosocial Research and Intervention. Ionnina, Greece*
[7]*Scoala Nationala de Sanatate Publica, Management si Perfectionare in Domeniul Sanitar, Bucharest, Romania*
[8]*Fundación Progreso y Salud, Consejeria de Salud de la Junta de Andalucia, Sevilla, Spain*
[9]*Santé Publique, Saint Maurice, France*
[*]*Siobhán Kennelly is not a member of the ADVANTAGE Joint Action*

Abstract

Introduction. Although frailty is common among community-dwelling older adults, its prevalence in Europe and how this varies between countries is unclear.

Methods. A systematic review and meta-analysis of literature on frailty prevalence in 22 European countries involved in the Joint Action ADVANTAGE was conducted.

Results. Sixty-two papers, representing 68 unique datasets were included. Meta-analysis showed an overall estimated frailty prevalence of 18% (95% confidence interval, CI, 15-21%). The prevalence in community (n = 53) *vs* non-community based studies (n = 15) was 12% (95% CI 10-15%) and 45% (95% CI 27-63%), respectively. Pooled prevalence in community studies adopting a physical phenotype was 12% (95% CI 10-14%, n = 45) *vs* 16% (95% CI 7-29%, n = 8) for all other definitions. Sub-analysis of a subgroup of studies assessed as high-quality (n = 47) gave a pooled estimate of 17% (95% CI 13-21%).

Conclusions. The considerable and significant heterogeneity found warrants the development of common methodological approaches to provide accurate and comparable frailty prevalence estimates at population-level.

Key words
- prevalence
- frailty
- systematic review
- meta-analysis
- ADVANTAGE JA
- Europe

INTRODUCTION

Frailty is an age-associated vulnerability to stressors that results in an increased risk of adverse healthcare outcomes [1]. Based on current ageing demographics [2], it is expected that the number of older adults with recognised frailty syndromes will increase such that frailty is now identified as an emerging public health priority [3]. Although the prevalence of frailty has been reported to range between 4-59.1% in community-based studies [4], there is marked variation in these in terms of methodological approaches, rendering geographical comparisons unclear. Longitudinal studies on ageing have shown that frailty is more common with greater age, female gender and socioeconomic factors, particularly lower education and less wealth [5], and that there is wide variation across European countries where data

Address for correspondence: Rónán O'Caoimh, Health Research Board Clinical Research Facility Galway, National University of Ireland, Galway, Geata an Eolais, University road, Galway City, Ireland. E-mail: rocaoimh@hotmail.com.

are available [6]. Two large population-based longitudinal studies, the Survey of Health and Retirement in Europe (SHARE) and the Study on Global AGEing and Adult Health (SAGE), reporting mean Frailty Index (FI) scores, found the lowest levels of frailty in Ireland, Greece and The Netherlands with the highest levels in Italy, Spain and Poland [5]. A recent systematic review in long-term (nursing home) care (LTC) estimated that half of residents aged ≥ 60 years can be classified as frail but noted that these studies were highly heterogeneous with mean prevalence of frailty ranging widely from 19% to 75.6% [7]. Individual studies have examined frailty in other populations but most studies reporting prevalence rates are limited to community-based samples with little data available from other important healthcare settings such as general practice, hospitals (inpatient or outpatient), or home care.

In order for healthcare planners and policy makers at local, national and European level to design and implement appropriate services for older adults, there is a need to determine the current prevalence of frailty in different settings using data from well designed population-based studies. The Joint Action (JA) initiative on Frailty, also called ADVANTAGE, co-funded by the European Third Health Programme (2014-2020), grant number #724099, aims to develop a holistic and comprehensive strategic framework for the prevention and management of frailty at European level. This JA brings together partners from 22 European countries (see www.advantageja.eu). One of its tasks is to explore the current state of knowledge on the epidemiology of frailty reviewing the existing literature on prevalence. This systematic review and meta-analysis aims to summarize and analyze the data on frailty prevalence in JA Member States (MSs). International data from non-JA MSs were also included, where available and relevant, to provide context and comparison.

METHODS

Data sources and search strategy

We conducted a systematic search of the literature published between the 1st of January 2002 and the 30th of April 2017 using PubMed, Embase, CINAHL, MEDLINE, Opengrey and the Cochrane databases. Grey literature and data from ongoing or unpublished frailty projects funded by the European Union or registered with the European Innovation Partnership on Active and Healthy Ageing [8, 9] were included based on information provided by MS partners about unpublished data or materials available through websites, reports, and academic thesis. Reference lists of included papers were also researched for relevant articles. The review protocol was registered and published in full on the Prospero website (protocol number CRD42017071866). This systematic review and meta-analysis was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [10]. The following search terms were applied: (Prevalence OR Incidence OR Epidemiology) AND (Elderly OR Aged OR "Older adult$" OR "Older person$" OR Geriatric$) AND (Frailty OR Frail) AND (Population-based OR "Population based") NOT ("Frailty model" OR "Frailty survival model"). Results relating to frailty incidence were then singled out and published in another paper of the present journal issue [11].

Inclusion and exclusion criteria

Prevalence of frailty was defined as the proportion of cases in a population in a specific moment (point prevalence) or over a specific period of time (period prevalence). Papers were included if they met all the following criteria: 1) Described data relating to frailty using any definition of frailty, irrespective of the method of data collection or instrument used, 2) Included participants aged ≥ 18 (no maximum limit), 3) Reported population-based prevalence data without a restriction on the setting i.e. findings that can be extrapolated to a larger population defined in terms of geographical area, age group and setting (e.g. general population, hospitals, and LTC). Data from specific settings, e.g. patients in geriatric wards, were included only if there was evidence that all individuals in the population could be recruited from that setting, 4) Reported data from a JA MS in English or any language of a MS partner, 5) Published data between the 1st of January 2002 and the 30th of April 2017. Papers published before 2002 were included on a case-by-case basis if discovered opportunistically and deemed relevant, 6) Presented data from original articles. Letters to the editor, abstract publications, conference proceedings, non-systematic reviews (narrative reviews etc.), and editorials were excluded. Relevant grey literature was included on a case by case basis. The following exclusion criteria were applied: 1) Replicated data, 2) not in English or language of JA partner, 3) not about the topic and 4) other reasons, including papers focusing on individuals with specific diseases.

Data extraction

Two pairs of reviewers independently assessed studies for inclusion. A third reviewer settled any disagreements. Data from articles assessed as eligible for inclusion were extracted and analyzed by a second pair of reviewers.

Quality and bias assessment

The Checklist for Prevalence Studies from the Joanna Briggs Institute (JBI) Critical Appraisal tools for use in JBI Systematic Reviews was preliminarly used to assess the methodological quality of each study and to determine the extent to which a study addressed the possibility of bias in its design, conduct and analysis [12]. All papers selected for inclusion in the systematic review were subjected to rigorous appraisal by two independent pairs of critical appraisers with disagreements settled by consensus. Risk of publication bias across studies was assessed using funnel plots and confirmed by Egger's test; a symmetric funnel plot indicates low risk of bias across studies.

Data synthesis and analysis

We conducted an initial descriptive analysis of the studies, followed by meta-analysis if there were more

than three meta-analyzable datasets. Due to the expected inherent heterogeneity of the included studies, a meta-analysis using an *a priori* random-effects model was chosen. In addition, subgroup analyses were performed according to: 1) the country in which data were collected; 2) the setting in which data were collected (community versus non-community); 3) the tools used to define frailty; and (4) the level of quality of the study as assed by means of the JBI Critical Appraisal tool (higher quality versus less high-quality studies).

The Freeman-Tukey double arcsine method, via *metaprop_one ftt* command in STATA (version 14.0), was used to perform the meta-analysis, in order to stabilize the inherent variance due to the nature of prevalence studies [13, 14]. Heterogeneity was assessed with Higgins' I^2 statistic to determine the extent of variation between studies. The following cut-offs for the degree of heterogeneity were used; I^2 = 0-40%: might not be important; I^2 = 30-60%: may represent moderate heterogeneity; I^2 = 50-90%: may represent substantial heterogeneity; I^2 = 75-100%: considerable heterogeneity [15]. The significance was determined using the χ^2 test with a p-value of < 0.05 considered significant.

RESULTS

The selection of relevant papers is depicted in a PRISMA flow diagram *(Figure 1)*. In summary, 68 unique datasets, derived from 62 papers reporting prevalence data, met the inclusion criteria and were included. The results from countries participating in the SHARE project were abstracted from a single paper [6], though presented as country-level data for this review. In addition, two systematic reviews reporting frailty prevalence data in older community-dwellers [4] and nursing home residents [7], that included results from JA MSs, were used to obtain relevant studies. Most papers were published since 2012 (52/68, 77%) and the majority evaluated persons aged 65 or over. The characteristics of the included studies reporting prevalence rates of frailty are summarised in *Table 1*.

Data were found across multiple settings at population level including primary care (n = 5), outpatient geriatric clinics (n = 4), LTC (n = 3), hospitals (n = 2), public health centres (n = 1) and in community-based samples (n = 53) recruited using observational, cross-sectional or cohort designs. Fifteen (68%) of the JA MSs had at least one published study reporting data on frailty prevalence rates, with the greatest number of

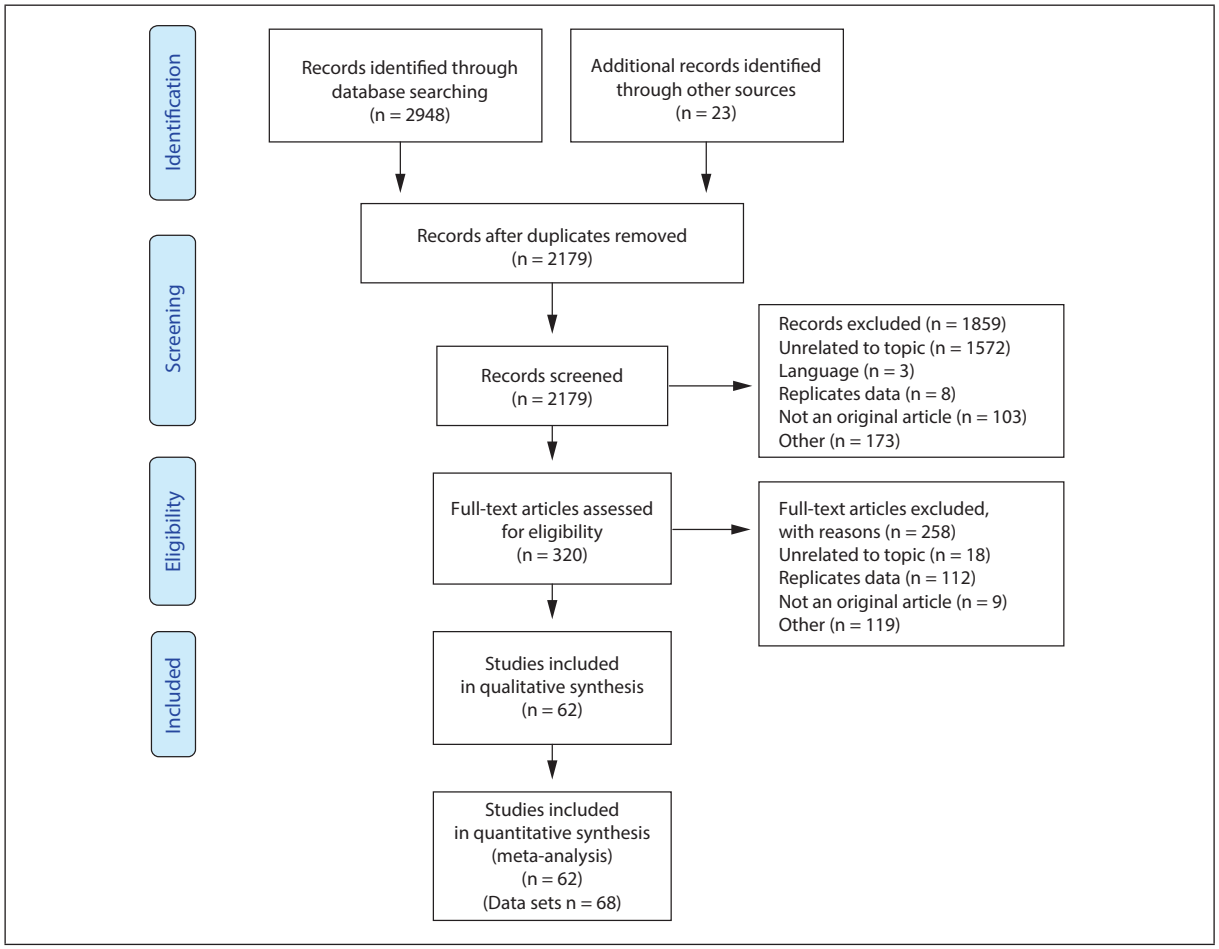

Figure 1
PRISMA flow diagram for the systematic review and meta-analysis of studies on the prevalence of frailty at population level in ADVANTAGE Joint Action (JA) Member States.

Table 1
Characteristics of studies reporting prevalence rates of frailty at population level in ADVANTAGE Joint Action (JA) Member States

Source	Frailty prevalence	Number of participants	Setting	Frailty definition	Age (years)	Women (%)
Austria						
Dorner *et al.*, 2014 [38]	54.1	133	Hospital - General inpatients	SHARE FI	≥ 65	60.9
Santos-Eggimann *et al.*, 2009 [5]	10.8	707	Community	SHARE FI	≥ 65	*Not reported*
Belgium						
Hoeck *et al.*, 2012 [39]	9.3	4777	Community	CHS	≥ 65	56
Theou *et al.*, 2013 [40]	20.0	3699	Community	SHARE FI	≥ 50	54.5
Boeckxstaens *et al.*, 2015 [41]	7.2	567	Community	CHS	≥ 80	62.8
Finland						
Koponen *et al.*, 2013 [42]	11.4	605	Community	CHS	≥ 75	70.1
France						
Santos-Eggimann *et al.*, 2009 [5]	15.0	687	Community	SHARE FI	≥ 65	*Not reported*
Avila-Funes *et al.*, 2008 [43]	7.0	6078	Community	CHS	≥ 65	61.3
Cesari *et al.*, 2012 [44]	2.9	523	Community	CHS	≥ 60	51
de Souto Barreto *et al.*, 2012 [45]	9.8	398	Community	CHS	≥ 60	64.3
Soler *et al.*, 2016 [46]	51.1	1648	Hospital - Geriatric Clinic	CHS	≥ 60	64.4
Le Cossec *et al.*, 2016 [47]	12.3	11089	Community	CHS	≥ 55	54.9
Le Cossec *et al.*, 2016 [47]	11.1	4236	Community	CHS	≥ 55	57
Germany						
Santos-Eggimann *et al.*, 2009 [5]	12.1	933	Community	SHARE FI	≥ 65	*Not reported*
Saum *et al.*, 2012 [48]	8.9	3,112	Community	CHS	≥ 59	52.5
Dapp *et al.*, 2014 [33]	15.8	1679	Community	FI	≥ 60	62.1
Bollwein *et al.*, 2013 [49]	15.5	206	Community	CHS	≥ 75	66
Buttery *et al.*, 2015 [20]	2.6	1843	Community	CHS	65-79	50.1
Vogt *et al.*, 2015 [50]	4.1	954	Community	CHS	≥ 65	49.1
Greece						
Santos-Eggimann *et al.*, 2009 [5]	14.7	784	Community	SHARE FI	≥ 65	*Not reported*
Italy						
Ble *et al.*, 2006 [51]	6.5	827	Community	CHS	≥ 65	54.0
Gallucci *et al.*, 2009 [52]	16.3	668	Community	Other	≥ 70	53.4
Bilotta *et al.*, 2010 [53]	38.0	302	Hospital - Geriatric Clinic	SOF	≥ 65	71.0
Solfrizzi *et al.*, 2012 [54]	7.6	2581	Community	CHS	65-84	45.2
Forti *et al.*, 2014 [55]	7.2	766	Community	SOF	≥ 65	53.4
Roppolo *et al.*, 2015 [56]	12.7	267	Community	CHS	≥ 65	59.9
Veronese *et al.*, 2016 [57]	10.0	1754	Community	CHS	≥ 65	64.0
Santos-Eggimann *et al.*, 2009 [5]	23.0	833	Community	SHARE FI	≥ 65	*Not reported*
Liotta *et al.*, 2017 [58]	21.5	1331	Community	Other	≥ 65	54.2
Ireland						
O'Halloran *et al.*, 2013 [19]	2.0	4858	Community	FI	≥ 50	52
Ntlholang *et al.*, 2014 [59]	32.0	257	Hospital - Geriatric Clinic/Day Hospital	SHARE FI	NA	64.8
O'Caoimh *et al.*, 2014 [60]	54.3	784	Public Health Centres	CFS	≥ 65	64.0
Kelly *et al.*, 2016 [61]	41.5	1312	Community	CFS	≥ 65	70.6

Continues

Table 1
Continued

Source	Frailty prevalence	Number of participants	Setting	Frailty definition	Age (years)	Women (%)
Theou *et al.*, 2013 [40]	15.0	1107	Community	SHARE FI	≥ 50	53.7
The Netherlands						
Santos-Eggimann *et al.*, 2009 [5]	11.3	830	Community	SHARE FI	≥ 65	*Not reported*
Peters *et al.*, 2012 [62]	62.1	124	Nursing home	GFI	≥ 65	62.9
Van Kempen *et al.*, 2013 [63]	24.0	141	Primary Care	Other	≥70	62.0
Metzelthin *et al.*, 2014 [26]	36.0	1101	Primary Care	GFI	≥ 70	*Not reported*
Etman *et al.*, 2014 [64]	24.8	408	Community	ISAR	≥ 65	52.9
Lahousse *et al.*, 2014 [65]	5.9	2833	Community	CHS	≥ 55	55.9
Cramm *et al.*, 2014 [66]	4.9	869	Community	TFI	≥ 70	57.1
Hoogendijk *et al.*, 2014 [67]	10.8	1205	Community	CHS	≥ 65	*Not reported*
Mijnarends *et al.*, 2015 [68]	8.4	227	Community	CHS	≥ 65	48.5
Op het Veld *et al.*, 2015 [69]	8.7	8,684	Community	CHS	≥ 65	53.2
Reijnierse *et al.*, 2015 [70]	28.6	299	Hospital - Geriatric Clinic	CHS	NA	66.0
Norway						
Langholz *et al.*, 2017 [71]	3.7	736	Community	CHS	≥ 65	51.4
Poland						
Matusik *et al.*, 2012 [17]	75.6	86	Nursing home	CFS	≥ 65	76.7
Theou *et al.*, 2013 [40]	42.0	2425	Community	SHARE FI	≥ 50	*Not reported*
Bieniek *et al.*, 2016 [72]	54.2	325	Hospital - Geriatric Ward	CHS	NA	67.0
Portugal						
Duarte *et al.*, 2014 [21]	60.0	50	Community	CHS	≥ 100	84.0
Duarte & Paul *et al.*, 2015 [73]	34.9	339	Community	CHS	≥ 50	53.4
Romania						
Olaroiu *et al.*, 2014 [18]	75.0	215	Primary Care	GFI	≥ 65	66.0
Spain						
Alcala *et* al., 2010 [74]	10.3	814	Community	CHS	≥ 65	51.4
Abizanda-Soler *et al.*, 2011 [75]	16.5	993	Community	CHS	≥ 70	60.5
Santos-Eggimann *et* al., 2009 [5]	27.3	816	Community	SHARE FI	≥ 65	*Not reported*
Jürschik Gimenez *et al.*, 2012 [76]	9.6	640	Community	CHS	≥ 75	60.3
Ferrer *et al.*, 2014 [77]	20.5	273	Community	CHS	85	60.8
Garcia-Garcia *et* al., 2011 [78]	8.4	1667	Community	CHS	≥ 65	56.1
Garre-Olmo *et al.*, 2013 [79]	17.3	875	Community	Other	≥ 75	58.2
León-Muñoz *et al.*, 2014 [80]	4.2	1815	Community	CHS	≥ 60	51.3
Gonzalez-Vaca, *et al.*, 2014 [23]	68.8	324	Nursing home	CHS	≥ 65	56.1
Acosta-Benito *et al.*, 2016 [81]	17.8	146	Community	FRAIL scale	≥ 70	54.7
Papiol *et* al., 2016 [27]	29.4	126	Primary Care	CHS	≥ 75	47.0
UK						
Hubbard *et al.*, 2010 [82]	9.7	3055	Community	CHS	≥ 65	56.0
Syddall *et al.*, 2010 [83]	6.3	642	Community	CHS	64-74	50.0
Bouillon *et al.*, 2013 [84]	2.8	3895	Community	CHS	45-69	27.0
Ramsay *et al.*, 2015 [85]	19.0	1622	Community	CHS	71-92	0
Palmer *et al.*, 2017 [24]	3.9	8095	Primary Care	CHS	50-65	54.0

CHS - Cardiovascular Health Study; CFS - Clinical Frailty Scale; FI - Frailty Index; FRAIL - Fatigue, Resistance, Ambulation, Illnesses, & Loss of Weight scale; GFI - Groningen Frailty Indicator; ISAR - Identification of Seniors at Risk tool; SHARE FI - Survey of Health, Ageing and Retirement in Europe Frailty Instrument; SOF - Study of Osteoporotic Fractures Index; TFI - Tilburg Frailty Indicator; NA = Not Available

studies found in Spain (n = 11) and The Netherlands (n = 11). Prevalence rates from Slovenia and Hungary were not included in the systematic review and meta-analysis because only sex-specific rates were available (Hungary 11.4% for females and 5.4% for males; Slovenia 6.1% for females and 2.3% for males, data available from SHARE in adults aged ≥ 50 years [16]). No published data were found for 5 JA MSs: Bulgaria, Croatia, Cyprus, Lithuania and Malta.

Frailty prevalence rates varied by setting and population characteristics. The highest rate was found among residents (≥ 65) in nursing homes in Poland (75.6%) [17] and patients (≥ 65) in primary care in Romania (75%) [18]. The lowest rate in longitudinal cohorts was shown in Ireland (2% in persons ≥ 50, according to a 32-item FI) [19], followed by Germany (2.6% in subjects aged 65-79, according to the Fried Frailty phenotype) [20]. Most of the community-based studies (48/53, 91%) reported prevalence rates lower than 30%, though results ranged widely from 2% among subjects aged ≥ 50 in Ireland [19] to 60% in those aged ≥ 100 years in Portugal [21], with a median prevalence of 10.8%, interquartile range (Q1-Q3) 7.2-16.5%. Two studies reported prevalence rates of 54% among hospital inpatients, while outpatients' studies reported figures approximating 30%. In LTC, the prevalence rate of frailty varied from 62.1% [22] and 68.8% [23] to 75.6% [17] for three studies that included patients aged ≥ 65 years.

Only five studies [18, 24-27] reported the prevalence rate of frailty in primary care, which also varied by sample characteristics and frailty instrument-classification. Three out of the five studies reported a prevalence rate of approximately 30% [25-27] with evident outlier results in Romania (75% in those ≥ 65 measured with the Groningen Frailty Indicator (GFI) [18] and the United Kingdom (3.9%, although in a younger population ranging from 50-65 years old and measured with the Frailty phenotype) [24].

We included all 68 unique datasets in the initial meta-analysis. The results showed that the overall estimated prevalence of frailty in JA MSs was 18% (95% CI 15-21%; 68 datasets; 13 932 individuals; I^2 = 99.36%, p < 0.001) *(Figure 2)*. The sub-analysis of studies from community-based studies, stratified by the tools used to define frailty, showed a lower prevalence of 12% (95% CI 10-15%; 53 datasets, 10 821 individuals; I^2 = 99.01%, p < 0.001) *(Figure 3)*. The estimated prevalence of frailty in non-community-based studies was considerably higher (45%; 95% CI 27-63%; 15 datasets; 3111 individuals; I^2 = 99.7%, p < 0.001) *(Supplementary Figure 1 available online)*. Sub-analysis of individual MSs only including community-based studies showed the lowest prevalence rates in the UK (9% with 95% CI 3-17%), France (9% with 95% CI 7-12%) and Germany (9% with 95% CI 5-14%). The highest estimated prevalence rates were found in Portugal (38% with 95% CI 33-43%) and Poland (42% with 95% CI 40-44%) *(Supplementary Figure 2 available online)*.

The estimated prevalence also varied depending on the tools used to define frailty status. The most commonly reported classification of frailty in JA MSs was the Fried frailty phenotype based on the findings of the Cardiovascular Health Study (CHS) [28] (n = 39/68 = 57%). The SHARE Frailty Instrument (SHARE-FI) [29], which captures similar physical parameters was the next most commonly used (n = 12), followed by the Groningen Frailty Indicator (n = 3) [30], the Clinical Frailty Scale (n = 3) [31], the Study of Osteoporotic Fractures (SOF) Index (n = 2) [32], and others (n = 9) including two studies that used a FI [19, 33]. The pooled prevalence according to the frailty classifications was estimated only for community studies; the CHS frailty phenotype had a lower estimated prevalence of 10% (95% CI 8-11%; I^2 99%; n = 33) compared to the similar SHARE FI, which had an estimated prevalence rate of 18% (95% CI 13-25%; I^2 99%; n=10) *(Figure 3)*. The two community-based studies using the FI had the lowest estimated rate: 4% (95% CI 4-5%; n = 2). Similarly, comparing the prevalence for the 45 community-based studies using measures of the physical phenotype, i.e. either CHS (n = 33), SHARE-FI (n = 10), SOF (n = 1) or FRAIL scale (n = 1) instruments, with studies using the other frailty classification approaches (n = 8) showed rates of 12% (95% CI 10-14%) and 16% (95% CI 7-29%) respectively *(Supplementary Figure 3 available online)*. When an extreme outlier including only centenarians [21] was excluded from this sub-analysis, the pooled estimated prevalence for studies classifiying frailty using physical parameters was similar: 11% (95% CI 9-13%).

Using the JBI checklist, 47 of the 62 papers were classified as high quality, meeting all nine of the checklist criteria, and were included in a subgroup analysis. Despite including only studies that were deemed of sufficiently high quality, the overall estimated prevalence was similar to that observed for all 62 papers (17%; 95% CI 13-21%) *(Supplementary Figure 4 available online)*.

There was considerable significant (p ≤ 0.05) heterogeneity among studies, which remained analysing studies by country or after dichotomizing them according to settings, tools used to define frailty and quality of the included studies. Generally, studies for each subgroup showed considerable heterogeneity, suggesting that differences in the effect size of included studies do exist. The Higgins' I^2 remains unchanged following sub-analyses, indicating the existence of variance derived from sources other than sampling error. Visual inspection of the funnel plots indicated that there was evidence of publication bias, which was confirmed by Egger test, with the exception of the sub-analysis for community-based studies (results not shown).

DISCUSSION

This systematic review found multiple published papers reporting on the prevalence rate of frailty in JA (ADVANTAGE) MSs, although there was considerable heterogeneity between studies in sample, setting and reporting. Our meta-analysis confirmed a relatively high pooled prevalence of 18% in all settings, which did not change considerably (17%) limiting the analysis to studies classified as of higher quality, albeit the CI widened. As expected, the highest prevalence rates were

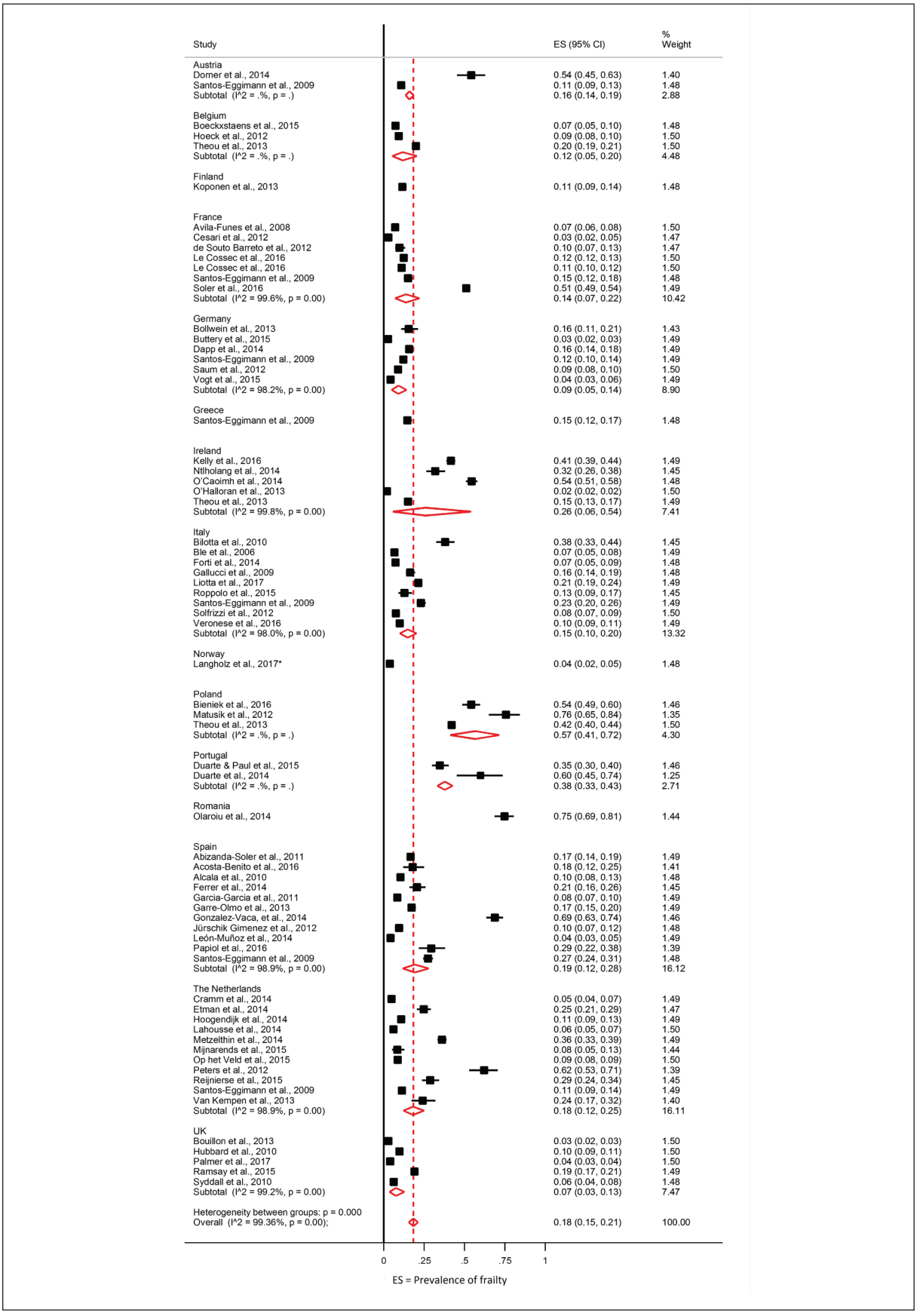

Figure 2
Estimated prevalence of frailty at population level in ADVANTAGE Joint Action Member States, n = 68 data sets.
ES = Effect Size

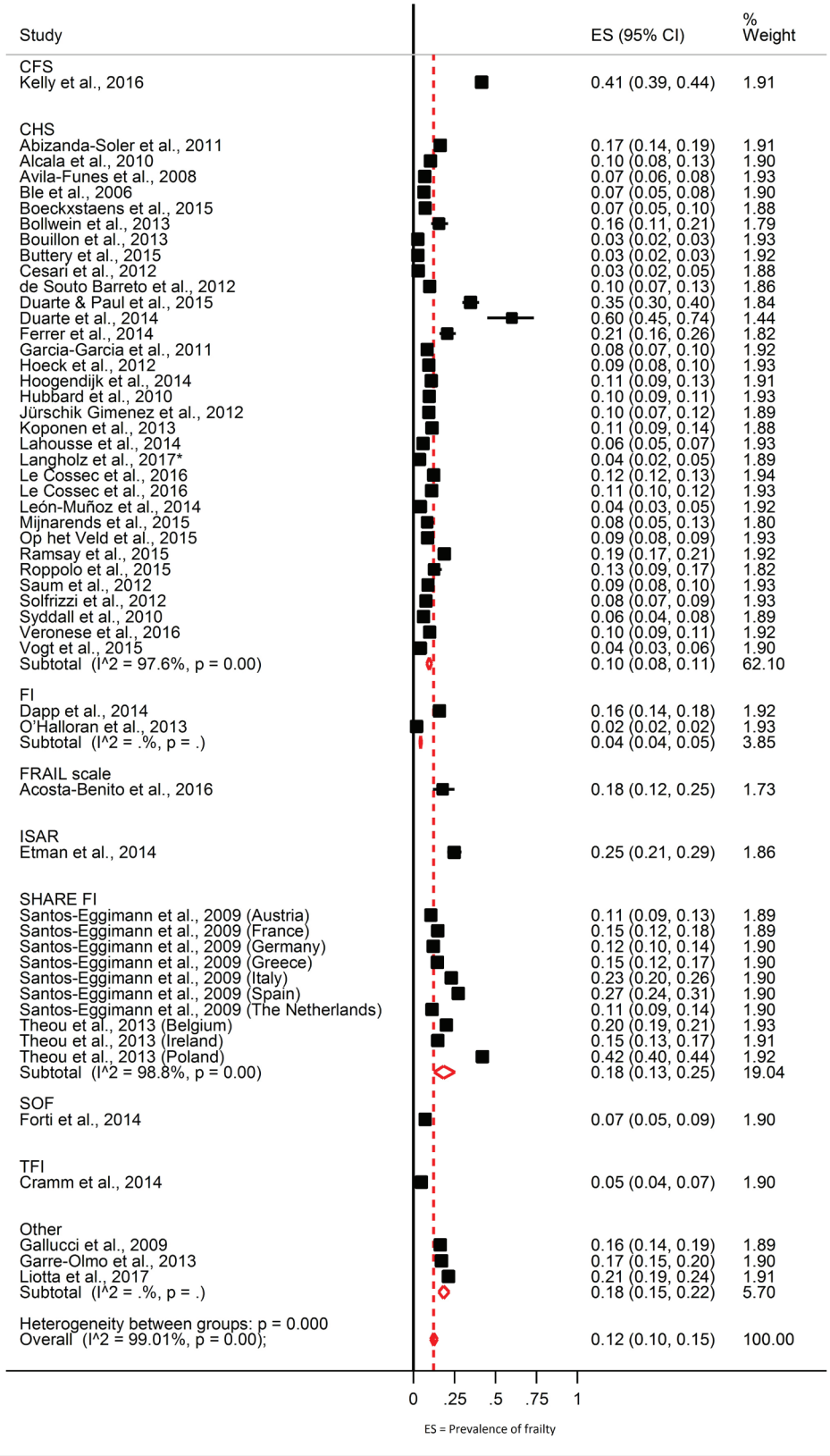

Figure 3
Estimated prevalence of frailty at population level in ADVANTAGE Joint Action Member States by tools used to define frailty. Data from community-based studies only, n = 53.
ES = Effect Size; CFS = Clinical Frailty Scale; CHS=Cardiovascular Health Study; FI = Frailty Index; FRAIL = Fatigue, Resistance, Ambulation, Illnesses, & Loss of Weight scale; ISAR = Identification of Seniors at Risk tool; SHARE FI = Survey of Health, Ageing and Retirement in Europe Frailty Instrument; SOF = Study of Osteoporotic Fractures Index; TFI = Tilburg Frailty Indicator.

from studies among hospital inpatients (around 50%) or set in LTC (more than 60%). Lower figures, around 30%, were found in studies in primary care and outpatient settings. The prevalence rates reported in community-based studies (i.e. removing those set in hospital or LTC settings) also varied, ranging from 2 [19] to 60% [21] with a median rate of 10.8%; most studies reported prevalence rates < 30%. The meta-analysis of community-based studies yielded a pooled estimate of 12%, consistent with the global weighted rate of 10.7% reported in community-based samples aged ≥ 65 years in 2012 [4] but lower than the prevalence rate of frailty in low and middle-income countries, which have recently been reported at 17.4% [34]. As expected, rates in non-community settings were markedly higher than in community samples, with a pooled estimate of 45% (95% CI 27-63%). This likely reflects fluctuations in frailty status during acute illness where frailty scores are significantly higher than at baseline after admission [35] and the high prevalence of disability and chronic multi-morbidity in nursing homes is associated with high levels of frailty [7]. As expected we found significant heterogeneity between studies in keeping with marked differences in the inclusion criteria. Moreover, the significant heterogeneity between studies remained irrespective of setting, confirming the differences evident in the systematic review.

Overall, while multiple papers on frailty prevalence were available, most came from just five JA ADVANTAGE countries (France, Germany, Italy, the Netherlands and Spain). Five countries belonging to the JA did not have prevalence data available. Poland seems to have an especially high prevalence rate, both in our review and in results from the SHARE data set [5]. The North-South divide between northern and southern European countries in terms of age and gender gradients of frailty, which have been reported previously [6], could not be verified by the present review due to the difficulties comparing the studies.

The Frailty phenotype (CHS) was the most commonly used frailty classification, though again there was marked heterogeneity in approaches to classify frailty across studies. This has importance given that no single consensus definition of frailty is as yet accepted [36] and the two most commonly used methods to define the syndrome, the FI and the Frailty Phenotype, while complementary, are not interchangeable, given that they measure different constructs [37]. Our meta-analysis showed that the estimated prevalence was dependent on the approach used to define frailty. In the community setting, the most frequently reported frailty model was the CHS phenotype (n = 33) [28], followed by the SHARE-FI (n = 10) [29]. The CHS criteria gave a lower prevalence of 10% (95% CI 8-11%) compared to a higher prevalence of 18% (95% CI 13-25%) for the the SHARE-FI *(Figure 3)*. Given the similarity between the two instruments [29], these results are unexpected but are likely explained by the high heterogeneity of the samples included in this review. Only two studies reported results using the FI to classify frailty. This may reflect the more common usage of the Frailty Phenotype in Europe and the relative ease of gathering the five CHS variables to construct this in clinical practice. The studies using the FI [19, 33] showed a lower estimated prevalence than those using the CHS criteria, different from the results of other studies where the FI consistently provides higher frailty rates [37]. This possibly occured by chance, given the limited number of studies using the FI to define frailty, but also likely reflects the different approaches used to modify the original Fried construct. However, the pooled estimate from studies using instruments capturing the physical phenotype (i.e. results from community-based studies using the CHS criteria, SHARE-FI, SOF and FRAIL scale) confirmed that this classification approach provides a lower estimate than an accumulation of deficits approach using an index (FI) or another multi-dimensional instrument (e.g. GFI) [37].

This review has a number of limitations. Although the approach to reviewing the literature used was standardized and the most important databases included, some papers may potentially have been missed. However, we included a very large number of datasets (n = 68) in this meta-analysis, mitigating this issue. Nevertheless, we are confident that most relevant results should have been published in peer-reviewed literature, and therefore, captured in our systematic review. Finally, there was a significant heterogeneity in the results as evidenced by the Higgin's I^2 value approaching 100%, inherent to the heteregenous population included in the studies. However, this heterogeneity could support the generalizability of the results for MS of JA. This degree of heterogeneity has been found in other similar meta-analysis of frailty prevalence rates e.g. that in low and middle-income countries [34].

CONCLUSIONS

The results of this systematic review and meta-anlysis show that frailty is common in European countries and varies by setting and definition of frailty. More studies are required to establish the prevalence rates of frailty in EU JA ADVANTAGE MSs. Prevalence data disaggregated by age, gender, socioeconomic and frailty severity status are of utmost importance to provide a reliable epidemiological picture of frailty. Further, as most data were available from community-based longitudinal studies and cross-sectional population-based surveys, more studies in different settings are required. Until a consensus definition of frailty is accepted and in an attempt to improve comparability and generalisability, studies should measure both the Frailty Phenotype and a FI with a standardised number of age-related health deficits e.g. 32 items. The inclusion of a common frailty instrument in national health surveys could contribute to the availability of more comparable population-based data at EU level, especially if this could be integrated in the European Health Interview Survey (EHIS), which is regulated by the European Commission and already collects comparable data across different domains (health status, health determinants, use of health care). It could also be incorporated into the European Health Examination Survey (EHES) funded by the European Commission.

Overall, well-designed and suitably powered prevalence studies of frailty at European level are necessary. The paucity and heterogeneity of data highlights the need to approach this in a standardised and harmonized way across the EU. Ongoing and future longitudinal studies could be adapted to support this.

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Conflict of interest statemet

There are no potential conflicts of interest or any financial or personal relationships with other people or organizations that could inappropriately bias conduct and findings of this study.

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REFERENCES

1. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. Lancet. 2013;381(9868):752-62. DOI: 10.1016/S0140-6736(12)62167-9
2. Rechel B, Grundy E, Robine JM, Cylus J, Mackenbach JP, Knai C, et al. Ageing in the European union. Lancet. 2013;381(9874):1312-22. DOI: 10.1016/S0140-6736(12)62087-X
3. Cesari M, Prince M, Thiyagarajan JA, De Carvalho IA, Bernabei R, Chan P, et al. Frailty: an emerging public health priority. J Am Med Dir Assoc. 2016;17(3):188-92. DOI: 10.1016/j.jamda.2015.12.016
4. Collard, R.M., Boter, H., Schoevers, R.A. and Oude Voshaar, R.C., 2012. Prevalence of frailty in community-dwelling older persons: a systematic review. J Am Geriatr Soc. 2012;60(8):1487-92. DOI: 10.1111/j.1532-5415.2012.04054.x
5. Santos-Eggimann B, Cuénoud P, Spagnoli J, Junod J. Prevalence of frailty in middle-aged and older community-dwelling Europeans living in 10 countries. J Gerontol A Biol Sci Med Sci. 2009;64(6):675-81. DOI: 10.1093/gerona/glp012
6. Harttgen K, Kowal P, Strulik H, Chatterji S, Vollmer S. Patterns of frailty in older adults: comparing results from higher and lower income countries using the Survey of Health, Ageing and Retirement in Europe (SHARE) and the Study on Global AGEing and Adult Health (SAGE). PloS one. 2013;8(10):e75847. DOI: 10.1371/journal.pone.0075847
7. Kojima G. Prevalence of frailty in nursing homes: a systematic review and meta-analysis. J AM MED DIR ASSOC. 2015;16(11):940-5. DOI: 10.1016/j.jamda.2015.06.025
8. Bousquet J, Michel JP, Strandberg T, Crooks G, Iakovidis I, Iglesia M. The European Innovation Partnership on Active and Healthy Ageing: the European geriatric medicine introduces the EIP on AHA column. Eur Geriatr Med. 2014;5:361-2 DOI: 10.1016/j.eurger.2014.09.010
9. O'Caoimh R, Sweeney C, Hynes H, McGlade C, Cornally N, Daly E, et al. COLLaboration on AGEing-COLLAGE: Ireland's three star reference site for the European Innovation Partnership on Active and Healthy Ageing (EIP on AHA). Eur Geriatr Med. 2015;5(6):505-11. DOI: 10.1016/j.eurger.2015.04.009
10. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. PLoS medicine. 2009;6(7):e1000100. DOI: 10.1371/journal.pmed.1000100
11. Galluzzo L, O'Caoimh R, Rodríguez-Laso Á, Beltzer N, Ranhoff AH, Van der Heyden J, Lamprini-Koula M, Ciutan M, Lopez-Samaniego L, Liew A on behalf of Work Package 5 of the Joint Action ADVANTAGE. Incidence of frailty: a systematic review of scientific literature from a public health perspective. Ann Ist Super Sanità. 2018;54(3):239-245.
12. Munn Z, Moola S, Riitano D, Lisy K. The development of a critical appraisal tool for use in systematic reviews addressing questions of prevalence. IJHPM. 2014;3(3):123. DOI: 10.15171/ijhpm.2014.71
13. Barendregt SAD, Lee YY, Norman RE, Vos T. Meta-analysis of prevalence. J Epidemiol Community Health. 2013;67(11):974-8. DOI: 10.1136/jech-2013-203104. DOI: 10.1136/jech-2013-203104.
14. Nyaga VN, Arbyn M, Aerts M. Metaprop: a Stata command to perform meta-analysis of binomial data. Arch Public Health. 2014;72(1):39. DOI: 10.1186/2049-3258-72-39.
15. Higgins JP, Thompson SG. Quantifying heterogeneity in a metaanalysis. Stat Med. 2002;21:1539-58. DOI: 10.1002/sim.1186
16. Romero-Ortuno R, Soraghan C. A Frailty Instrument for primary care for those aged 75 years or more: findings from the Survey of Health, Ageing and Retirement in Europe, a longitudinal population-based cohort study (SHARE-FI75+). BMJ open. 2014;4(12):e006645. DOI: 10.1136/bmjopen-2014-006645
17. Matusik P, Tomaszewski K, Chmielowska K, Nowak J, Nowak W, Parnicka A, et al. Severe frailty and cognitive impairment are related to higher mortality in 12-month follow-up of nursing home residents. Arch Gerontol Geriatr. 2012;55(1):22-4. DOI: 10.1016/j.archger.2011.06.034
18. Olaroiu M, Ghinescu M, Naumov V, Brinza I, Heuvel WV. The psychometric qualities of the Groningen Frailty Indicator in Romanian community-dwelling old citizens. Fam Pract. 2014;31(4):490-5. DOI: 10.1093/fampra/cmu022
19. O'Halloran AM, Finucane C, Savva GM, Robertson IH, Kenny RA. Sustained attention and frailty in the older adult population. J Gerontol B Psychol Sci Soc Sci. 2013;69(2):147-56. DOI: 10.1093/geronb/gbt009
20. Buttery AK, Busch MA, Gaertner B, Scheidt-Nave C, Fuchs J. Prevalence and correlates of frailty among older adults: findings from the German health interview and examination survey. BMC geriatr. 2015;15(1):22. DOI: 10.1186/s12877-015-0022-3
21. Duarte N, Teixeira L, Ribeiro O, Paul C. Frailty phenotype criteria in centenarians: Findings from the Oporto Centenarian Study. Eur Geriatr Med. 2014;5(6):371-6. DOI: 10.1016/j.eurger.2014.09.015
22. Peters LL, Boter H, Buskens E, Slaets JP. Measurement

properties of the Groningen Frailty Indicator in home-dwelling and institutionalized elderly people. J AM MED DIR ASSOC. 2012;13(6):546-51. DOI: 10.1016/j.jamda.2012.04.007
23. González-Vaca J, de la Rica-Escuín M, Silva-Iglesias M, Arjonilla-García MD, Varela-Pérez R, Oliver-Carbonell JL, et al. Frailty in INstitutionalized older adults from ALbacete. The FINAL Study: rationale, design, methodology, prevalence and attributes. Maturitas. 2014;77(1):78-84. DOI: 10.1016/j.maturitas.2013.10.005
24. Palmer KT, Dangelo S, Harris EC, Linaker C, Gale CR, Evandrou M, et al. Frailty, prefrailty and employment outcomes in Health and Employment After Fifty (HEAF) Study. Occup Environ Med. 2017;74(7):476-82. DOI:10.1136/oemed-2016-104103
25. van Kempen JA, Schers HJ, Jacobs A, Zuidema SU, Ruikes F, Robben SH, et al. Development of an instrument for the identification of frail older people as a target population for integrated care. Br J Gen Pract. 2013;63(608):e225-31. DOI: 10.3399/bjgp13X664289
26. Metzelthin SF, van Rossum E, de Witte LP, Ambergen A, Hobma S, Sipers W et al. Thuiswonende ouderen in een kwetsbare positie: Effecten van een interdisciplinair eerstelijnszorgprogramma. Ned Tijdschr Geneeskd. 2014;158. A7355.
27. Papiol M, Serra-Prat M, Vico J, Jerez N, Salvador N, Garcia Met al. Poor muscle strength and low physical activity are the most prevalent frailty components in community-dwelling older adults. J Aging Phys Act. 2016;24(3):363-8. DOI: 10.1123/japa.2015-0114
28. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci. 2001;56(3):M146-57. DOI: 10.1093/gerona/56.3.M146
29. Romero-Ortuno R, Walsh CD, Lawlor BA, Kenny RA. A frailty instrument for primary care: findings from the Survey of Health, Ageing and Retirement in Europe (SHARE). BMC Geriatr. 2010;10(1):57. DOI: 10.1186/1471-2318-10-57
30. Peters LL, Boter H, Buskens E, Slaets JP. Measurement properties of the Groningen Frailty Indicator in home-dwelling and institutionalized elderly people. J Am Med Dir Assoc. 2012;13:546-51. DOI: 10.1016/j.jamda.2012.04.007
31. Rockwood K, Song X, MacKnight C, Bergman H, Hogan DB, McDowell I, et al. A global clinical measure of fitness and frailty in elderly people. CMAJ. 2005;173(5):489-5. DOI:10.1503/cmaj.050051
32. Ensrud KE, Ewing SK, Taylor BC, Fink HA, Cawthon PM, Stone KL, et al. Comparison of 2 frailty indexes for prediction of falls, disability, fractures, and death in older women. Arch Intern Med. 2008;168(4):382-9. DOI:10.1001/archinternmed.2007.113
33. Dapp U, Minder CE, Anders J, Golgert S, von Renteln-Kruse W. Long-term prediction of changes in health status, frailty, nursing care and mortality in community-dwelling senior citizens-results from the longitudinal urban cohort ageing study (LUCAS). BMC geriatr. 2014;14(1):141. DOI: 10.1186/1471-2318-14-141
34. Siriwardhana DD, Hardoon S, Rait G, Weerasinghe MC, Walters KR. Prevalence of frailty and prefrailty among community-dwelling older adults in low-income and middle-income countries: a systematic review and meta-analysis. BMJ Open 2018;8:e018195. DOI: 10.1136/bmjopen-2017-018195
35. Morrison L, Costello M, Flannery A, Small C, Nevin R, Havelin A, et al. Frailty in an acute hospital: Point prevalence and change in baseline status during hospitalisation. Age Ageing 2017;46(S3):11-2. DOI: 10.1093/ageing/afx145.1
36. Rodríguez-Mañas L, Féart C, Mann G, Viña J, Chatterji S, Chodzko-Zajko W, et al. Searching for an operational definition of frailty: a Delphi method based consensus statement. The frailty operative definition-consensus conference project. J Gerontol A Biol Sci Med Sci. 2012;68(1):62-7. DOI: 10.1093/gerona/gls119
37. Cesari M, Gambassi G, Abellan van Kan G, Vellas B. The frailty phenotype and the frailty index: different instruments for different purposes. Age Ageing. 2013;43(1):10-2. DOI: 10.1093/ageing/aft160
38. Dorner TE, Luger E, Tschinderle J, Stein KV, Haider S, Kapan A, et al. Association between nutritional status (MNA®-SF) and frailty (SHARE-FI) in acute hospitalised elderly patients. J Nutr Health Aging. 2014;18(3):264-9.DOI: 10.1007/s12603-013-0406-z
39. Hoeck S, François G, Geerts J, Van der Heyden J, Vandewoude M, Van Hal G. Health-care and home-care utilization among frail elderly persons in Belgium. Eur J Public Health. 2011;22(5):671-7. DOI: 10.1093/eurpub/ckr133
40. Theou O, Brothers TD, Rockwood MR, Haardt D, Mitnitski A, Rockwood K. Exploring the relationship between national economic indicators and relative fitness and frailty in middle-aged and older Europeans. Age Ageing. 2013;42(5):614-9. DOI: 10.1093/ageing/aft010
41. Boeckxstaens P, Vaes B, Legrand D, Dalleur O, De Sutter A, Degryse JM. The relationship of multimorbidity with disability and frailty in the oldest patients: A cross-sectional analysis of three measures of multimorbidity in the BELFRAIL cohort. Eur J Gen Pract. 2014:1-6. DOI: 10.3109/13814788.2014.914167
42. Koponen MP, Bell JS, Karttunen NM, Nykänen IA, Desplenter FA, Hartikainen SA. Analgesic use and frailty among community-dwelling older people. Drugs Aging. 2013;30(2):129-36. DOI: 10.1007/s40266-012-0046-8
43. Avila-Funes JA, Helmer C, Amieva H, Barberger-Gateau P, Goff ML, Ritchie K, et al. Frailty among community-dwelling elderly people in France: the three-city study. J Gerontol A Biol Sci Med Sci. 2008;63(10):1089-96. DOI: 10.1093/gerona/63.10.1089
44. Cesari M, Demougeot L, Boccalon H, Vellas B. Prevalence of frailty and mobility limitation in a rural setting in France. J Frailty Aging. 2012;1(4):169-73. DOI: 10.14283/jfa.2012.26
45. de Souto Barreto P, Greig C, Ferrandez AM. Detecting and categorizing frailty status in older adults using a self-report screening instrument. Arch Gerontol Geriatr. 2012;54(3):e249-54. DOI: 10.1016/j.archger.2011.08.003
46. Soler V, Sourdet S, Balardy L, Van Kan GA, Brechemier D, Bugat MR, et al. Visual impairment screening at the Geriatric Frailty Clinic for Assessment of Frailty and Prevention of Disability at the Gérontopôle. J Nutr Health Aging. 2016;20(8):870-7. DOI: 10.1007/s12603-015-0648-z
47. Le Cossec C, Perrine AL, Beltzer N, Fuhrman C, Carcaillon-Bentata L. Pre-frailty, frailty, and multimorbidity: prevalences and associated characteristics from two French national surveys. J Nutr Health Aging. 2016;20(8):860-9. DOI: 10.1007/s12603-016-0802-2
48. Saum KU, Müller H, Stegmaier C, Hauer K, Raum E, Brenner H. Development and evaluation of a modification of the Fried frailty criteria using population-independent cutpoints. J Am Geriatr Soc. 2012;60(11):2110-5. DOI: 10.1111/j.1532-5415.2012.04192.x
49. Bollwein J, Volkert D, Diekmann R, Kaiser MJ, Uter W, Vidal K, et al. Nutritional status according to the mini nutritional assessment (MNA®) and frailty in commu-

nity dwelling older persons: a close relationship. J Nutr Health Aging. 2013;17(4):351-6. DOI: 10.1007/s12603-013-0009-8
50. Vogt S, Decke S, de Las Heras Gala T, Linkohr B, Koenig W, Ladwig KH, et al. Prospective association of vitamin D with frailty status and all-cause mortality in older adults: Results from the KORA-Age Study. Prev Med. 2015;73:40-6. DOI: 10.1016/j.ypmed.2015.01.010
51. Ble A, Cherubini A, Volpato S, Bartali B, Walston JD, Windham BG, et al. Lower plasma vitamin E levels are associated with the frailty syndrome: the InCHIANTI study. J Gerontol A Biol Sci Med Sci. 2006;61:278-83. DOI: 10.1093/gerona/61.3.278
52. Gallucci M, Ongaro F, Amici GP, Regini C. Frailty, disability and survival in the elderly over the age of seventy: Evidence from "The Treviso Longeva (TRELONG) Study". Arch Gerontol Geriatr. 2009;48:281-3. DOI: 10.1016/j.archger.2008.02.005
53. Bilotta C, Casè A, Nicolini P, Mauri S, Castelli M, Vergani C. Social vulnerability, mental health and correlates of frailty in older outpatients living alone in the community in Italy. Aging Ment Health. 2010;14(8):1024-36. DOI: 10.1080/13607863.2010.508772
54. Solfrizzi V, Scafato E, Frisardi V, Sancarlo D, Seripa D, Logroscino G, et al. Frailty syndrome and all-cause mortality in demented patients: the Italian Longitudinal Study on Aging. Age. 2012;34(2):507-17. DOI: 10.1007/s11357-011-9247-z
55. Forti P, Maioli F, Lega MV, Montanari L, Coraini F, Zoli M. Combination of the clock drawing test with the physical phenotype of frailty for the prediction of mortality and other adverse outcomes in older community dwellers without dementia. Gerontology. 2014;60(3):204-11. DOI: 10.1159/000356701
56. Roppolo M, Mulasso A, Gobbens RJ, Mosso CO, Rabaglietti E. A comparison between uni-and multidimensional frailty measures: prevalence, functional status, and relationships with disability. Clin Interv Aging. 2015;10:1669. DOI: 10.2147/CIA.S92328
57. Veronese N, Stubbs B, Fontana L, Trevisan C, Bolzetta F, De Rui M, et al. Frailty is associated with an increased risk of incident type 2 diabetes in the elderly. J Am Med Dir Assoc. 2016;17(10):902-7. DOI: 10.1016/j.jamda.2016.04.021
58. Liotta G, O'Caoimh R, Gilardi F, Proietti MG, Rocco G, Alvaro R, et al. Assessment of frailty in community-dwelling older adults residents in the Lazio region (Italy): a model to plan regional community-based services. Arch Gerontol Geriatr. 2017;68:1-7. DOI: 10.1016/j.archger.2016.08.004
59. Ntlholang O, Kelly RE, Romero-Ortuno R, Cosgrave S, Kelly D, Crowe M, et al. The Role the Frailty Syndrome Can Play in Advocacy and Resource Allocation for Our Ageing Population - Findings in a Dublin Day Hospital. J Frailty Aging. 2014;3(1):21-4. DOI: 10.14283/jfa.2014.5
60. O'Caoimh R, Gao Y, Svendrovski A, Healy E, O'Connell E, O'Keeffe G, et al. Screening for markers of frailty and perceived risk of adverse outcomes using the Risk Instrument for Screening in the Community (RISC). BMC geriatr. 2014;14(1):104. DOI: 10.1186/1471-2318-14-104
61. Kelly S, O'Brien I, Smuts K, O'Sullivan M, Warters A. Prevalence of frailty among community dwelling older adults in receipt of low level home support: a cross-sectional analysis of the North Dublin Cohort. BMC geriatrBMC geriatr. 2017;17(1):121. DOI.org/10.1186/s12877-017-0508-2
62. Peters LL, Boter H, Buskens E, Slaets JP. Measurement properties of the Groningen Frailty Indicator in home-dwelling and institutionalized elderly people. Journal of the American Medical Directors Association. 2012;13(6):546-51. DOI: 10.1016/j.jamda.2012.04.007
63. van Kempen JA, Schers HJ, Jacobs A, Zuidema SU, Ruikes F, Robben SH, et al. Development of an instrument for the identification of frail older people as a target population for integrated care. Br J Gen Pract. 2013;63(608):e225-31. DOI: 10.3399/bjgp13X664289
64. Etman A, Burdorf A, Van der Cammen TJ, Mackenbach JP, Van Lenthe FJ. Socio-demographic determinants of worsening in frailty among community-dwelling older people in 11 European countries. J epidemiol community health. 2012;66(12):1116-21. DOI: 10.1136/jech-2011-200027
65. Lahousse L, Maes B, Ziere G, Loth DW, Verlinden VJ, Zillikens MC, et al. Adverse outcomes of frailty in the elderly: the Rotterdam Study. European journal of epidemiology. 2014;29(6):419-27. DOI: 10.1007/s10654-014-9924-1
66. Cramm JM, Twisk J, Nieboer AP. Self-management abilities and frailty are important for healthy aging among community-dwelling older people; a cross-sectional study. BMC geriatr. 2014;14(1):28. DOI: 10.1186/1471-2318-14-28
67. Hoogendijk EO, van Hout HP, Heymans MW, van der Horst HE, Frijters DH, van Groenou MI, et al. Explaining the association between educational level and frailty in older adults: results from a 13-year longitudinal study in the Netherlands. Ann Epidemiol. 2014;24(7):538-44. DOI: 10.1016/j.annepidem.2014.05.002
68. Mijnarends DM, Schols JM, Meijers JM, Tan FE, Verlaan S, Luiking YC, et al. Instruments to assess sarcopenia and physical frailty in older people living in a community (care) setting: similarities and discrepancies. J Am Med Dir Assoc. 2015;16(4):301-8. DOI: 10.1016/j.jamda.2014.11.011
69. Op het Veld LPE, van Rossum E, Kempen GI, de Vet HC, Hajema K, Beurskens AJ. Fried phenotype of frailty: cross-sectional comparison of three frailty stages on various health domains. BMC geriatr. 2015;15(1):77 DOI: 10.1186/s12877-015-0078-0
70. Reijnierse EM, Trappenburg MC, Blauw GJ, Verlaan S, de van der Schueren MA, Meskers CG, et al. Common ground? The concordance of sarcopenia and frailty definitions. J Am Med Dir Assoc. 2016;17(4):371-e7. DOI: 10.1016/j.jamda.2016.01.013
71. Langholz PL, Strand BH, Cook S, Hopstock LA. Frailty phenotype and its association with all-cause mortality in community-dwelling Norwegian women and men aged 70 years and older: The Tromsø Study 2001-2016. Geriatr Gerontol Int. 2018 May 29. DOI: 10.1111/ggi.13447
72. Bieniek J, Wilczyński K, Szewieczek J. Fried frailty phenotype assessment components as applied to geriatric inpatients. Clin Interv Aging. 2016;11:453. DOI: 10.2147/CIA.S101369
73. Duarte M, Paúl C. Prevalence of phenotypic frailty during the aging process in a Portuguese community. Rev Bras Geriatr Gerontol. 2015;18(4):871-80. DOI: org/10.1590/1809-9823.2015.14160
74. Alcala MV, Puime A, Santos MT, Barral A, Montalvo JI, Zunzunegui MV. Prevalence of frailty in an elderly Spanish urban population. Relationship with comorbidity and disability. Aten Primaria. 2010;42:520-7. DOI: 10.1016/j.aprim.2009.09.024
75. Abizanda-Soler P, Lopez-Torres Hidalgo J, Romero Rizos L, Lopez Jimenez M, Sanchez Jurado PM, Atienzar Nuñez P, et al. Frailty and dependency in albacete

(The FRADEA Study): Rationale, design and methods. Rev Esp Geriatr Gerontol. 2011;46:81-8. DOI: 10.1186/1471-2318-14-2
76. Jürschik Gimenez P, Escobar Bravo MA, NuinOrrio C, Botigué ST. Frailty criteria in the elderly: a pilot study. Aten Primaria. 2011;43:190-6. DOI: 10.1016/j.aprim.2010.03.020
77. Ferrer A, Formiga F, Sanz H, Monserrate E, Verges D; Grupo Octabaix. Successful aging and indicators of frailty in the elderly. Octabaix Study. Aten Primaria. 2014;46:475-82. DOI: 10.1016/j.aprim.2014.01.004
78. Garcia-Garcia F, Gutierrez G, Alfaro-Acha A, Amor MS, Lanza MAT, Escribano MV, et al. The prevalence of frailty syndrome in an older population from Spain. The Toledo Study for Healthy Aging. J Nutr Health Aging. 2011;15(10):852-6. DOI: 10.1186/1471-2318-14-2
79. Garre-Olmo J, Calvó-Perxas L, López-Pousa S, de Gracia Blanco M, Vilalta-Franch J. Prevalence of frailty phenotypes and risk of mortality in a community-dwelling elderly cohort. Age Ageing. 2012;42(1):46-51. DOI: 10.1093/ageing/afs047
80. León-Muñoz LM, Guallar-Castillón P, López-García E, Rodríguez-Artalejo F. Mediterranean diet and risk of frailty in community-dwelling older adults. J Am Med Dir Assoc. 2014;15(12):899-903. DOI: 10.1016/j.jamda.2014.06.013
81. Acosta-Benito MA, Sevilla-Machuca I. Using prefrailty to detect early disability. J Family Community Med. 2016;23(3):140. DOI: 10.4103/2230-8229.189106
82. Hubbard RE, Lang IA, Llewellyn DJ, Rockwood K. Frailty, body mass index, and abdominal obesity in older people. J Gerontol A Biol Sci Med Sci. 2010;65:377-81. DOI: 10.1093/gerona/glp186
83. Syddall H, Roberts HC, Evandrou M, Cooper C, Bergman H, Sayer AA. Prevalence and correlates of frailty among community-dwelling older men and women: Findings from the Hertfordshire Cohort Study. Age Ageing. 2010;39:197-203. DOI: 10.1093/ageing/afp204
84. Bouillon K, Batty GD, Hamer M, Sabia S, Shipley MJ, Britton A, et al. Cardiovascular disease risk scores in identifying future frailty: the Whitehall II prospective cohort study. Heart. 2013;99(10):737-42. DOI: 10.1136/heartjnl-2012-302922
85. Ramsay SE, Arianayagam D, Whincup PH, Lennon LT, Cryer J, Papacosta AO, et al. Cardiovascular risk profile and frailty in a population-based study of older British men. Heart. 2015;101(8):616-22. DOI: 10.1136/heartjnl-2014-306472