Oral frailty and its determinants in older age: a systematic review

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Poor oral health is common among older adults and can impair essential activities of daily living and contribute to frailty. We did a systematic review of studies on the relationship between oral health factors and frailty among older adults (>60 years), consulting six different electronic databases for studies published from database inception to March 20, 2021. In total, 39 articles met the eligibility requirements, including 12 different indicators of poor oral health related to frailty, which we grouped in four different categories: oral health status deterioration; deterioration of oral motor skills; chewing, swallowing, and saliva disorders; and oral pain. Factors of oral health status deterioration (52%), in particular few remaining teeth (29%), were most frequently associated with frailty. Reduced oral motor skills (27%), especially masticatory function (9%), oral diadochokinesis (5%), occlusal force (7%), and chewing, swallowing, and saliva disorders (20%), especially chewing difficulties [11%]), were less frequent but were similarly considered to be associated with frailty. Our findings could help to assess the contribution of each oral health item to a possible operational definition of this novel frailty phenotype, defined as an age-related gradual loss of oral function together with a decline in cognitive and physical functions.

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Introduction

Global demography is shifting and ageing populations are projected to grow exponentially. Such population growth projections over the next decade are worrying, raising concerns that resources might be unable to satisfy the health demands of almost 9 billion people. From a generational perspective, older people will contribute substantially to health-care demands, as this population has a decline in general wellbeing and quality of life and is generally more frail than the younger population. Frailty is a biophysiological disorder that affects many activities of daily living, characterised by diminishing physiological reserves and resistance to stressogenic insults.[1,2] This crucial intermediate status of the ageing process can be defined as either a unidimensional entity, on the basis of physical or biological factors according to the construct derived from the Cardiovascular Health Study,[2] or as a non-specific multidimensional status, on the basis of a deficit accumulation model[3] with interconnected domains. Frailty actually has a multidimensional and multisystemic nature leading to a marked susceptibility to a cluster of adverse health-related events such as falls, injuries, disability, hospitalisation, institutionalisation, dementia, and death.[1–3] A large systematic review and meta-analysis of reports in 62 countries suggested a pooled prevalence of 12% of frailty in a sub-analysis of population-based studies using physical phenotype measures.[4] Using the same unidimensional physical frailty phenotype,[2] we found a 14·8% prevalence of physical frailty in an older southern Italian population.[5]

However, because of the multidimensional and challenging nature of frailty, both clinicians and researchers must consider different domains, including physical,[2] cognitive,[6] social or biopsychosocial,[7] and nutritional[8] frailty phenotypes. Moreover, emerging questions about prioritising domains in frailty contexts are still being debated and there is no universal consensus on this issue. Therefore, poor oral health is a new concept when considering the frail older population and increased life expectancy is contributing to the growing scientific interest on this topic. From a multi-item perspective, the oral frailty phenotype is a novel construct proposed as a conceptualisation of age-related gradual loss of oral function, driven by a set of impairments that worsen oral daily functions—eg, loss of teeth, poor oral hygiene, inadequate dental prostheses, or difficulty in chewing associated with age-related changes in swallowing.[9,10] Oral frailty has been defined as a decrease in oral function together with a decline in cognitive and physical functions, such as oral microbiota and Alzheimer's disease neurodegeneration.[11]

From a single-item perspective, the oral cavity has several essential functions, such as chewing, swallowing, and communicating. Therefore, oral health is an essential aspect of health, life satisfaction, quality of life, and self-perception. Impairment of oral functions is very common in older adults and this adverse feature of ageing can indirectly interact with several frailty domains through multiple pathways. An overt example of this relationship is age-related functional oral deterioration, characterised by poor dental hygiene, inadequate dental prostheses, and dietary deficiencies, which leads to a high risk of nutritional frailty.[8,12]

Many studies have described the association between oral health and frailty, concluding that oral health problems in older age could be possible exposure risk factors for a frailty syndrome. Also, an impaired eating or swallowing ability,[13] and oral motor skills,[14] deterioration of hard and soft oral tissues,[15,16] and pain[17] might interact with the oral frailty condition. A positive association between frailty and poor oral health, particularly having few remaining teeth and an impaired oral function, has also been suggested in systematic reviews.[18,19] However,

these systematic reviews of oral health and frailty in older age included few studies (only two reports of an established frailty model and ten reports of physical frailty components),[18] given that many reports on this topic have been published only in the past 5 years or were focused only on longitudinal studies.[19] Most of the studies on this topic applied heterogeneous qualitative measurements, resulting in a substantial heterogeneity of the protocols, which means that results are difficult to compare. The complexity and multidimensional nature of oral health make it difficult to clarify its true role in inducing frailty. In this systematic review, we aimed to summarise the parameters used when investigating oral health aspects in older people, and their predictive role in assessing frailty risk.

Methods

Search strategy and selection criteria

We followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines, adhering to the PRISMA 27-item checklist.[20] The protocol was established and registered on PROSPERO (CRD42021231450). We searched PubMed, MEDLINE, Embase, Scopus, Ovid, and Google Scholar databases to find original research articles on the association between exposure to poor oral health and frailty (appendix p 1). Databases were searched for articles published in any language from database inception to March 20, 2021. The selected exposure factors included any indicators of poor oral health, regardless of the measurement method (eg, clinical examination or self-reported) and the outcomes, including any validated frailty tools (ie, scales, indexes, scores, questionnaires, instruments, evaluations, screening, and indicators).

See Online for appendix

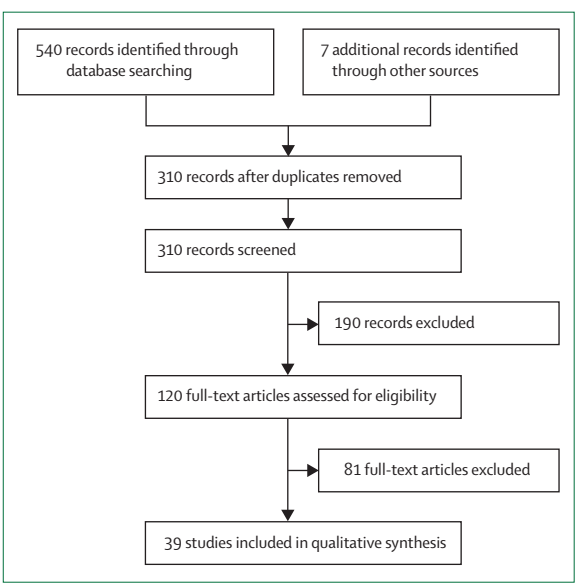

Figure 1: **Oral health factors associated with the four categories identified from the study selection**
All included oral health factors were identified as being related to frailty.

Two investigators (VD and RZ) searched for articles, screened titles and abstracts of the retrieved articles separately and in duplicate, checked the complete texts, and selected records for inclusion.

Studies of people aged older than 60 years was an inclusion criterion applied when screening for relevant articles. No screening was applied to the recruitment settings (eg, care home, hospital, or community) or general health status. Technical reports, letters to the editor, and systematic and narrative review articles were excluded.

The following information was extracted by the two investigators (VD, RZ), separately and in duplicate in a piloted form: name of the tool used to assess frailty (eg, scales, indexes, scores, questionnaires, instruments, evaluations, screening, and indicators), general information on single studies (eg, author, year of publication, country, settings, design, sample size, and age), and oral items that are associated with poor oral health. The exposure included every oral health factor measured at least once in the study, regardless of the form of measurement (eg, clinical examination or self-reported). For data collection, all references selected for retrieval from the databases were managed using Microsoft Excel. All duplicated records were excluded. Potentially eligible articles were identified by reading the abstract and then, in cases of potential inclusion, reading the full-text version of the articles. Data were cross-checked, any discrepancies were discussed, and disagreements were resolved by a third investigator (FP).

Quality assessment

The methodological quality of included studies was independently appraised by paired investigators (VD and RZ or ML), using the National Institutes of Health quality assessment toolkits for quantitative studies.[21] The ratings high (good), moderate, or poor were assigned to studies according to the criteria stated in the toolkit (ie, study question, population, participation rate, inclusion criteria, sample size justification, time of measurement of exposure or outcomes, timeframe, extent of exposure, defined exposure, masking, repeated exposure, defined outcomes, loss to follow-up, and confounding factors). Disagreements regarding methodological quality of the included studies were resolved through discussion until a consensus was reached, or resolved by a fourth investigator (FP). A modified version of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) rating system was used to assess the overall quality of evidence of the included studies.[22] The following factors were considered: the strength of association for poor oral health indicators and frailty outcomes, methodological quality and design of the studies, consistency, directedness, precision, size, and (if applicable) dose-response gradient of the estimates of effects across the evidence base. Evidence was graded as

very low, low, moderate, or high, similar to a GRADE rating system.

Results

The preliminary systematic literature search yielded 540 records. After excluding duplicates, 310 were considered potentially relevant and retained for analysis of the titles and abstracts. Then 190 articles were excluded because they did not meet the characteristics of the approach, or the review goal. After reviewing the full text of the remaining 120 articles, only 39 met the inclusion criteria and were included in the final qualitative analysis (figure 1).[12,15,16,23–58] The endpoint of the screening process yielded 39 eligible articles focused on 12 different oral health factors: masticatory function; tongue pressure; occlusal force; oral diadochokinesis; difficulty swallowing; difficulty chewing; dry mouth; oral health; periodontal disease; oral dysbiosis; number of teeth; and tooth or mouth pain. Given the original heterogeneous labelling which prevented a rapid conceptual interpretation, we grouped oral health factors in four separate categories: oral health status deterioration; deterioration of oral motor skills; chewing, swallowing, and saliva disorders; and oral pain (figures 2, 3).

Details of the study design, sample size, sex ratio (%), minimum age, mean age, setting, country, main findings, and quality assessment of individual studies are shown in table 1. Given the mixed recruitment settings for a small percentage of selected studies (2 [5%] of 39), the distribution resulted as follows: 31 studies in communities (78%), seven studies in hospitals (18%), and two studies in the home (5%). Asia led the geographical distribution of selected studies (20 [51%] of 39 studies), followed by 11 (28%) studies in Europe, five (13%) studies in North America, two (5%) studies in Oceania, and one (3%) study in South America. This geographical perspective highlighted both the dyshomogeneous geographical distribution and the inadequate representativeness of all countries. There were more women (63%) than men (37%) in the total of 164499 participants. Among the included studies, a cross-sectional design was more common than a longitudinal cohort design (26 [67%] cross-sectional studies *vs* 13 longitudinal cohort studies [33%]).

Prevalence of frailty and assessment tools

The type of assessment tool and the prevalence of frailty were recorded when tabulating the overview of selected studies (table 1). Prevalence estimates of frailty ranged from 2%[38] to 67%;[45] such variations were probably due to the assessment tool, diagnostic criteria used, or study setting. Regarding the different types of frailty assessment tools, the physical frailty phenotype (defined as patients having three or more of five frailty components from the Cardiovascular Health Study was most frequently used (17 [40%] of 43 studies), followed by the Kihon Checklist score (six [14%] studies), the Groningen Frailty Indicator (3 [7%] studies),

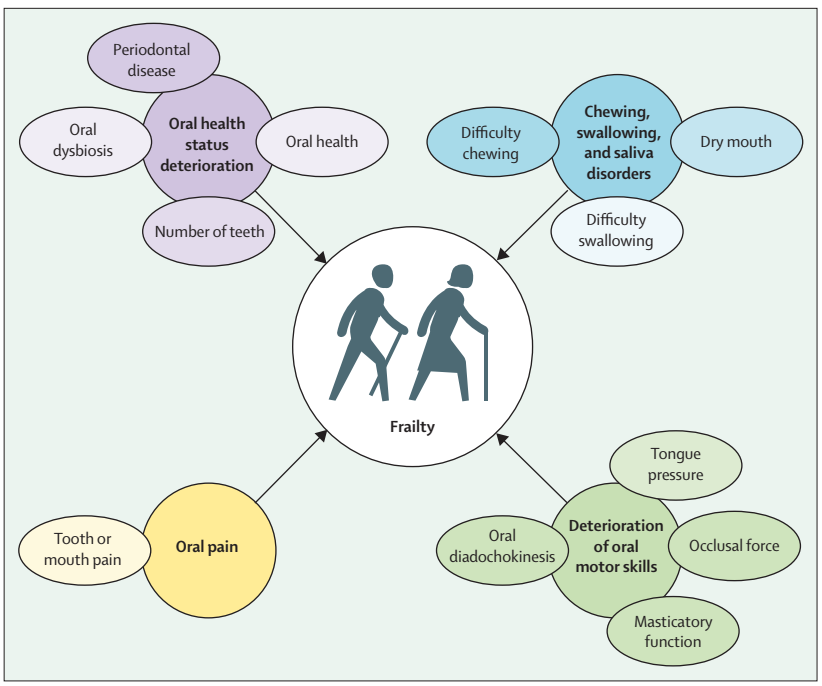

Figure 2: **Four categories of oral health items and the associated 12 indicators of oral health and relative metrics**
The four categories of oral health factors were the topics reported in the 39 articles that were included in the systematic review

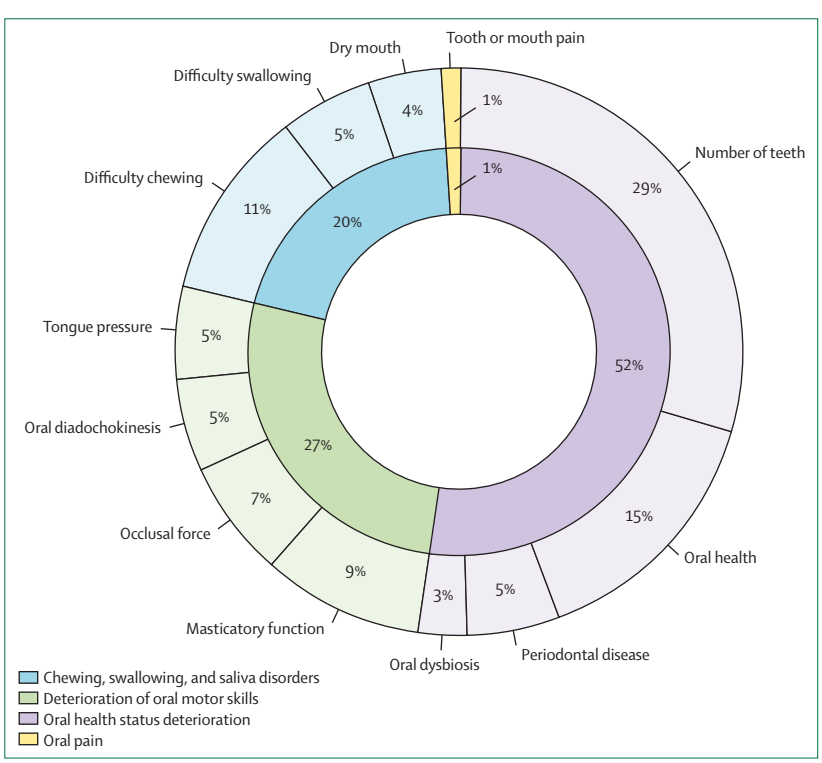

Figure 3: **Methodological quality assessment within studies**
Percentages are rounded.

	Frailty assessment tool	Oral factors	n	Frailty prevalence	Design (follow-up)	Inclusion age	Average age	Setting	Continent (country)	Quality assessment	Main findings
Castrejón-Pérez et al (2012)[23]	Physical frailty phenotype	Number of teeth, oral health, periodontal disease, and difficulty chewing	838	15% frail	Cross-sectional	≥70 years	77·9 years (6·3)	Community	North America (Mexico)	High	Use of dental services and self-perception of oral health were associated with a higher probability of being frail
de Andrade et al (2013)[24]	Physical frailty phenotype	Number of teeth	1374	8·5% frail, 40·7% pre-frail, 50·8% robust	Cross-sectional	≥60 years	..	Community	South America (Brazil)	High	Participants with 20 or more teeth had a lower chance of being frail than edentulous individuals
Komulainen et al (2014)[25]	Physical frailty phenotype	Number of teeth	165	57·1% pre-frail plus frail	Cross-sectional	≥75 years	81·3 years (4·3)	Community	Europe (Finland)	High	Older individuals with a need for dental prostheses were significantly more likely to be pre-frail and frail
Hoeksema et al (2017)[26]	Groningen Frailty Indicator	Number of teeth, oral health, dry mouth, and difficulty chewing	1026	22% frail	Cross-sectional	≥75 years	Median age 83 years (IQR 78–88)	Community	Europe (Netherlands)	Moderate	Older people with remaining teeth were less frail, had better quality of life and activities of daily living, and used fewer drugs than edentulous older people
Kamdem et al (2017)[27]	Physical frailty phenotype	Masticatory function and tooth or mouth pain	992	35·4% pre-frail plus frail	Cross-sectional	≥65 years	74·9 years (1·4)	Community	Europe (Switzerland)	High	Self-reported oral pain and masticatory impairment had a significant relationship with frailty
Rapp et al (2017)[28]	Physical frailty phenotype	Oral health	1314	46·8% frail, 42·6% pre-frail, 10·6% robust	Cross-sectional	≥75 years	74·9 years (1·4)	Hospital	Europe (France)	Moderate	Physical frail participants had significantly increased OHAT score
Watanabe et al (2017)[29]	Physical frailty phenotype	Occlusal force, number of teeth and oral diadochokinesis	4720	11·3% frail, 57·0% pre-frail, 31·7% robust	Cross-sectional	≥65 years	72·1 years (5·6)	Community	Asia (Japan)	High	Frail group had fewer present teeth (women aged ≥70 years), lower occlusal force, lower masseter muscle thickness, and lower oral diadochokinesis rate than the robust group
Castrejón-Pérez et al (2017)[30]	Physical frailty phenotype	Number of teeth and periodontal disease	237	14·8% frail	Longitudinal (3 years)	≥70 years	76·4 years (5·2)	Community	North America (Mexico)	High	Oral health conditions at baseline were associated with incident frailty at 3 years, whereas the probability of developing frailty was reduced for each additional tooth present
Okura et al (2017)[31]	Kihon Checklist	Masticatory function	5083	32·1% frail	Longitudinal (3 years)	≥65 years	..	Community	Asia (Japan)	High	The presence of kyphosis or poor masticatory function was related to mortality and there was an additive effect of these two factors related to frailty
Ewan et al (2018)[32]	Canadian Study of Health and Aging Clinical Frailty Scale, Barthel Index, and Hierarchical Balance and Mobility Scale	Oral dysbiosis	53	9·4% frail according to Clinical Frailty Scale; 37·7% frail according to Barthel Index; 96·2% frail according to Hierarchical Balance and Mobility Scale	Longitudinal (3, 5, 7, and 14 days)	≥65 years	82·9 years (6·4)	Hospital	Europe (UK)	High	Oral microbial community structure was related to frailty

(Table 1 continues on next page)

	Frailty assessment tool	Oral factors	n	Frailty prevalence	Design (follow-up)	Inclusion age	Average age	Setting	Continent (country)	Quality assessment	Main findings
(Continued from previous page)											
Woo et al (2018)[33]	FRAIL Questionnaire	Difficulty chewing	2259	18·1% frail, 46·1% pre-frail, 35·8% robust	Cross-sectional	≥60 years	..	Community	Asia (China)	High	Chewing difficulties were associated with all the domains of comprehensive geriatric assessment, including frailty
Iwasaki et al (2018)[34]	Physical frailty phenotype	Masticatory function	141	22·7% frail, 55·3% pre-frail	Cross-sectional	≥60 years	Median age 72 years (IQR 66–78)	Community	Asia (Thailand)	High	Objectively measured masticatory ability was significantly associated with frailty
Ramsay et al (2018)[35]	Physical frailty phenotype	Number of teeth, dry mouth, oral health, and periodontal disease	1622	19% frail	Longitudinal (2 years)	≥71 years	79·2 years (4·8)	Community	Europe (UK)	High	Tooth loss, dry mouth, and cumulative oral health problems were independently associated with incident frailty
Tanaka et al (2018)[12]	Physical frailty phenotype	Tongue pressure, number of teeth, masticatory function, oral diadochokinesis, difficulty chewing, and difficulty swallowing	2011	7·2% frail	Longitudinal (2 years)	≥65 years	73 years (5·5)	Community	Asia (Japan)	High	Accumulated poor oral status strongly predicted the onset of adverse health-related outcomes, including physical frailty
Iwasaki et al (2018)[36]	Physical frailty phenotype	Occlusal force	322	15·2% frail	Longitudinal (5 years)	≥75 year	..	Community	Asia (Japan)	High	Poor oral function, as indicated by low maximum occlusal force, increased the risk of the development of frailty
Iwasaki et al (2018)[37]	Physical frailty phenotype	Number of teeth	322	14·9% frail	Longitudinal (5 years)	≥75 years	..	Community	Asia (Japan)	High	Association of functional dentition with the development of frailty
Yamanashi et al (2018)[38]	Physical frailty phenotype	Tongue pressure	1603	1·9% frail, 37·7% pre-frail, 60·4% robust	Cross-sectional	≥60 years	72·8 years (7·4)	Community	Asia (Japan)	High	Maximum isometric tongue pressure is independently associated with frailty
Hoeksema et al (2018)[39]	Groningen Frailty Indicator	Number of teeth	103	Two thirds of the participants (n=68) were identified as frail	Cross-sectional	≥65 years	Median age 79 years (IQR 72–85)	Home care	Europe (Netherlands)	Moderate	Frailty, health, and quality of life were better in community-dwelling older people who recently (<6 months) received formal home care with remaining teeth
Horibe et al (2018)[40]	Kihon Checklist	Masticatory function and difficulty chewing	418	9·6% frail, 29·4% pre-frail, 61% robust	Longitudinal (2 years)	≥65 years		Community	Asia (Japan)	High	Mixing ability and subjective chewing ability were associated with frailty progression
Horibe et al (2018)[41]	Kihon Checklist	Occlusal force, difficulty chewing, and masticatory function	659	14% frail, 33·4% pre-frail, 52·7% robust	Cross-sectional	≥65 years	72·7 years (5·2)	Community	Asia (Japan)	High	All three masticatory functions (maximum bite force, mixing ability, and self-reported chewing ability) were associated with pre-frailty or frailty
da Mata et al (2019)[42]	Seattle Care Pathway recommendations	Oral health	327	28·4% frail	Cross-sectional	≥60 years	74 years (6·9)	Hospital	Europe (Ireland)	Moderate	Frail older people presented with poorer oral-health-related quality of life compared to healthier participants

(Table 1 continues on next page)

	Frailty assessment tool	Oral factors	n	Frailty prevalence	Design (follow-up)	Inclusion age	Average age	Setting	Continent (country)	Quality assessment	Main findings
(Continued from previous page)											
Satake et al (2019)[43]	FRAIL questionnaire	Tongue pressure and number of teeth	467	10·1% frail	Cross-sectional	≥60 years	71·6 years (7·1)	Community	Asia (Japan)	High	Fewer teeth and lower tongue pressure were associated with frailty
Gu et al (2019)[44]	38-Item Frailty Index	Number of teeth	3635	27·68% frail	Cross-sectional	≥65 years	84·3 years (9·9)	Community	Asia (China)	High	The presence of fewer teeth was significantly associated with frailty status
Hasegawa et al (2019)[16]	Kihon Checklist	Oral dysbiosis, number of teeth and dry mouth	308	6·5% frail, 27·6% pre-frail, 69·5% robust	Cross-sectional	≥65 years	72·7 years (7·1)	Community	Asia (Japan)	Moderate	Physical frailty may affect the oral hygiene status and condition of the remaining teeth
Shwe et al (2019)[45]	Reported Edmonton Frail Scale	Oral health	168	66·7% frail	Cross-sectional	≥65 years		Hospital	Oceania (Australia)	High	Poor self-reported oral health was found to be independently associated with frailty
Hakeem et al (2020)[15]	(1) 34-Item Frailty Index (2) Physical frailty phenotype	Number of teeth	356	43·5% frail according to (1); 20·8% frail, 54% pre-frail, and 25·2% robust according to (2)	Cross-sectional	≥60 years	67·2 years (6·5)	Community and hospital	Asia (Saudi Arabia)	High	Significant associations were found between oral health indicators, namely number of teeth, functional dentition and self-rated oral health, and both physical frailty phenotype and Frailty Index
Hakeem et al (2020)[46]	49-Item Frailty Index	Oral health	2368	50·3% frail	Cross-sectional (two different baseline assessments: NHANES 2011 and 2013)	≥60 years		Community	America (USA)	High	Poorer self-rated oral health is associated with higher rates of frailty
Tuuliainen et al (2020)[47]	Abbreviated comprehensive geriatric assessment scale	Oral health	231	62% frail, 26·7% pre-frail, 11·3% robust	Longitudinal (6 months)	≥75 years	84·4 years (5·4)	Home care	Europe (Finland)	High	Frail participants had poorer oral cleaning habits and hygiene, and they had lost more teeth than non-frail participants
Tai et al (2020)[48]	Physical frailty phenotype (assessed only with the IADL Scale)	Difficulty chewing and number of teeth	2905	8·2% frail	Cross-sectional	≥60 years	69·5 years (9·3)	Community	Asia (Taiwan)	High	Chewing impairment was associated with frailty
Hironaka et al (2020)[49]	Physical frailty phenotype	Tongue pressure, number of teeth, masticatory function, oral diadochokinesis, difficulty chewing, and difficulty swallowing	682	3·5% frail, 45·7% pre-frail, 50·7% robust	Cross-sectional	≥65 years	73·3 years (6·6)	Community	Asia (Japan)	Moderate	Physical frailty was directly related to oral frailty
Zhang et al (2020)[50]	Physical frailty phenotype	Number of teeth	4037	6·7% frail, 47% pre-frail, 46·3% robust	Cross-sectional	≥60 years	67·8 years (5·9)	Community	Asia (China)	High	Frailty was associated with having fewer teeth (≤20 teeth)

(Table 1 continues on next page)

	Frailty assessment tool	Oral factors	n	Frailty prevalence	Design (follow-up)	Inclusion age	Average age	Setting	Continent (country)	Quality assessment	Main findings
(Continued from previous page)											
Valdez et al (2020)[51]	Physical frailty phenotype	Oral health, number of teeth	601	19·3% frail, 56·2% pre-frail, 24·5% robust	Cross-sectional	≥70 years		Community	Oceania (Australia)	High	Dentate status and self-reported perception of oral health were associated with frailty
Nishida et al (2020)[52]	Kihon Checklist	Difficulty swallowing	3475	Not reported	Cross-sectional	≥65 years	75·8 years (6·8)	Community	Asia (Japan)	Moderate	Dysphagia was independently associated with oral, physical, cognitive, and psychological frailty
Shimazaki et al (2020)[53]	Kihon Checklist	Occlusal force, oral diadochokinesis, difficulty swallowing	978	9% frail, 26·4% pre-frail, 64·6% robust	Cross-sectional	≥65 years	Median age 73 years (IQR 69–77)	Community	Asia (Japan)	High	Many community-dwelling older people have reduced oral function or oral hypofunction, which is significantly associated with frailty
Chalittikul et al (2020)[54]	Physical frailty phenotype diagnosed by physical function limitation (difficulty in climbing stairs or walking or dressing or bathing)	Number of teeth	114 602	28% frail	Cross-sectional	≥65 years	..	Community	America (USA)	High	There was a significant association between the number of extracted teeth and physical function limitation
Hakeem et al (2021)[55]	49-Item Frailty Index	Periodontal disease and number of teeth	2368	38·7% frail	Cross-sectional (two different baseline assessments: NHANES 2011 and 2013)	≥60 years	..	Community	America (USA)	High	Periodontal disease has a significant but weaker association with frailty compared with number of teeth
Noetzel et al (2021)[56]	CGA-based MPI	Oral health and number of teeth	100	19·8% low-risk of death (MPI-1), 63·7% moderate-risk of death (MPI-2), 16·5% high-risk of death (MPI-3)	Longitudinal (6 months)	≥65 years	76·9 years (6·4)	Hospital	Europe (Germany)	High	Oral health examination showed significant results in association to CGA-based MPI prognosis
Ogawa et al (2021)[57]	Physical frailty phenotype diagnosed by Short Physical Performance Battery	Number of teeth and occlusal force	457	24·3% frail	Cross-sectional	≥60 years	..	Hospital	Asia (Japan)	High	The number of teeth present and the prevalence of occlusal support were significantly lower in patients with than without physical frailty
Everaars et al (2021)[58]	(1) Utrecht Periodic Risk Identification and Monitoring system (2) Groningen Frailty Indicator	Oral health	1202	53% at risk for frailty according to (1); 19% frail according to (2)	Cross-sectional	≥60 years	73 years (8)	Community	Europe (Netherlands)	High	Poor self-reported oral health problems were associated with frailty

Average age data are mean (SD), unless otherwise stated. Unless otherwise stated, all reference to physical frailty phenotypes were defined as patients having three or more of five frailty components from the Cardiovascular Health Study. CGA=Comprehensive Geriatric Assessment. IADL=instrumental activities of daily living. NHANES=National Health and Nutrition Examination Surveys. MPI=Multidimensional Prognostic Index. OHAT=oral health assessment tool.

Table 1: **Selected studies investigating oral health items and frailty in older age (people 60 years and older, n=39) and quality appraisal summary**

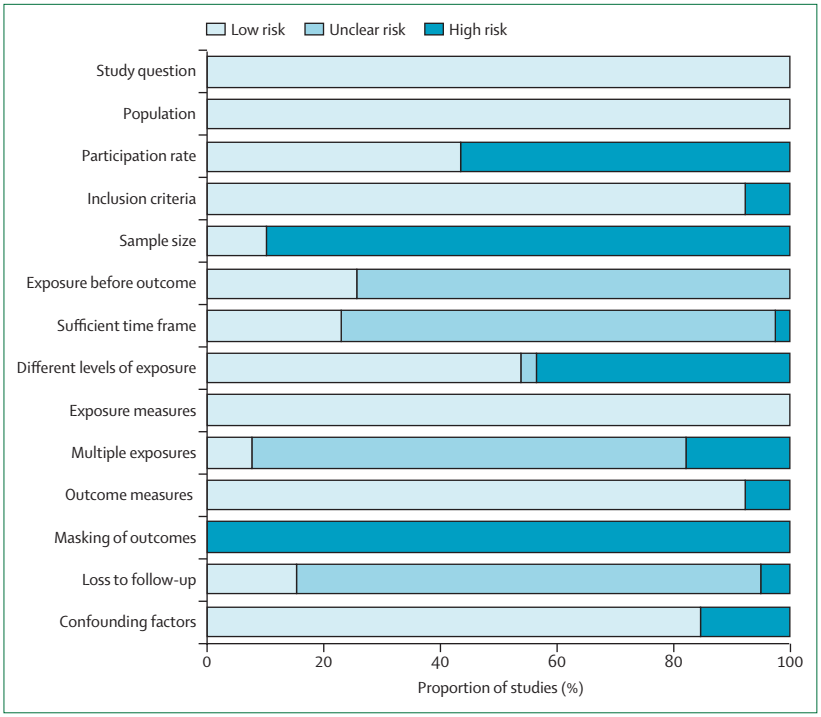

Figure 4: **Overall quality assessment across studies**

FRAIL Questionnaire (two [5%] studies), and the 49-Item Frailty Index (two [5%] studies). The following assessment tools were each used by one (2%) of the 43 studies: the Canadian Study of Health and Aging Clinical Frailty Scale, 38-Item Frailty Index, 34-Item Frailty Index, abbreviated Comprehensive Geriatric Assessment scale, Barthel Index, Hierarchical Balance and Mobility Scale, Seattle Care Pathway recommendations, Comprehensive Geriatric Assessment-based Multidimensional Prognostic Index, Reported Edmonton Frail Scale, instrumental activities of daily living scale, physical function limitation (ie, difficulty in climbing stairs or walking or dressing or bathing, Short Physical Performance Battery, and Utrecht Periodic Risk Identification and Monitoring system. Among these tools, the last four tools (ie, the instrumental activities of daily living scale, physical function limitation, Short Physical Performance Battery, and Utrecht Periodic Risk Identification and Monitoring system) were used as proxy estimates of the physical frailty phenotype as assessed by the Cardiovascular Health Study, whereas the Seattle Care Pathway recommendations was used as a proxy estimate of the deficit accumulation model (ie, frailty index). However, 3 (8%) of the 39 selected studies adopted more than a single frailty assessment tool; therefore, the representativeness of each frailty assessment tool was calculated on what amounted to a total of 43 studies.

Associations among oral health items and frailty

For the first category identified, we recorded markers of oral health status deterioration (52%), which was affected by the number of teeth (22 [29%] of 75 oral health factors), whereas the items oral health (11 [15%]), periodontal disease (four [5%]), and oral dysbiosis (two [3%]) were less common (figures 1, 2).

The burden of items belonging to the oral motor skills (20 [27%] of 75 oral health factors) and the chewing, swallowing, and saliva disorders categories was similar (15 [20%]). For the deterioration of oral motor skills category, the item masticatory function was found to be the factor most often associated with frailty (seven [9%]), whereas tongue pressure (four [5%]), occlusal force (five [7%]) or oral diadochokinesis (four [5%]) were less common (figure 1 and 2). For the chewing, swallowing, and saliva disorders category, difficulty chewing was most often associated with frailty (eight [11%]) compared with dry mouth (three [4%]) or difficulty swallowing (four [5%]). Oral pain was the least common category, accounting for only one [1%] of the items related to frailty (figure 1, 2).

Overall quality of evidence

Examining all the 39 reports included in this systematic review, studies were considered to be of moderate (seven studies) to high (32 studies) methodological quality (table 1). An overview of the quality assessment of the studies is in the appendix (p 2) and figure 4 highlights study components with a higher or lower risk assessment. Bias was detected predominantly as sample size justification (selection bias); 35 (90%) of 39 studies were associated with a high risk of bias and all 39 (100%) were associated with a high risk of detection bias as blinded assessment was not used. 16 (41%) studies were associated with a higher risk of bias regarding the participation rate and different levels of exposure (figure 4).

Using the GRADE approach, the overall quality of evidence of our four categories was judged as moderate for oral health status deterioration and deterioration of oral motor skills, but low for chewing, swallowing, and saliva disorders and very low for oral pain (table 2). The oral health items most associated with frailty in older age were number of teeth (very strong association, moderate quality of evidence), decreased masticatory function (very strong association, moderate quality of evidence), difficulty chewing (very strong association, moderate quality of evidence), deterioration of oral health (strong association, moderate quality of evidence), oral diadochokinesis (strong association, moderate quality of evidence), and reduced occlusal force (strong association, moderate quality of evidence), followed by reduced tongue pressure (low strength of association, low quality of evidence), dry mouth (low strength of association, low quality of evidence), periodontal disease (low strength of association, low quality of evidence), and difficulty swallowing (low strength of association, low quality of evidence). Finally, oral dysbiosis and tooth or mouth pain linked to frailty showed a very low strength of association and a very low quality of evidence (table 2).

Discussion

We identified four different categories of variables, covering 12 determinants of poor oral health that were judged using the perspective of contributing to frailty exposure, regardless of the nature of the frailty assessment tool (ie, scales, indexes, scores, questionnaires, instruments, evaluations, screening, and indicators). For this purpose, the exposure variable needed to be considered while disregarding the inconsistency among frailty assessment tools, so the selected studies had a high amount of discrepancy. The overall quality of evidence was judged as moderate for the categories oral health status deterioration and deterioration of oral motor skills. In fact, drivers of oral health status deterioration (52%), generally consisting of having few remaining teeth (29%), were most frequently associated with frailty, followed by poor oral health (15%), an impaired masticatory function (9%), and difficulty chewing (11%), oral diadochokinesis (5%), and occlusal force (7%). By comparison with these oral factors, tongue pressure (5%), periodontal disease (5%), difficulty swallowing (5%), and dry mouth (4%) had a low association with frailty and low quality of evidence. The contributing role of oral dysbiosis (3%) and tooth or mouth pain (1%) was found to be irrelevant.

Two other systematic reviews of oral health and frailty in older age have been reported.[18,19] In 2015, the first systematic review concluded that none of the longitudinal

	Evidence base	Strength of evidence (GRADE)	Strength of association	Comments
Oral health status deterioration				
Number of teeth[12,15,16,23–26,29,30,35,37,39,43,44,48–51,54–57]	22 studies (n=142771)	Moderate	Oral frailty/incident physical frailty (HR 2·41, 95% CI 1·27–4·55);[12] teeth/frailty (RR 0·99, 95% CI 0·98–0·99);[15] low number of remaining teeth/frailty p<0·001;[16] number of teeth/frailty (p<0·001);[23] >21 teeth/frailty (OR 0·25, 95% CI 0·07–0·91);[24] edentulous/frail (OR 3·2, 95% CI 1·2–8·3);[25] remaining teeth/less frail (p≤0·01);[26] functional teeth/frailty (p<0·001);[29] number of teeth/incident frailty (risk ratio 0·97, 95% CI 0·94–1·01);[30] edentulous/frailty (OR 1·90, 95% CI 1·03–3·52);[35] good functional dentition/incident frailty (HR 0·50, 95% CI 0·25–0·98);[37] remaining teeth/less frailty (p=0·01);[39] number of teeth/frailty (OR 0·963, 95% CI 0·930–0·997);[43] no teeth (OR 2·07, 95% CI 1·53-2·80), 1–10 teeth (OR 1·77, 95% CI 1·31–2·38);[44] no dental prosthesis/frailty (OR 1·61, 95% CI 1·11–2·35);[48] oral frailty/physical frailty (p<0·001);[49] ≤20 teeth and no denture use/frailty (OR 7·56, 95% CI 5·22–10·94), ≤20 teeth and denture use/frailty (OR 5·33, 95% CI 3·89–7·30);[50] number of teeth/frailty (OR 2·49, 95% CI 1·17–5·30);[51] DMFT Index/frailty (OR 106, 95% CI 1.00–1.12);[54] teeth/frailty (RR 0·99, 95% CI 0·98–0·99);[55] edentulous/frailty (OR 1·36, 95% CI 1·22–1·52), six teeth or more/frailty (OR 1·35, 95% CI 1·23–1·48);[56] remaining teeth/frailty (β 0·08, p=0·02);[57]	Very strong association with estimates provided; very large sample size and several studies included
Oral health[23,26,28,35,42,45,46,47,51,54,58]	11 studies (n=8340)	Moderate	Self-rated oral health/frailty (p=0·006);[23] self-rated oral conditions/frailty (p≤0·001);[26] OHAT score/frailty (p<0·001);[28] poor self-rated oral health/frailty (OR 1·56, 95% CI 1·18–2·07);[35] OHIP-14 score/frailty (p<0·001);[42] GOHAI score/frailty (p=0·019);[45] poor self-related oral health/frailty (rate ratio 1·41, 95% CI 1·28–1·54);[46] low frequency of tooth brushing/frailty (OR 0·4, 95% CI 0·1–0·9, low denture cleaning/frailty (OR 0·3, 95% CI 0·1–0·8);[47] ACDS/frailty (OR 3·01, 95% CI 1·50–6·08);[51] BOHSE/frailty (OR 1·34, 95% CI 1·15–1·56); GOHAI/frailty (OR 0·87, 95% CI 0·81–0·94);[54] self-reported oral discomfort (OR 2·07, 95% CI 1·52–2·81)[58]	Strong association with estimates provided; large sample size and multiple studies included
Oral dysbiosis[16,32]	Two studies (n=361)	Very low	Lower salivary bacterial count/frailty (p<0·05);[16] Shannon index/frailty (t −3·057965, p=0·0035)[32]	Uncertain association because there is a low number of studies and small sample size
Periodontal disease[23,30,35,55]	Four studies (n=3206)	Low	Severe periodontitis/frailty (OR 3·8, 95% CI 0·93–15·4, not significant);[23] severe periodontitis/frailty (risk ratio 2·13, 95% CI 1·01–4·50);[30] periodontal disease markers/frailty not significant (p value not provided);[35] moderate–severe periodontitis/frailty (RR 1·08, 95% CI 1·02–1·14)[55]	Despite multiple studies included and a large sample size, mixed evidence regarding strength of association and significance
Deterioration of oral motor skills				
Masticatory function[12,27,31,34,40,41,49]	Seven studies (n=9784)	Moderate	Oral frailty/incident physical frailty (HR 2·41, 95% CI 1·27–4·55);[12] masticatory ability/frailty (OR 1·70, 95% CI 1·07–2·72);[27] good masticatory ability/frailty (OR 0·38, 95% CI 0·32–0·44);[31] masticatory ability/frailty (OR 1·05, 95% CI 1·01–1·10);[34] mixing ability/frailty (OR 1·49, 95% CI 1·14–1·96);[40] mixing ability/frailty (OR 1·91, 95% CI 0·96–3·77);[41] oral frailty/physical frailty (p<0·001)[49]	Very strong association with estimates provided; large sample size and several studies included
Oral diadochokinesis[12,29,49,53]	Four studies (n=8391)	Moderate	Oral frailty/incident physical frailty (HR 2·41, 95% CI 1·27–4·55);[12] oral diadochokinesis (p<0·001);[29] oral frailty/physical frailty (p<0·001);[49] tongue–lip motor function/frailty (OR 2·2, 95% CI 1·1–4·6)[53]	Strong association with large sample size and multiple studies included
Occlusal force[29,36,41,53,57]	Five studies (n=6679)	Moderate	Occlusal force (p<0·001);[29] lower tertile MBF/frailty (HR 2·78, 95% CI 1·15–6·72);[36] MBF/frailty (OR 2·02, 95% CI 1·04–3·91);[41] decreased occlusal force/frailty (OR 2·7, 95% CI 1·7–4·4);[53] poor occlusion support/frailty (p=0·003)[57]	Strong association with estimates provided; large sample size and multiple studies included
Tongue pressure[12,38,43,49]	Four studies (n=4763)	Low	Oral frailty/incident physical frailty (HR 2·41, 95% CI 1·27–4·55);[12] MIP/frailty (OR 0·37, 95% CI 0·26–0·54);[38] tongue pressure/frailty (OR 0·956, 95% CI 0·919–0·996);[43] oral frailty/physical frailty (p<0·001)[49]	Despite multiple studies included and a large sample size, in half of the studies, the measure of tongue pressure came from the operational definition of oral frailty

(Table 2 continues on next page)

	Evidence base	Strength of evidence (GRADE)	Strength of association	Comments
(Continued from previous page)				
Chewing, swallowing, and saliva disorders				
Difficulty chewing[12,23,26,33,40,41,48,49]	Eight studies (n=10798)	Moderate	Oral frailty/incident physical frailty (HR 2·41, 95% CI 1·27–4·55);[12] chewing difficulties/frailty (OR 1·97, 95% CI 1·29–3·00);[23] chewing difficulties/frailty (p≤0·001);[26] chewing difficulties/frailty (OR 2·21, 95% CI 1·61–3·04);[33] self-reported chewing ability/frailty (OR 0·59, 95% CI 0·36–0·99);[40] self-reported chewing ability/frailty (OR 5·61, 95% CI 3·05–10·33);[41] OHIP-7T Q3 score (uncomfortable to eat)/frailty (OR 1·33, 95% CI 1·19–1·49, p<0·001);[48] oral frailty/physical frailty (p<0·001)[49]	Very strong association with estimates provided; large sample size and several studies included
Dry mouth[16,26,35]	Three studies (n=6782)	Low	Dry mouth/frailty not significant (p value not provided);[16] dry mouth/frailty (p<0·04);[26] ≥3 dry mouth symptoms/frailty (OR 2·03, 95% CI 1·18–3·48)[35]	Uncertainty because there is a low number of studies and mixed evidence regarding strength of association and significance, notwithstanding a large sample size
Difficulty swallowing[12,49,52,53]	Four studies (n=3671)	Low	Oral frailty/incident physical frailty (HR 2·41, 95% CI 1·27–4·55);[12] oral frailty/physical frailty (p<0·001);[49] swallowing difficulties/frailty (OR 2·19, 95% CI 1·66–2·90);[52] reduced swallowing function/frailty (OR 10·2, 95% CI 5·4–19·1)[53]	Despite multiple studies included and a large sample size, in half of the studies, the measure of difficulties swallowing came from the operational definition of oral frailty
Oral pain				
Tooth or mouth pain[27]	One study (n=992)	Very low	Oral pain/frailty (OR 1·72, 95% CI 1·17–2·53)[27]	Uncertainty due to evidence coming from a single study although with a relevant sample size

A modified version of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) rating system was used to assess the overall quality of evidence of the included studies.[22] Moderate means that further research is likely to have an important impact on our confidence in the estimate of effect and might change the estimate. Low means that further research is likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. Very low means that any estimate of effect is very uncertain. Solidus represents association. ACDS=active coronal decayed surface. BOHSE=Brief Oral Health Status Examination. DMFT=decayed, missing, and filled teeth. GOHAI=general oral health assessment index. HR=hazard ratio. MBF=maximum bite force. MIP=maximum isometric tongue pressure. OHAT=oral health assessment tool. OHIP=oral health impact profile. RR=relative risk. OR=odds ratio.

Table 2: **Summary of findings on oral health items associated with frailty in older adults**

studies showed whether poor oral health could increase the likelihood of developing signs of frailty.[18] However, this systematic review only identified two studies—neither was longitudinal—that used an established frailty definition, namely the physical frailty phenotype.[23,24] The second systematic review, published in 2019, identified five longitudinal studies that provided evidence of a longitudinal relationship between number of teeth and masticatory function, where frailty was measured using the physical frailty phenotype.[19] However, evidence of a relationship between periodontal diseases and frailty was inconclusive.[19]

Several pathways have been followed to explain the relationship between oral health and frailty. The first plausible pathway is the interplay between poor oral health and nutrition, food intake, and selection of food intakes on the basis of oral health (eg, remaining teeth). The evidence suggests that nutritional status could be a substantial risk factor for the development of frailty.[59] For the same reason, nutritional status could mediate the association between oral health and frailty, which could lead to difficulties eating. The cross-sectional association between oral frailty and malnutrition among community-dwelling older adults has been previously reported.[12] In the past 5 years, the construct of oral frailty, defined as accumulating deficits in oral health, has started to emerge.[8,10] In 2020, the Japan Dental Association described oral frailty as a series of processes that lead to age-associated changes in various oral conditions (eg, number of remaining teeth, oral hygiene, and oral dysfunction), together with a decreased interest in oral health and reduced physical and cognitive functions.[10]

Another possible link between oral health and frailty is the inflammatory pathway. Periodontal disease can increase prevalence of inflammatory markers,[30,60] and a relationship between inflammation and frailty has been suggested.[61] However, our findings, and the findings by Hakeem and colleagues[19] regarding the association between periodontal status and frailty, were inconclusive. Findings from the National Health and Nutrition Examination Surveys suggested that periodontal disease had a weaker association with frailty compared with the number of teeth.[55] However, an analysis considering people who were wholly or partially dentate (ie, 1–32 teeth) observed that individuals with severe periodontitis had a 2·1-times higher risk of 3-year incidence of frailty than those without severe periodontitis.[30] Periodontal disease could be relevant to frailty prevention, even if it was only evaluated in 4% of the studies included in our systematic review; the omission of periodontal disease is probably because the assessment is time-consuming, particularly in population-based settings. It is important to consider that periodontal disease affects teeth, whereas the studies included in the present systematic review reported results in older people with few or no teeth (36 [92%] of 39 studies). Tooth loss due to periodontal disease and its

effect on food selection and nutritional status might also mediate the association between oral health and extent of frailty. Furthermore, periodontal disease is generally due to mouth bacteria infecting the tissue around the teeth. A research interest in the role that oral microbiota might have in the microbiota–gut–brain axis has developed over the past 5 years.[62] Between dental plaque bacteria and the innate host defence system there is a dynamic equilibrium, and perturbation of this balance can lead to dental caries (tooth decay) and periodontal disease. The contribution of severe periodontal disease to the development of frailty should be explored in larger longitudinal population-based analyses. In our systematic review, we selected only two studies linking oral dysbiosis to frailty,[16,32] and the low strength of association was due to uncertainty owing to the low number of reports and the small sample size (two studies, n=361). However, in one of these studies, loss of species richness in oral microbiota was associated with increased frailty,[32] reflecting other evidence on gut microbiota.[63] These findings suggested a pathway in which the major trend in oral dysbiosis was related to the extent of frailty and multimorbidity, both of which are related to age.[32]

The relationship between poor oral health and frailty could have other intermediate psychosocial factors that should be researched. For example, the social effects of oral health deterioration and its effect on quality of life,[64] given that loneliness could also contribute to the development of frailty.[65] Furthermore, late-life depression can affect both frailty[66] and oral health status,[67] and late-life depression has been associated with a disinterest in maintaining good oral hygiene and having a cariogenic diet, diminished salivary flow, rampant dental decay, advanced periodontal disease, and oral dysesthesias.[67] Another pathway linking oral health and frailty could involve the role of socioeconomic factors in both frailty and oral health. Older adults with less education were more frail compared with those with more education,[68] and consistent socioeconomic inequalities have been reported for a number of oral health determinants.[69]

Our findings support the development of the concept of oral frailty as a possible independent frailty phenotype. To date, only one operational definition of oral frailty has been introduced, by Tanaka and colleagues,[12] which was based on the identification of six oral health items (ie, number of teeth, masticatory function, difficulty chewing, oral diadochokinesis, tongue pressure, and difficulty swallowing). Oral frailty was defined as poor status in three or more of these six oral health measures and oral pre-frail status as poor status in two or less measures.[12] This novel frailty phenotype was substantially associated with an increased risk of physical frailty, sarcopenia, disability, and all-cause mortality. These findings have been partially replicated by at least one other independent study using the same criteria and show an association between oral and physical frailty.[49] The first four oral items suggested by Tanaka and colleagues'[12] operational definition are among the measures mostly identified in our systematic review (ie, number of teeth, masticatory function, difficulty chewing, and oral diadochokinesis). Subsequent steps could be to assess the contribution of each oral health item to a possible operational definition of oral frailty, thereby defining the items that could best identify this new frailty phenotype.

In this systematic review, among the studies in which the physical frailty phenotype (as defined by the Cardiovascular Health Study) was the most prevalent (about half of the sample, n=17), the predictors most commonly associated with different frailty models were the low number of remaining teeth and poor oral health. Both tooth loss due to periodontal disease (a major cause of tooth loss) and irregular tooth brushing were associated with a higher risk of dementia.[70] Periodontal disease, generally due to oral bacteria, causes tooth loss associated with Alzheimer's disease risk. Although not explicitly evaluated, tooth loss could be related to infectious diseases due to poor oral dental care and irregular tooth brushing. However, tooth loss can be associated with an increased risk of dementia even without periodontal disease. In fact, a masticatory disorder due to tooth loss can lead to poor nutrition, reducing cerebral blood flow, often linked to memory deficits.[70]

Another possible definition of oral frailty included difficulty chewing associated with age-related changes in swallowing (presbyphagia).[9,71] The masticatory function was the third most compromised predictor of frailty in the deterioration of oral motor skills category. Sarcopenia, a progressive, generalised skeletal muscle disorder involving accelerated loss of muscle mass and function, could be the connection and could also depict a novel frailty phenotype.[71] Sarcopenia is now recognised as a whole-body process also affecting masticatory and swallowing muscles.[72] Linked to both nutritional and oral frailty, sarcopenia could share a bidirectional relationship with cognition, encompassing muscle dysfunction, slow gait, and cognitive dysfunction. In older age, these links suggest the coexistence of both cognitive and motor dysfunctions, characterising the proposed conditions of motoric cognitive risk syndrome, defined by slow gait plus cognitive complaints, and cognitive frailty, as another frailty phenotype characterised by coexisting physical frailty and mild cognitive impairment.[73] It is important to consider that the gait parameter could influence the estimated frailty models and health-related outcomes of the various studies (ie, clinical, cognitive, physical, and nutritional outcomes).[73]

The last predictor of frailty measures, included in the chewing, swallowing, and saliva disorders category, was difficulty swallowing. Considering the social, psychological, and biological factors associated with the process of swallowing and eating, a new term "eating capability" has been coined by Laguna and colleagues[74] to describe various quantifiable endogenous factors in the

well-coordinated eating process, which might help to characterise the food handling and oral processing abilities of older individuals. A reduced nutrient intake in older individuals is directly or indirectly associated with a progressive loss of muscle mass, a decline of oral functions, and coordination capabilities, all of which partly or jointly affect the intricate process of eating.[74] These complex physiological age-related changes are not yet fully understood but are thought to be related to the lifelong accumulation of impairments at molecular, tissue, and organ level. Although the process of swallowing and eating is often underestimated, it involves a systematic series of well-coordinated actions, including opening packages, lifting objects, manipulating cutlery, carrying food to the mouth, closing the mouth, chewing, saliva incorporation, bolus formation, and swallowing. An older adult might have difficulty executing one or more of these important operations in the overall eating process, resulting in a reduced food intake. However, focusing only on swallowing could result in underestimating some of the challenges faced during the whole process of transporting food to the mouth.

In this systematic review, owing to the heterogeneity of different variables in oral health assessment, a quantitative meta-analysis might be unreliable. Some other limitations of the present systematic review should also be considered. First, the study designs were different in the selected studies. The statistical survey of oral factors associated with frailty, even using the same definition, was different among the studies, in terms of the rating tools used and the definition of the oral items. Second, the number of oral items and the sample size varied between the included studies. Given the original heterogeneous labelling, we subjectively grouped oral health indicators in four separate categories, driven by the oral health items found in the reviewed studies, with some degree of overlap between these categories (eg, deterioration of oral motor skills and chewing, swallowing, and saliva disorders). Finally, owing to the lack of a consensus about oral frailty operationalisation, we had to use a framework based on oral items extracted from the selected studies without any process of selection. In future studies, oral deficits could be used to compute a frailty index, so the contribution of oral diseases to frailty can be reflected also by the deficit accumulation model.[3]

Our findings highlight the importance of oral health as a possible predictor of frailty, providing evidence showing the use of applying oral health indicators in health-care surveys and clinical practice. However, routine oral health assessment could pose several challenges in non-gerodontologic settings. In this context, tooth count could serve as a good marker for general health, reflecting the net accumulation of problems over time, ranging from poor hygiene habits to the development of caries, periodontal disease, and trauma. Furthermore, tooth count is clinical-friendly information that can be easily retrieved during the comprehensive geriatric assessment of older people. It could provide useful insights supporting the design of the most appropriate intervention with the aim of achieving maintenance and improvement of oral function and nutritional status. Over the next decade, the gerodontologist might have a greater effect on the prevention and maintenance of oral and general health status, and need to expend less effort on treatment.

Poor oral health could be a marker for frailty onset. Maintaining or increasing oral function, and so decreasing the effect of oral frailty, can be associated with an improved nutritional and functional status in older people, and could be implicated in reducing the mortality risk and other adverse health-related outcomes, including dementia and Alzheimer's disease. In fact, oral health implications could be subdivided into research outlooks, investigating the underlying mechanisms linking oral health status and frailty, and clinical implications. A further subgrouping is necessary to distinguish immediate clinical implications from typical multidimensional syndromes including late-life cognitive decline and dementia[70] and the risk of falls.[75] Preventive management of these syndromes is now imperative, and the oral health perspective, including a complete clinical oral examination, falls within a multidisciplinary approach to an efficacious Comprehensive Geriatric Assessment for managing older individuals.

Contributors
VD, RZ, and FP conceptualised this systematic review. RS, ML, FC, ADi, ADa, GDP, IB, LL, and GG contributed to data collection. VD, RZ, RS, ML and FP contributed to data interpretation. All authors contributed to drafting, revising, and approving of the submitted paper.

Declaration of interests
We declare no competing interests.

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