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Chewing and its influence on swallowing, gastrointestinal and nutrition-related factors: a systematic review

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ABSTRACT

The study aimed to evaluate the hypothesis that chewing is a mechanical and physiological contributor to swallowing, physiologic/pathologic processes of the gastrointestinal tract (GIT), and nutrition-related factors. A search strategy was applied to three different databases to investigate if chewing function in adults affects the swallowing, physiologic/pathologic processes of the GIT, and nutrition-related factors compared to controls with no exposure. The included studies were evaluated for methodological quality and risk of bias and certainty of evidence. The results showed 71 eligible studies. Overall, the results showed that 46 studies supported the hypothesis while 25 refuted it. However, the GRADE analysis showed low to very low certainty of the evidence to support the hypothesis that chewing is an important contributor in the swallowing process, and physiologic/pathologic processes in the GIT. The GRADE analysis also showed a moderate to very low certainty of the evidence to suggest that chewing function contributes to nutrition-related parameters. The overall results of the current study showed that a majority (64.7%) of the studies (46 out of 71) supported the hypothesis. However, robust studies with proper design, adequate sample size, and well-defined outcome parameters are needed to establish conclusive evidence.

KEYWORDS

Chewing efficiency; chewing performance; gastrointestinal disorders; oral rehabilitation; sensorimotor; videofluorography; narrative synthesis

Introduction

Mastication or chewing is a rhythmic process with finely synchronized movements coordinated by the components of the masticatory system. The rhythmic act of chewing results primarily in the physical comminution of large aggregates of food morsels and the formation of a soft bolus. The soft bolus, thus formed by mixing food with saliva, is easier and safer to swallow (Lund 1991; Mishellany et al. 2006; Prinz and Lucas 1997). Chewing increases the release of flavor and aromatic molecules that enhance the aroma and taste of food. In addition, the masticatory system is also involved in several other vital functions including respiration (Hasegawa et al. 2009), digestion and speech. Besides, there is compelling evidence, mainly from animal studies, indicating that chewing increases the cortical blood flow, particularly to the prefrontal cortex and hippocampus. Chewing may thus play a substantial role in improving subjective alertness, working memory, and cognition; for reviews, please see (Azuma et al. 2017; Ono et al. 2010; Weijenberg et al. 2019; Weijenberg, Scherder, and Lobbezoo 2011). Therefore, an impaired masticatory system will result in impaired chewing, which may have adverse effects on

multiple bodily functions (Nakata 1998; Miquel, Aspiras, and Day 2018).

Although chewing and swallowing processes have been extensively studied, their coordination during eating has been overlooked (Yamashita, Sugita, and Matsuo 2013). Studies suggest that poor masticatory performance due to removable dentures contributes to impaired swallowing function in older individuals (Son et al. 2013; Monaco et al. 2012). The absence of dentures in edentulous individuals may alter the anatomical structure and functional movement of the pharynx resulting in poor bolus transport (Yamamoto et al. 2013). However, it has been shown that people with higher masticatory performance do not necessarily swallow their food after fewer chewing strokes than those with lower masticatory performance (Gonçalves et al. 2021). Subsequently, it has also been reported that people with poor chewing performance do not necessarily swallow food morsels after fewer chewing cycles or poorly prepared blouses (Gonçalves et al. 2021; Homsí et al. 2021). Therefore, there is a greater need for studies investigating the precise relationship between chewing and swallowing functions.

The role of mastication in the digestive process has not received adequate attention from medical and dental

Table 1. PECO criteria for inclusion and exclusion of studies.

	Inclusion criteria	Exclusion criteria
Population (P)	Adults and older individuals Edentulous and/or dentulous Healthy and/or not healthy With or without different medical conditions	Children below 18 years
Exposition (E)	Chewing, mastication, physical breakdown of food Direct objective assessment of chewing function or chewing/ eating intervention or intentional/deliberate change in chewing behavior	Self- or proxy-assessed (indirect) masticatory function Subjective assessments measured by questionnaires and interviews evaluating the status of dentition, prosthesis use, and eating behavior
Comparison (C)	Healthy cohort, younger/older participants. Control condition without chewing intervention of condition.	No restrictions/exclusions were applied based upon presence/ absence of comparator groups.
Outcomes (O)	Bolus formation and properties, swallowing threshold, and dysphagia Gastric emptying, gastric hormones, pathological conditions of the gastrointestinal tract Nutritional status, body mass index, micronutrient concentrations, body composition, malnutrition	No direct relationship between chewing intervention and outcome No clear finding related to chewing and outcome Effect of gum chewing on postoperative ileus and recovery of the bowel function after cesarean section
Studies design (S)	Randomized control trials Prospective cohort Prospective observational study with/without comparison group Cross sectional study with or without comparison group English-language studies	All reviews (narrative or systematic), meta-analysis, opinion pieces. Study protocols, conference abstracts, letters to editors, commentaries, preprints. Case reports, invitro, and animal studies. Articles published in languages other than English Article not published in peer-reviewed journals

researchers. It is believed that impaired chewing function affects the oral bacterial flora and increases the risk of gastrointestinal pathologies (Tosello et al. 2001). Fragments of food that are too large to be digested completely can result in bacterial overgrowth in the colon which may lead to indigestion, bloating and constipation (Mercier and Poitras 1992; Ghoshal, Shukla, and Ghoshal 2017). Loss of (molar) teeth decreases the trituration ability, resulting in delayed gastric emptying and impaired digestive function (Hattori, Mito, and Watanabe 2008). Efficient chewing affects gut signaling and ultimately digestive and absorptive processes (Li et al. 2011). Hence, mastication and swallowing not only prepare food to safely pass from the oral cavity to the esophagus but also aid in the subsequent events that occur in the stomach (Kimura et al. 2006).

Impaired chewing function may also be an important contributing factor to malnutrition (Marshall et al. 2002; Mann, Heuberger, and Wong 2013). Edentulous or partially edentulous individuals have been shown to consume significantly lower amounts of fruits and vegetables compared to individuals with a natural dentition (Joshiyura, Willett, and Douglass 1996). Fiber-rich foods are probably more difficult for them to chew. Due to chewing difficulties older individuals may be particularly vulnerable to nutritional deficiencies because they subsequently exclude high-fiber foods from their diet. A significant association has been demonstrated between impaired chewing ability, food avoidance, and digestive distress in the older adults (Altenhoevel et al. 2012). Thorough mastication has been shown to affect postprandial plasma glucose concentrations and increase the absorption of key nutrients (Suzuki et al. 2005). As a result of impaired chewing function, chewed food may have varying physical characteristics, which may affect swallowing function, digestion kinetics, and nutritional status (Grundy et al. 2015).

Although the process of chewing, swallowing, digestion, and absorption of nutrients processes have all separately

been extensively studied, little attention has been given to how they inter-relate. Furthermore, the specific role of chewing on swallowing, digestion, and nutrition related parameters is not clearly evident. Hence, the current systematic review was designed to evaluate the available literature regarding the hypothesis that chewing is a mechanical and physiological “contributor” to the swallowing process, to physiologic/pathologic processes of the gastrointestinal tract (GIT), and to nutrition-related factors, in adult humans.

Material and methods

The current systematic review was performed in accordance with the revised guidelines set forth by Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 (Page et al. 2021). The protocol for the review was registered a priori on the International prospective register of systematic reviews PROSPERO: ID = CRD42018112209.

Search strategy

The current systematic review evaluated original, cross-sectional, clinical cohort, and randomized clinical trials (RCTs) in humans investigating the effects of chewing or physical breakdown of food on swallowing or bolus formation, digestion kinetics, and associated physiologic or pathologic processes of the GIT, and nutritional absorption or other nutrition-related parameters. The Population, Exposure, Comparator, and Outcomes (PECO) was defined as “in adult humans, does chewing function affect the swallowing function, physiologic/pathologic processes of the GIT, and nutrition-related factors compared to controls with no (or other) exposure.” Table 1 provides a detailed explanation of the inclusion exclusion criteria based on PECO.

All publications were searched, identified, and selected from three databases, Medline (OVID), Embase (Elsevier),

and the Cochrane Library (Wiley). A comprehensive search strategy was planned and applied on 08.09.2018, revised on 07.07.2021 and updated on 16.03.2022 by a team of experienced librarians (see acknowledgments). A detailed description of the search strategy and the MeSH/search terms used for the systematic searches are presented in supplementary file, [Supplementary Table 1A–C](#). There were no restrictions according to the date of publication, but only English-language studies were included. An additional manual search of gray literature with Google Scholar was conducted using free text terms such as chewing and “digestion,” “chewing and gastrointestinal,” and “chewing and nutrition.” Furthermore, references of included studies were also searched for potentially eligible studies through cross-referencing.

Study selection

All the studies identified through the systematic search were imported to the Rayyan web application for systematic reviews (Ouzzani et al. 2016). After the removal of the duplicates, two authors assessed the titles and abstracts of the publications for eligibility. The studies were included if the relationship between direct objective assessment of chewing function (Gonçalves et al. 2021) or chewing intervention/exposure and one of the measures of swallowing function, physiologic/pathologic processes of the GIT, or nutrition-related factors were presented. The authors categorized all the articles into “included,” “excluded” and “undecided.” All undecided articles were further included or excluded after mutual discussion to consensus. The inter-rater agreement between the two reviewers in excluding or including the studies was assessed using the Intraclass Correlation Coefficient (two-way mixed model with absolute agreement). The results showed good inter-rater agreement (0.793, 95% CI [0.722–0.845], P value < 0.0001). Further, full texts of all the publications published from inception that met or appeared to meet the inclusion criteria were retrieved. All reviews (narrative or systematic), meta-analysis, study protocols, conference abstracts, letters to editors, opinion pieces, commentaries, case reports, invitro, and animal studies were excluded. Further, studies were only included if the chewing function was objectively assessed (i.e., measured chewing performance or chewing efficiency) or if there was an intentional/deliberate change in chewing behavior or similar interventions/exposures. Studies investigating self- or proxy-assessed (indirect) masticatory function (e.g., bite force) (Gonçalves et al. 2021) or other subjective assessments measured by questionnaires and interviews evaluating the status of dentition, prosthesis use, and eating behavior, were excluded.

Data extraction and quality assessment

Data extraction was independently performed by three authors (A.K., N.A. and J.J.M.) using customized tables specifically created for the current study. The information about the authors, year, study design, study participants, or participant groups (sample size, age, and sex), intervention/

exposure, outcome, major results and conclusions and remarks (if any) were extracted from each study. All selected studies were further evaluated with the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Analytical cross-sectional, cohort, and randomized clinical trials. The purpose of this appraisal is to assess the methodological quality and to determine whether the possibility of bias has been taken into consideration in the design, conduct, and analysis of this study. Accordingly, the included studies were assessed for study quality addressing the risk of bias by two authors (NA and MT). Cumulative scores were calculated by adding the positive responses to the questions in the instrument for each study. Based on the percentage of the cumulative scores of each study, the included studies were rated as high (80%–100%), moderate (60%–79%) or low (less than 60%) quality. The certainty of evidence was assessed with the Grading of Recommendations Assessment Development and Evaluation (GRADE) approach (Guyatt et al. 2008).

Results

The systematic search strategy using the search terms ([Supplementary Table 1](#)) yielded 10,855 publications and 6,982 after removing the duplicates. All the publications were imported to the Rayyan web application for systematic reviews (Ouzzani et al. 2016) and the abstracts and titles of all the eligible publications were carefully read. In total, 523 publications were shortlisted and selected for evaluation of their full texts according to the study objectives. Screening of the full text of the publications led to the exclusion of 452 studies because they did not comprehend the study objectives. Further four more articles, identified through cross-referencing, were added to the final list leading to a total of seventy-one articles eligible for the systematic review. The PRISMA flowchart used to guide the selection of the studies is presented in [Figure 1](#). Out of the seventy-one publications, sixty-two were cross-sectional studies, four cohort studies, and five randomized control trials. Studies were further divided into the effect of chewing on the swallowing process (24 studies), physiologic/pathologic processes in the GIT (10 studies), and nutrition-related factors (37 studies), based on their outcomes. An overview of the data extraction and quality assessment of each study is presented in [Table 2](#).

Characteristics of included publications

Although the methods used to measure chewing function, swallowing, digestion, and nutrition-related factors differed in most publications, there were certain similarities that are described below.

Intervention/exposure: chewing assessment methods

Masticatory performance was objectively (direct) assessed by either food comminution, mixing ability, swallowing threshold or other objective chewing tests (Gonçalves et al.

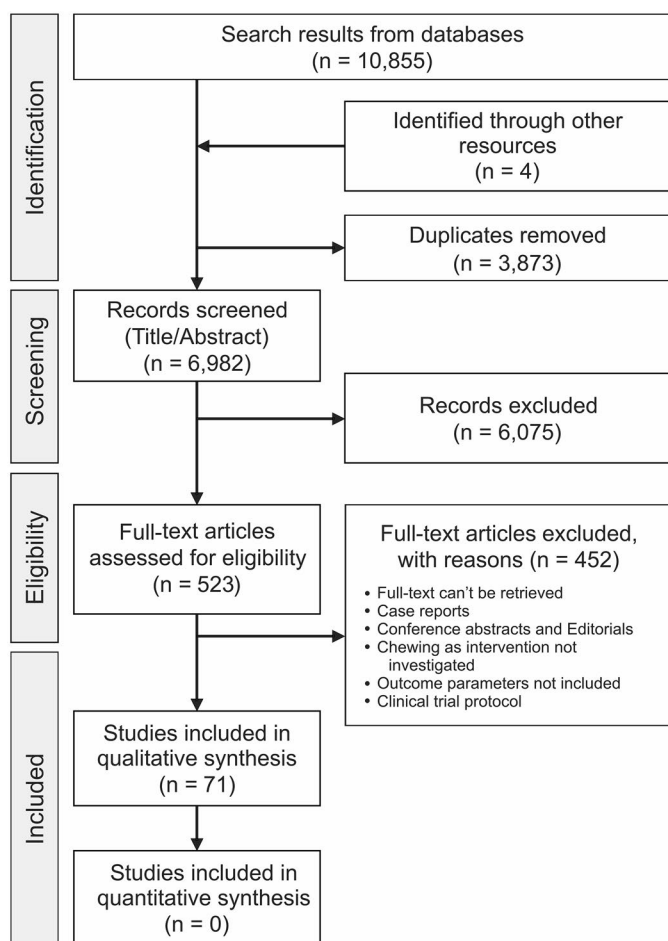


Figure 1. PRISMA flow diagram showing the screening and study selection.

2021). Specifically, studies calculated the median particle size distribution of natural and edible test food such as peanuts (Hattori, Mito, and Watanabe 2008), almonds (Cassady et al. 2009) carrots (Leischker, Kolb, and Felschen-Ludwig 2010; Lucas and Luke 1986), ham (Pera et al. 2002), chicken (Sumonsiri et al. 2019) gummy jelly (Iwasaki et al. 2022a), representative inedible test food such as Optosil/Optocal tablets (Engelen, Fontijn-Tekamp, and van der Bilt 2005; Sierpinska et al. 2007; Carretero et al. 2011; Flores-Orozco et al. 2016; Isabel et al. 2015; Sanchez-Ayala, Campanha, and Garcia 2013; Campos, Goncalves, and Rodrigues Garcia 2014; Goncalves, Campos, and Garcia 2015; Amaral et al. 2019; Flores-Orozco et al. 2020) or chewing gums (Magara et al. 2022). Masticatory performance was also objectively assessed by color-changing chewing gums (Furuya et al. 2014; Wada, Goto, et al. 2017; Koike et al. 2013; Okada et al. 2010; Kimura et al. 2013; Bayram et al. 2021; Motokawa et al. 2021; Saksono et al. 2019), two colors chewing gum mixing test (Müller et al. 2013; Liedberg et al. 2007; Wallace et al. 2018; Liedberg et al. 2004; Aquilanti et al. 2020; Medeiros et al. 2020; de Medeiros et al. 2021), or by estimating the glucose in the supernatant liquid collected by washing the chewed pieces of a standardized candy in water (Son et al. 2013; Fujimoto et al. 2020; Takeshima, Fujita, and Maki 2019; Ohta et al.

2022; Nishi et al. 2022; Sawada et al. 2021; Karawekpanyawong et al. 2022; Onuki et al. 2021).

Chewing as the intervention was investigated by asking edentulous participants to eat with and without dentures (Yamamoto et al. 2013) or by experimentally shortening the dental arches (Hattori, Mito, and Watanabe 2008). Interventions in normal chewing were performed by eating food (Idris et al. 2021) of a different type (Ranawana, Henry, et al. 2010), size (Goto et al. 2015), consistency (Suzuki et al. 2005; Kohyama et al. 2007; Saitoh et al. 2007; Berretin-Felix et al. 2009; Kim and Han 2005; Pennings et al. 2013; Dubey and Nundy 1984) or chewing duration (Lucas and Luke 1986; Kochi et al. 2021).

Some studies reported the effect of intentional/deliberate changes in the chewing behavior by asking the participants to either chew the test food naturally or with a conscious effort (with volition) (Furuya et al. 2014) or to chew and spit out the food after a certain chewing duration (Maeda et al. 2020). Similar intentional changes in the chewing behavior were done by asking the participants to eat the test food naturally or deliberately change the number of chewing strokes (Ono et al. 2007; Fukatsu et al. 2015; Abe and Tsubahara 2011; Zhu and Hollis 2014a, 2014b; Arya et al. 2017; Madhu et al. 2016) or chewing rate/speed before swallowing (Suzuki et al. 2005; Kokkinos et al. 2010; Goh, Chatonidi, et al. 2021; Goh, Choy, et al. 2021; Paphangkorakit et al. 2019; Hamada and Hayashi 2021).

Outcome measures swallowing assessment methods

The effects of chewing on the swallowing process were investigated in twenty-four original research studies, including twenty-three cross-sectional studies (Yamashita, Sugita, and Matsuo 2013; Son et al. 2013; Yamamoto et al. 2013; Lucas and Luke 1986; Engelen, Fontijn-Tekamp, and van der Bilt 2005; Magara et al. 2022; Furuya et al. 2014; Bayram et al. 2021; de Medeiros et al. 2021; Takeshima, Fujita, and Maki 2019; Onuki et al. 2021; Goto et al. 2015; Kohyama et al. 2007; Saitoh et al. 2007; Kim and Han 2005; Kochi et al. 2021; Maeda et al. 2020; Fukatsu et al. 2015; Mioche, Bourdiol, and Monier 2003; Matsuno et al. 2017; Abe, Furuya, and Suzuki 2011; Fontijn-Tekamp et al. 2004; Wada, Kawate, et al. 2017) and one cohort study (Berretin-Felix et al. 2009). Videofluorography/endoscopy was the most common method to assess swallowing function (Yamashita, Sugita, and Matsuo 2013; Son et al. 2013; Yamamoto et al. 2013; Furuya et al. 2014; Saitoh et al. 2007; Fukatsu et al. 2015; Abe, Furuya, and Suzuki 2011; Matsuno et al. 2017). Swallowing threshold (Medeiros et al. 2020; de Medeiros et al. 2021) or oral transit time was assessed by counting the number of chewing strokes until swallowing while eating a standardized portion of test food (Son et al. 2013; Lucas and Luke 1986; Campos, Goncalves, and Rodrigues Garcia 2014; Takeshima, Fujita, and Maki 2019; Kim and Han 2005; Fontijn-Tekamp et al. 2004). Swallowing movement has also been monitored by an array of pressure sensors and sound detected from microphones connected to an amplifier (Kohyama et al. 2007). Further the effect of chewing (gum)

Table 2. Summary of the included studies.

ID	Authors (year)	Study design	Study group (N, age, sex)	Comparison group (if applicable)	Intervention /exposure (Chewing)	Outcome measurement	Results	Study quality
Effect of chewing on swallowing								
1	Saitoh, Shibata (Saitoh et al. 2007)	Cross-sectional	N = 15 Age = 30 ± 5.2 yrs. Sex: 6 women		Chew and swallow food with 4 different consistencies	Video fluorography of 4 stages of swallowing The duration of each stage was calculated.	Chewing reduced the effectiveness of the posterior tongue-palate seal, allowing oral contents to spill into the pharynx. Consuming foods with both solid and liquid phases increase the risk of aspiration in dysphagic individuals Higher EMG for the hard meat and more saliva in the spitted bolus than tender meat.	High
2	Mioche, Bourdiol (Mioche, Bourdiol, and Monier 2003)	Cross-sectional	N = 25 Age = 25-30 yrs. Sex: 11 Women		Chewing two samples of meat (hard and tender) for 7s and spitting them. EMG for masseter and temporalis muscle was recorded.	Meat samples were weighed before and after chewing to determine weight changes due to saliva incorporation and the release of meat juice		High
3	Berretin-Felix, Machado (Berretin-Felix et al. 2009)	Cohort	N = 15 Age = 60-76 yrs. Sex: 10 Women	Pre-tx (removable denture) and post-tx 3, 6, and 18 months after implant overventure tx	Chewing ability (interview) and chewing/swallowing of water, paste, and hard consistencies. Chewing cycles and bolus formation evaluated	Subjective evaluation Swallowing: Lip seal, bolus propulsion duration, oral food residue, and amplitude of laryngeal elevation	Patients reported more masticatory and swallowing disturbances before tx as compared to after tx. Swallowing of liquids is not affected in the removable denture, but bolus propulsion of solid foods was affected before tx and improved after tx.	Moderate
4	Fukatsu, Nohara (Fukatsu et al. 2015)	Cross-sectional	N = 33 Age = 25.6 ± 3.5 yrs. Sex: 20 women		Eating 5g of cooked rice (white and green; 3 trials) in the usual manner or chewed well. Chewing cycles were counted. 3 volumes (0.5, 1, and 2) of 3 foods: boiled rice, fish sausage, and peanuts. Spitted at 50%, 100% or 120% chewing	Videoescopy to evaluate swallowing. Food bolus was graded subjectively into 3 categories. Physical properties of solidity, adhesiveness, and cohesiveness were measured in the bolus	The grinding of the swallowed food bolus increases with the increase in chewing cycles. The number of chews significantly increased with an increase in the mouthful volume for all of the foods. No change in bolus properties	High
5	Goto, Nakamich (Goto et al. 2015)	Cross-sectional	N = 15 Age = 20.2 ± 0.54 yrs. Sex = all women,					Moderate
6	Kim and Han (Kim and Han 2005)	Cross-sectional	N = 10 (Stroke patients) Age 50-82 yrs. Sex: 5 Women	N = 10 Healthy controls Age = 51-75 yrs. Sex: 5 women	Chew different pudding, thick rice gruel, curd-type yogurt, and liquid barium. Spit before swallowing. Also, chewing and swallowing thick rice gruel.	Food bolus viscosity (spit food). Also, chewing time and the number of chews was counted for the Thich rice gruel.	No differences in food bolus viscosity. But stroke patients used more chewing cycles and chewing time than healthy individuals.	Moderate

(Continued)

Table 2. (Continued).

ID	Authors (year)	Study design	Study group (N, age, sex)	Comparison group (if applicable)	Intervention /exposure (Chewing)	Outcome measurement	Results	Study quality
7	Kohyama, Sawada (Kohyama et al. 2007)	Cross-sectional	N = 15, Age = 20-42 yrs. Sex: All women		The participants ate 2 cubes of standard rice cake (6 and 9 g), and a modified cylindrical rice cake for the older adults (9 g).	Swallowing was measured by EMG of suprahyoid muscle, laryngeal movement, and swallowing sound.	Food size and texture affected chewing behavior but not swallowing behavior. Swallowing was induced whenever the food bolus was ready for swallowing.	High
8	Matsumoto, Nohara (Matsumoto et al. 2017)	Cross-sectional	N = 30 Age = 73.7 ± 6.3 yrs. Sex: 14 women	N = 30 Age = 25.6 ± 3.5 yrs. Sex: 19 women	Participants ate 5 g of cooked rice (white and green). Chewing cycles were counted.	Videofluoroscopy to evaluate swallowing. Food bolus was graded subjectively into 3 categories.	Old adults showed similar food mixing and grinding scores to young adults, but with longer chewing cycles and lower food bolus aggregation scores.	Moderate
9	Abe, Furuya (Abe, Furuya, and Suzuki 2011)	Cross-sectional	N = 10 27.1 ± 1.7 yrs. Sex: 5 women		Rice cake cubes (2 green layers and one white layer in between) eaten in two ways: usual or well-chewing and under 4 restricted chewing cycles (10, 15, 20 or 30 cycles).	Videofluoroscopy to evaluate swallowing. Food bolus was evaluated with the bolus formation index (BFI) (ratio of nonwhite rice pixels to the total food bolus pixels)	The BFI score increased with the increase in chewing times and cycles. BFI scores also increased with the well-chewing than usual chewing.	Moderate
10	Yamashita, Sugita (Yamashita, Sugita, and Matsuo 2013)	Cross-sectional	N = 25 Age = 20-37 yrs. Sex: 10 women		Participants ate 7 g of gummy jelly (3 trials). Number of chewing cycles pre- and post-stage II food transport.	Videofluoroscopy to determine the onset of stage II food transport (bolus aggregation on the oropharynx).	The number of chewing cycles for pre-stage II transport was significantly higher than that for post-stage II transport. Bolus aggregation in the pharynx is related to the number of chewing strokes	High
11	Son, Seong (Son et al. 2013)	Cross-sectional	N = 20 (edentulous) Age = 73.3 ± 11.4 yrs. Sex: 10 Women	Measurements before and after the removal of the removable denture	Chewing performance was measured with chewing soft candy (30 cycles; with dentures only) then the particles were dissolved in water and the glucose contents were analyzed and categorized into: 0%—25%, 25%—50% and ≥50%.	Videofluorography of swallowing a mixture of younger and water-soluble barium. Food bolus oral and pharyngeal transit times, food residue, and aspiration.	Wearing dentures delayed the oral transit time of food bolus. Aspiration and food residue did not differ with or without wearing the dentures.	Moderate
12	Yamamoto, Furuya (Yamamoto et al. 2013)	Cross-sectional	N = 15 (edentulous) Age = 78 ± 5.6 yrs. Sex: 11 women	Measurements before and after the removal of the removable denture	10 g of minced agar jelly (with barium) was ingested with and without dentures (3 times each).	Videofluorography of 4 swallowing stages: 1- oral cavity, 2- upper oropharynx, 3- valleculae, and 4- hypopharynx. Duration of each stage was calculated.	Swallowing onset without dentures was delayed, with poorer food bolus aggregation. With dentures, food transit time was shorter than without dentures.	Moderate

Table 2. (Continued).

ID	Authors (year)	Study design	Study group (N, age, sex)	Comparison group (if applicable)	Intervention /exposure (Chewing)	Outcome measurement	Results	Study quality
13	Furuya, Hara (Furuya et al. 2014)	Cross-sectional	N = 25 Age = 27.6 ± 2.9 yrs. Sex: 8 women	With or without volition.	Masticatory performance was evaluated by color-changeable chewing gum.	Solid agar jelly (with barium) was ingested with or without volition (3 times each). Videofluorography of 4 swallowing stages: 1- oral cavity, 2- upper oropharynx, 3- valleculae, and 4- hypopharynx. Duration of each stage was calculated.	With volition, the food chewing and the onset of swallowing were delayed than without volition. However, chewing with volition showed faster transport of food bolus transport with swallowing.	Moderate
14	Engelen, Fontijn-Tekamp (Engelen, Fontijn-Tekamp, and van der Bilt 2005)	Cross-sectional	N = 266 Age = 42 ± 12 Sex: 187 women		Communication test Optical plus 15 chewing strokes Besides, participants also chewed carrot, peanut, and cheese.	Swallowing threshold	The chewing performance showed small, but significant correlations with the swallowing thresholds of the relatively hard to chew products Hard and dry products require more chewing cycles and longer time in mouth until swallowing	Moderate
15	Fontijn-Tekamp, Slagter (Fontijn-Tekamp et al. 2004)	Cross-sectional	N = 87 Age = 41.6 ± 12 Sex: 62 Women		Median particle sizes (X50) for Optocal Plus after 15 chewing strokes and at the moment of swallowing Swallowing threshold tests were performed with peanuts, carrots, and cheese	Swallowing threshold	The number of chewing strokes for bolus preparation correlated significantly with the size of food. Food with suitable texture for swallowing was positively associated with masticatory efficiency.	High
16	Wada, Kawate (Wada, Kawate, et al. 2017)	Cross-sectional	N = 100 Age ≥ 65 Sex: 67 Women		Color-changeable chewing gum 120s of chewing	Food bolus texture at the swallowing threshold	With larger portion sizes, subjects needed significantly more chewing strokes and time until swallowing.	Moderate
17	Bayram, Ilgaz (Bayram et al. 2021)	Cross-sectional	N = 55 older participants with dysphagia	62 older participants without dysphagia	Mixing ability test Color-changeable chewing gum	Dysphagia risk evaluated by Eating Assessment Tool (EAT-10).	Poor oral health and decreased masticatory performance are directly associated with dysphagia and may lead to a decrease in ADL	Low

(Continued)

Table 2. (Continued).

ID	Authors (year)	Study design	Study group (N, age, sex)	Comparison group (if applicable)	Intervention /exposure (Chewing)	Outcome measurement	Results	Study quality
18	Maeda, Takei (Maeda et al. 2020)	Cross-sectional	N=29 Age= 29.6±6.8 Sex= 14 women		Chew the food in their usual manner and then spit it out at 50%, 100% and 150% of chewing duration, In the swallowing test, participants were asked to chew the food in the same manner and then to swallow at 50%, 100% and 150% of chewing duration, cued by the investigator	Bolus analysis done to measure rheological properties such as hardness, adhesiveness, and cohesiveness	Hardness, cohesiveness, and adhesiveness changed with increasing the number of chewing cycles but not the adhesiveness at least changed with chewing duration.	High
19	Lucas and Luke (Lucas and Luke 1986)	Cross-sectional	N=35 Age = 18-41 (median 21 years)	6 participants with partial dentures Age (41-74) mean 60	Chew and spit food varying numbers of chews and median particle size calculated	Number of chews needed to swallow the food sample	Within the limitations of the study the no. of chews before swallow was correlated with median particle size in dentate individuals	Moderate
20	Takeshima, Fujita (Takeshima, Fujita, and Maki 2019)	Cross-sectional	N = 120	Group 1: primary dentition N=20, Age= 5.68±0.68 Sex: 10 girls Group 2: early mixed dentition N=20 Age = 7.75±0.96 Sex = 10 girls Group 3: late mixed dentition stage N=20 Age = 10.40±1.09 10 females, Group 4: permanent dentition N=20, age, 16.50±2.25 years Sex: 10 women, Group 5 permanent dentition (n=40), age= 25.05±2.89 20 women	Communion text Concentration of dissolved glucose obtained from a cylindrical shaped (diameter, 15 mm; height, 8 mm) gummy jelly consisting of 40% maltose	Participants were instructed to chew until feeling the desire to swallow Number of chewing cycles and chewing duration to the onset of swallowing was recorded	Swallowing threshold did not coincide with masticatory performance according to dental formula stage	High

Table 2. (Continued).

ID	Authors (year)	Study design	Study group (N, age, sex)	Comparison group (if applicable)	Intervention /exposure (Chewing)	Outcome measurement	Results	Study quality
21	Kochi, Takei (Kochi et al. 2021)	Cross sectional	N = 24 adults Age= 29±6.1 Sex: 10 women		Chew 8 g of steamed rice and spit it out at 50%, 100% and 150% of their own chewing duration, defined as the time of chewing from onset of the first chewing cycle to onset of the first swallow	Bolus properties, i.e., hardness, cohesiveness, and adhesiveness as well as water content of the bolus were measured	Bolus hardness decreased, and the cohesiveness and water content of the bolus did not change up to 50% of chewing duration followed by a slight but significant increase Variation of chewing duration and swallowing initiation was not dependent on bolus properties during the chewing of steamed rice, but mainly depended on the surface lubrication of the bolus There was a significant negative correlation between time and hardness, and positive correlations between time and cohesiveness, and adhesiveness and between time and water content The masticatory performance and swallowing threshold were not correlated.	High
22	Medeiros, Figueredo (de Medeiros et al. 2021)	Cross-sectional	N = 179 Age: 78.9 ± 9.0 years Sex: 119 women		Mixing ability test with two-colored chewing gum	Swallowing thresholds were evaluated by asking them to chew a 3.7-g portion of unsalted roasted peanuts		High
23	Magara, Onuki (Magara et al. 2022)	Cross-sectional	N = 20 healthy subjects Age= 28.1 ± 3.2 years Sex= 10 women		Freely chewing gum for three min	Repeated swallowing 1 ml of water (at 36 °C) delivered to the posterior dorsal tongue using an infusion catheter	Masticatory movement may suppress swallowing related activity within the pharyngeal motor circuit	High
24	Onuki, Magara (Onuki et al. 2021)	Cross-sectional	209 patients median age, 72 years (69.0–77.0); 128 women)		Comminution test Masticatory performance evaluated by estimating the glucose concentration after chewing gummy jellies with Gluco sensor device	Dysphagia screening questionnaire	Deterioration of swallowing function was related to reduced occlusal force and decreased masticatory performance	High
Effect of chewing on physiologic/pathologic processes of the GIT								
25	Hattori, Mito (Hattori, Mito, and Watanabe 2008)	Cross-sectional	N = 13 Age range = 20–21 yrs. Sex: All men	With or without splint (on separate days, 7 days in between)	Comminution test 3 g of peanut (20 cycles) Mandibular intraoral appliance covering the teeth anterior to the second premolars	Gastric emptying rate measured by ¹³ C-octanoic acid breath test after a solid test meal	Chewing performance decreased with the splint. No change in gastric emptying with or without the splint.	High

(Continued)

Table 2. (Continued).

ID	Authors (year)	Study design	Study group (N, age, sex)	Comparison group (if applicable)	Intervention /exposure (Chewing)	Outcome measurement	Results	Study quality
26	Sierpinska, Golebiewska (Sierpinska et al. 2007)	Cross-sectional	N = 40 (Dyspeptic patients with a suspected masticatory deficiency), Age = 24–65 yrs. Sex: 18 women	N = 40 (Dyspeptic patients without masticatory deficiency), Age = 24–70 yrs. Sex: 17 women	Comminution test (Optosil tablets chewed for 20, 40, 60, and 80 chewing strokes).	Histopathologic changes of gastric mucosa and severity of Helicobacter pylori infection scored according to Sydney Classification of Chronic Gastritis.	Reduced masticatory efficiency was associated with more severe chronic inflammatory changes and Helicobacter pylori infection of the gastric mucosa.	Moderate
27	Arya, Agarwal (Arya et al. 2017)	Cross-sectional	N = 12 (Diagnosed with GERD) Age = 44.6 ± 11.6 Sex: 7 women		Chewing normal Vs increasing the chewing cycles 20 times or until the food becomes a puree.	48-hour pH monitoring DeMeester score	An increase in chewing cycles did not influence the DeMeester score significantly.	Moderate
28	Kimura, Nomura (Kimura et al. 2006)	Cross-sectional	N = 30 (Tubal feeding without mastication and swallowing) Age = 74 ± 4.3 Sex: 24 women	N = 30 Ingested food with mastication and swallowing) Age = 77.2 ± 6.1 Sex: 18 women	Ingestion of 250 ml of a liquid diet.	Before and 30 min after ingestion, the electrogastrography (for gastric motility) and abdominal ultrasonography (for gastric emptying) were measured.	Gastric motility increased for both the groups, but the ratio of the increase was lower in the tube-fed group than in controls. Gastric excretion was lower in tube-fed individuals than controls.	Moderate
29	Pera, Bucca (Pera et al. 2002)	Cross-sectional	N = 12 Age range = 8–35 yrs. Sex: 3 women		Comminution test Evaluated by chewing ham for 50 cycles and passed through a sieve.	Solid meal consists of egg with 100 mg sodium octanoate, ham (21 g), crackers (25 g), and water (500 ml). Eaten with 50 cycles in one session, while in another session only the egg and crackers chewed for 25 cycles and swallowed the ham.	Masticatory performance was inversely related to both lag phase and gastric half-emptying time. Both lag phase and gastric half-emptying time were shorter during 50 chewing cycles than 25 chewing cycles.	Moderate
30	Penning, Groen (Penning et al. 2013)	Cross-sectional	N = 10, Age = 74 ± 2 yrs. Sex: all men		Participants consumed 135 g of L-[1- ¹³ C] phenylalanine-labeled beef both as beef steak and minced beef	Gastric emptying using the ¹³ C-octanoic acid breath test Lag phase and gastric half-emptying time were measured. Blood sample to evaluate postprandial protein kinetics and insulin and amino acid levels.	Minced beef is more rapidly digested than beef steak leading to increased amino acid availability and greater postprandial protein retention Does not result in greater postprandial muscle protein synthesis rates	Low

Table 2. (Continued).

ID	Authors (year)	Study design	Study group (N, age, sex)	Comparison group (if applicable)	Intervention /exposure (Chewing)	Outcome measurement	Results	Study quality
31	Koike (Koike et al. 2013)	Cross-sectional	N=11 (With malocclusion) Age= 25.5 ±4.8 yrs. Sex: all women	N=11 (With normal occlusion) Age= 26 ±5–1.0 yrs. Sex: all women	Masticatory ability was evaluated with questionnaires. Masticatory efficiency was measured with color-changeable gums.	Gastric emptying was assessed using a [13C]-labelled acetate breath test with a liquid meal Frequency scale for symptoms of gastroesophageal reflux disease (FSSG) Questionnaire on food intake	Masticatory function in patients with malocclusion was significantly lower than in subjects with normal occlusion No difference in the FSSG results between the two groups Malocclusion group showed lower CO2 excretion with a slower gastric emptying rate Masticatory performance of subjects presenting with dyspepsia and 0–4 occlusal pairs was significantly lower when compared to the control group.	Moderate
32	Carretero, Sanchez-Ayala (Carretero et al. 2011)	Cross-sectional	N=38, (Non-ulcerative functional dyspepsia) Age= 71.8 ±7.7 yrs. 16 women	N=38, (Healthy) Age = 71.9 ±7.0 15 women	Number of occluding teeth pairs and Communion test (Optosil 20 chewing strokes)	--	Masticatory performance of subjects presenting with dyspepsia and 0–4 occlusal pairs was significantly lower when compared to the control group.	High
33	Dubey, Nundy (Dubey and Nundy 1984)	Cross-sectional	22 patients with duodenal ulcer Age = 36 ±17	30 control subjects without any gastrointestinal disease	A masticatory and a non-masticatory (homogenized) meal having the same chemical composition.	Gastric acid secretion by intubation	No difference in the gastric acid response to a masticatory or a non-masticatory diet. However, a masticatory diet has a buffer capacity after ingestion which is significantly greater than that of a non-masticatory diet. Masticatory diets may play a part in protecting individuals from developing duodenal ulcer.	Moderate
34	Sumonsiri, Thongudomporn (Sumonsiri et al. 2019)	Cross-sectional	N=40 healthy subjects Age= 23.9 ±3.8 years Sex= 25 women		Food comminution test with chicken sausage cubes where participants chewed and expectorated the cubes after 30 cycles Median particle size was calculated by the multiple sieving method	Gastric emptying was measured by scintigraphy	No significant relationships between masticatory performance, and number of chewing cycles, and any parameter of gastric emptying scintigraphy using frankfurter sausage as a test food in healthy dentate subjects.	High
Effects of chewing on nutrition-related parameters								
35	Flores-Orozco, Tiznado-Orozco (Flores-Orozco et al. 2016)	Cross-sectional	N=100 Age = 21.9 Women 47		Comminution test (Optosil tablets chewed for five trials with 20 cycles/trial).	Anthropometric measurements and blood samples were collected.	No relation between masticatory performance and any nutritional status indicator	Moderate

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Table 2. (Continued).

ID	Authors (year)	Study design	Study group (N, age, sex)	Comparison group (if applicable)	Intervention /exposure (Chewing)	Outcome measurement	Results	Study quality
36	Okada, Enoki (Okada et al. 2010)	Cross-sectional	N = 200 Age 76.6±7.1 yrs. Sex: 122 women		Masticatory performance was measured with color-changeable gums.	Anthropometric measurements and blood samples were collected.	Serum albumin concentrations were well-correlated with chewing performance and anthropometric measurements	Moderate
37	Leischker, Kolb (Leischker, Kolb, and Felschen-Ludwig 2010)	Cross-sectional	N = 31 Age ≥70 yrs. Sex: 13 women		Comminution test (Standardized slices of carrots chewed for 45s)	MNA, anthropometric measurements, and more extensive blood samples were collected.	The nutritional status was higher in patients with a better chewing function, but these correlations were not significant.	Low
38	Kimura, Ogawa (Kimura et al. 2013)	Cross-sectional	N = 269 Age = 80.6±4.7 yrs. Sex: 181 Women		Masticatory efficiency was measured with color-changeable gums. Chewing ability A questionnaire was used for self-assessment of chewing. Comminution test (Optosil tablets chewed 20 cycles)	The 11-item Food Diversity Score Kyoto (FDSK-11).	Participants with low chewing performance had lower food variety and less frequent intake of beans, vegetables, seaweed, and nuts.	Low
39	Isabel, Moysés (Isabel et al. 2015)	Cross-sectional	N = 160, Age = 17.8-34.3 yrs. Sex: 80 Women		Mixing ability test (Two colored chewing gum chewed 10 strokes, 3 times) Chew an almond until swallowing	BMI	Chewing parameters did not differ between different BMI groups.	High
40	Liedberg, Stoltze (Liedberg et al. 2007)	Cross-sectional	N = 481, Age = 67-68 yrs. Sex: All men		Chewing ability (Interviews for self-assessment of chewing)	Nutritionist used dietary history interview by Steen at al. BMI, 24-hour urinary nitrogen excretion.	No significant differences between those with adequate or inadequate nutrition were found regarding chewing performance, including self-assessed chewing. Inadequate dietary habits were associated with high BMI.	High
41	Wallace, Samietz (Wallace et al. 2018)	Randomized controlled clinical trial	N = 44 (RDPD) Age = 79.7 ± 5.41 yrs. Sex: 23 Women	N = 45, (SDA) Age = 79.6 ± 6.4 Sex: 20 women	Mixing ability test Two colored chewing gum chewed 20 cycles	MNA and blood samples at baseline and 12 months post-treatment.	Masticatory performance and MNA increased significantly in both groups with no significant differences between the groups.	Moderate
42	Zhu and Hollis (Zhu and Hollis 2014b)	Randomized crossover design	N = 45 Age = 20.9-27.1 yrs. Sex: 25 Women	Normal = N = 16 Overweight N = 16. Obese N = 15	Pizza chewed 100%, 150%, or 200% of the normal number of chews	Weighing the plate before and after serving	Nutritional status could not be predicted from the masticatory performance. Food intake was reduced significantly by increasing the number of chews. Meal duration was prolonged, eating rate reduced but subjective appetite the same.	Low
43	Zhu and Hollis (Zhu and Hollis 2015b)	Cross-sectional	N = 64 Age = 20.9-25.4 yrs. Sex: 39 Women		Consumed five portions of pizza rolls	BMI	Negative correlation between body mass index and the number of chewing cycles Chewing behavior is associated with body weight status in fully dentate healthy adults	High

Table 2. (Continued).

ID	Authors (year)	Study design	Study group (N, age, sex)	Comparison group (if applicable)	Intervention /exposure (Chewing)	Outcome measurement	Results	Study quality
44	Ranawana Viren, Henry (Ranawana, Henry, et al. 2010)	Randomized non-blind	N = 11 Age = 18-65 yrs. Sex: 8 Women		Consumed rice or spaghetti on six nonconsecutive days, each food tested on 3 random days	Fasting blood samples at -5, 0 minutes before consumption and at 15, 30, 45, 60, 90, and 120 minutes after.	Significant correlations between the degree of breakdown during mastication and the GR were observed for rice, but none for spaghetti. 40 chews compared to 10 and 25 chews, induced more satiety and higher PYY and GLP-1 levels but not ghrelin, glucose, or insulin levels	Low
45	Cassady, Hollis (Cassady et al. 2009)	Randomized crossover trial	N = 13 Age = 19-43 yrs. Sex: 5 Women		Comminution test 5 g of raw almonds chewed 10, 25, or 40 times before swallowing	Particle sieving and stool samples were collected. Blood glucose, insulin, plasma lipids, ghrelin, PYY, and GLP-1 at 15, 30, 45, 60, 90, 120, and 180 min after almond consumption.		Low
46	Campos, Goncalves (Campos, Goncalves, and Rodrigues Garcia 2014)	Cross-sectional	N = 8 Age: 60.1 ± 6.6 yrs. Sex: 6 Women	RPD before and after implant support (2 months interval)	Comminution test measured with Optocal.	Swallowing threshold and subjective nutrient intake.	Smaller particle size and improved subjective nutrient intake with the implant, compared to no implant.	Moderate
47	Müller, Duvernay (Müller et al. 2013)	Randomized clinical trial	N = 16 IOD group: Age = 85.0 ± 6.19 yrs.	CD group: 18, 84.1 ± 5.55 yrs.	Maximum bite force Masticatory performance with a two-color mixing ability test	MNA and blood samples (hemoglobin, albumin, folic acid, vitamin B12, and C-reactive protein) at baseline, 3- and 12-months post-treatment.	IOD compared to CD, had higher bite force but no differences in masticatory performance or MNA or blood markers.	Moderate
48	Suzuki, Fukushima (Suzuki et al. 2005)	Cross-sectional	N = 10 Type2 diabetes: Age = 44.1 ± 4.4 yrs. Sex = 2 women	Control: 16, 7 F; 9 M, 35.6 ± 2.1 yrs.	Chewing and eating 130g hamburger steak and 100g rice in the "usual" manner and "thoroughly"	Plasma glucose and serum insulin concentrations were measured for 3 hours postprandially	Thorough mastication in subjects with type 2 diabetes elicited a higher postprandial plasma glucose concentration Postprandial plasma glucose concentration was lower during thorough mastication in controls	High
49	Kokkinos, le Roux (Kokkinos et al. 2010)	Cross-sectional	N = 17 Age = 29.7 ± 1.2 Sex: All men		Eating ice cream fast (5 min) vs slow (30 min)	Blood glucose, insulin, plasma lipids, ghrelin, PYY, and GLP-1	Eating slowly induced more satiety and higher PYY and GLP-1 levels but not ghrelin, glucose, or insulin levels	Moderate
50	Zhu, Hsu (Zhu, Hsu, and Hollis 2013)	Cross-sectional	N = 21 Age = 18-40 yrs. Sex: all men		Consumed equal-sized portions of pizza either in 15 or 40 chewing cycles.	Appetite was determined subjectively. Blood sample to evaluate satiety-related hormones, glucose, insulin, and GIP concentrations.	Subjective hunger and desire to eat were lower during the 40 cycles than 15 cycles. Glucose, insulin, and GIP concentrations were higher with 40 than 15 cycles.	High

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Table 2. (Continued).

ID	Authors (year)	Study design	Study group (N, age, sex)	Comparison group (if applicable)	Intervention /exposure (Chewing)	Outcome measurement	Results	Study quality
51	Wöstmann, Michel (Wöstmann et al. 2008)	Cross-sectional	N=47 Age = 72.6±6.7 Sex: 28 women		Chew a standardized cube of carrot (45 seconds) and degree of breakdown evaluated	MNA and Albumin, pre-albumin and zinc	Despite an improvement in masticatory ability and efficiency, no change in nutritional status particularly albumin, zinc, and MNA values remained unchanged	Moderate
52	Goncalves, Campos (Goncalves, Campos, and Garcia 2015)	Cross-sectional	N=12 Age = 62.6±7.8 Sex: 8 women		Communion test with Optocal until swallow	Nutritional intake measured by dietary dairies and BMI	Efficient mastication as a result of Implant-supported fixed partial prosthesis improves dietary intake	Low
53	Liedberg, Norlén (Liedberg et al. 2004)	Cohort	N=44 FPDs Age = 67–68 Sex: All men	N=40 RPDs Age = 67–68 Sex: All men	Chewing gum color mixing and bolus-shaping Almonds used to record the swallowing threshold	Body mass index and Participants interviewed for the choice of food	Chewing gum bolus differed between the two groups No changes in energy intake and nutrients or body mass index between the groups	High
54	Sanchez-Ayala, Campanha (Sanchez-Ayala, Campanha, and Garcia 2013)	Cross-sectional	N=100 Age = 39.7±16.6 Sex: 67 Women		Comminution test The participants chewed Optosil cubes for 20 chewing cycles	Patients were weighed on a scale arm bascule determine body fat BMI	Lower masticatory efficiency maybe at risk for increased body fat	High
55	Amaral, Souza (Amaral et al. 2019)	Cross-sectional	N=12 Age = 68.6±5.2 years 8 women		40 cycles of Optocal mastication performed	Computerized dietary tables were used to evaluate intake of energy	Improved masticatory performance after participants with conventional complete dentures were rehabilitated with single-implant overdentures. Intake of nutrients remains the same except sodium ingestion, which was decreased.	High
56	Aquilanti, Alia (Aquilanti et al. 2020)	Cross-sectional	N=76 Age: 75.8±5.6 Sex: 34 women		Two-color mixing test	Qualitative and a quantitative food interview to assess nutritional status	No association between reduced masticatory performance and a worsening of nutritional parameters or bioimpedance parameters such as Impedance, Resistance, Phase Angle and Reactance	High

Table 2. (Continued).

ID	Authors (year)	Study design	Study group (N, age, sex)	Comparison group (if applicable)	Intervention /exposure (Chewing)	Outcome measurement	Results	Study quality
57	de Medeiros, Pinheiro (Medeiros et al. 2020)	Cross-sectional	N= 344 Older adults Age= 77.7 ±9.1 Sex: 206 Women		Masticatory performance using two-color chewing gum	Swallowing threshold evaluated while eating peanuts Mini-Nutritional Assessment—Short Form Body composition was assessed by a bioelectrical impedance analysis	Nutritional status and body composition of institutionalized older adults was not correlated with their poor masticatory performance and swallowing threshold. Worse masticatory performance and swallowing threshold negatively impacted the OHRQoL.	High
58	Flores-Orozco, Pérez-Rodríguez (Flores-Orozco et al. 2020)	Cross-sectional	N= 100 non-indigenous population Age= 21.9 Sex: 53 women	N=42 indigenous population Age =40years Sex: 31 women	Chewing 2g of silicon for 20 cycles. Tablets of Optosil (5 mm thick, 20 mm in diameter) (Optosil P Plus ®)	Weight, height, and body circumferences were recorded	No relation between any aspect of masticatory function (masticatory performance, masticatory laterality, and chewing rate) and nutritional status indicator was detected in the indigenous group	High
59	Fujimoto, Suito (Fujimoto et al. 2020)	Cross-sectional	N=153 Age= 75.3 ±6.5 year 47 Women		Comminution text with gummy jelly and glucose concentration in the supernatant liquid collected by washing the chewed pieces was measured	Body height and weight were self-reported in participant interviews and were subsequently used to calculate the BMI for assessing the nutritional status	BMI not associated with objective masticatory efficiency*	High
60	Motokawa, Mikami (Motokawa et al. 2021)	Cross-sectional	N=509 community-dwelling older 294 women		Mixing ability text Color-changeable chewing gum	BMI blood serum albumin values Food Frequency Questionnaire	Chewing performance was related to nutrient and food group intake among community-dwelling older adults After adjusting for BMI, the chewing ability was significantly related to undernutrition	High
61	Paphangkorakit, Kanpittaya (Paphangkorakit et al. 2019)	Cross-sectional	N=30 Age range= 20–24 yr, 20 women		Participants were asked to eat a meal and chewing rate was calculated	BMI	Neither chewing rate nor the number of chews per mouthful was correlated with BMI.	Moderate
62	Saksono, Hijryana (Saksono et al. 2019)	Cross-sectional	N= 158 Age = 67 117 women	Two groups based on the Eichner Index A2–B3 (with at least one posterior support zone) (n = 114) and Eichner Index B4–C3 with no posterior support zone) (n = 44)	Color-changeable chewing gum	Mini-Nutritional Assessment (MNA) Food-frequency questionnaire (FFQ)	Despite significant differences between masticatory performance no significant differences in nutrition intake*	Moderate

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Table 2. (Continued).

ID	Authors (year)	Study design	Study group (N, age, sex)	Comparison group (if applicable)	Intervention /exposure (Chewing)	Outcome measurement	Results	Study quality
63	Iwasaki, Motokawa (Iwasaki et al. 2022b)*	Cohort	N = 715 adults Age = ≥65 years Sex: 436 women		Comminution test Chew gummy jelly for 30 strokes. The degree of comminution evaluated compared to a visual reference scored on a scale of 0 to 9.	MNA	7-component oral hypofunction (which includes masticatory performance in food comminution test) phenotype contributed to the increase in the odds of the presence and severity of malnutrition	High
64	Madhu, Shirali (Madhu et al. 2016)	Cross-sectional	N = 100 Normoglycaemic 37.9 ± 14.2 Sex = 43 Women	N = 100 Dysglycaemic 56.74 ± 11.78 Sex = 44 Women	Chew test food normally and chew 40 times	fasting and post-prandial blood sugar values estimated	Postprandial blood glucose concentration upon thorough mastication was significantly lower, due to early-phase insulin secretion in Normoglycaemic group	Low
65	Goh, Chatonidi (Goh, Chatonidi, et al. 2021)	Cross-sectional	Slow chewers N = 24 Age = 26.0 ± 4.2 Sex = all men	Fast chewers N = 15 Age = 27.3 ± 4.6 Sex = all men	Participants classified into Slow chewers/eaters' Fast chewers eaters based on chewing rate	Bolus and saliva properties Post-prandial glucose response	Eating rate, oral exposure time and saliva uptake were shown to be the main contributors to an increase in post-prandial glycemic responses in slow eaters.	High
66	Goh, Choy (Goh, Choy, et al. 2021)	Cross-sectional	Slow chewers N = 15 Age = 48.1 (8.8) Sex = women	Fast chewers N = 15 Age = 43.0 (9.5) Sex = 3 women	Participants with higher risk for type 2 diabetes classified into Slow chewers and Fast chewers based on chewing rate	Bolus and saliva properties Plasma glucose, insulin, and satiety measures	Increased chews per bite and a longer oral sensory exposure, led to increased bolus particle surface area and greater saliva uptake and were associated with higher PP glucose, PP insulin and satiety responses.	High
67	Ohta, Imamura (Ohta et al. 2022)*	Cross-sectional	Sixty patients Age = 82.5 ± 7.0 Sex: 38 women		Comminution test Masticatory performance evaluated by estimating the glucose concentration after chewing gummy jellies with Gluco sensor device	Nutritional risk was screened using the Mini-Nutritional Assessment Short Form (MNA-SF) Nutritional Risk Screening (NRS) scores Malnutrition was assessed according to the Global Leadership Initiative on Malnutrition (GLIM) criteria	Oral hypofunction that included masticatory function correlated with nutritional risk, evaluated by the MNA-SF and Nutritional Risk Screening score	High
68	Nishi, Ohta (Nishi et al. 2022)*	Cross-sectional	117 women 73, mean age: 50 ± 7 years		Comminution test Masticatory performance evaluated by estimating the glucose concentration after chewing gummy jellies with Gluco sensor device	Multi-frequency bioelectrical impedance analysis (MF-BIA)	No association between masticatory performance and nutritional status.	High

Table 2. (Continued).

ID	Authors (year)	Study design	Study group (N, age, sex)	Comparison group (if applicable)	Intervention /exposure (Chewing)	Outcome measurement	Results	Study quality
69	Sawada, Takeuchi (Sawada et al. 2021)	Cross-sectional	203 Age = 74.0 (70.0, 79.0) 150 women		Comminution test Masticatory performance evaluated by estimating the glucose concentration after chewing gummy jellies with Gluco sensor device	Mini Nutritional Assessment	Masticatory function was not associated with national status	High
70	Karawekpanyawong, Nohno (Karawekpanyawong et al. 2022)	Cross-sectional	N = 84 Sex: 45 women		Comminution test Masticatory performance evaluated by estimating the glucose concentration after chewing gummy jellies with Gluco sensor device	Brief-Type Self-Administered Diet History Questionnaire, Body mass index (BMI) assessments	Masticatory performance <173 mg/dL had lower intake of folic acid and vitamin A than those with masticatory performance \geq 173 mg/dL Lower masticatory performance, lower SF and fewer teeth were associated with a lower intake of several micronutrients, such as vitamin A, β -carotene, and folic acid	High
71	Hamada and Hayashi (Hamada and Hayashi 2021)	Cross-sectional	N = 11 Healthy participants Age = 23 \pm 1 years		Participants chewed 20-mL test drink for 30s at a frequency of once per second, and then swallowed it	Gas-exchange variables, DIT, and substrate oxidation.	Oral stimuli (i.e., the duration of tasting food in the mouth and the duration of chewing) increase DIT	Moderate

GIT: gastrointestinal tract; Tx: treatment; MNA: mini nutritional assessment; BMI: body mass index; RDPD: removable partial dental prosthesis; SDA: shortened dental arch; GR: glycemic response; GERD: gastroesophageal reflux disease; GIP: glucose-dependent insulintropic peptide; GLP-1: glucagon-like peptide; PYY: peptide YY; IOD: implant overdenture; CD: complete removable denture; IBS: irritable bowel syndrome; ADL: activities of daily living; EMG: electromyography; Co2: carbon dioxide; OHRQoL: Oral Health Related Quality of Life; DIT: diet induced thermogenesis.
*Partial finding.

on swallowing-related neural pathways were also studied by transcranial magnetic stimulation (Magara et al. 2022).

Boluses preparation during swallowing was assessed by evaluating the amount of saliva incorporated and mechanical properties of the food bolus (Kochi et al. 2021; Fukatsu et al. 2015; Goh, Chatonidi, et al. 2021; Goh, Choy, et al. 2021; Mioche, Bourdiol, and Monier 2003; Matsuno et al. 2017; Wada, Kawate, et al. 2017). Evaluation was performed either by visual inspection of the spat-out food (Berretin-Felix et al. 2009) or by fiberoptic endoscopic evaluation/video endoscopy of swallowing movements (Yamamoto et al. 2013; Furuya et al. 2014; Goto et al. 2015; Saitoh et al. 2007; Fukatsu et al. 2015; Matsuno et al. 2017; Abe, Furuya, and Suzuki 2011). The criteria for boluses inspection during endoscopy were grinding, mixing, and aggregation of the food bolus (Yamashita, Sugita, and Matsuo 2013; Kochi et al. 2021; Fukatsu et al. 2015; Matsuno et al. 2017). Boluses were also evaluated for solidity, adhesiveness, and cohesiveness (Kochi et al. 2021; Maeda et al. 2020) by the force-time graph obtained from a creep meter (Goto et al. 2015). Further, dysphagia risk was evaluated by the Eating Assessment Tool (EAT-10) (Bayram et al. 2021) and Dysphagia screening questionnaire (Onuki et al. 2021).

Physiologic/pathologic processes of the GIT and assessment methods

The effect of chewing on physiologic/pathologic processes of the GIT was investigated in ten cross-sectional studies (Hattori, Mito, and Watanabe 2008; Kimura et al. 2006; Pera et al. 2002; Sierpiska et al. 2007; Koike et al. 2013; Dubey and Nundy 1984; Arya et al. 2017; Pennings et al. 2013; Carretero et al. 2011; Sumonsiri, Thongudomporn, and Paphangkorakit 2018). The effect of chewing on gastric emptying was assessed by a [¹³C]-labeled acetate breath test (Hattori, Mito, and Watanabe 2008; Pera et al. 2002; Koike et al. 2013), abdominal ultrasonography (Kimura et al. 2006) and scintigraphy (Sumonsiri et al. 2019). The effect of chewing on gastric acid secretion (Dubey and Nundy 1984), and pathologic processes of the GIT was measured by DeMeester score to assess for Gastroesophageal Reflux Disease (GERD) (Arya et al. 2017) and the frequency scale for symptoms of gastroesophageal reflux disease (FSSG) (Koike et al. 2013). Histopathologic changes of gastric mucosa and severity of *Helicobacter pylori* infection were scored according to the updated Sydney Classification of Chronic Gastritis (Sierpiska et al. 2007). Studies have also evaluated chewing function in clinically diagnosed groups of non-ulcerative functional dyspepsia (Carretero et al. 2011).

Nutrition-related parameters

In general, nutrition status is assessed using energy balance indicators, resulting in undernutrition and overweight. Variables such as body weight, body mass index (BMI), body composition, change in blood glucose concentration, and level of certain minerals (e.g., Fe, Mg) in tissue fluids are suggested to be good indicators of nutrition. Accordingly, the effect of chewing on nutrition-related factors was

investigated in thirty-seven studies with twenty-nine cross-sectional (Leischker, Kolb, and Felschen-Ludwig 2010; Iwasaki et al. 2022a; Isabel et al. 2015; Sanchez-Ayala, Campanha, and Garcia 2013; Campos, Goncalves, and Rodrigues Garcia 2014; Flores-Orozco et al. 2020; Okada et al. 2010; Motokawa et al. 2021; Saksono et al. 2019; Liedberg et al. 2007; Liedberg et al. 2004; Aquilanti et al. 2020; Medeiros et al. 2020; Fujimoto et al. 2020; Ohta et al. 2022; Nishi et al. 2022; Sawada et al. 2021; Karawekpanyawong et al. 2022; Madhu et al. 2016; Kokkinos et al. 2010; Goh, Chatonidi, et al. 2021; Goh, Choy, et al. 2021; Paphangkorakit et al. 2019; Hamada and Hayashi 2021; Flores-Orozco et al. 2016; Kimura et al. 2013; Zhu and Hollis 2015b; Zhu, Hsu, and Hollis 2013), three cohort (Suzuki et al. 2005; Goncalves, Campos, and Garcia 2015; Amaral et al. 2019; Wöstmann et al. 2008), and five RCT (Cassady et al. 2009; Müller et al. 2013; Wallace, McKenna, and Schimmel 2017; Zhu, Hsu, and Hollis 2014; Ranawana, Monro, et al. 2010) design studies. Anthropometric measurements such as BMI were studied in fourteen of the included publications (Leischker, Kolb, and Felschen-Ludwig 2010; Flores-Orozco et al. 2016; Isabel et al. 2015; Sanchez-Ayala, Campanha, and Garcia 2013; Flores-Orozco et al. 2020; Okada et al. 2010; Motokawa et al. 2021; Liedberg et al. 2007; Fujimoto et al. 2020; Karawekpanyawong et al. 2022; Idris et al. 2021; Zhu and Hollis 2014a; Paphangkorakit et al. 2019; Zhu and Hollis 2015a). Other measures of body composition such as body water percentage, body fat mass, muscle and bone mass (Flores-Orozco et al. 2016; Flores-Orozco et al. 2020; Medeiros et al. 2020; Nishi et al. 2022), and body weight and dimensions such as mid-upper-arm circumference, triceps skinfold, and grip strength were also recorded (Okada et al. 2010).

Nutritional status was screened by the mini nutritional assessment tool (MNA) to identify the risk of malnutrition (Leischker, Kolb, and Felschen-Ludwig 2010; Iwasaki et al. 2022a; Saksono et al. 2019; Müller et al. 2013; Medeiros et al. 2020; Ohta et al. 2022; Sawada et al. 2021; Wöstmann et al. 2008; Wallace, McKenna, and Schimmel 2017). Food and nutrient intake were assessed with a 24-hour recall survey method (Kwon et al. 2017), food frequency questionnaire (Motokawa et al. 2021; Saksono et al. 2019) or dietary interviews (Amaral et al. 2019; Liedberg et al. 2007; Aquilanti et al. 2020; Karawekpanyawong et al. 2022). In one study, food diversity was assessed by an 11-item Food Diversity Score Kyoto (FDSK-11) (Kimura et al. 2013). Another study monitored food intake by weighing food plates before and after they were served (Zhu and Hollis 2014a).

Blood samples were collected for analysis of nutritional parameters such as blood serum and albumin level (Suzuki et al. 2005; Cassady et al. 2009; Leischker, Kolb, and Felschen-Ludwig 2010; Flores-Orozco et al. 2016; Okada et al. 2010; Motokawa et al. 2021; Müller et al. 2013; Wallace et al. 2018; Pennings et al. 2013; Kokkinos et al. 2010; Zhu, Hsu, and Hollis 2013; Ranawana, Monro, et al. 2010). In particular, the level of blood glucose (Madhu et al. 2016), insulin, and Glucagon-like peptide-1 (GLP-1) and diet induced thermogenesis (Hamada and Hayashi 2021) was

evaluated at regular intervals of time (Suzuki et al. 2005; Ranawana, Henry, et al. 2010; Madhu et al. 2016). Nutrient absorption was also measured in terms of the concentration of gut hormones, insulin, and plasma concentrations of glucose/glucose-dependent insulinotropic peptide (Cassady et al. 2009; Goh, Chatonidi, et al. 2021; Goh, Choy, et al. 2021; Zhu, Hsu, and Hollis 2013). Other studies investigated the effect of chewing and swallowing on protein kinetics (Pennings et al. 2013), the plasma concentration of gut hormone (Zhu, Hsu, and Hollis 2013), and the postprandial response of the orexigenic hormone ghrelin and the anorexigenic peptides (peptide YY and glucagon-like peptide-1) (Kokkinos et al. 2010).

Quality assessments, narrative synthesis, and GRADE analysis

In total, thirty-six studies were rated as high quality (based on JBI criteria) with low risk of bias, twenty-six as moderate, and nine as low-quality studies with high risk of bias (Supplementary Table 2A-C). Studies with a common intervention/exposure and outcome variables were congregated (based on narrative synthesis) and the average score from the quality assessment (JBI criteria) for each congregated outcome was calculated. Thus, the quality assessment of the congregated outcome was based on the average score of the individual studies in the group. The cumulative representation of the intervention/exposure and the congregated outcome variables (swallowing process, physiologic/pathologic processes of the GIT, and nutrition-related parameters) are presented in Figure 2A-C.

It was hypothesized (as mentioned above) that chewing is an important mechanical and physiological contributor in the swallowing process, physiologic/pathologic processes of the GIT, and in nutrition-related parameters, in humans. Studies were considered to “support the hypothesis” if there was any change (increased or decreased) in the expression of the outcome measures (see, 3.1.2) obtained in the chewing intervention (see 3.1.1). Similarly, a study was adjusted as “refuting the hypothesis” if the chewing intervention did not result in a change in the outcome measures. The overall results of the narrative synthesis showed that 46 out of 71 (64.7%) studies supported the hypothesis. Only 25 (35.3%) studies refuted the hypothesis (Figure 3A). Specifically, the notion that chewing function contributes to either the swallowing process, the process of the GIT, or nutrition-related factors was supported by 19 out of 24; 6 out of 10; and 21 out of 37 investigations, respectively (Figure 3B).

The overall certainty of the evidence was evaluated with an adapted GRADE framework. The GRADE analysis was performed for the congregated outcomes consisting of a minimum of 3 studies (Please see circles marked with “#” in Figure 2A-C.) The evidence for specific outcomes were evaluated based on the study design, risk of bias, inconsistency, indirectness, and imprecision. The overall quality of evidence for all the congregated outcomes (Figure 2A-C) ranged from moderate to very low according to the GRADE criteria (see Table 3, A-C). The level of evidence was

downgraded due to limitations in study designs, imprecision (studies with small sample size), and inconsistency because of evident heterogeneity across populations, interventions/exposure, and indirectness.

Discussion

The current systematic review is a comprehensive analysis of the available literature on chewing as a mechanical and physiological contributor to swallowing and digestive process and nutrition-related factors in adults. The overall results of the current study showed that a majority of the studies (64.7%) supported the hypothesis to some degree. However, the GRADE analysis showed low to very low certainty of the evidence to support the hypothesis that chewing is an important mechanical and physiological contributor in the swallowing process, and in physiologic/pathologic processes in the GIT. Further, the grade analysis also showed a moderate to very low certainty of the evidence to suggest that chewing function contributes to nutrition-related parameters. The results of the study imply that impaired or improved chewing function may affect (impair or improve) swallowing function, digestive process, and nutrition-related parameters. However, more robust studies with proper design, adequate sample size, well defined outcome parameters and large effect size are needed to establish conclusive evidence.

Assessment of chewing function

Measuring chewing function is a challenging task, and various methods have been used to quantify chewing ability (subjective) and chewing efficiency/performance (objective). However, studies have often shown disagreements between subjective and objective measures of chewing function (Pedroni-Pereira et al. 2018; Aimajiang, Otomaru, and Taniguchi 2016). For example, in a study by Leischker et al., eighty-one percent of participants reported having no problems with chewing. However, objective tests showed that about 42% of participants were unable to adequately chew a carrot slice (Leischker, Kolb, and Felschen-Ludwig 2010). It has been argued that subjective assessment of chewing function in the older individuals provide “overly optimistic” results (Tada and Miura 2018). One reason could be that chewing impairment is a gradual process and people often do not recognize the difficulties at early stages. In addition, chewing impairment is often compensated by changing the eating habits and food preparation methods, either by overcooking foods or by avoiding hard-to-chew foods altogether (Pera et al. 2002). Therefore, in the current study it was decided to include the studies evaluating chewing efficiency/performance rather than subjectively evaluated chewing ability.

Consequently, in the current study different methods were used to quantify chewing function (see, intervention/exposure in results). Chewing function tests have primarily focused on the ability of the individual to comminute the test food to smaller pieces/particles or knead two plastic test foods into a bolus. While some studies have used natural foods for comminution tests others have used artificial

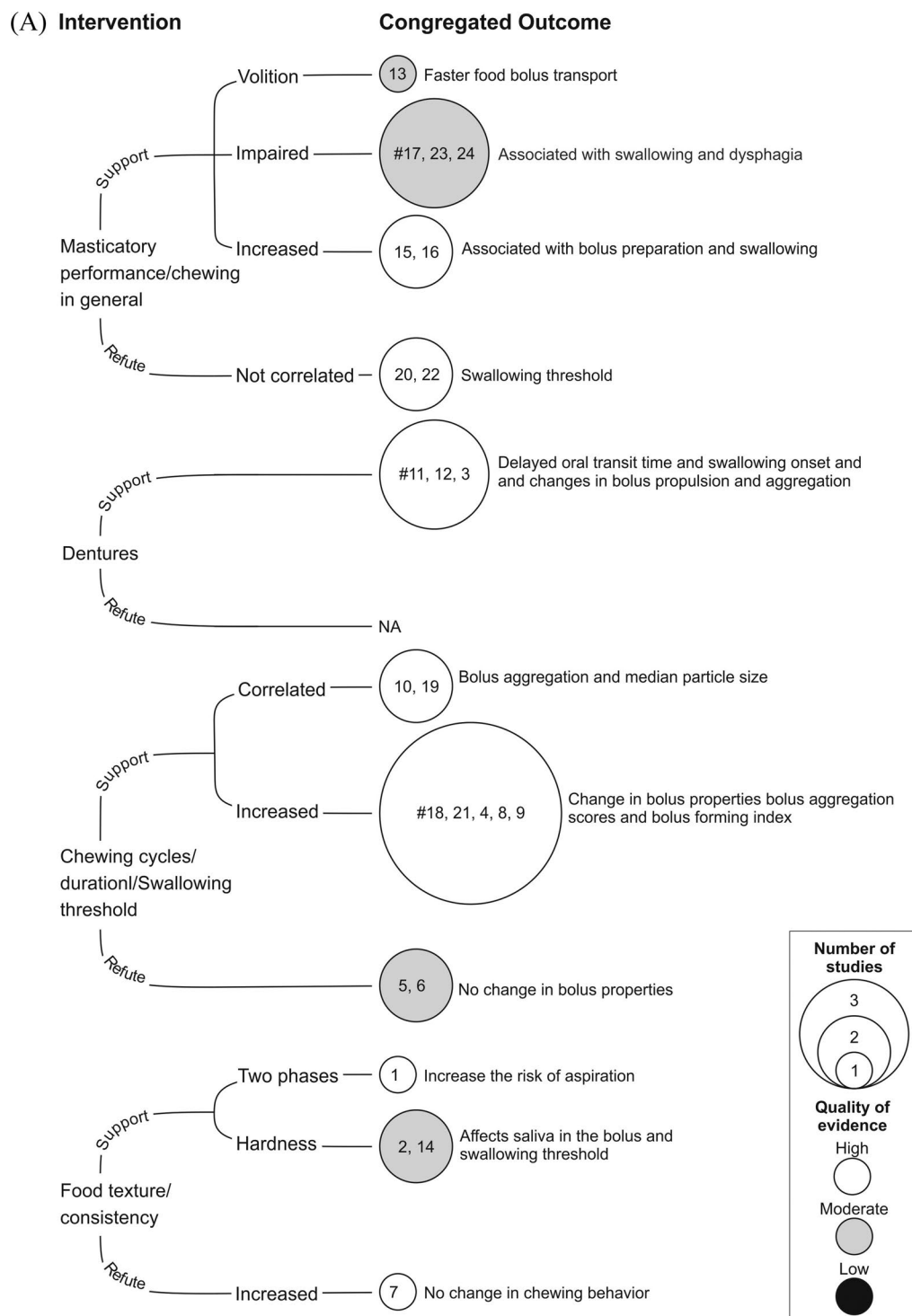


Figure 2. Diagram showing narrative synthesis based on quality assessment using the Joanna Briggs Institute Critical Appraisal Checklist for Analytical cross-sectional, cohort, and randomized clinical trials investigating if chewing is a mechanical or physiological contributor in the (A) process of swallowing, (B) physiologic/pathologic processes in the gastrointestinal tract, and (C) nutrition-related parameters. The interventions/exposure are classified into studies supporting and refuting the hypothesis. The common intervention and outcome parameters are grouped together to form the congregated outcomes. The size of the circles denotes the number of studies, and the color of the circles denote the quality of the congregated outcomes. The numbers in the circles denote the ID number from the studies in Table 1. Circles marked with “#” are assessed for certainty of evidence with the Grading of Recommendations Assessment Development and Evaluation (GRADE) approach.

or representative test foods. Although natural food has the obvious advantage of being normally consumed the texture and size may vary, influencing the quantification of masticatory performance (Isabel et al. 2015). Artificial test substances such as silicon based Optosil cubes (comminution

test), chewing gums, and molding waxes (mixing ability test) are also accepted to be good alternatives to standardize chewing tasks. However, chewing is a cumulative process of simultaneous food comminution/breakdown and mixing/lubrication of food with saliva (Prinz and Lucas 1997).

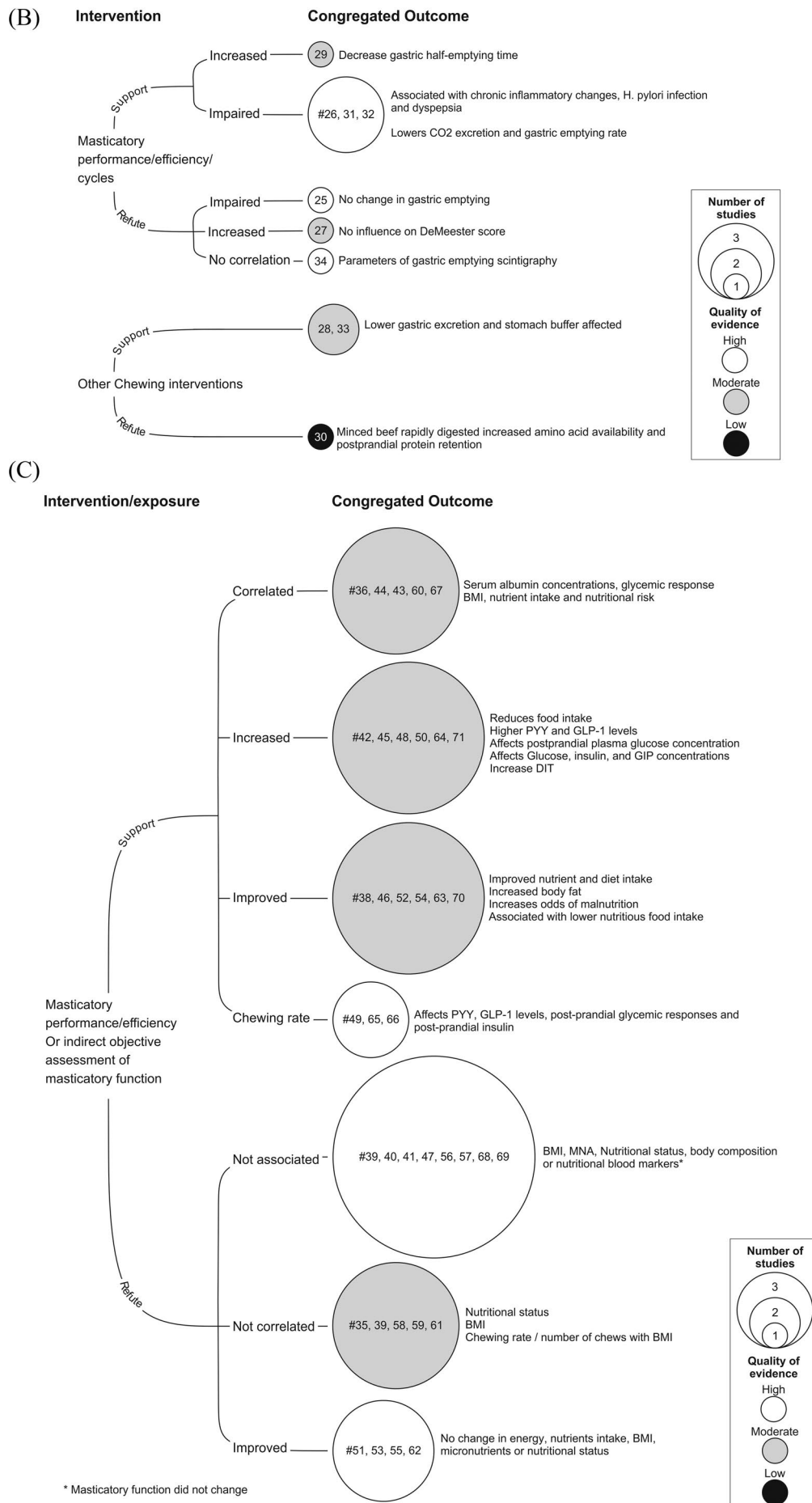


Figure 2. Continued.

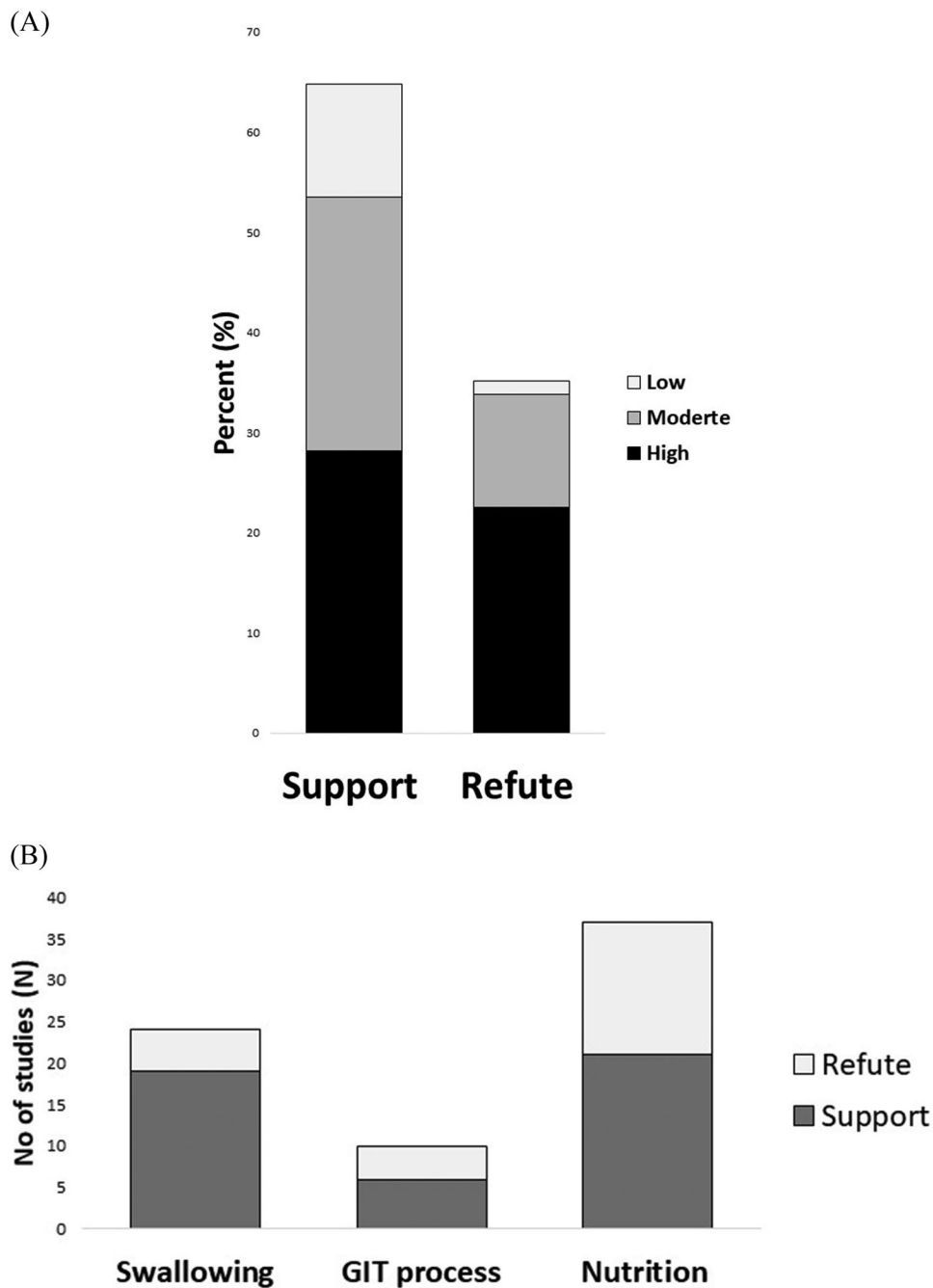


Figure 3. Bar graphs showing the overall A) number of studies (in percent) supporting and refuting the hypothesis that chewing is a mechanical or physiological contributor in the swallowing process, physiologic/pathologic processes of the gastrointestinal tract, and nutrition-related parameters. The different shades of the bars represent the methodological quality of the studies based on the Joanna Briggs Institute (JBI) Critical Appraisal Checklist. B) showing the number of studies (N) supporting and refuting the hypothesis.

Therefore, it is rational to assume that chewing function can be better quantified by considering the comminution, mixing, and preparation of boluses of test food with a different texture, hardness, or size, in accordance with the previous suggestions (van der Bilt 2011; Slagter et al. 1992).

Effect of chewing on swallowing

Chewing disintegrates the food morsels and with adequate help of the tongue and orofacial muscles, incorporates saliva (Mioche, Bourdiol, and Monier 2003) to form a bolus.

Swallowing, like chewing, is one of the most complex sensorimotor behaviors in humans. It was shown that volitional chewing during eating can expedite bolus transport, delay swallowing onset, and enable smooth bolus transit (Furuya et al. 2014). Studies have shown a positive correlation between the number of chewing strokes/cycles and the bolus forming index (Yamashita, Sugita, and Matsuo 2013; Abe, Furuya, and Suzuki 2011). Studies on food bolus analysis have shown higher grinding and mixing scores (Fukatsu et al. 2015) and better bolus aggregation in the pharynx (Yamashita, Sugita, and Matsuo 2013) in participants who exhibit a higher number of chewing cycles. The relationship

between food transport and swallowing initiation is influenced by chewing and the initial consistency and size of the food (Engelen, Fontijn-Tekamp, and van der Bilt 2005; Saitoh et al. 2007; Fontijn-Tekamp et al. 2004; Wada, Kawate, et al. 2017). A decrease in food volume per morsel has been suggested to increase the number of chewing strokes, resulting in appropriate bolus properties for swallowing (Goto et al. 2015). Impaired mastication is associated with dysphagia (Bayram et al. 2021) and causes impaired swallowing in stroke patients (Kim and Han 2005). These findings indicate that the greater the number of chewing strokes before swallowing, the better is the bolus formation and the swallowing function.

Older individuals are less capable of preparing boluses in comparison to younger (Matsuno et al. 2017). Feeding without dentures delays swallowing onset and also results in a significant delay of pharyngeal swallowing, despite a greater volume of food bolus penetrating the hypopharynx (Yamamoto et al. 2013). While removable dentures impair the masticatory performance and increase the oral transit time and oropharyngeal swallow efficiency (Son et al. 2013). Replacement of removable partial dentures with fixed implant-supported dentures results in improved chewing and subsequent swallowing function (Berretin-Felix et al. 2009). Further, improved chewing function also results in reduced bolus propulsion time and reduced oral residue once the bolus is transported from the oral cavity (Berretin-Felix et al. 2009). These studies indicate that chewing performance is indeed increased after oral rehabilitation and this, in turn, results in better swallowing function.

Although chewing is influenced by the size of the morsel and texture of the food these factors may (Saitoh et al. 2007; Maeda et al. 2020; Mioche, Bourdiol, and Monier 2003; Fontijn-Tekamp et al. 2004) or may not (Kohyama et al.

2007) affect swallowing function. The properties of the bolus such as hardness, cohesiveness, and adhesiveness change as the number of chewing cycles is increased or decreased (Kochi et al. 2021; Maeda et al. 2020; Fukatsu et al. 2015; Matsuno et al. 2017). However, studies have also suggested that bolus aggregation scores are independent of the chewing conditions (Saitoh et al. 2007; Fukatsu et al. 2015). The number of chewing cycles and swallowing threshold were similar in people with implant-supported partial dentures and people with conventional removable partial dentures, although the implant patients showed better masticatory performance in food comminution tests (Campos, Goncalves, and Rodrigues Garcia 2014). Masticatory performance did not coincide/correlate with swallowing threshold (de Medeiros et al. 2021) in a group of participants of different ages (Takeshima, Fujita, and Maki 2019). Video endoscopy during rice-eating showed that older adults required a greater number of chewing cycles but achieved lower bolus aggregation scores than younger controls (Matsuno et al. 2017). Bolus aggregation specifically does not seem to depend on the number of chewing cycles or whether the participants chewed food (rice) in a “usual” manner as compared to “chewed-well” (Fukatsu et al. 2015). It was also suggested that the urge to swallow food could be triggered by a threshold determined by the food particle size and the degree of lubrication of the food bolus (Prinz and Lucas 1995). It is therefore suggested that swallowing is perhaps induced when the bolus properties become suitable for swallowing. Healthy individuals are often capable of adjusting their chewing techniques according to the food texture and food volume (Kohyama et al. 2007). In the present study, although majority (N=19) of the studies supported the hypothesis and indicated that chewing function affects the swallowing process, the certainty of evidence was *very low*

Table 3. A. Question: Does chewing function affect or contribute to swallowing function

No. of studies	Study design	Risk of bias	Inconsistency	Certainty assessment			Bibliography
				Indirectness	Imprecision	Certainty	
Impaired masticatory function is associated with swallowing function and dysphagia[#]							
3	Cross-sectional	Serious	Very serious	Not serious	Not serious	⊕○○○ Very low	Magara et al. 2022; Bayram et al. 2021; Onuki et al. 2021
Chewing with dentures causes delayed oral transit time, swallowing onset and changes in bolus propulsion and aggregation[#]							
3	Cross-sectional (2) Cohort (1)	Not serious	Very serious	Serious	Serious	⊕○○○ Very low	Son et al. 2013; Yamamoto et al. 2013; Berretin-Felix et al. 2009
Increased chewing cycles/duration/swallowing threshold causes changes in bolus properties, bolus aggregation and bolus forming index[#]							
5	Cross-sectional	Not serious	Serious	Not serious	Serious	⊕⊕○○ Low	Kochi et al. 2021; Maeda et al. 2020; Fukatsu et al. 2015; Matsuno et al. 2017; Abe, Furuya, and Suzuki 2011

B. Question: Does chewing function affects or contributes to the physiologic/pathologic processes of gastrointestinal tract

No. of studies	Study design	Risk of bias	Inconsistency	Certainty assessment			Bibliography
				Indirectness	Imprecision	Certainty	
Impaired masticatory performance is associated with physiologic/pathologic processes of gastrointestinal tract[#]							
3	Cross-sectional	Not serious	Very serious	Serious	Very serious	⊕○○○ Very low	Sierpiska et al. 2007; Koike et al. 2013; Carretero et al. 2011

(Continued)

Table 3. (Continued)

C. Question: Does chewing function affects or contributes to nutrition-related factors

No. of studies	Certainty assessment					Certainty	Bibliography
	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision		
Masticatory function was correlated with nutrition-related factors**#							
5	Cross-sectional (4) Randomized control trials (1)	Serious	Very serious	Serious	Serious	⊕○○○ Very low	Okada et al. 2010; Motokawa et al. 2021; Ohta et al. 2022; Ranawana, Henry, et al. 2010; Zhu and Hollis 2015b
Increased masticatory function reduces food intake and affects postprandial glucose concentration and gut hormones***#							
6	Cross-sectional (4) Randomized control trials (2)	Serious	Very serious	Very serious	Very serious	⊕○○○ Very low	Suzuki et al. 2005; Cassady et al. 2009; Zhu and Hollis 2014a; Madhu et al. 2016; Hamada and Hayashi 2021; Zhu, Hsu, and Hollis 2013
Improved masticatory function results in improved diet and nutritional intake increased risk of fat and associated with malnutrition#							
6	Cross-sectional (5) Cohort (1)	Serious	Very serious	Serious	Serious	⊕○○○ Very low	Iwasaki et al. 2022a; Sanchez-Ayala, Campanha, and Garcia 2013; Campos, Goncalves, and Rodrigues Garcia 2014; Goncalves, Campos, and Garcia 2015; Karawekpanyawong et al. 2022; Kimura et al. 2013
Chewing rate affects expression of gut hormones***#							
3	Cross-sectional	Not serious	Not serious	Not serious	Serious	⊕⊕⊕○ Moderate	Goh, Chatonidi, et al. 2021; Goh, Choy, et al. 2021; Kokkinos et al. 2010
Masticatory function is not associated with BMI, nutritional status body composition or nutritional biomarkers#							
8	Cross-sectional (6) Randomized control trials (2)	Not serious	Serious	Not serious	Serious	⊕⊕○○ Low	Isabel et al. 2015; Müller et al. 2013; Liedberg et al. 2007; Wallace et al. 2018; Aquilanti et al. 2020; Medeiros et al. 2020; Nishi et al. 2022; Sawada et al. 2021; Zhu and Hollis 2014b
Masticatory function is not correlated with BMI and nutritional status#							
5	Cross-sectional	Serious	Not serious	Not serious	Not serious	⊕⊕⊕○ Moderate	Isabel et al. 2015; Flores-Orozco et al. 2020; Fujimoto et al. 2020; Paphangkorakit et al. 2019; Flores-Orozco et al. 2016
Improved masticatory function does not change the nutritional intake BMI or nutrition status#							
4	Cross-sectional (3) Cohort (1)	Not serious	Very serious	Very serious	Serious	⊕○○○ Very low	Amaral et al. 2019; Saksono et al. 2019; Liedberg et al. 2007; Wöstmann et al. 2008

#Congregated outcomes with 3 or more studies have been analyzed.

*Chronic inflammatory changes in the gastrointestinal tract, helicobacter infection, dyspepsia, lowers CO₂ excretion and gastric emptying.

**Serum albumin concentrations, glycemic responses, body mass index, nutrient intake, and nutritional risk.

***Gut hormones: peptide YY, glucagon-like peptide, post-prandial glycemic responses, and post-prandial insulin.

to low (GRADE criteria). Specifically, the grade assessment showed a *very low* certainty of evidence to support the finding that impaired masticatory performance is associated with swallowing and dysphagia and that chewing with dentures causes delayed oral transit time and changes in bolus propulsion and aggregation. Further there was also low

certainty of evidence to suggest that increased chewing cycles or duration or increasing the swallowing threshold causes changes in bolus properties (Table 3, A).

Overall, the included studies on sensorimotor regulation of swallowing behavior and dysphagia have largely focused on the pathophysiology of the pharyngeal phase and little

consideration has been given to the oral phase. The oral phase of food processing that involves the breakdown and mixing of food morsels with saliva can be an important determinant of swallowing thresholds and swallowing function (Kim and Han 2005). Thus, future studies on the pathophysiology of swallowing should also consider the oral phase.

Effect of chewing on digestion

Gut hormones play an essential physiological and pathophysiological role in regulating energy homeostasis. Ghrelin, an intestinal hormone responsible for regulating appetite, is affected by oral stimulation/mastication (Simonian et al. 2005). Therefore, mastication may play an important role in the gut hormone profile and consequently influence energy intake (Li et al. 2011). It has been suggested that decreased masticatory efficiency increases the functional load on the stomach and affects the function of the GIT system (Koike et al. 2013). The loss of molar teeth decreases the ability to triturate food and results in delayed gastric emptying and impaired digestive function (Hattori, Mito, and Watanabe 2008). Accordingly, a higher incidence of digestive complaints is reported in patients with subjective chewing problems and/or discomfort with dentures or ill-fitting dentures (Altenhoevel et al. 2012). A significant relationship has been demonstrated between chewing ability and the use of medications for gastrointestinal disorders or digestive complaints (Pera et al. 2002). In addition, chewing inefficiency was associated with a higher prevalence of irritable bowel syndrome in adolescents (Khayatzadeh et al. 2018). Hence, in the current study, it was reasonable to hypothesize that chewing is an important contributor to the normal physiological process of the GIT, and impaired chewing would potentially result in digestive distresses and associated problems.

Poor oral trituration has been associated with severe chronic inflammatory changes and *H. pylori* infection of the gastric mucosa in dyspepsia patients (Sierpinska et al. 2007). People with fewer occlusal pairs and decreased masticatory performance presented greater odds of being functional dyspeptics (Carretero et al. 2011). The gastric excretion function was significantly lower in a group of older individuals with tubal feeding (without chewing) in comparison to individuals who chewed and swallowed their food (Kimura et al. 2006). Further, foods that require chewing have a higher buffering capacity that could neutralize duodenal acidity than foods that do not require chewing (Dubey and Nundy 1984). In addition, a randomized controlled, clinical trial reported that minced beef was more rapidly digested and absorbed than beef steak in older adult men (Pennings et al. 2013). On one hand, an experimental increase in the number of chewing strokes from 25 to 50 chewing cycles appears to decrease gastric emptying time (Pera et al. 2002). On the other hand, reduction in food trituration caused by the shortening of the dental arch did not significantly affect gastrointestinal digestive function (Hattori, Mito, and Watanabe 2008). Further, prolonged mealtime (30 min) was associated with a more pronounced

anorexigenic gut peptide response than eating very fast (5 min) (Kokkinos et al. 2010). People with impaired chewing efficiency show a longer maximum ^{13}C exhalation time as determined by the ^{13}C -acetate breath test (Koike et al. 2013) and minced beef is digested more rapidly than beak steak (Pennings et al. 2013). Therefore, currently, it is not fully understood if mastication influences gastrointestinal functions. The prevalence of gastrointestinal disorders, especially the ones related to gastrointestinal motor dysfunctions, is high in older people and increases with aging (Dumic et al. 2019; Grassi et al. 2011). However, although majority (6 out of 10) of the included studies supported the hypothesis, yet the certainty of evidence based on GRADE analysis showed that there was a *moderate* to *very low* level of evidence to support and refute the hypothesis on different congregated outcomes (see Figure 2B and Table 3, B).

Effects of chewing on nutrition-related factors

Nutritional assessments are the prerequisites for interpretation of data that determines the nutritional status of an individual (or a group). In the current study, different methods were used for assessments of nutrition-related parameters. Compromised oral health and impaired chewing function are suggested to be important determinants of nutritional status. These determinants may influence the eating habits and the supply of key ingredients, especially in the older adults (Motokawa et al. 2021; Sheiham and Steele 2001). Previous studies have shown that chewing efficiency/performance influences food choices (Mioche, Bourdiol, and Peyron 2004) and, subsequently, dietary and nutrient intake, especially in older adults (Goncalves, Campos, and Garcia 2015; Motokawa et al. 2021). People with chewing difficulties tend to consume a lower amount of fruits and vegetables resulting in lower nutrients such as calcium (Kwon et al. 2017), potassium, and vitamin C, compared to controls (Kimura et al. 2013; Kwon et al. 2017). Further, community-dwelling older individuals with lower chewing efficiency tend to consume lesser food variety and lesser frequency of beans, vegetables, seaweeds, and nuts (Kimura et al. 2013). One study showed that the replacement of conventional removable partial dentures with fixed implant-supported dentures resulted in better masticatory performance and an increased protein, fiber, and carbohydrate intake (Campos, Goncalves, and Rodrigues Garcia 2014). Recently, a randomized control trial reported that nutritional status could be predicted from masticatory performance (Wallace et al. 2018). Further, it was suggested that oral hypofunction (which includes masticatory performance in food comminution tests) contributed to greater odds of presence and severity of malnutrition (Iwasaki et al. 2022b). Based on these findings, it was hypothesized that chewing function may also affect the nutrition status in adults.

BMI is one of the low-cost, easy to measure, and widely used indicators of nutritional status, nutritional risk, and obesity (Nuttall 2015). High correlations have been established between BMI, body fat, and morbidity and mortality

(Flegal et al. 2013; Kong et al. 2017). Negative correlations between BMI and the number of chewing cycles, and chewing duration have been reported (Zhu and Hollis 2015b). Studies have also shown significant associations between chewing function, body fat (Sanchez-Ayala, Campanha, and Garcia 2013), and anthropometric measurements (Okada et al. 2010). Masticatory efficiency was suggested to be a risk factor for increased body fat (Sanchez-Ayala, Campanha, and Garcia 2013). Underweight people were shown to chew slowly and more asymmetrically than normal weight or obese counterparts (Flores-Orozco et al. 2016). Chewing efficiency and swallowing threshold were significantly associated with BMI and people with higher BMI had higher scores of chewing performance (Isabel et al. 2015; Sanchez-Ayala, Campanha, and Garcia 2013). The reported correlations and associations potentially indicate that chewing function can influence BMI in accordance with the previous studies (Motokawa et al. 2021; Okubo et al. 2018; White et al. 2015).

Chewing function was reported to be a good predictor of serum albumin concentrations; an important biomarker of nutrition (Okada et al. 2010). The degree of mastication and chewing rate was shown to be significantly correlated with the glycemic response (Ranawana, Henry, et al. 2010; Goh, Chatonidi, et al. 2021), PP insulin and satiety responses (Goh, Chatonidi, et al. 2021). Thorough mastication affects the postprandial glucose concentration and absorption of nutrients (Suzuki et al. 2005; Madhu et al. 2016). The initial postingestive glucagon-like peptide-1 concentrations were also reported to be increased after chewing almonds for 40 strokes as compared to 25 strokes (Cassady et al. 2009). Similarly, it was reported that minced meat results in increased amino acid availability and greater postprandial protein retention but does not result in greater postprandial muscle protein synthesis rates (Pennings et al. 2013). Therefore, food texture including hardness is an important factor that influences not only the chewing behavior (Grigoriadis, Johansson, and Trulsson 2014; Grigoriadis et al. 2019; Grigoriadis and Trulsson 2018) but also the bolus formation (Engelen, Fontijn-Tekamp, and van der Bilt 2005; Saitoh et al. 2007; Mioche, Bourdiol, and Monier 2003), digestion (Pennings et al. 2013), and nutrition.

Contradictory to the above-mentioned findings it was shown that inadequate dietary intake was independent of dental status and both, masticatory ability, and performance (Liedberg et al. 2007). Studies have reported that neither chewing rate nor the number of chews per morsel were correlated with BMI (Paphangkorakit et al. 2019). Studies have also reported that masticatory performance (or improved masticatory performance) is not associated with nutritional status (Flores-Orozco et al. 2016; Amaral et al. 2019; Aquilanti et al. 2020), BMI (Flores-Orozco et al. 2020; Liedberg et al. 2007; Fujimoto et al. 2020) or body composition (Medeiros et al. 2020). There was no significant difference in energy and nutrients intake or BMI despite improved masticatory performance due to fixed dentures as compared to removable (Saksono et al. 2019; Liedberg et al. 2004). The postprandial plasma glucose concentration

was reduced with thorough mastication (Suzuki et al. 2005) although it could be anticipated that thorough mastication increases the plasma glucose concentration. Further, even though the hospitalized geriatric patients with acute diseases and with good chewing function had higher scores on the mini nutritional assessment (MNA) and had higher concentrations of vitamins and trace elements, yet there were no significant correlations. (Leischker, Kolb, and Felschen-Ludwig 2010). The authors also reported that patients with poor masticatory function tended to show lower (yet not significant) serum levels of Vitamin B1, Niacin, Vitamin C, Vitamin A, and Selenium (Leischker, Kolb, and Felschen-Ludwig 2010). Further, it is also shown that dental status and self-assessed masticatory ability have little influence on the dietary selection in older individuals (Österberg et al. 2002). Hence, it is suggested that masticatory efficiency is not the only factor affecting or determining the nutritional status and restoring the dental status alone apparently cannot improve nutritional status (Müller et al. 2013; Wöstmann et al. 2008). Chewing problems may be one of several factors that make older adults susceptible to nutrition deficiencies. Based on the narrative synthesis, 21 studies (out of 37) supported the hypothesis, whereas 16 of them refuted it (Figure 3B). However, the certainty of evidence based on GRADE analysis on the congregated outcomes (Figure 2C) showed that there was a *moderate* level of evidence to support of the chewing rate affects gut hormones (Table 3, B).

Strengths, limitations, and implications

A meta-analysis was not appropriate to implement in the present study as selected studies are largely heterogeneous in terms of study participants involved, interventions/exposures, and outcomes to provide a reasonable overview (see, intervention/exposure 3.1.1 and outcome 3.1.2 above). Accordingly, findings from the included studies are interpreted using narrative synthesis, an approach that uses words and text to summarize and explain results from multiple studies (Yellowitz 2016). In the current study since there were different chewing interventions and several outcomes it was rather pragmatic to adopt this approach. A majority of the studies in the current systematic review use a cross-sectional design (N=62) and can therefore not demonstrate causal relationships between chewing impairment and the assessed outcome variables. The quality assessment of the individual studies was evaluated to determine the bias in the design, conduct, and analysis of the data. Accordingly, it was found that 7 studies were of low quality. In spite of this, all studies that met the inclusion criteria, regardless of quality or small sample size, were included in the analysis to provide a holistic overview of the topic. The figures (Figure 2A–C) are formed by the narrative synthesis of the congregated outcomes and provide a logical representation of the *cluster* of studies supporting and refuting the hypothesis. Further, the GRADE criteria were only applied to the congregated outcomes (see “#” in Figure 2A–C) with three or more studies for evaluating the certainty of evidence.

This approach may provide a more focused impression of the cluster of evidence and is considered as a positive attribute of the current study.

Despite a comprehensive hypothesis, only a limited number of studies (N=71) were found eligible according to the inclusion criteria. Therefore, there is an undeniable need to establish strong evidence through large studies with adequate sample size and power. Given that chewing is an important step in food oral processing, multidisciplinary collaboration is needed to construct high-quality studies with broad perspectives on the issue. A major problem in clinical practice is that chewing and swallowing dysfunctions are managed by several clinical specialties and the interdisciplinary collaboration is often limited (Yellowitz 2016). A striking observation is that although chewing and swallowing functions are very closely related, dentists and speech therapists rarely work together. Similarly, there is also lack of strong collaboration between dentists and dieticians. Furthermore, modern dentistry is primarily directed toward structural rehabilitation of the dentition, and not toward functional rehabilitation of the masticatory system. The problem is further accentuated because, at present, there are no reliable, clinical, and easy to use tests to identify the signs of impaired chewing and swallowing behavior. Thus, this area of research could be better served by interdisciplinary collaborations. Moreover, a switch of tracks toward functional rehabilitation instead of structural restoration is warranted.

Conclusion

The results of the current systematic review study showed that the hypothesis was overall supported by forty-six studies and refuted by twenty-five. The results of the study provide pragmatic and preliminary indication on the role of chewing in the measured outcome parameters. However, the overall results also suggest a “moderate” to “very low” certainty of the evidence to support the hypothesis that chewing is an important mechanical and physiological contributor in the swallowing process, and physiologic/pathologic processes in the GIT and various nutrition-related parameters, in humans. It is suggested that chewing function, gastrointestinal disorders, and malnutrition have a complex multifactorial etiology with at least partly similar risk factors (Altenhoevel et al. 2012). Impaired chewing function may result from functional disturbances, tooth loss, or poor dentures; however, the extent to which these factors may impact an individual's overall health is also dependent on somatic, social, and psychological factors. This review also highlights the lack of interdisciplinary collaborations between different specialties of healthcare in constructing well designed studies. Chewing function is one of the important physiological contributors to overall general health and general quality of life. Well-designed studies able to show causality, with sufficient sample size, studying the relationship chewing function as exposé and swallowing, GIT system, and nutrition-related factors as outcomes are needed to establish stronger, conclusive evidence for their complex inter-play.

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Data availability statement

Data can be obtained from the corresponding author on reasonable request.

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