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ORIGINAL ARTICLE—ALIMENTARY TRACT

Systematic review of the epidemiology of gastroesophageal reflux disease in Japan

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Abstract
Background Epidemiological studies of gastroesophageal reflux disease (GERD) in Japan vary in design. This systematic review examines the prevalence of GERD in Japan, distinguishing between study methodologies, and reports on changes over time and factors potentially associated with GERD.
Methods PubMed and Embase searches identified studies reporting the prevalence of GERD in the general population, primary care patients, and individuals undergoing routine health checks.
Results Of the twenty eligible studies, half excluded individuals taking acid-suppressive medication, so these studies would have been likely to have underestimated the prevalence by 2–3%. Nine studies reported the prevalence of at least weekly reflux symptoms (the definition closest to the Montreal definition): in seven studies this was 6.5–9.5%, but in two studies that included individuals who underwent upper gastrointestinal endoscopy the prevalence was 19.0 and 21.8%. Eight studies used symptom scores: prevalence estimates ranged from 10.2 to 29.0% in five studies using the Carlsson–Dent self-administered questionnaire (QUEST), and from 27.0 to 37.6% in three studies using the frequency scale for the symptoms of GERD. Prevalence estimates were 15.1–24.3% in three studies that reported the presence of reflux symptoms of undefined frequency. Six studies reported the prevalence of reflux esophagitis as 4.9–8.2%. Changes in prevalence over time and factors associated with reflux symptoms were inconsistent.
Conclusions Few studies have reported the prevalence of GERD in Japan using standardized criteria. Thus, prevalence estimates vary substantially, reflecting differences in study populations and GERD definitions. However, seven studies reported that the prevalence of at least weekly symptoms was 6.5–9.5%, a finding which approaches that reported in Western populations (10–20%).

Keywords Japan · Gastroesophageal reflux disease · Prevalence · Epidemiology

Abbreviations

BMI	Body mass index
95% CI	95% confidence interval
FSSG	Frequency scale for the symptoms of GERD
GERD	Gastroesophageal reflux disease
LA	Los Angeles
OR	Odds ratio
QUEST	Carlsson–Dent self-administered questionnaire

Introduction

The prevalence of gastroesophageal reflux disease (GERD), defined as the presence of at least weekly

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heartburn and/or acid regurgitation, is reported to be 10–20% in Europe and North America, but seems to be lower in Asia (<5%) [1, 2]. However, prevalence estimates depend on a variety of factors, including the definition of GERD used and the characteristics of the study cohort. The Montreal definition defines GERD as a condition that develops when the reflux of stomach contents causes troublesome symptoms [3]. In population-based studies, mild symptoms occurring on two or more days per week or moderate or severe symptoms occurring on at least 2 days per week are often considered troublesome and consistent with a diagnosis of GERD [3].

In Japan, epidemiological studies of GERD conducted in the general population are rare, and they do not use the Montreal definition. Most of these studies recruit individuals attending routine health checks, which should be reasonably representative of the general population because Japanese law requires that annual routine health checks are performed on all individuals in employment [4–6], and all those aged over 40 years are offered routine health checks [7].

The aim of this systematic review was to examine the epidemiology of GERD in Japan by critically distinguishing between study designs, populations, and the definitions of GERD in the published English and Japanese literature. This review also reports on changes in the prevalence of GERD over time and examines factors that are potentially associated with GERD.

Methods

Study selection

Studies were identified by systematic searches of PubMed and Embase up to 20 November 2009, with no language limits. Additional sources were also searched: the authors' libraries, the reference lists of recent reviews [2, 8, 9], and the abstracts from Digestive Disease Week and United European Gastroenterology Week in 2008 and 2009.

The studies were screened mainly on the basis of titles and abstracts, with the full article being examined when additional information was required. A flow chart of the literature searches is shown in Fig. 1. Studies were selected that reported the prevalence or incidence of GERD in adults in Japan, and that recruited the general population, primary care patients, or individuals undergoing routine health checks. Studies were excluded if they were conducted in highly selected populations. The studies used for the analysis of factors associated with GERD were limited to those that also reported the prevalence of GERD.

Results

Search results

The literature searches identified 20 eligible studies that reported the prevalence of reflux symptoms in Japan (Table 1). Eighteen of the studies were published peer-reviewed articles and two were abstracts from international meetings [10, 11]. Manual screening excluded seventeen studies because they were conducted in various highly selected populations (see Table in supplementary online material).

The source populations differed between the studies. Fifteen of the studies recruited individuals undergoing routine health checks, the studies by Stanghellini [12] and Kusano and Fujimoto [11] were conducted in the adult general population, one study recruited current and retired members of a rugby association [13], one study recruited medical students [10], and one study was performed in primary care patients [14]. The study designs and definitions used to identify individuals with GERD also varied, so we conducted a subanalysis of groups of studies that used the same definition of GERD.

Studies reporting the prevalence of at least weekly reflux symptoms

Nine studies reported the prevalence of at least weekly reflux symptoms (Fig. 2). Using this definition, the prevalence of GERD was 9.4% in the one population-based study [12]. In six studies [5, 6, 15–18] that were conducted as part of routine health checks, the prevalence was 6.5–9.5%. Two of these studies [17, 18] excluded individuals who had endoscopically confirmed reflux esophagitis, and the others did not include endoscopy; thus, the presence of reflux esophagitis was not assessed.

Higher prevalence estimates of 19.0 [19] and 21.8% [10] were reported by two studies of individuals confirmed endoscopically not to have reflux esophagitis. These studies included mostly individuals who elected to undergo an endoscopy, reflecting a selected cohort of individuals.

Studies reporting the prevalence of reflux symptoms by symptom score

Eight studies estimated the prevalence of GERD from a symptom score (Fig. 2). Three of these studies [20–22] defined GERD as ≥6 points on the Carlsson–Dent self-administered questionnaire (QUEST) [23] and reported the prevalence to be 10.2–16.3%. The studies by Sudou et al. [24] and Suganuma et al. [13] used a less stringent threshold of ≥4 points on QUEST and reported higher prevalence estimates, of 17.0 and 29.0%. QUEST was

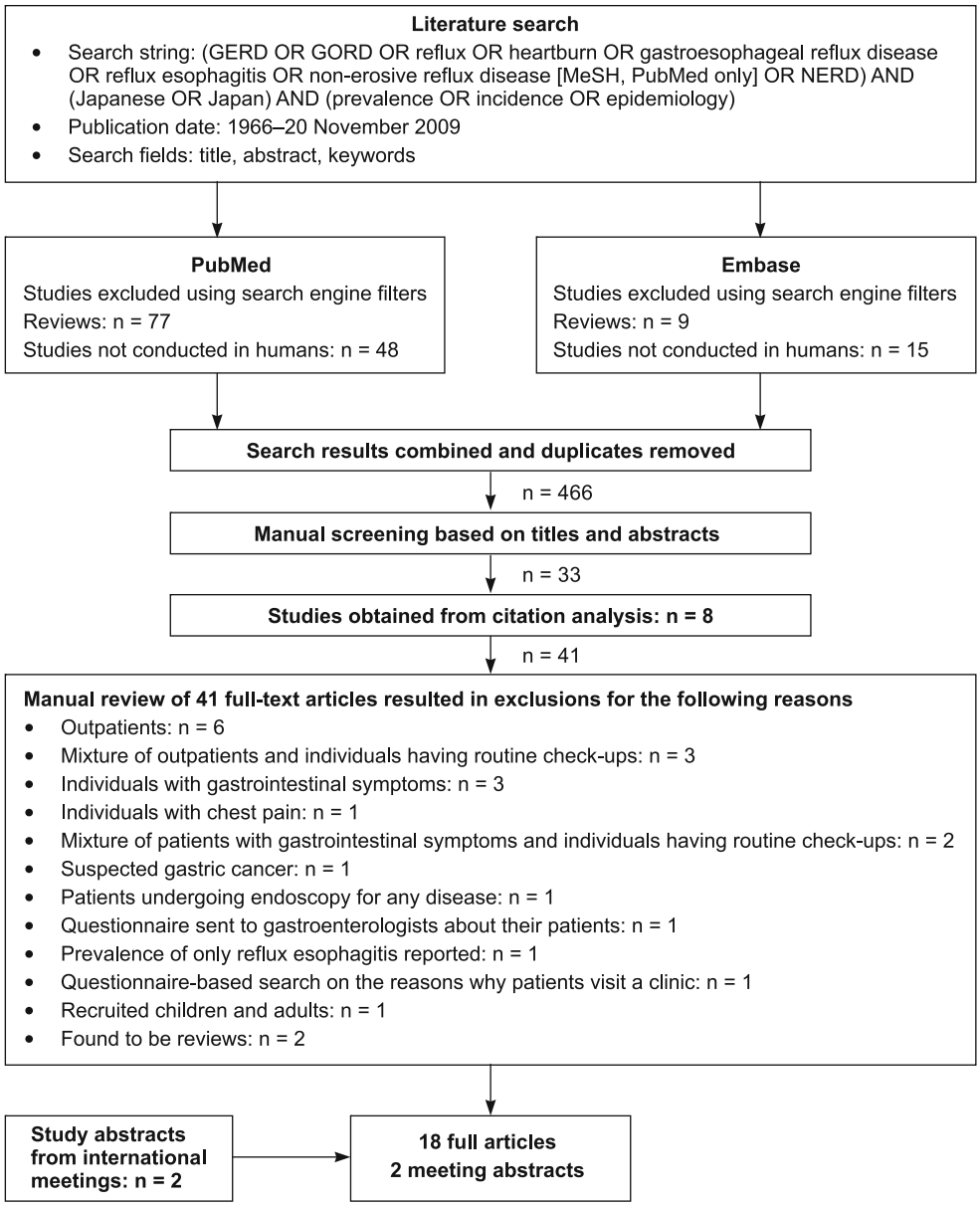

Fig. 1 Literature search strategy

developed to diagnose GERD based on symptoms (and does not determine symptom frequency or severity), and a score of >4 was shown in the original questionnaire to have poor specificity (46%) and thus to be of limited value in excluding individuals without GERD [23]. A cut-off score of ≥6 (specificity of 60%) is considered more likely to exclude individuals who do not have GERD and, hence, to reflect the true prevalence of GERD.

The other three studies reporting the prevalence of reflux symptoms by symptom score [11, 14, 25], which defined GERD using a cut-off score of ≥7 on the self-administered frequency scale for the symptoms of GERD (FSSG) [26], all reported high prevalence estimates (27–37.6%). The FSSG was formulated to evaluate the response of GERD symptoms to medical therapy (measuring the frequency but not severity of symptoms); when the cut-off score was set at 8 points, the FSSG showed a similar level of specificity to QUEST (59%) [26].

Studies using other reflux symptom definitions

Three studies that were conducted in individuals undergoing routine health checks used various definitions of GERD (Fig. 2). 'Presence of symptoms' of heartburn,

Table 1 Identified studies reporting the prevalence and incidence of GERD in Japan

Reference	Population	Method of data collection	Endoscopy	*n*	Response rate	Recall period	Definition of GERD	Prevalence of GERD
At least weekly symptoms								
[17]	Routine health checks (excluded those with ulcers, cancer, or lesions in the GI tract)	Standardized but non-validated questions	Yes (excluded individuals with reflux esophagitis)	911	NA	1 year	Heartburn and/or acid regurgitation ≥ once weekly and ≥ once monthly	3–10% ≥ once weekly[a], 9–24% ≥ once monthly[a], 6.5% (overall for all ages)[b]
[5]	Routine health checks (excluded users of acid-suppressives and those with past dyspepsia or gastric surgery)	Self-report questionnaire (non-validated)	No	6035	86.4%	1 year	Heartburn and/or acid regurgitation ≥ twice weekly	6.6%
[6]	Routine health checks (excluded users of acid-suppressives, those with peptic ulcers, dyspepsia, or history of gastrectomy)	Self-report questionnaire (non-validated)	No	4095	85.7%	1 year	Heartburn and/or acid regurgitation ≥ twice weekly (options given: daily, twice weekly, twice monthly, less than monthly)	6.7%
[15]	Routine health checks (excluded users of acid-suppressives, those with digestive diseases or a history of upper GI surgery)	Self-report questionnaire (non-validated)	No	7386	NR	NR	Heartburn ≥ twice weekly	8.4%
[16]	Employees	Questionnaire (non-validated)	No	1662	NA	NR	Heartburn ≥ once weekly	8.7%
[12]	General population	Interview with questionnaire (DIGEST)[46]	No	500	37.2% response rate among eligible contacts or 26.5% overall	3 months[45]	At least moderate severity of upper GI symptoms and occurring ≥ once weekly	9.4%
[18]	Routine health checks, excluded individuals with reflux esophagitis, those who had undergone *Helicobacter pylori* eradication, and those taking acid-suppressives)	Not clear	Yes (excluded individuals with reflux esophagitis in the prevalence of GERD study)	497	NR	NR	Heartburn ≥ twice weekly	9.5% in 1998

Table 1 continued

Reference	Population	Method of data collection	Endoscopy	*n*	Response rate	Recall period	Definition of GERD	Prevalence of GERD
[10]	Medical students	Interview	Yes (confirmed by author to be ~80%)	678	NA	NR	Mild symptoms ≥ 2 days weekly, or moderate/severe symptoms occurring ≥ 1 day weekly	21.8% NERD; 7.7% reflux esophagitis; 5.2% reflux esophagitis without symptoms
[19]	Routine health checks (excluded individuals with gastroduodenal ulcers, a history of gastrectomy, and those taking PPIs)	Questionnaire (non-validated)	Yes	3818	NR	NR	Heartburn ≥ twice weekly	19.0% NERD; 5.3% reflux esophagitis
QUEST								
[20]	Routine health checks (excluded users of acid-suppressives and those who had been previously diagnosed with GERD)	Self-report questionnaire (QUEST)	No	322 in 1998 241 in 2004	NR follow-up rate 83.4%	NR	≥6 points on QUEST	In 1998: 10.2%; in 2004: 15.4%
[21]	Routine health checks (excluded individuals who had had *H. pylori* eradication or gastric surgery or acid-suppressives in the previous 2 months)	Self-report questionnaire (Japanese QUEST)	Yes	2760	NA	NR (also not stated in [23])	>6 points on QUEST and/or endoscopically proven reflux esophagitis (LA grade A–D)	NERD 10.9%; 7.1% reflux esophagitis; 12.7% by QUEST alone
[22]	Routine gastric cancer screens (excluded individuals who had had *H. pylori* eradication or gastric surgery and users of acid-suppressives)	Self-report questionnaire (QUEST)	Yes	539 in 2000 539 in 2005	NR rate 100%	NR	>6 points on QUEST and/or endoscopically proven reflux esophagitis (LA grade A–D)	Reflux symptoms: in 2000, 16.3% and in 2005, 10.8% with reflux esophagitis (all mild): in 2000, 8.2% and in 2005, 9.8% reflux esophagitis without symptoms: in 2000, 5.4% and in 2005, 7.6%.
[24]	Routine health checks	Self-report questionnaire (QUEST)	In 7.4% of individuals	869	NA	Recent	>4 points on QUEST	17%
[13]	Active and retired members of a rugby association	Self-report questionnaire (QUEST, with additional questions)	No	475	81.9%	NR	≥4 points on QUEST for GERD and sleep problems graded on 5-point scale	29%

Table 1 continued

Reference	Population	Method of data collection	Endoscopy	*n*	Response rate	Recall period	Definition of GERD	Prevalence of GERD
FSSG								
[25]	Routine health checks (excluded individuals taking GI medication)	Self-report questionnaire (FSSG)	Yes	659	NA	NR	>8 points on FSSG	27% NERD; reflux esophagitis 4.9% (disregarded FSSG for individuals with reflux esophagitis)
[11]	General population	FSSG questionnaire via the internet	No	15814	NR	NR	>8 points on FSSG	35.8%
[14]	Primary care	Self-report questionnaire (FSSG)	No	4139	NR	NR	≥7 points on FSSG	37.6%
Other GERD definitions								
[27]	Routine health checks	Yes or no to presence of symptoms	Yes	6307	NA	1 month	Presence of symptoms	Heartburn 15.1%[a]
[28]	Routine health checks	Do you have discomfort in your chest or stomach?	No	531	NA	NR	Presence of discomfort in chest or stomach	24.3%
[7]	Routine health checks	Self-report questionnaire (non-validated)	No	160848	99%	1 month	Heartburn usually or sometimes	17.7%

[a] Data obtained by approximation from graph in referenced publication

[b] Study reports the prevalence of GERD stratified by age and the number of individuals in each age group. The average prevalence for any age was calculated (e.g., ≤39 years, $n = 161$ and the prevalence of GERD was 3%. The study sample size was $n = 911$. Thus, the contribution of this age group was 3 (161/911) = 0.5%. This was added to the contribution of the other age groups

FSSG frequency scale of symptoms of GERD, *GERD* gastroesophageal reflux disease, *GI* gastrointestinal, *LA* Los Angeles classification scale for reflux esophagitis, *NA* not applicable, *NERD* non-erosive reflux disease, *NR* not reported, *QUEST* Carlsson–Dent self-administered questionnaire, *PPI* proton pump inhibitor

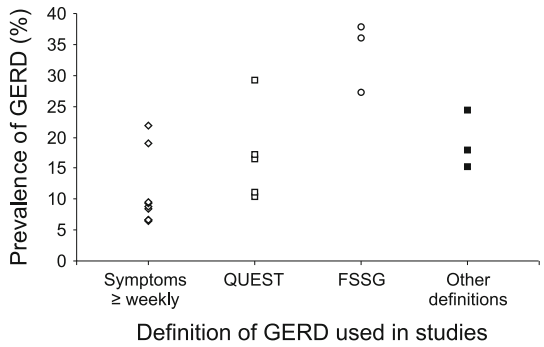

Fig. 2 The prevalence of gastroesophageal reflux disease (*GERD*) in Japan. The values plotted are the prevalence of GERD without reflux esophagitis (because three studies excluded individuals with reflux esophagitis or endoscopy was not included in the study). Only the first value in the two longitudinal studies is plotted because the study designs of the follow-up differed [20, 22]. *FSSG* frequency scale for the symptoms of GERD, *QUEST* Carlsson–Dent self-administered questionnaire

dysphagia, and abdominal pain had a prevalence of 15.1% (value obtained from graph in Fig. 2) [27], 'discomfort in the chest or stomach' had a prevalence of 24.3% [28], and 'heartburn usually or sometimes' had a prevalence of 17.7% [7].

Changes in prevalence of gastroesophageal reflux disease over time

Two articles were longitudinal studies reporting changes in the prevalence of GERD over time, as assessed by QUEST, in individuals undergoing routine health checks [20, 22]. The study by Miyamoto et al. [20], which did not include endoscopy, reported an increase of symptom-defined GERD from 10% in 1998 to 15% in 2004, whereas the study by Azumi et al. [22] reported a decrease, from 16% in 2000 to 11% in 2005. However, Azumi et al. found that 8% of individuals without reflux symptoms in 2000 had symptoms in 2005, and the number of individuals with reflux esophagitis had increased from 8 to 10%. Furthermore, their study reported that 74% of the individuals with GERD defined by QUEST in 2000 did not have symptoms 5 years later. The differences between the findings in these two studies may be explained by differences in their study designs. Importantly, in the study by Miyamoto et al., individuals who had a positive QUEST result in the first period of the study were excluded from the follow-up, whereas the study by Azumi et al. assessed the same individuals at both times.

Prevalence of reflux esophagitis

Endoscopic examination was included in nine of the studies, and reflux esophagitis was mostly graded using the Los Angeles (LA) classification [29]. Three studies reported the prevalence of LA grade A–D reflux esophagitis to be 4.9–8.2% in individuals undergoing routine health checks [21, 22, 25]. Funatsu et al. [25] disregarded the FSSG score for individuals with reflux esophagitis. One study used a revised version of the LA classification system [30] and reported the prevalence of minimal changes to the lower esophageal mucosa or reflux esophagitis to be 5.3% [19]. Another study reported the prevalence of reflux esophagitis (defined as the presence of mucosal breaks) to be 7.7% [10]. One study reported that the prevalence of heartburn (undefined frequency) significantly increased with the LA classification grading of reflux esophagitis, but did not specify the prevalence of reflux esophagitis [27]. The studies by Hirakawa et al. [17] and Kawanishi [18] excluded individuals with reflux esophagitis at baseline from the prevalence study, but did not specify how many individuals were excluded on this basis. In the final study, endoscopy was performed only in some patients [24].

Incidence of gastroesophageal reflux disease and reflux esophagitis

One study aimed to report the incidence of GERD using QUEST in a population with a mean age of almost 60 years [20]. However, the incidence was reported as a percentage rather than the more comparable measure of person-years. When contacted, the author did not have any additional data and advised that the incidence per 1000 person-years should be calculated from the numbers in the publication. Hence, the incidence in that study was estimated to be 25.6 per 1000 person-years (37 new cases in 6 years/241 individuals in the population initially at risk).

Another study reported the incidence of reflux esophagitis in a population with a mean age of approximately 48 years, but again as a percentage [18]. Attempts to contact the author were unsuccessful. Thus, the incidence of reflux esophagitis was estimated from the values in the article to be 72.3 per 1000 person-years in the subgroup who had heartburn twice or more weekly at baseline and 22.7 per 1000 person-years in the subgroup who had heartburn less than twice weekly. Overall, the estimated incidence of reflux esophagitis was approximately 27.4 per 1000 person-years.

Factors potentially associated with gastroesophageal reflux disease

Demographic and lifestyle factors

Thirteen cross-sectional studies examined demographic or lifestyle factors potentially associated with the prevalence of GERD or reflux symptoms (Fig. 3). Three of the studies used multiple regression analysis to assess factors

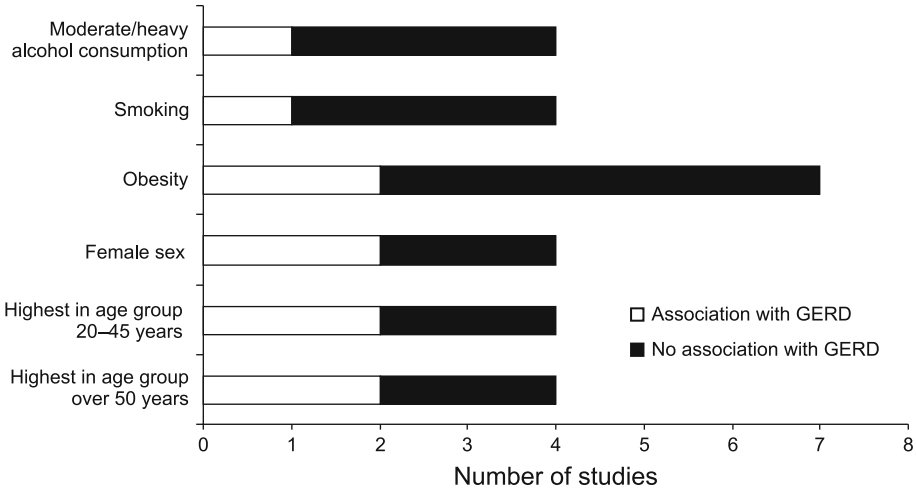

Fig. 3 Demographic and lifestyle factors associated with gastroesophageal reflux disease (*GERD*). *GERD* gastroesophageal reflux disease

potentially associated with GERD [6, 15, 21] but most of the studies used the χ^2 test to compare binary proportions between two groups.

Whether reflux symptoms were associated with age was examined in seven studies. Of four studies that defined GERD as the presence of at least weekly reflux symptoms, one found that the prevalence of reflux symptoms was highest in those older than 50 years but did not report statistical significance [15], while one study reported that the prevalence of reflux symptoms was significantly higher in the 50- to 59-year age group than in the younger-than-40-year age group ($p < 0.05$) [17]. However, two studies found no relationship between age and the prevalence of at least weekly reflux symptoms [5, 6]. One study that used a GERD definition of >4 on QUEST reported the highest prevalence to be in individuals aged in their early 30 s and early 40 s ($p < 0.05$) [13]. A study that used the FSSG to identify individuals with reflux symptoms reported the highest prevalence to be in the 20- to 29-year age group ($p < 0.05$) [14].

The potential association between GERD and sex was examined in five studies. One study found an association between female sex and heartburn (frequency not specified) only in the 60- to 89-year age group ($p < 0.0001$) [7], and another study reported a higher prevalence of reflux symptoms (determined using the FSSG) in women than in men ($p < 0.05$) [14]. Two other studies found no significant relationship between sex and the prevalence of at least weekly reflux symptoms [5] or a QUEST score of >6 [21].

One study found that a body mass index (BMI) of ≥25 kg/m^2 was associated with an increased prevalence of at least weekly reflux symptoms ($p < 0.05$) [15]. However, five studies reported no association between BMI and the prevalence of reflux symptoms [6, 12, 13, 16, 21].

One study reported that current smoking was associated with at least weekly reflux symptoms compared with non-smoking [odds ratio (OR) 1.35; 95% confidence interval (CI) 1.01–1.82] [6]. The same study also found that moderate and heavy alcohol consumption (≥16 mL/day) was associated with at least weekly symptoms compared with light consumption (OR 1.47; 95% CI 1.01–215). However, three studies found no significant association with these factors [16, 18, 19].

Comorbidities

Six studies examined the possible relationships between comorbidities and reflux symptoms. One study reported that *Helicobacter pylori* infection was associated with at least weekly reflux symptoms only in individuals younger than 40 years of age (OR 2.41; 95% CI 1.52–3.82) [15], although another study found no significant association with *H. pylori* [18]. The studies by Kawanishi [18] and Mishima et al. [21] found an association between hiatus hernia and at least weekly reflux symptoms ($p < 0.01$) or a QUEST score of >6 (OR 1.48; 95% CI 1.17–1.89) [18, 21].

Risk factors associated with gastroesophageal reflux disease

Two longitudinal studies examined risk factors potentially associated with a QUEST score of ≥6 using multivariate analysis [20, 22]. Both studies found that smoking and alcohol consumption were not significant risk factors for reflux symptoms. One of the studies reported that *H. pylori* negativity (OR 17.81; 95% CI 2.80–113.23) was a risk factor for reflux symptoms [20]. The other study found that hiatus hernia was not a significant risk factor for reflux symptoms (OR 1.53; 95% CI 0.77–3.03) [22]. This study also reported that the presence of reflux symptoms was not a significant risk factor for the presence of reflux esophagitis after 5 years (OR 1.76; 95% CI 0.82–3.74) [22]. Furthermore, this study found that the presence of reflux esophagitis was not a significant risk factor for reflux

symptoms after 5 years (OR 1.69; 95% CI 0.68–4.22). A third longitudinal study reported that the presence of at least weekly reflux symptoms was a risk factor for the development of reflux esophagitis after 5 years [hazard ratio (HR) 3.83; 95% CI 2.29–6.61] [18].

Discussion

Our systematic review of the literature identified 20 studies that reported the prevalence of GERD in Japan, based largely on data from studies in the general population and data from routine health checks. When GERD was defined as the presence of at least weekly reflux symptoms, the prevalence ranged from 6.5 to 9.5% in seven studies that either did not perform an endoscopy or that excluded individuals with reflux esophagitis.

The presence of at least weekly reflux symptoms is the definition of GERD that is closest to that described by the Montreal Consensus Group.The Montreal definition states 'in population-based studies, mild symptoms occurring 2 or more days a week, or moderate/severe symptoms occurring 1 or more days a week, are often considered troublesome by patients' [3]. In order to establish the true prevalence of GERD, a symptom threshold must be defined which adequately selects for patients whose quality of life is impaired as a result of their disease [1]. Although GERD symptoms experienced at least twice weekly are thought to be sufficient to impair quality of life [1], some of the epidemiological studies reviewed here that used a symptom frequency threshold defined GERD as symptoms occurring at least once a week, while some defined GERD as symptoms occurring at least twice a week. Thus, at least weekly symptoms represents the definition used in the Japanese literature that gives the most realistic prevalence estimate.

The prevalence of at least weekly symptoms was high (19.0 and 21.8%) in two studies. In the first study, Yagi et al. [19] selected 3818 participants who had chosen to have endoscopy from among 9236 patients who had attended for a routine medical health check up. In the second study [10], the participants were medical students (Shimatani et al., personal communication), who may have had greater awareness of and willingness to report their symptoms than the general population; approximately 80% of the students agreed to endoscopy. Thus, these two studies are likely to have overestimated the prevalence of GERD, because individuals who had experienced symptoms may have been more likely to be willing to undergo endoscopy.

Prevalence estimates were also higher in studies that used reflux symptom scores to define GERD. QUEST does not include measures of frequency or severity, instead using seven questions that focus on symptoms in relation to timing, food intake, and actions such as bending [31]. Thus, the prevalence of GERD may be higher when defined using QUEST scores than when defined by the frequency of typical reflux symptoms. Using QUEST is likely to include individuals with infrequent and/or non-severe typical reflux symptoms, as well as those with more frequent and/or severe symptoms.

QUEST uses 'word pictures' for symptoms. For example, heartburn may be described as a burning feeling rising from your stomach or lower chest up towards your neck. Such word pictures may have been better understood by the study participants than the use of terms such as 'heartburn' for symptoms, because this term has been reported to be poorly understood by >80% of East Asian individuals, including those from Japan [32]. Moreover, a recent survey conducted in Japan reported that patients with GERD without reflux esophagitis were less likely than physicians to recognize a 'burning sensation in the chest' as heartburn, and they confused stomach ache with heartburn [33].

The studies that used the FSSG to define GERD and estimate its prevalence reported higher prevalence estimates (27–37.6%) than studies using other definitions of GERD. The study that reported the highest prevalence (37.6%) of reflux symptoms defined using the FSSG [14] was conducted in the primary care setting; these individuals were seeking medical advice so they may have been more likely to have symptoms than the general population. The FSSG [26] consists of twelve questions relating to the frequency of symptoms, including heartburn, bloating, regurgitation, burping, heavy stomach, and feeling sick or full with meals. The participants rate their symptoms as never, occasionally (around 30% of the time), sometimes (50%), often (70%), or always (100%). Seven of the questions assess reflux symptoms and the remaining five assess symptoms that can also be caused by dyspepsia. As the questions are all equally weighted, the FSSG is likely to rate a substantial proportion of individuals with dyspeptic symptoms falsely as having GERD. Indeed, a comparison of FSSG and QUEST scores at Japanese centers reported that the FSSG total score was inferior to QUEST in terms of distinguishing GERD from other conditions [34].

However, the FSSG was developed with significant input from patients in Japan, rather than merely being translated from an English survey, as was done for QUEST, and FSSG scores have been shown to correlate with endoscopic improvement in patients with mild or severe GERD [26]. Kusano et al. [26] reported that a cut-off score of 8 points on the FSSG had a sensitivity of 62% and a specificity of 59% for detecting endoscopically diagnosed GERD [26], while Nagano et al. [35] reported that the Japanese translation of QUEST had sensitivities of 72 and 65% and specificities of 54 and 74%, when the cut-off scores were 4 and 6 points, respectively.

The prevalence estimates from the three studies [7, 27, 28] that used vague definitions of GERD are unlikely to be as reliable as the other estimates, which are based on clearer definitions of GERD that include the frequency of symptoms.

About half (9/20) of the studies excluded individuals who were taking acid-suppressive medication. In four of these studies, this accounted for 2–3% of individuals [5, 6, 15, 22], whereas the other five studies did not indicate the number of individuals excluded on this basis. Assuming that a substantial proportion of these individuals were taking acid-suppressive medication for reflux symptoms, it is likely that these studies underestimated the prevalence of GERD by up to 2–3%.

Four studies excluded individuals with different gastrointestinal diseases, dyspeptic symptoms, or a past diagnosis of GERD [5, 6, 15, 20]. Individuals with dyspepsia are more likely than those without dyspepsia to also have GERD [36, 37]. Thus, excluding individuals with gastrointestinal diseases is likely to lead to an underestimation of the prevalence of symptom-defined GERD.

The two longitudinal studies that reported changes in the prevalence of GERD defined by QUEST scores [20, 22] had inconsistent findings; they had both recruited small study samples, but they had different study designs. The data reported by Azumi et al. [22] suggest that there was spontaneous symptom improvement or that GERD was cycling between symptoms and remission, whereas the study by Miyamoto et al. [20] reported the occurrence of new cases. The incidence of GERD estimated from the data reported by Miyamoto et al. [20], of 26 per 1000 person-years, and the incidence of reflux esophagitis reported by Kawanishi [18], of 27 per 1000 person-years in Japanese populations, are higher than the reported incidences in Western populations. Studies that used the United Kingdom General Practice Research Database reported the incidence of GERD to be 3.8–4.5 per 1000 person-years [38, 39]. Similarly, Dent et al. [1] calculated the incidence of GERD in the United States to be 5.4 per 1000 person-years. A potential explanation for these large differences in the estimated incidence between the populations include the relatively small (322 and 497) sample sizes of the Japanese studies [20, 22], compared with the United States and United Kingdom studies (at least 7159), suggesting that the Western studies may provide a more accurate estimate of the incidence of GERD than those conducted in Japan.

There were few consistent inter-study data on factors associated with GERD. Overall, cross-sectional studies that used the definition of GERD most similar to the Montreal definition (symptoms at least once weekly) indicate that BMI, smoking, and alcohol consumption are not associated with GERD in Japan.

A major difference between Asia and the West is the age at which endoscopy is used before any treatment is given [9], which is often by the age of 35 years in Japan. The prevalence of reflux esophagitis in Japan in the studies reviewed here (4.9–8.2%) [10, 19, 21, 22, 25] is similar to the prevalence in China (6.4%) [40] and is lower than that in Western countries (11.8–15.5%). The longitudinal data assessed in this review are inconclusive with regard to whether symptomatic GERD is a risk factor for the development of reflux esophagitis and vice versa [18, 22]. This may reflect difficulties in symptom recognition in Japan, because patients with GERD have demonstrated problems in recognizing heartburn, and have confused it with stomach ache [33].

A major strength of the present review is that it has critically distinguished between study designs, definitions of GERD, and study populations, enabling relevant subanalyses to be performed. Additionally, studies that recruited hospital outpatients were excluded because these populations were deemed to have been too selective to provide an estimate of prevalence in the general population.

This review highlights how few studies on the epidemiology of GERD in Japan have used standardized criteria for GERD and representative study populations. Surveys that recruit individuals undergoing routine health checks will not be fully representative of the general population because they are likely to exclude students and unemployed and sick people. A study of a nationally representative population sample aged 25–59 years found that the proportions showing non-attendance at general health checks were 27.5% for men and 42.3% for women [41]. A second study found a marked variation among prefectures in the health-check participation rates for people older than 40 years (range 26.2–61.1%) [41].

A further limitation of the studies we examined is that many of them excluded individuals who were taking acid-suppressive therapy, those with dyspeptic symptoms or other gastrointestinal diseases, and/or those with reflux esophagitis. Importantly, these studies may have excluded individuals with GERD and thus may have reported a lower than actual prevalence; many of these studies did not report the number of individuals excluded on this basis, making total prevalence estimates difficult.

Most of the studies did not use the recent Montreal definition of GERD. This reflects the findings of a recent questionnaire-based survey [42], which reported that approximately half of Japanese physicians do not use guidelines (i.e., Montreal, Asian-Pacific Consensus, American College of Gastroenterology, Genval Workshop Report, and others) when diagnosing GERD. However, this survey did not include the GERD workshop guidelines [43] as a named response option. Furthermore, the National Guidelines on GERD [44] of the Japanese Society of

Gastroenterology were published after the survey [42] was conducted.

The prevalence of at least weekly reflux symptoms was 6.5–9.5% in seven studies that were conducted in the general population or as part of a routine health check. However, the actual prevalence is likely to be higher because of study exclusions, particularly as four of these studies excluded individuals who were taking acid-suppressive medication (2–3% of the population cohort studied). The prevalence of reflux esophagitis was reported to be 4.9–8.2% in five studies conducted as part of a routine health check or among medical students.

There is a need for more high-quality population-based studies in Japan. Our searches identified only two population-based studies, one of which formed part of an international study and had a low response rate [12], while the other did not report the response rate to their internet questionnaire [11]. It is also recommended that future studies use specific standardized definitions of GERD, such as the Montreal definition [3].

In conclusion, the variation in prevalence estimates of GERD tends to reflect differences in study populations, study designs, and definitions of GERD. In agreement with previous findings in Western and Asian populations [1], we found a lack of consensus on the threshold used to determine the presence of symptom-defined GERD in epidemiological studies, which makes comparison of studies to estimate the prevalence of GERD difficult. No studies in Japan were identified that directly reported the incidence of GERD in person-years, and the data for changes in prevalence over time and the evidence for factors associated with GERD were inconclusive. However, the evidence suggests that the prevalence range of at least weekly symptoms in Japan is within the lower end of that reported for Europe and North America.

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