Original research

Global prevalence of self-reported non-coeliac gluten and wheat sensitivity: a systematic review and metaanalysis

Mohamed G Shiha , ^{1,2} Francesca Manza, ^{3,4} Oscar G Figueroa-Salcido, ⁵ Noé Ontiveros, ⁶ Giacomo Caio, ^{4,7} Claire L Jansson-Knodell, ⁸ Alberto Rubio-Tapia , ⁸ Imran Aziz, ^{1,3} David S Sanders ^{1,3}

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For numbered affiliations see end of article.

Correspondence toDr Mohamed G Shiha;

Dr Mohamed G Shiha; mohamed.shiha1@nhs.net

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ABSTRACT

Background Non-coeliac gluten/wheat sensitivity (NCGWS) is characterised by gastrointestinal and extraintestinal symptoms related to gluten or wheat ingestion in individuals without coeliac disease or wheat allergy.

Objective A systematic review and meta-analysis was conducted to estimate the global burden and clinical characteristics of self-reported NCGWS.

Design We searched for studies evaluating the prevalence of self-reported NCGWS in the general population. Pooled prevalence estimates and odds ratios (ORs) and their 95% confidence intervals (CIs) were calculated using random-effects meta-analysis.

Results Twenty-five studies comprising 49 476 participants from 16 countries were included in the analysis. The pooled prevalence of self-reported NCGWS was 10.3% (95% CI 7.0% to 14.0%), with marked variations between countries. Among individuals reporting NCGWS, 40% (95% CI 25.2% to 55.0%) adhered to a gluten-free diet. The most common symptoms were bloating (71.0%; 95% CI 62.8% to 79.1%), abdominal discomfort (46.0%; 95% CI 39.0% to 52.7%), abdominal pain (36.0%; 95% CI 28.6% to 43.2%) and fatigue (32.1%; 95% CI 25.3% to 39.0%). Self-reported NCGWS was significantly more common in females than in males (OR 2.29; 95% CI 1.80 to 2.90; p<0.001). Individuals who self-reported NCGWS were significantly more likely to report anxiety (OR 2.95; 95% CI 1.56 to 5.57; p<0.001), depression (OR 2.42; 95% CI 1.80 to 3.24; p<0.001) and irritable bowel syndrome (OR 4.78; 95% CI 3.48 to 6.57; p<0.001) than controls.

Conclusion Approximately one in 10 people worldwide self-report NCGWS, with a female predominance and a significant association with psychological distress and irritable bowel syndrome. Our findings suggest positioning NCGWS within the spectrum of disorders of gut—brain interaction once organic pathologies have been excluded.

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INTRODUCTION

Non-coeliac gluten/wheat sensitivity (NCGWS) is an umbrella term encompassing a broad spectrum of gastrointestinal and extraintestinal symptoms triggered by gluten or wheat ingestion in

individuals without coeliac disease or wheat allergy. Symptoms of NCGWS typically improve with gluten or wheat avoidance and recur on re-exposure. Unlike coeliac disease or wheat allergy, the

WHAT IS ALREADY KNOWN ON THIS TOPIC

- ⇒ Non-coeliac gluten/wheat sensitivity (NCGWS) is a condition characterised by gastrointestinal and extraintestinal symptoms following gluten or wheat ingestion in individuals without coeliac disease or wheat allergy.
- ⇒ Self-reported NCGWS has emerged as a global phenomenon over the past decade.
- There are no comprehensive global estimates of the pooled prevalence of NCGWS, nor any synthesis of its clinical characteristics and associated factors.

WHAT THIS STUDY ADDS

- ⇒ This study provides the first comprehensive and methodologically robust global synthesis of the prevalence and clinical features of self-reported NCGWS.
- ⇒ Approximately 10% of people worldwide report symptoms related to gluten or wheat despite not having coeliac disease or wheat allergy.
- ⇒ NCGWS is significantly associated with female sex (OR 2.29), anxiety (OR 2.95), depression (OR 2.42) and irritable bowel syndrome (OR 4.78).
- ⇒ Around 40% of individuals with self-reported NCGWS follow a gluten-free diet.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

- ⇒ NCGWS is a common condition worldwide and may represent an umbrella term for foodtriggered symptomatology within disorders of qut-brain interaction.
- ⇒ The widespread use of gluten-free products, often without a clear diagnosis, highlights the clinical uncertainty surrounding this condition.
- Our findings call for research into validated diagnostic criteria and evidence-based management strategies to support patients and clinicians.



Neurogastroenterology

pathophysiology of NCGWS remains unclear and no specific serological markers have been identified. Nonetheless, awareness and interest in NCGWS have grown significantly over the past decade, driven in part by increased public demand and a widespread perception of health benefits associated with glutenfree products.²

Diagnosing NCGWS poses a clinical challenge. The Salerno Expert's criteria proposed a rigorous double-blind, placebo-controlled, crossover gluten challenge as the gold standard method for confirming the diagnosis of NCGWS.³ However, trials that adopted this approach found a strong nocebo effect, with only a small proportion of patients showing gluten-specific symptoms.^{4 5} In routine practice, NCGWS is diagnosed by the exclusion of coeliac disease and wheat allergy in individuals who report adverse symptoms after eating gluten or wheat. Although self-reported NCGWS may not always represent true sensitivity to gluten or wheat, it reflects the burden of symptoms attributed to these dietary components in the general population.⁶

Despite an expanding body of research, the global burden of NCGWS in the general population remains unknown. In this systematic review and meta-analysis we aimed to estimate the worldwide prevalence and clinical features of self-reported NCGWS.

METHODS

This systematic review and meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) 2020 guidelines (see online supplemental material).⁸ The review protocol was prospectively registered with the International Prospective Register of Systematic Reviews (PROSPERO; registration number: CRD420251050152) published on 19 May 2025.

Data sources and search strategy

We systematically searched MEDLINE, Embase, Scopus and Web of Science for studies reporting the prevalence of self-reported NCGWS in the general population. The search strategy was developed in collaboration with an experienced medical librarian from Sheffield Teaching Hospitals NHS Foundation Trust. Searches included all records up to 27 May 2025, with no restrictions on publication date or language. The reference lists of included studies were also manually screened to identify additional eligible articles. The full search strategy is provided in the online supplemental material.

Study selection and eligibility criteria

Search results were exported to EndNote 20 (Clarivate Analytics, London, UK) and duplicate records were removed. Two reviewers (MGS and FM) screened titles and abstracts for eligibility. Full-text articles were assessed for inclusion based on the predefined criteria outlined in the published protocol. We included studies reporting the prevalence of self-reported NCGWS in general population samples such as probability samples, school or workplace-based surveys, nationally representative health surveys or large convenience samples with a clearly defined denominator. We excluded studies limited to hospital or clinic populations unless prevalence in a general population control group was reported. Gluten-challenge trials, case reports, editorials, letters and clinical guidelines were excluded. Studies only reporting the prevalence of gluten/wheat avoidance in the general population were also excluded.

Study outcomes

The primary outcome was the global prevalence of self-reported NCGWS in the general population. Secondary outcomes included the prevalence of gastrointestinal and extraintestinal symptoms in individuals with self-reported NCGWS, the prevalence of gluten/wheat avoidance in those with NCGWS, sex-based differences in NCGWS prevalence, and the odds of NCGWS in patients with irritable bowel syndrome (IBS) compared with non-IBS controls.

Data extraction

Two reviewers (MSG and FM) independently extracted data using a standardised Excel spreadsheet (Microsoft Corp, Redmond, Washington, USA). The following data were extracted from each study where available: study authors, publication year, country, setting, study design, population characteristics, period of data collection, definition of NCGWS, diagnostic criteria for IBS, and all relevant study outcomes. Any discrepancies were resolved by discussion.

Quality assessment

The risk of bias was independently assessed by two reviewers (MGS and FM) using the Newcastle–Ottawa Scale, adapted for cross-sectional studies. This tool evaluates studies based on three broad domains: selection of participants, comparability of study groups and the ascertainment of the outcome. Each study was assigned a score from 0 to 9, with scores of 7–9 indicating a low risk of bias (high quality), 4–6 indicating a moderate risk of bias (moderate quality) and 1–3 indicating a high risk of bias (low quality). Discrepancies between reviewers were resolved through discussion.

Data synthesis and statistical analyses

We used a random-effects meta-analysis model to estimate the pooled prevalence rates of self-reported NCGWS with their 95% confidence intervals (CIs). Pooled odds ratios (ORs) were calculated for comparative outcomes. We assessed heterogeneity using the I² statistic, with I² values of 25%, 50% and 75% considered low, moderate and high heterogeneity, respectively. Where ≥ 10 studies were available, we assessed publication bias using funnel plots and the Egger's test. We performed subgroup and sensitivity analyses to explore potential sources of heterogeneity and to assess the robustness of our findings. A p value of < 0.05 was considered statistically significant. All statistical analyses were performed using the 'meta' command on Stata version 18 (StataCorp, College Station, Texas, USA).

RESULTS

Study selection and characteristics

The systematic literature search identified 13 954 records across the four databases. After removing 5439 duplicate records, 8515 articles were screened by title and abstract. Of these, 54 articles were assessed in full text and 24 studies met the inclusion criteria. One additional study was identified through consultation with co-authors, are resulting in a total of 25 studies included in the meta-analysis (figure 1).

The characteristics of the included studies are summarised in online supplemental table 1. The 25 included studies comprised 49 476 participants from 16 countries representing five WHO regions: the Americas, Europe, Western Pacific, South-East Asia and Eastern Mediterranean. The studies were published between 2014 and 2024. All used a cross-sectional design with most focusing on adult populations; only two studies assessed

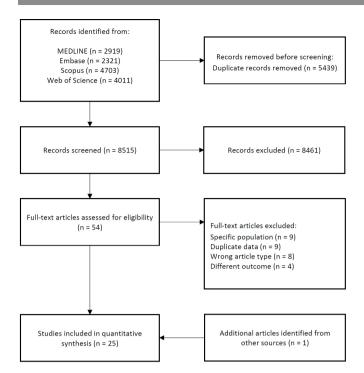


Figure 1 PRISMA flow diagram of study selection.

the prevalence of self-reported NCGWS in paediatric cohorts. Data were collected using self-administered, postal or online questionnaires in community-based settings.

Prevalence of self-reported NCGWS

The pooled prevalence of self-reported NCGWS in the general population was 10.3% (95% CI 7.0% to 14.0%), with high between-study heterogeneity (I²=99.7%) (figure 2). There was evidence of funnel plot asymmetry, suggesting publication bias or small-study effects (Egger's test, p<0.0001; see online supplemental figure 1). Leave-one-out sensitivity analysis demonstrated stability of the pooled estimates, with prevalence rates consistently ranging between 9.0% and 11.0%, indicating that no single study disproportionately influenced the overall results (see online supplemental figure 2).

The overall and subgroup prevalence rates of self-reported NCGWS are shown in table 1. Subgroup analyses revealed significant variations in the prevalence of self-reported NCGWS between countries (p<0.001) and WHO regions (p<0.001) (figure 3). Individuals in high-income countries were more likely to self-report NCGWS than those in middle-income countries (p=0.002). There was no statistically significant difference in the prevalence rates between studies conducted in adult and paediatric populations (p=0.11).

To explore the sources of heterogeneity further we conducted meta-regression analyses using study-level covariates. A higher proportion of female participants was associated with a significant increase in the prevalence of self-reported NCGWS (p=0.02) (see online supplemental figure 3). No significant associations were observed for the total sample size (p=0.35), year of publication (p=0.33), country (p=0.06), WHO region (p=0.11) or number of participants with IBS (p=0.78).

The sex differences in the prevalence of self-reported NCGWS were reported in 17 studies. ¹⁰⁻¹² ¹⁶⁻¹⁹ ²¹⁻²³ ²⁵ ²⁶ ²⁹⁻³² ³⁴ The pooled prevalence of self-reported NCGWS in females was 14.0% (95% CI 9.0% to 19.1%) compared with 7.6% (95% CI 3.6% to 11.6%) in males. Females were significantly more likely

than males to report NCGWS (OR 2.29; 95% CI 1.80 to 2.90; p<0.001) (figure 4). However, there was evidence of high between-study heterogeneity ($I^2=79.0\%$).

Clinical characteristics of patients with self-reported NCGWS

The pooled proportions of gastrointestinal and extraintestinal symptoms in patients with self-reported NCGWS are summarised in table 2. Bloating was the most frequently reported gastrointestinal symptom (71.0%; 95% CI 62.8% to 79.1%), followed by abdominal discomfort (46.0%; 95% CI 39.0% to 52.7%) and abdominal pain (36.0%; 95% CI 28.6% to 43.2%). Constipation (26.1%; 95% CI 21.1% to 31.2%) and diarrhoea (20.8%; 95% CI 15.8% to 25.8%) were also commonly reported, while nausea was less prevalent (13.4%; 95% CI 9.3% to 17.5%). Regarding extraintestinal symptoms, fatigue was the most frequently reported (32.1%; 95% CI 25.3% to 39.0%), followed by headache (18.2%; 95% CI 12.6% to 23.7%), arthralgia (9.8%; 95% CI 8.0% to 11.6%) and rash (7.3%; 95% CI 4.8% to 9.7%).

Association with psychological distress

The prevalence rates of psychological distress in individuals with self-reported NCGWS and controls were reported in seven studies. ¹⁰ ¹¹ ¹⁵ ¹⁸ ²¹ ²² ³¹ Individuals with self-reported NCGWS were significantly more likely to report anxiety (OR 2.95; 95% CI 1.56 to 5.57; p<0.001) and depression (OR 2.42; 95% CI 1.80 to 3.24; p<0.001) than controls. Two studies reported the composite endpoint of psychological distress also found significantly higher odds in individuals with self-reported NCGWS compared with controls (OR 1.50; 95% CI 1.20 to 1.88 and OR 2.24; 95% CI 1.84 to 2.72, respectively). ²¹ ³¹

Association with IBS

Twelve studies reported the prevalence of self-reported IBS among patients with self-reported NCGWS and controls. $^{10\,11\,15\,17\,18\,21\,23\,27\,31-34}$ The pooled proportion of patients reporting IBS-type symptoms among those with self-reported NCGWS was 28.0% (95% CI 21.0% to 35.2%; I^2 =94.1%). The odds of reporting IBS-type symptoms among individuals with self-reported NCGWS were significantly higher than controls (OR 4.38; 95% CI 3.34 to 5.75; p<0.001; I^2 =77.2%). This remained significant when restricting the analysis to eight studies that used validated Rome III or Rome IV criteria for IBS (OR 4.78; 95% CI 3.48 to 6.57; p<0.001; I^2 =79.7%), with a similar pooled proportion of 27.5% (95% CI 18.6% to 36.4%; I^2 =95.6%). I^0 15 18 21 23 27 31 33

Gluten avoidance among individuals with NCGWS

A total of 16 studies reported the rates of gluten avoidance among individuals with self-reported NCGWS. $^{10-12}$ $^{14-18}$ $^{21-26}$ 31 32 The pooled proportion of individuals with self-reported NCGWS who adhered to a gluten-free diet was 40.0% (95% CI 25.2% to 55.0%; $I^2=99.3\%$).

Proportion of individuals with physician-diagnosed NCGWS

Eight studies reported the rates of seeking medical advice or formal diagnosis among individuals with self-reported NCGWS. ¹⁵ ¹⁶ ¹⁸ ²² ^{24–26} ³¹ The pooled proportion of those who reported a physician diagnosis of NCGWS was 32.0% (95% CI 17.2% to 46.8%; I^2 =96.8).

Prevalence of self-reported coeliac disease and wheat allergy

The pooled prevalence of self-reported coeliac disease in 20 studies was 0.7% (95% CI 0.4% to 1.0%), 10-12 15-28 31 32 34 with

Study	Participants with self-reported NCGWS	Total participa	nts	Prevalence with 95% CI	Weight (%)
Aziz et al., 2014	129	1,002	-	0.13 [0.11, 0.15]	4.00
Golley et al., 2015	87	1,184		0.07 [0.06, 0.09]	4.02
Ontiveros et al., 2015	96	1,237		0.08 [0.06, 0.09]	4.02
Vu et al., 2015	126	976		0.13 [0.11, 0.15]	3.99
Gasparre et al., 2015	643	4,833		0.13 [0.12, 0.14]	4.04
van Gils et al., 2016	49	785	-	0.06 [0.05, 0.08]	4.01
Cabrera-Chávez et al., 2016	55	1,207		0.05 [0.03, 0.06]	4.03
Cabrera-Chávez et al., 2017	76	1,209		0.06 [0.05, 0.08]	4.03
Carroccio et al., 2017	68	555		0.12 [0.10, 0.15]	3.95
Ontiveros et al., 2018	13	1,326	-	0.01 [0.00, 0.02]	4.05
Zanini et al., 2018	35	746	-	0.05 [0.03, 0.06]	4.02
Potter et al., 2018	464	3,115		0.15 [0.14, 0.16]	4.03
Croall et al., 2019	329	1,004		0.33 [0.30, 0.36]	3.94
Potter et al., 2020	179	1,322	-	0.14 [0.12, 0.15]	4.01
Arámburo-Gálvez et al., 2020	28	1,630	-	0.02 [0.01, 0.02]	4.05
Araya et al., 2020	9	1,203	-	0.01 [0.00, 0.01]	4.05
Ontiveros et al., 2021	55	1,058		0.05 [0.04, 0.07]	4.03
Reuzé et al., 2021	355	15,103	-	0.02 [0.02, 0.03]	4.05
Dhoble et al., 2021	23	604	-	0.04 [0.02, 0.05]	4.02
Cha et al., 2022	80	386		0.21 [0.17, 0.25]	3.84
Figueroa-Salcido et al., 2022	20	850		0.02 [0.01, 0.03]	4.04
Jansson-Knodell et al., 2023	108	2,133	—	0.05 [0.04, 0.06]	4.04
Brindicci et al., 2024	608	5,108	_	0.12 [0.11, 0.13]	4.04
El-Gamal et al., 2024	179	500		— 0.36 [0.32, 0.40]	3.83
Soares et al., 2024	78	400		0.20 [0.16, 0.23]	3.86
Overall			•	0.10 [0.07, 0.14]	
Heterogeneity: $\tau^2 = 0.01$, $I^2 = 99$	9.73% , $H^2 = 364.27$				
Test of $\theta_i = \theta_j$: Q(24) = 2556.43,	p = 0.00				
Test of θ = 0: z = 5.73, p = 0.00					
			0.00 0.10 0.20	0.30 0.40	

Random-effects REML model

Figure 2 Forest plot of the pooled prevalence of self-reported non-coeliac gluten/wheat sensitivity (NCGWS) in the general population.

significant between-study heterogeneity ($I^2=96.0\%$). Thirteen studies reported the prevalence of self-reported wheat allergy. ^{121316–1924–2628313234}The pooled prevalence of self-reported wheat allergy was 0.8% (95% CI 0.4% to 1.2%; $I^2=93.7\%$).

Risk of bias assessment

The methodological quality of the 25 included studies assessed using the Newcastle–Ottawa Scale was generally high. In total, 17 studies (68.0%) were rated as high quality, six (24.0%) as moderate quality and two (8.0%) as low quality (see online supplemental table 1). There were no statistically significant differences in the reported prevalence of NCGWS according to study quality (p=0.01). However, high-quality studies provided more conservative prevalence estimates (table 1). Excluding the two studies with low quality, the pooled prevalence of self-reported NCGWS in the remaining studies was 9.8% (95% CI 6.0% to 13.5%; I^2 =99.7%).

DISCUSSION

In this systematic review and meta-analysis we synthesised data from over 49 000 individuals across 16 countries to estimate the global burden and clinical characteristics of self-reported NCGWS. We found that approximately 10% of the general population report symptoms attributed to gluten or wheat ingestion despite the absence of coeliac disease or wheat allergy. Commonly reported symptoms included gastrointestinal symptoms such as bloating, abdominal pain and diarrhoea and also extraintestinal manifestations such as fatigue, headache and arthralgia. Self-reported NCGWS was significantly more prevalent among females and was associated with anxiety, depression and IBS. Almost half of the individuals with self-reported NCGWS follow a gluten-free diet, often without formal medical advice or diagnosis.

Self-reported NCGWS is a global phenomenon, but its prevalence rates varied widely between countries in our analysis. The pooled prevalence estimates ranged from 0.7% in Chile to 23% in the UK and 36% in Saudi Arabia. This variability may reflect multiple factors including study design, cultural attitudes toward gluten and health, and availability and marketing of gluten-free products.³⁵ Historically, adherence to a gluten-free diet was limited to people with coeliac disease. However, the growing public awareness and interest in gluten-free products

	Studies (n)	Participants (n)	Self-reported NCGWS (n)	Prevalence (95% CI)	l ²
Overall general population	25	49476	3892	10.3% (7.0% to 14.0%)	99.7%
By sex					
Male	17	10232	639	7.6% (3.6% to 11.6%)	99.4%
Female	17	14136	1914	14.0% (9.0% to 19.1%)	99.3%
By age					
Adults	23	44 088	3181	10.1% (6.2% to 14.0%)	99.7%
Children	2	5388	711	13.2% (12.3% to 14.1%)	0.2%
By sample size					
<1000	9	5802	658	13.0% (6.0% to 20.0%)	99.1%
≥1000	16	43 674	3234	8.8% (5.0% to 12.6%)	99.7%
By survey method					
In-person	15	22 489	2281	10.2% (5.8% to 14.7%)	99.6%
Postal	5	7343	891	10.7% (6.8% to 14.6%)	96.6%
Online	5	19644	717	12.0% (0% to 22.5%)	99.9%
By study period				,	
2009–2014	3	3162	342	11.0% (7.3% to 14.7%)	91.3%
2015–2019	18	38 798	2685	9.4% (5.5% to 13.3%)	99.7%
2020–2024	4	7516	862	13.7% (0% to 28.5%)	99.8%
By methodological quality				,	/
Low	2	5233	721	16.1% (10.1% to 22.1%)	89.1%
Moderate	6	19948	868	13.1% (2.6% to 23.5%)	99.8%
High	17	24295	2203	8.6% (5.0% to 12.2%)	99.4%
By country	.,	21233	2203	0.0 /0 (5.0 /0 to 12.2 /0)	33.170
Argentina	1	1209	76	6.3% (4.9% to 7.7%)	_
Australia	4	6597	856	12.2% (9.0% to 15.5%)	93.9%
Brazil	2	2030	106	10.5% (0% to 28.0%)	98.7%
Chile	1	1203	9	0.7% (0.3% to 1.2%)	-
Colombia	2	2057	75	3.4% (1.3% to 5.6%)	87.0%
El Salvador	1	1326	13	1.0% (0.5% to 1.5%)	-
France	1	15103	355	2.4% (2.1% to 2.6%)	
India	1	604	23	3.8% (2.3% to 5.3%)	
Italy	4	11 242	1354	10.5% (6.6% to 14.4%)	97.3%
Mexico	1	1237	96	7.8% (6.3% to 9.3%)	97.570
Netherlands	1	785	49	6.2% (4.5% to 7.9%)	
			55		
Paraguay	1	1058		5.2% (3.9% to 6.5%)	_
Saudi Arabia		500	179	35.8 (31.6% to 40.0%)	_
South Korea	1	386	80	20.7% (16.7% to 24.8%)	- 00.40/
UK	2	2006	458	22.8% (3.3% to 42.3%)	99.1%
USA	1	2133	108	5.1 (4.1% to 6.0%)	_
By income category of country		20055	2442	42.00/ /0.40/ 47.50/ \	00.70/
High income	16	39 955	3448	13.0% (8.1% to 17.6%)	99.7%
Upper middle income	8	8917	421	6.0% (2.0% to 9.7%)	99.1%
Lower middle income	1	604	23	3.8% (2.3% to 5.3%)	
By WHO region				5 00/ /0 40/ · 5 55/	
Americas	10	12 253	538	5.2% (2.1% to 8.3%)	99.2%
Eastern Mediterranean	1	500	179	35.8 (31.6% to 40.0%)	-
Europe	8	29136	2216	12% (5.6% to 18.4%)	99.6%
South-East Asia	1	604	23	3.8% (2.3% to 5.3%) 13.7% (9.7% to 17.7%)	_

has led to a broader adoption of gluten avoidance among individuals without coeliac disease, either due to perceived symptom relief or misconstrued beliefs about general health benefits. ^{36 37} A UK survey has shown a >2-fold increase in the prevalence of self-reported NCGWS over a 3-year period, despite a stable prevalence of coeliac disease. ²² Therefore, the public perception

of gluten may be driving the marked rise in the number of individuals who believe they are 'gluten sensitive'.

A recent randomised double-blind placebo-controlled trial showed that negative expectancy, rather than gluten intake, was the primary cause of symptoms in individuals with self-reported NCGWS.⁵ This nocebo effect has been consistently observed

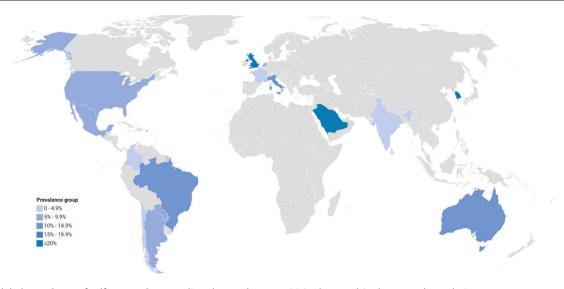


Figure 3 Global prevalence of self-reported non-coeliac gluten/wheat sensitivity (NCGWS) in the general population.

across similar trials, suggesting that psychological factors and the gut-brain axis play the central role in the pathophysiology of NCGWS. 4 38 Our findings reinforce this conclusion. We found that individuals with self-reported NCGWS were significantly more likely to report anxiety, depression and overlapping IBS compared with controls. Furthermore, individuals with self-reported NCGWS have a wide range of extraintestinal symptoms, decidedly resembling symptoms reported by patients with disorders of gut-brain interaction (DGBI). 39 40 These associations support the notion that NCGWS lies closer to the

biopsychosocial model of DGBI than to the immune-mediated spectrum of coeliac disease. However, it is important to note that gluten may still play a role in a subset of individuals with self-reported NCGWS, particularly those with more acute and severe symptoms who are often under-represented in gluten challenge trials due to anticipated ill effects. Hechanistic studies exploring immune activation, intestinal barrier dysfunction and dysbiosis in this subgroup are needed to clarify potential biological pathways. Moreover, careful clinical assessment and baseline investigations are necessary to exclude other diagnoses

Chardin		ales		iles				Odds r		Weight
Study	NCGWS	Controls	NCGWS	Controls				with 95	% CI	(%)
Aziz et al., 2014	102	449	27	424		-	_	3.57 [2.29	5.56]	6.70
Golley et al., 2015	69	557	16	511				3.96 [2.27	6.91]	5.91
Ontiveros et al., 2015	71	607	25	534			-	2.50 [1.56	4.00]	6.52
Cabrera-Chávez et al., 2016	39	637	16	515			-	1.97 [1.09	3.57]	5.67
Cabrera-Chávez et al., 2017	61	573	15	560				3.97 [2.23	7.08]	5.78
Carroccio et al., 2017	46	318	22	169	_	_		1.11 [0.65	1.91]	6.02
Ontiveros et al., 2018	9	646	4	667	_	-		2.32 [0.71	7.58]	2.77
Potter et al., 2018	348	1,306	116	1,345		-	-	3.09 [2.47	3.86]	8.11
Croall et al., 2019	218	376	111	299				1.56 [1.19	2.05]	7.83
Potter et al., 2020	136	538	43	605		-	_	3.56 [2.48	5.11]	7.27
Araya et al., 2020	6	600	3	594		-		1.98 [0.49	7.95]	2.20
Ontiveros et al., 2021	48	641	7	362				3.87 [1.73	8.65]	4.38
Cha et al., 2022	55	184	25	122	-			1.46 [0.86	2.47]	6.13
Figueroa-Salcido et al., 2022	17	435	3	395			_	5.15 [1.50	17.69]	2.61
Jansson-Knodell et al., 2023	73	1,361	35	664	-	_		1.02 [0.67	1.54]	6.92
Brindicci et al., 2024	486	2,780	122	1,720				2.46 [2.00	3.03]	8.19
El-Gamal et al., 2024	130	214	49	107	-			1.33 [0.89	1.98]	6.99
Overall						•		2.29 [1.80	2.90]	
Heterogeneity: $\tau^2 = 0.17$, $I^2 = 7$	9.01%, H ² =	4.77								
Test of $\theta_i = \theta_j$: Q(16) = 66.82, p	0.00									
Test of θ = 0: z = 6.81, p = 0.00)									
					0.5	1 2	4 8	16		

Random-effects REML model

Figure 4 Forest plot of the odds of self-reported non-coeliac gluten/wheat sensitivity (NCGWS) in females compared with males.

Table 2 Gastrointestinal and extraintestinal symptoms in patients with self-reported non-coeliac gluten/wheat sensitivity (NCGWS)							
	Studies (n)	Self-reported NCGWS (n)	Proportion (95% CI)	l ²			
Gastrointestinal symptoms							
Abdominal pain	11	1919	36.0% (28.6% to 43.2%)	89.9%			
Abdominal discomfort	10	1141	46.0% (39.0% to 52.7%)	81.7%			
Nausea	14	2415	13.4% (9.3% to 17.5%)	89.4%			
Bloating	14	2415	71.0% (62.8% to 79.1%)	95.3%			
Diarrhoea	13	2236	20.8% (15.8% to 25.8%)	87.2%			
Constipation	14	2415	26.1% (21.1% to 31.2%)	87.0%			
Extraintestinal symptoms							
Fatigue	13	1833	32.1% (25.3% to 39.0%)	88.7%			
Headache	13	1833	18.2% (12.6% to 23.7%)	89.6%			
Rash	12	1810	7.3% (4.8% to 9.7%)	72.1%			
Arthralgia	12	1753	9.8% (8.0% to 11.6%)	24.9%			

with similar presentations that require specific treatment such as coeliac disease, inflammatory bowel disease, microscopic colitis, bile acid diarrhoea and other relevant gastrointestinal disorders before making a diagnosis of NCGWS.⁴²

Approximately 40% of individuals with self-reported NCGWS adhere to a gluten-free diet. Although symptomatic improvement after excluding gluten has been reported, 43 44 many individuals with self-reported NCGWS continue to experience gastrointestinal and extraintestinal symptoms despite long-term adherence to a gluten-free diet. 45 An Italian tertiary-centre study found a significant post-pandemic decline in outpatient NCGWS diagnoses, indicating that many individuals no longer seek medical evaluation for this condition and may adopt a gluten-free diet without pursuing a formal diagnosis. 46 Following a gluten-free diet without medical or dietetic oversight is associated with an increased risk of nutritional deficiencies, psychological burden and unnecessary economic cost. 47 A detailed assessment of both physical and psychological factors, including evaluation for overlapping DGBI, is therefore essential to avoid unnecessary dietary restrictions. In many cases, symptoms attributed to gluten may instead be triggered by food containing fermentable oligosaccharides, disaccharides, monoaccharides, and polyols (FODMAPs), particularly fructans, which are commonly found in wheat-based foods like bread.⁴⁸ This is supported by a recent global survey which showed that individuals in countries with the highest IBS prevalence and severity were consuming diets rich in FODMAPs, particularly pasta and bread.⁴⁹ Interestingly, a large proportion of individuals with self-reported NCGWS do not follow a strict gluten-free diet and the nuances of their dietary habits, including partial avoidance, self-modification or intermittent adherence, cannot be fully captured in crosssectional studies.

Our findings have implications for clinical practice and research. To date, most research and funding have been focused on the role of gluten in triggering symptoms in NCGWS or on the search for specific disease biomarkers. ^{50 51} Reclassifying NCGWS as a DGBI and the development of standardised symptom-based criteria for diagnosis could shift the focus toward a more holistic, biopsychosocial understanding of this heterogeneous condition. Such a shift would support more individualised approaches to diagnosis and management. Future research should prioritise identifying the clinical phenotypes of NCGWS, exploring the role of the gut—brain axis and psychological comorbidities, and evaluating the effectiveness of multidisciplinary interventions beyond the gluten-free diet.

Strengths and limitations

Our study has several strengths. This is the first comprehensive and methodologically robust systematic review and metaanalysis of the global prevalence of self-reported NCGWS. Second, our analysis included over 49 000 participants from 16 countries representing five out of six WHO regions, providing a geographically diverse representation of the prevalence of selfreported NCGWS worldwide. Third, we followed a rigorous methodology including a prospectively registered protocol, a highly sensitive literature search with an experienced librarian, duplicate screening and data extraction, and quality assessment using a validated tool adapted for cross-sectional studies. Fourth, we performed extensive subgroup and sensitivity analyses to explore the sources of heterogeneity and to assess the robustness of our results. Fifth, we offered novel insights into the clinical profile of patients with self-reported NCGWS by synthesising data on associated symptoms, dietary behaviours and psychological comorbidities.

The limitations of our study should also be acknowledged. There was evidence of substantial heterogeneity in most of the analyses, which could not be fully explained despite subgroup and meta-regression analyses. Such heterogeneity is common in prevalence meta-analysis and reflects a combination of residual confounding factors, variability in diagnostic criteria, true differences in prevalence across populations and countries, and potential publication bias. Another limitation is that we relied on self-reported NCGWS, which may be subject to recall or misclassification bias. The reliance on self-reported data is an inherent limitation to most global prevalence studies of DGBI, which similarly depend on symptom-based, self-reported data. Nonetheless, such studies provide essential insights to guide clinical practice, inform public health priorities and shape future research directions. Importantly, the pooled prevalence of self-reported coeliac disease and wheat allergy in the same populations aligns with the widely accepted global figures, 52 53 supporting the validity of the self-reported data. Despite the wide geographical representation, data remain limited or entirely lacking from several countries and regions, which may limit the generalisability of our findings to these populations. Finally, several authors of this meta-analysis contributed to a subset of the included studies. While this may introduce a potential risk of bias, it also allowed for accurate verification of data and study characteristics.

CONCLUSION

Self-reported NCGWS affects approximately one in 10 people worldwide, with a considerable geographical variation and

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strong association with female sex, psychological distress and IBS. Recognising NCGWS within the DGBI framework and the development of symptom-based diagnostic criteria are needed to guide a more tailored management approach focusing on individual symptom patterns and dietary triggers beyond gluten and to reduce unnecessary dietary restriction in this common condition.

Author affiliations

¹Division of Clinical Medicine, School of Medicine and Population Health, The University of Sheffield, Sheffield, UK

²Department of Gastroenterology, University Hospitals of Leicester NHS Trust, Leicester, UK

³Academic Unit of Gastroenterology, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK

⁴Department of Translational Medicine, St Anna Hospital, University of Ferrara, Ferrara, Italy

⁵Nutrition Ściences Postgraduate Program, Autonomous University of Sinaloa, Culiacán, Mexico

⁶Clinical and Research Laboratory (LACIUS, C.N., CONAHCYT National Laboratory, LANIBIOC), Department of Chemical, Biological, and Agricultural Sciences (DC-QB), Faculty of Biological and Health Sciences, University of Sonora, Sonora, Mexico
⁷Mucosal Immunology and Biology Research Centre, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts, USA

⁸Division of Gastroenterology, Hepatology, and Nutrition, Department of Medicine, Cleveland Clinic, Cleveland, Ohio, USA

Social media Mohamed G Shiha, X @Mo_Shiha

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Contributors Conception and design: MGS, IA, DSS. Literature search and data extraction: MGS, FM. Statistical analysis and data visualisation: MGS. Quality assessment: MGS, FM. Initial drafting of the manuscript: MGS, IA, DSS. Data interpretation, critical revision of the manuscript and final approval of the submitted version: all authors. All authors approved the final draft of the manuscript. MGS is the guarantor.

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ORCID iDs

Mohamed G Shiha http://orcid.org/0000-0002-2713-8355 Alberto Rubio-Tapia http://orcid.org/0000-0001-6964-4072

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