

Obesity, Metabolic Syndrome, and Cardiovascular Risk in Gluten-Free Followers Without Celiac Disease in the United States: Results from the National Health and Nutrition Examination Survey 2009–2014

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Abstract

Background Despite unclear benefits of gluten-free diets (GFD) in the general population, gluten-free followers without medical indications are driving the market. Few studies have investigated health benefits of GFD in the general population.

Aims To estimate metabolic and cardiovascular disease (CVD) risk profiles among gluten-free followers without celiac disease (CD).

Methods Data were obtained from the National Health and Nutrition Examination Survey (NHANES) 2009–2014. There were 13,523 persons without CD who had GFD information. People with known CVD were excluded. We compared gluten-free followers without CD and the general population by selective metabolic and CVD risk profiles using survey-weighted generalized logistic regression.

Results There were 155 gluten-free followers without CD and CVD, corresponding to a weighted prevalence of 1.3% (3.2 million Americans). Gluten-free followers tended to be women and have a smaller waist circumference and higher HDL cholesterol. They also had a lower BMI with a borderline *p* value (0.053) and significant self-reported weight loss (−1.33 kg) over one year. Moreover, gluten-free followers were more likely to consider their weight appropriate. There was no statistical difference by age,

smoking, hypertension, total cholesterol, triglyceride cholesterol, HbA1c, or fasting glucose. Despite a lower probability of having metabolic syndrome (33.0 vs 38.5%) and lower 10-year CVD risk score (4.52 vs 5.70%) in gluten-free followers, there was no statistical difference.

Conclusions Although being on a GFD may be beneficial in weight management, there was no significant difference in terms of prevalence of metabolic syndrome and CVD risk score in gluten-free followers without CD.

Keywords Gluten-free diet · Obesity · Metabolic syndrome · Cardiovascular risk

Introduction

Gluten-free diets (GFD) have seen an enormous growth in popularity and availability in recent years, with an annual market growth rate of 10.4% from \$4.63 billion spent in 2015 to \$7.59 billion expected in 2020 [1]. While up to 30% of Americans have reportedly endorsed trying a gluten-free diet [2], the prevalence of celiac disease (CD), the main medical indication for GFD, in the USA is estimated to be around 0.7%—or 1.76 million Americans—and has remained stable in recent years [3]. It has been suggested that gluten-free followers without medical indications are driving the market growth [2]. Celebrity endorsements have also caused an increased awareness of the diet among the general population, as they have advocated its beneficial effects on maintaining body shape and weight loss [4, 5].

While strict adherence to a GFD is the treatment of choice with proven benefits in CD patients [6–9], the health benefits of a GFD in the general population remains unclear. Despite this, being on a GFD is generally

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perceived as being “healthier,” promoting weight loss and improving metabolic parameters. Furthermore, non-celiac gluten sensitivity (NCGS), an entity with clinical signs suggestive of celiac disease without the typical enteropathy or serology, has gained attention. Increasing evidence suggesting clinical improvement in NCGS patients who adhere to a GFD has provoked debates about the appropriateness of a GFD in the general population [10–12].

Often, the health effect of a diet is measured by its effect on metabolic and cardiovascular disease (CVD) risk profiles. Other popular diets, such as vegetarian [13–15] and Mediterranean [16] diets, have large bodies of evidence of their health benefits on metabolic and cardiovascular diseases. To our knowledge, there is no published literature that has investigated the effect of GFD on obesity, metabolic syndrome, and cardiovascular disease in the general population. Thus, the purpose of this study was to evaluate whether there was an association between being a gluten-free follower without CD and likelihood of obesity, metabolic syndrome, or elevated cardiovascular disease risk, using nationally representative data.

Methods

Data Collection

The National Health and Nutrition Examination Survey (NHANES) is a series of cross-sectional surveys conducted every two years by the National Center for Health Statistics of the Centers for Disease Control and Prevention. This survey is conducted by a complex, stratified, and multi-stage probability sampling design that obtains information using standardized household interviews, physical examinations, and testing of biologic samples. Currently, NHANES is the only nationally representative survey that has measured celiac disease serology coupled with questions about medical conditions. For our study, we combined 3 cycles of NHANES data (2009–2010, 2011–2012, and 2013–2014) to obtain an adequate sample size. The NHANES protocol was approved by the human subjects review board, and written informed consent was obtained from all participants.

Participants

In the NHANES 2009–2014, there were 22,278 individuals aged 6 years or older who participated in serologic testing for CD and completed a comprehensive set of questionnaires (Fig. 1). The overall unweighted response rates for the 2009–2010, 2011–2012, and 2013–2014 surveys were 77.3, 69.5, and 68.5%, respectively. We defined gluten-free followers without CD as those who reported being on a

GFD in a medical question (MCQ 086: “Are you on a gluten-free diet?”) without meeting our CD definition [17]. As described in previous studies [3, 18], CD was defined as having either double-positive serology on IgA tissue transglutaminase (IgA tGA) and IgA Endomysial antibody (IgA EMA) (Serologic CD, by LBXTTG and LBXEMA variable) or a reported diagnosis of CD by a healthcare provider coupled with being on a GFD (reported clinical CD, by MCQ 082: “Ever been told you have celiac disease?”). Overall participation rate for celiac disease serologic testing among individuals aged greater than 6 in the NHANES was 90.2%. Persons with or without available CD serologic testing did not substantially differ by major demographic variables (age, sex, and race). Among them, there were 13,591 persons aged between 20 and 80 years who did not report having a prior diagnosis of CVD. In total, there were 68 participants who met our CD criteria (19 reported clinical CD and 50 serologic CD). One participant met both serologic and reported clinical criteria. After excluding CD patients ($n = 68$), 13,523 persons met our selection criteria, including 155 gluten-free followers (Fig. 1).

Blood Pressure and Anthropometric Measurements

Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured in the mobile examination center (MEC) after participants rested for 5 min quietly in a sitting position and after determining maximum inflation level. Hypertension was defined if SBP ≥ 130 mmHg or DBP ≥ 85 mmHg or patient was on treatment with hypertensive medications. Waist circumference was measured during a health examination in the MEC and was measured at the highest point of the iliac crest at minimal respiration. BMI (kg/m^2) was categorized as: underweight (≤ 18.5); normal (18.5–24.9); overweight (25.0–29.9); or obese (≥ 30.0) according to the World Health Organization (WHO) criteria [19].

Metabolic Syndrome

The metabolic syndrome was defined according to the NCEP/ATP III revised diagnostic criteria proposed by AHA/NHLBI [20]. Specifically, individuals with three or more of the following five criteria were defined as having metabolic syndrome: (1) abdominal obesity (waist circumference >102 cm for men and >88 cm for women); (2) serum triglyceride cholesterol (TG) levels ≥ 150 mg/dl (≥ 1.7 mmol/l) or treatment for elevated TG; (3) HDL concentration <40 mg/dl (<1.04 mmol/l) for men and <50 mg/dl (<1.3 mmol/l) for women or treatment for low HDL; (4) SBP ≥ 130 mmHg or DBP ≥ 85 mmHg or treatment with antihypertensive medications; and (5)

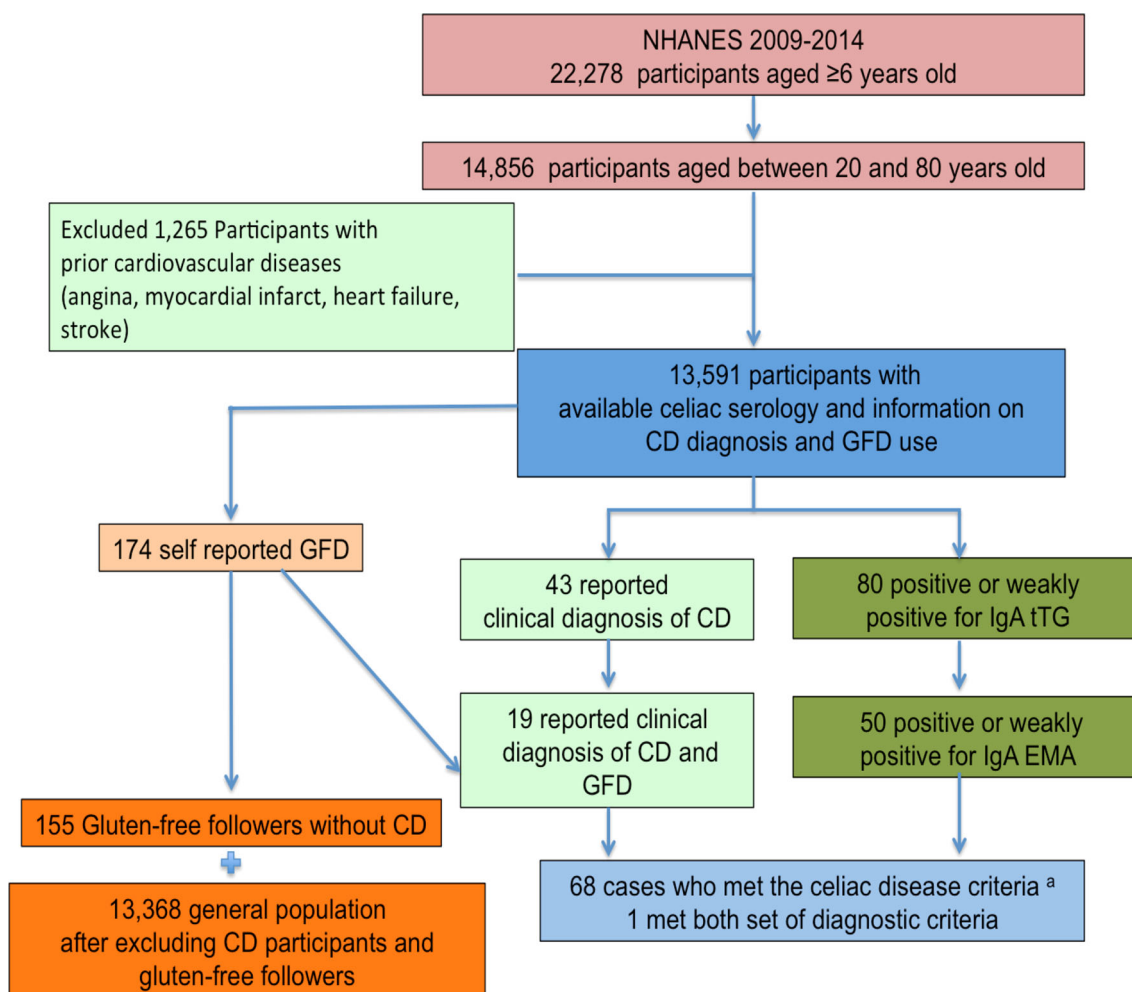


Fig. 1 Selection criteria ^a Celiac disease (CD) was defined as having either double-positive serology on IgA tissue transglutaminase (IgA tGA) and IgA Endomysial antibody (IgA EMA) or a reported

fasting glucose ≥ 100 mg/dl (≥ 5.5 mmol/l) or treatment with glucose-lowering medications.

CVD Risk Profile

The 10-year CVD risk profile score or Framingham Risk Score (FRS) was derived based on the formula in the Framingham Heart Study [21]. FRS represents the estimated 10-year risk of myocardial infarction, angina, ischemic or hemorrhagic stroke, transient ischemic attack, heart failure, or peripheral artery disease. FRS incorporates age, sex, SBP, treatment for hypertension, current smoking, diabetes, and serum total and HDL cholesterol levels.

Covariates

In order to investigate the association of GFD with metabolic parameters and cardiovascular risk in gluten-free

followers, we explored the data that are needed to assess the status of metabolic syndrome and FRS: age (divided into age groups: 20–39 years old, 40–59 years old, and 60–79 years old), sex (male or female), current smoking status (yes or no), self-reported weight change over one year (kg), self-reported weight status (overweight, underweight, or about the right weight), BMI (kg/m^2), waist circumference (cm), hypertension diagnosis (yes or no), being on any blood pressure medication (yes or no), serum total cholesterol (mg/dL), serum HDL cholesterol (mg/dL), serum TG cholesterol (mg/dL), HbA1c (%), fasting glucose level, and being on any diabetes medication (yes or no). Serum total cholesterol levels and TG levels were measured enzymatically (Roche/Hitachi Modular P Chemistry Analyzer). Serum HDL levels were measured using the direct HDL immunoassay method (Roche/Chemistry Cobas 6000 Analyze). Fasting glucose levels were analyzed using a hexokinase assay (Roche Diagnostics), and

HbA1c was measured by the A1c G7 HPLC Glycohemoglobin Analyzer (Tosoh Medics, Inc). The self-reported weight change was calculated by the difference between self-reported current weight (WHD020 question) and weight one year ago (WHD050 question) [22].

Statistical Analysis

Data were analyzed using R software version 3.2.2, using the “survey” package [23]. We used appropriate study design and published weights for all analyses to account for oversampling and nonparticipation in the household interview and physical examination. All variance calculations took into consideration the design effects of the survey using Taylor series linearization [24]. We compared gluten-free followers without CD and the general population using survey-weighted generalized logistic regression in the selected variables as mentioned in the covariate section. Obesity, metabolic syndrome, and FRS were utilized to summarize the overall risk. All statistical tests were adjusted by age, sex, and race.

Results

Demographics

As summarized in Fig. 1 and Table 1, 155 gluten-free followers without CD met the inclusion criteria, corresponding to a weighted prevalence of 1.3% [95% confidence interval (CI) 0.9–1.6], or 3.2 million Americans. Most of them were young or middle-aged adults aged between 40 and 59 (43.3%), followed by age group 20–39 (41.2%) and age group 60–79 (15.6%). There was no statistical age difference compared to the general population (43.5 years old in gluten-free followers vs 44.6 years old in the general population, p value 0.39). Moreover, gluten-free followers tended to be women (64.6 vs 51.6%, p value < 0.01), born in the USA (86.7 vs 80.9%, p value < 0.05), and have a higher education level (p value < 0.05) and household income (poverty index \geq 1.85: 77.5 vs 61.7%, p value < 0.01).

Obesity and Weight Change

The mean BMIs of gluten-free followers without CD and the general population were 27.2 [95% CI 25.9–28.5] and 28.8 [95% CI 28.6–29.1], respectively, with p value of 0.053 (Table 2). According to the World Health Organization classification of obesity, 1.41% [95% CI –0.13 to 2.95], 42.5% [95% CI 32.4–52.7], 26.4% [95% CI 17.4–35.3], and 29.7% [95% CI 20.8–38.6] of gluten-free followers and 1.59%, [95% CI 1.31–1.86], 28.8% [95% CI

27.3–30.3], 33.8% [95% CI 32.5–35.0], and 35.9% [95% CI 34.5–37.2] of the general population were classified as underweight, normal, overweight, and obese, respectively. Although gluten-free followers were more likely to have a normal BMI range (18.5–25), this composition was not statistically different when compared to the general population with a borderline p value of 0.09 after adjusting for age, sex, and race. In addition, gluten-free followers without CD had a statistically significant self-reported weight change over one year (–1.33 kg vs +0.01 kg, p value 0.04) and were more likely to consider their weight status as being “about the right weight.”

Metabolic Syndrome and Framingham 10-Year Cardiovascular Disease Risk

Metabolic and cardiovascular risk profiles of gluten-free followers are summarized in Table 3. Gluten-free followers had a smaller waist circumference (92.7 cm [95% CI 88.7–95.8] vs 98.4 cm [95% CI 97.9–98.9], p value < 0.01) and a higher serum HDL cholesterol level (58.1 mg/dL [95% CI 54.4–61.9] vs 53.2 mg/dL [95% CI 52.7–53.6], p value < 0.05) after adjusting for age, sex, and race. There was no significant difference between gluten-free followers and the general population in terms of smoking status (current smoker: 15.6 vs 20.4%, p value 0.36), mean systolic blood pressure (117 vs 121 mmHg, p value 0.33), proportion of people on blood pressure medications (14.1 vs 19.0%, p value 0.32), serum total cholesterol level (199 vs 195 mg/dL, p value 0.25), serum triglyceride cholesterol level (132 vs 152 mg/dL, p value 0.37), mean HbA1c (5.48 vs 5.57%, p value 0.52), or proportion of people with an elevated fasting glucose or on diabetes medications (29.6 vs 29.9%, p value 0.65). Moreover, the prevalence of metabolic syndrome in gluten-free followers was not significantly different from that in the general population (33.0% [95% CI 20.4–45.7] vs 38.5% [95% CI 37.1–40.0], p value 0.42). In the FRS comparison, gluten-free followers had a lower risk score (4.52% [95% CI 3.35–5.86] vs 5.70% [95% CI 5.66–5.94]), but it did not reach statistical significance (p value 0.63).

Discussion

While the prevalence of CD has been stable in recent years, the popularity of GFD has grown disproportionately [3]. Thus, it becomes important to evaluate the “real” versus “perceived” health benefits of this diet, especially in light of the costs of such foods. Gluten-free foods can cost up to five times as much as equivalent gluten-containing foods, and the cost difference has remained high over the past decade [25–27]. However, to our knowledge, there is no

Table 1 Demographics of gluten-free followers without celiac disease

	Gluten-free followers without CD <i>N</i> = 155 Weighted prevalence: 1.3% [95% CI 0.9–1.6]	General population <i>N</i> = 13,368	Age, sex, race adjusted <i>p</i> value
Age (%)			
20–39	41.2% [95% CI 30.0–52.4]	40.4% [95% CI 38.4–42.4]	0.45
40–59	43.3% [95% CI 32.3–54.2]	40.2% [95% CI 38.8–41.6]	
60–79	15.6% [95% CI 6.85–24.3]	19.4% [95% CI 18.3–20.5]	
Mean, 95% CI	43.5 [95% CI 40.0–47.0]	44.6 [95% CI 44.0–45.3]	0.39
Sex (%)			
Male	35.4% [95% CI 27.0–43.8]	48.4% [95% CI 47.5–49.4]	<0.01
Female	64.6% [95% CI 56.2–73.0]	51.6% [95% CI 50.6–52.5]	
Race (%)			
Non-Hispanic whites	71.0% [95% CI 61.2–80.7]	66.0% [95% CI 61.9–70.1]	0.14
Non-Hispanic blacks	9.73% [95% CI 5.85–13.6]	11.0% [95% CI 9.16–12.9]	
Hispanics	10.1% [95% CI 5.12–15.0]	15.2% [95% CI 12.2–18.3]	
Others	9.23% [95% CI 3.84–14.6]	7.78% [95% CI 6.61–8.95]	
Born in the USA			
No	13.3% [95% CI 6.87–19.7]	19.1% [95% CI 16.8–21.5]	<0.05
Yes	86.7% [95% CI 80.3–93.1]	80.9% [95% CI 78.5–83.3]	
Education level (%)			
Below high school	10.5% [95% CI 4.13–16.9]	16.0% [95% CI 14.3–17.6]	<0.05
High school	12.3% [95% CI 5.48–19.2]	21.2% [95% CI 19.8–22.6]	
Above high school	77.1% [95% CI 68.5–85.8]	62.9% [95% CI 60.4–65.3]	
Poverty index^a (%)			
≤1.3	13.3% [95% CI 6.21–20.4]	26.3% [95% CI 24.2–28.4]	<0.01
1.3–1.85	9.22% [95% CI 5.30–13.1]	12.0% [95% CI 11.1–12.9]	
≥1.85	77.5% [95% CI 69.6–85.4]	61.7% [95% CI 59.3–64.2]	

^a It was calculated by dividing family income by the poverty guidelines, specific to family size, as well as the appropriate year and state. The index was grouped into three categories with cutoffs of 1.30 and 1.85 according to the poverty guidelines

Table 2 Prevalence of obesity in the gluten-free followers without celiac disease

	Gluten-free followers without celiac disease (%) [95% CI]	General population (%) [95% CI]	Age, sex, race adjusted <i>p</i> value
BMI			
<18.5	1.41% [−0.13 to 2.95]	1.59% [1.31–1.86]	0.09
18.5–25	42.5% [32.4–52.7]	28.8% [27.3–30.3]	
25–30	26.4% [17.4–35.3]	33.8% [32.5–35.0]	
≥30	29.7% [20.8–38.6]	35.9% [34.5–37.2]	
Mean [95% CI]	27.2 [25.9–28.5]	28.8 [28.6–29.1]	0.053
Weight change over 1 year (Mean, [95% CI])	−1.33 kg [−2.28 to 0.12]	0.01 kg [−0.20 to 0.22]	0.04
Perceived weight status			
Overweight	45.5% [33.5–57.5]	56.0% [54.5–57.5]	0.03
Underweight	1.91% [−0.11 to 3.93]	4.3% [3.9–4.7]	
About the right weight	52.6% [40.8–64.4]	39.7% [38.2–41.2]	

CI confidence interval

published article that has investigated the health effects of the GFD in the general population without CD. In the current study, we assessed obesity, metabolic syndrome, and FRS in gluten-free followers without CD.

Our findings show that gluten-free followers tend to be women, born in the USA, and have higher education levels (above high school) and household incomes. Gluten-free followers had a lower BMI (27.2 kg/m² [2] in gluten-free followers vs 28.8 kg/m² in the general population) with a borderline *p* value of 0.053 and a smaller waist circumference (92.7 vs 98.4 cm, *p* value < 0.05). Moreover, they had a statistically greater self-reported weight loss over one year (−1.33 vs +0.01 kg, *p* value 0.04), and a higher proportion of them viewed their weight as appropriate. This is congruent with claims made by marketing surveys, celebrities, and athletes who advocate for the benefits of GFD in weight loss [4, 5]. However, these findings need to be interpreted cautiously. Several previous studies about the effect of GFD in CD patients have suggested weight gain after GFD treatment, although contradictory findings exist and findings in CD patients may not apply to the general population [28–31]. A study from Ireland suggested that being on a GFD resulted in weight gain in already overweight CD patients, raising concern about morbidities from worsening BMI [28]. Kabbani et al. [31]

also reported that BMI in CD patients increased on GFD, especially in those who adhered closely to it. On the GFD, 15.8% of patients moved from a normal or low BMI class into an overweight BMI class, and 22% of patients overweight at diagnosis gained weight. Furthermore, the fact that demographic characteristics of gluten-free followers include more women and those with higher education levels and household incomes—which are all factors associated with better weight control via a healthier lifestyle [32, 33]—may have contributed to our finding of improved weight profiles since the statistical significance of “weight loss over one year” became borderline significant (*p* value 0.07) after adding poverty index and education variables in the model.

Additionally, our study suggests that gluten-free followers without CD had a higher average serum HDL cholesterol level, a protective factor in the progression of atherosclerosis and in developing coronary artery disease. Higher HDL cholesterol in gluten-free followers is consistent with previous studies that showed improved lipid profiles in CD patients after GFD treatment [34–36]. It is suggested that the improvement in lipid profiles in CD patients is in part due to a recovered intestine, a major source of absorption of both HDL and apo-A1, the main apo-protein of circulating HDL. However, the mechanism

Table 3 Metabolic syndrome and FRS of gluten-free followers

	Gluten-free followers without CD	General Population	Age, sex, race adjusted <i>p</i> value
Smoking			
Yes	15.6% [95% CI 6.26–24.9]	20.4% [95% CI 19.1–21.7]	0.36
No	84.4% [95% CI 75.1–93.7]	79.6% [95% CI 78.3–80.9]	
Waist circumference (cm) (Mean, 95% CI)	92.7 [95% CI 88.7–95.8]	98.4 [95% CI 97.9–98.9]	<0.01
Hypertension			
Systolic BP (mmHg) (Mean, 95% CI)	117 [95% CI 114–121]	121 [95% CI 120–122]	0.33
BP treatment (%)	14.1% [95% CI 7.64–20.5]	19.0% [95% CI 17.7–20.3]	0.32
Total cholesterol (mg/dL) (Mean, 95% CI)	199 [95% CI 190–209]	195 [95% CI 194–196]	0.25
HDL Cholesterol (mg/dL) (Mean, 95% CI)	58.1 [95% CI 54.4–61.9]	53.2 [95% CI 52.7–53.6]	<0.05
TG Cholesterol (mg/dL) (Mean, 95% CI)	132 [95% CI 109–155]	152 [95% CI 148–156]	0.37
HbA1c (%)	5.48 [95% CI 5.33–5.63]	5.57 [95% CI 5.55–5.59]	0.52
Elevated fasting glucose or on diabetes medication (%)	29.6% [95% CI 19.9–39.3]	29.9% [95% CI 28.7–31.0]	0.65
Who met metabolic syndrome criteria (%)	33.0% [95% CI 20.4–45.7]	38.5% [95% CI 37.1–40.0]	0.42
Framingham CVD 10-year risk %	4.52 [95% CI 3.35–5.86]	5.70 [95% CI 5.66–5.94]	0.63

for improvement in lipid profiles in gluten-free followers without the malabsorption found in CD may be different and needs further investigation. Despite higher HDL levels and lower waist circumferences, gluten-free followers did not have more favorable overall CVD risk, estimated by FRS (4.52 vs 5.70%, *p* value 0.63). There was also no significant difference in other elements of metabolic syndrome: hypertension, triglycerides, and elevated fasting glucose or being on diabetic medications.

Several elements likely play into this finding that GFD is not associated with lower prevalence of metabolic syndrome and beneficial CVD risk profiles. The simplest explanation is that a GFD may not, in fact, be healthier. Analyses of patients on GFD suggest that they may be consuming more carbohydrates and sugars and becoming deficient in several vitamins and minerals [37, 38]. Many gluten-free products do not contain the same levels of magnesium, zinc, selenium, folate, calcium, B-vitamins, iron, and fiber as their wheat-containing counterparts [39, 40]. Following a GFD also may change the gut

microbiome, reducing concentrations of beneficial bacteria and increasing levels of pathogenic bacteria [41, 42]. However, given the cross-sectional survey design, this finding needs to be interpreted with the caveat that no causal relationships could be investigated. Moreover, the relatively small sample size could be a reason for not reaching statistical significance. Finally, while elements of metabolic syndrome and FRS are useful surrogates for CVD risk and overall health, they are not perfect markers. FRS may underestimate CVD risk in women and some racial/ethnic minorities and does not capture nontraditional CVD risk factors related to inflammation and oxidative stress [43, 44]. Many young patients with a first myocardial infarction turn out to have a low FRS [45].

While our study did not demonstrate a significant difference in terms of metabolic syndrome and CVD risk score, gluten-free followers without CD consume gluten-free products with different reasons and goals. Gluten-free followers may obtain an improved sense of well-being as a result of potential weight loss and eliminating highly

processed foods and refined carbohydrates such as white bread and pizza from their diet, while increasing consumption of fruit and vegetables [46]. This can be supported by our findings that gluten-free followers are more likely to perceive their weight as being normal (Table 2). Furthermore, there is increasing evidence that people with NCGS report improved gastrointestinal and extra-intestinal symptoms, including mental confusion, depression, and fatigue after the adoption of a GFD [10–12]. However, the definition and prevalence of NCGS is still unclear as symptoms overlap with irritable bowel syndrome. Additionally, there have been debates about whether avoiding the gluten component was the major responsible factor in alleviating symptoms, since there are other components in gluten-containing products—particularly, fermentable, oligo-, di-, monosaccharides, and polyols (FOMADS), which are poorly absorbed carbohydrates. Moreover, by embarking on a self-imposed GFD before medical evaluation, these people may lose their opportunity to be accurately diagnosed with CD or NCGS. In our current study, the proportion of NCGS participants among the gluten-free followers could not be assessed.

Strengths of this study are that NHANES data provide a unique opportunity to describe gluten-free followers in a healthy general population with comprehensive demographic, physical exam, and biochemical lab values to investigate associations of the diet with metabolic/cardiovascular risks. This allows us to use strict, objective criteria to define those with CD, metabolic syndrome, and CVD risk. There are also multiple limitations to our study. Patient preference for GFD is self-reported with potential recall bias, and the degree and duration of adherence to the diet could not be assessed. As mentioned previously, causal relationships could not be determined and the number of gluten-free followers was small (although the authors are not aware of any larger cohort of patients on a GFD that have been examined for their metabolic/cardiovascular risk factors).

In conclusion, gluten-free diet followers are a heterogeneous group with different reasons and goals for being on the diet. Our study found that being on a GFD is associated with healthier waist circumference and HDL levels with potential benefits in weight, but not with decreased prevalence of metabolic syndrome or cardiovascular risk as determined by FRS. Given little proven health benefit of GFD in the general population and existing concerns of nutritional deficiencies and false negatives in CD serology by self-imposed GFD, gluten-free followers should consider having a medical evaluation and dietary review with an experienced gastroenterologist and dietician before starting the diet. Further prospective studies are warranted in order to better assess the health benefits of GFD in individuals without CD.

Author's contributions HSK and SKA are involved in study and design. All authors are involved in acquisition, analysis, or interpretation of data. All authors are involved in drafting of the manuscript. All authors are involved in critical revision of the manuscript for important intellectual content. HSK is involved in statistical analysis. All authors are involved in administrative, technical, or material support. HSK, MFD, NK, MF, SKA are involved in study supervision. Dr. H.S. Kim had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. All authors approved the final version of the manuscript.

Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

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