Low Rates of Screening for Celiac Disease Among Family Members

Adam S. Faye,[*,a] Fernanda Polubriaginof,[‡,a] Peter H. R. Green,[*] David K. Vawdrey,[‡] Nicholas Tatonetti,[‡] and Benjamin Lebwohl[*]

*Division of Gastroenterology and Hepatology, ‡Division of Biomedical Informatics, Columbia University Medical Center/New York-Presbyterian Hospital, New York, New York

BACKGROUND & AIMS: **Given the increased morbidity and potential mortality of celiac disease, guidelines recommend screening high-risk individuals, including first-degree relatives of patients. We assessed how commonly celiac disease testing occurs in these individuals and identified factors that influence testing.**

METHODS: **Relatives of 2081 patients with biopsy-diagnosed celiac disease and followed up at Columbia University Medical Center were identified using relationship inference from the electronic health record—a validated method that uses emergency contact information to identify familial relationships. We manually abstracted data from each record and performed univariate and multivariate analyses to identify factors associated with testing relatives for celiac disease.**

RESULTS: **Of 539 relatives identified, 212 (39.3%) were tested for celiac disease, including 50.4% (193 of 383) of first-degree relatives and 71.5% (118 of 165) of symptomatic first-degree relatives. Of the 383 first-degree relatives, only 116 (30.3%) had a documented family history of celiac disease. On multivariate analysis, testing was more likely in adults (odds ratio [OR], for 18–39 y vs younger than 18 y, 2.27; 95% CI, 1.12–4.58); relatives being seen by a gastroenterologist (OR, 15.16; 95% CI, 7.72–29.80); relatives with symptoms (OR, 3.69; 95% CI, 2.11–6.47); first-degree relatives of a patient with celiac disease (OR, 4.90, 95% CI, 2.34–10.25); and relatives with a documented family history of celiac disease (OR, 11.9, 95% CI, 5.56–25.48).**

CONCLUSIONS: **By using an algorithm to identify relatives of patients with celiac disease, we found that nearly 30% of symptomatic first-degree relatives of patients with celiac disease have not received the tests recommended by guidelines. Health care providers should implement strategies to identify and screen patients at increased risk for celiac disease, including methods to ensure adequate documentation of family medical history.**

Keywords: RIFTEHR; Gluten; Transglutaminase; Antibody; Risk Factor.

Celiac disease is a genetically linked autoimmune disease triggered by the ingestion of gluten. Currently, it is estimated that approximately 1% of the population has celiac disease, with recent studies showing an increasing prevalence of the disease worldwide.[1–3] Given the myriad presenting symptoms, diagnosis of celiac disease can be missed, placing individuals at risk for increased morbidity and possibly mortality.[4,5] Recent studies have suggested that asymptomatic individuals identified via screening have benefited from initiation of a gluten-free diet; patients had fewer gastrointestinal symptoms, improved histologic findings on biopsy, and lower anxiety without impairment in quality of life.[6–8] As a result, emphasis has been placed on identifying and ensuring early diagnosis of patients with celiac disease.

Current strategies focus on testing patients with a higher pretest probability of disease. Included in this population are those with a family history of celiac disease, who are known to be at a higher risk. One recent study estimated that 10% of first-degree relatives of those with celiac disease also were found to have celiac disease.[9] Guidelines thus recommend testing for celiac disease in symptomatic first-degree relatives, and to

[a]Authors share co-first authorship.

Abbreviations used in this paper: EHR, electronic health record; RIFTEHR, relationship inference from the electronic health record.

1542-3565/$36.00
https://doi.org/10.1016/j.cgh.2018.06.016

consider screening of asymptomatic first-degree relatives.[10,11]

Little is currently known about adherence to these guidelines. One study screening asymptomatic individuals found that of 35 individuals newly diagnosed with celiac disease in a population-based mass screening program, 10 (29%) had a positive family history for the disease that should have prompted prior testing.[7] Given the paucity of data, our goal was to use a novel validated algorithm identifying familial relationships from the electronic health record (EHR) to study current screening practices in relatives of celiac disease patients at our institution, and to identify the factors that influence testing to improve future adherence rates.

What You Need to Know

Background

Undiagnosed celiac disease may increase morbidity. As a result, guidelines suggest screening high-risk individuals, including first-degree relatives of affected patients.

Findings

Almost 30% of symptomatic first-degree relatives were not tested for celiac disease. We found that having a documented family history of celiac disease and seeing a gastroenterologist were significant predictors.

Implications for patient care

Emphasis should be placed on ensuring adequate documentation of family history, and on educating primary care physicians as to the importance of celiac disease testing in relatives.

Methods

We conducted a retrospective analysis examining relatives of patients (n = 2081) with biopsy-diagnosed celiac disease in a prospectively maintained database at New York-Presbyterian Hospital/Columbia University Medical Center. Relatives of index cases were identified using an algorithm named Relationship Inference From The Electronic Health Record (RIFTEHR); a novel validated method that uses the first name, last name, phone number, and ZIP code of the emergency contact provided to identify familial relationships from existing clinical databases. The emergency contact information also includes an individual's relationship to the patient, which allows our algorithm to differentiate a spouse from a relative who shares the same last name. Once the relationships are identified, RIFTEHR infers additional relationships according to family structure. The identified relationships were validated previously using both clinical and genetic data in 3 distinct institutions.[12]

We manually reviewed each record to extract celiac disease testing information from the EHR. The manual review included extraction of the following elements: (1) serology results, (2) duodenal biopsy results, (3) occurrence of a visit with a gastroenterologist, (4) presence of signs or symptoms of celiac disease in clinical notes and/or International Classification of Diseases codes, and (5) documentation of a family history of celiac disease. Demographic information such as sex, age, race, and ethnicity were queried from the EHR database. We defined celiac disease screening to include either antibody testing or endoscopic evaluation with duodenal biopsy.

In our institution, race and ethnicity were collected in 2 distinct fields. To adequately capture the diverse population seen in our institution while dealing with missing data, we transformed the 2 fields into a single field. Patients with reported ethnicity of Hispanic are reported in this study as Hispanic. Patients without ethnicity data are reported using the race information available (eg, white, black or African American, Asian).

We also extracted the number of visits family members had after the index case had been diagnosed with celiac disease.

We then used SAS software (Cary, NC) version 9.4 to perform both univariate and multivariate analyses to identify predictors of celiac disease screening. We tested the following variables a priori and included all variables in the multivariable analysis. All reported *P* values are 2-sided. The Institutional Review Board of Columbia University Medical Center approved this study.

Results

Demographic Information

We applied the RIFTEHR algorithm to identify family members of the 2081 index cases of celiac disease, yielding 379 distinct families and 852 relatives. Our inclusion criteria included only relatives seen at our institution after the index case was diagnosed, which resulted in a total of 272 distinct families and 539 relatives that we then included in the analysis (Table 1).

There was a relatively even distribution of men (47.1%) and women (52.9%), and those ≥18 years (52.5%) compared with those younger than 18 years (47.5%). The majority of individuals identified were first-degree relatives (71.1%) of patients with celiac disease and had been seen more than once (88.3%) at our institution after their relative was diagnosed. Non-Hispanic white (58.6%) and Hispanic (28.9%) were the 2 most commonly documented ethnicities in our study population. On manual review of the EHR to provide the highest accuracy, 316 of the 539 total relatives (58.6%) did not have any of the included associated symptoms or conditions related to celiac disease documented.

Table 1. Demographics of Relatives (n = 539)

	N (%)
Age, *y*	
<18	256 (47.5)
18–39	114 (21.2)
40–69	133 (24.7)
≥70	36 (6.7)
Sex	
Male	254 (47.1)
Female	285 (52.9)
Race	
Non-Hispanic white	316 (58.6)
African American	14 (2.6)
Hispanic	156 (28.9)
Other/unknown	53 (9.8)
Relative	
First	383 (71.1)
All other	156 (28.9)
Number of times seen at CUMC	
1	63 (11.7)
2–5	206 (38.2)
>5	270 (50.1)
CD signs/symptoms during any visit	
Diarrhea	54 (10.0)
Bloating	18 (3.3)
Abdominal pain	136 (25.2)
Fatigue	2 (0.4)
Fe. def. anemia	14 (2.6)
Osteoporosis/osteoarthritis	29 (5.4)
GERD	62 (11.6)
Type 1 diabetes mellitus/IgA deficiency/primary biliary cholangitis	11 (2.0)
None of the above	316 (58.6)

CD, celiac disease; CUMC, Columbia University Medical Center; GERD, gastroesophageal reflux disease.

Screening Practices

Of the 539 total relatives, 212 (39.3%) were tested for celiac disease. Of those 212 tested for celiac disease, 61 (28.7%) had serologic testing alone, 24 (11.3%) had endoscopic evaluation with biopsy alone, and 127 (60%) had both serologic and endoscopic evaluation with biopsy.

Among first-degree relatives, we found that 193 of the 383 (50.4%) had been screened for celiac disease (Table 2). When restricting this analysis to first-degree relatives with associated symptoms or conditions related to celiac disease, we found that 71.5% (118 of 165) were tested. Because screening practices largely are influenced by the available data at the time of the visit, we manually reviewed each patient's EHR to determine if a family history of celiac disease had been documented anywhere within the record. Of all 539 relatives, only 120 (22.3%) had a family history of celiac disease documented. When subcategorized by degree of relative, we found that 30.3% of first-degree relatives had documentation of a family history of celiac disease, compared with only 2.6% for all other degrees of relatives. Of note, there were 32 individuals tested for celiac disease who either had additional signs and symptoms of celiac disease not included in our analysis (eg, short stature), or limited documentation with no family history, or associated sign or symptoms, documented.

Factors Associated With Celiac Disease Testing

On univariate analysis, there were several factors that were associated with a higher likelihood of being tested (Table 3). Only 5.6% of relatives older than age 69 were tested, a far lower rate compared with all other age categories, which ranged from 35.3% to 44.1%. Screening practices also varied by race, with 58.6% of non-Hispanic whites, 25% of Hispanics, and 0% of African Americans tested. In addition, the presence of symptoms (59.2% vs 25.3%; $P < .0001$), whether the relative was seen by a gastroenterologist (87.1% vs 20.1%; $P < .0001$), whether there was documentation of a family history of celiac disease in the EHR (89.2% vs 25.1%; $P < .0001$), and the degree of relative (first-degree 50.4% vs all other degrees 12.2%; $P < .0001$), were associated with testing for celiac disease. Notably, neither sex (male 39% vs female 39.7%; $P = .87$) nor the number of times a relative had been seen at our institution after the initial family member had been diagnosed (once 36.5% vs 2–5 times 45.2% vs >5 times 35.6%; $P = .09$) affected the likelihood of celiac disease testing.

On multivariate analysis (Table 4), we found that age, the number of visits to our institution, being seen by a gastroenterologist, the presence of symptoms or conditions associated with celiac disease, a documented family history of celiac disease, and the degree of relative to be significant predictors of screening. Specifically, we found that relatives aged 18 to 39 were more than 2 times more likely to be screened than relatives younger than age 18 (odds ratio [OR], 2.27; 95% CI, 1.12–4.58; $P = .02$). When the number of visits was considered as a binary variable, those seen more than 5 times were less

Table 2. Screening and Charting Practices Based on Degree of Relative

Variable	Total	First-degree relative	All other relatives	*P* value
Tested for CD	212/539 (39.3%)	193/383 (50.4%)	19/156 (12.2%)	**<.0001**
Family history lists CD	120/539 (22.3%)	116/383 (30.3%)	4/156 (2.6%)	**<.0001**

NOTE. The percentage of symptomatic first-degree relatives tested for celiac disease was 71.52% (118 of 165).
CD, celiac disease.

Table 3. Factors Associated With Screening: Univariate Analysis

Variable	Screened (%)	*P* value
Age, *y*		
<18	113/256 (44.1)	**<.0001**
18–39	50/114 (43.9)	
40–69	47/133 (35.3)	
≥70	2/36 (5.6)	
Sex		
Male	99/254 (39.0)	.87
Female	113/285 (39.7)	
Race		
Non-Hispanic white	149/316 (58.6)	**<.0001**
African American	0/14 (0)	
Hispanic	39/156 (25)	
Other/unknown	24/53 (45.3)	
CD signs/symptoms		
Symptoms documented	132/223 (59.2)	**<.0001**
No symptoms documented	80/316 (25.3)	
Visits, n		
1	23/63 (36.5)	.09
2–5	93/206 (45.2)	
>5	96/270 (35.6)	
Seen by a gastroenterologist		
Yes	135/155 (87.1)	**<.0001**
No	77/384 (20.1)	
Family history lists CD		
Yes	107/120 (89.2)	**<.0001**
No	105/419 (25.1)	
Degree of relative		
First	193/383 (50.4)	**<.0001**
Other	19/156 (12.2)	

CD, celiac disease.

Table 4. Multivariate Analysis Examining Patient Factors Associated With Screening in All Relatives

Variable	Adjusted OR[a]	95% CI	*P* value
Age, *y*			
<18	1.0	Ref	Ref
18–39	2.27	1.12–4.58	**.02**
40–69	1.03	0.53–2.02	.93
≥70	0.27	0.05–1.43	.12
Sex			
Female	1.0	Ref	Ref
Male	0.882	0.52–1.51	.65
Race/ethnicity			
Non-Hispanic white	1.0	Ref	Ref
Hispanic	0.75	0.39–1.46	.40
Other/unknown	1.16	0.52–2.57	.72
Number of visits to CUMC			
1–5 visits	1.0	Ref	Ref
>5 visits	0.57	0.32–0.999	**.0495**
Seen by a gastroenterologist			
No	1.0	Ref	Ref
Yes	15.16	7.72–29.80	**<.0001**
Any documented symptom/sign of celiac disease[b]			
No	1.0	Ref	Ref
Yes	3.69	2.11–6.47	**<.0001**
Family history lists CD			
No	1.0	Ref	Ref
Yes	11.9	5.56–25.48	**<.0001**
Degree of relative			
Other	1.0	Ref	Ref
First	4.90	2.34–10.25	**<.0001**

CD, celiac disease; CUMC, Columbia University Medical Center.
[a]Adjusted for all variables listed in Table 4.
[b]Symptoms/signs of celiac disease include diarrhea, bloating, abdominal pain, fatigue, osteoporosis, osteoarthritis, gastroesophageal reflux disease, type 1 diabetes, autoimmune thyroid disease, IgA deficiency, and primary biliary cholangitis.

likely to be screened compared with those seen 1 to 5 times, although this was of borderline significance (OR, 0.57; 95% CI, 0.32–1.00; $P = .05$). Other significant predictors included the presence of any condition or symptom related to celiac disease (OR, 3.69; 95% CI, 2.11–6.47; $P < .0001$) and being a first-degree relative (OR, 4.90; 95% CI, 2.34–10.25; $P < .0001$). The 2 factors most strongly associated with screening were whether the relative had been seen by a gastroenterologist (OR, 15.16; 95% CI, 7.72–29.80; $P < .0001$) and whether there was documentation in the EHR of a family history of celiac disease (OR, 11.9; 95% CI, 5.56–25.48; $P < .0001$). Race and sex were not associated with celiac disease testing on multivariate analysis.

Biopsy-Proven Celiac Disease

A total of 79 of the 539 relatives (14.7%) had biopsies consistent with celiac disease. Seventy-six of these individuals were first-degree relatives, with 30 (39.4%) age 18 years and older, and 46 (60.5%) younger than age 18 years. Fourteen individuals had biopsy-proven celiac disease but no record of antibody testing recorded within the EHR. Of the 82 patients who tested positive for celiac antibodies (endomysial, transglutaminase, and/or gliadin peptide), 80 (97.6%) were first-degree relatives, and a total of 65 (79.3%) had a biopsy confirming the diagnosis.

Discussion

Although the recent US Preventative Services Task Force recommendations concluded that "current evidence is insufficient to assess the balance of benefits and harms of screening for celiac disease in asymptomatic persons,"[13] both adult and pediatric guidelines[10,11] suggest a benefit from screening first-degree relatives of people with celiac disease to decrease morbidity.[14,15] Although much of this is based on consensus data, at our celiac disease center we similarly have found that 25% of children seen were diagnosed through screening high-risk groups,[16] as were 10% of adults.[17]

In this study, we showed the clinical utility of RIFTEHR, an algorithm that extracts familial relationships from existing clinical databases, to identify patients at risk for developing celiac disease. Our study found that almost 50% of all first-degree relatives were not tested,

including nearly 30% of symptomatic first-degree relatives. Previous research has suggested similar findings for a myriad of different diseases, most notably in relation to cancer screening.[18–20]

There are a number of different contributing factors to the overall low adherence to screening rates. As hypothesized and previously noted in other conditions, being seen by a specialist in that discipline is associated with a higher likelihood of being screened.[21] In our study, only 39% of relatives were seen by a gastroenterologist, and those who did were significantly more likely to be screened. In addition, in adherence with American College of Gastroenterology guidelines, which recommend testing of first-degree symptomatic relatives,[10] we found that both being a first-degree relative and being symptomatic were associated independently with an increased likelihood of being tested for celiac disease. Those patients seen more than 5 times without being tested were overall less likely to be tested. This may be owing to a significant number of acute conditions that dictated numerous visits and took precedence over celiac disease screening, or reflect that after several visits, the provider and patient may no longer be as cognizant of the family member who previously was diagnosed with celiac disease, and, as a result, were less likely to be tested.

Although many factors were found to influence the likelihood of being tested for celiac disease, one strong and modifiable predictor we identified was the care provider having access to a patient's relevant clinical information during a visit. In our study, we found that individuals with a documented family history of celiac disease had an 11.9 times greater odds of being tested compared with those who had no EHR documentation of a family history of celiac disease. Although family health history has been described previously as "a core element of clinical care,"[22] many EHR implementations do not store family history in a centralized or standardized fashion.[23] As such, family history data often are absent or collected and stored as free-text as part of clinical notes, making the extraction and use of this information during patient visits difficult.[24,25] Standardizing the input of this information across all EHRs may improve future adherence to screening practices because it would allow clinicians to easily identify those at higher risk for both celiac and other diseases.

Although having a standardized information technology process for collecting and displaying clinical information may improve screening rates, providers still are met with challenges, including short visit times[26] and an overwhelming amount of data in the EHR[27] that may preclude screening. Future directions may include using health information technology tools, such as the RIFTEHR algorithm, to identify high-risk patients eligible for screening. This, in addition to other EHR-based algorithms,[28] may be able to be used to alert physicians of such eligibility during the clinical visit.[29] Before implementation, however, there are ethical issues that would need to be addressed properly, including a patient's right to privacy and the clinician's duty to warn relatives of potential genetic risks.

Overall, 14.7% of our cohort had biopsy-confirmed celiac disease. This likely is higher than previously reported percentages[30] owing to a high number of referrals given the presence of a specialized celiac disease center at our institution. Of the 82 individuals who had any positive celiac antibody and a biopsy in our system, 65 were found to have biopsy-proven celiac disease. This results in a positive predictive value of 79.2% in our cohort, similar to previously reported findings.[31,32]

One limitation and strength of our study was that it was undertaken at a single center that has a specialized Celiac Disease Center. Although this may limit the generalizability of our results, our study was performed in New York City, which has both a large and diverse patient population. Of note, the high proportion of Hispanic individuals in our study likely resulted from 3 different causes: (1) a high proportion of Hispanic individuals seen at our institution, (2) increased awareness and thus prevalence of celiac disease in ethnicities other than non-Hispanic whites,[33] and (3) transformation of the race and ethnicity pairs into a single race/ethnicity variable. Moreover, by using only individuals seen at our institution, we were able to use a cohort of 2081 patients with confirmed celiac disease, rather than relying on a patient population identified by International Classification of Diseases codes, which often includes many patients without true celiac disease.[34] In addition, our screening rate for first-degree relatives with symptoms was only approximately 70% at our institution, and, although not generalizable, likely represents a higher percentage than those tested at other hospitals and institutions that do not specialize in celiac disease care. Finally, our study identified several associations that may predict celiac disease testing, but further investigation is necessary to determine causality.

In summary, we extracted familial relationships from existing clinical databases to identify patients at risk for developing genetically linked diseases. In this study, we found poor overall adherence to celiac screening guidelines and identified significant and actionable predictors of screening. Our results suggest that we may significantly increase the adherence rate to these guidelines by educating primary care physicians on the importance of testing relatives of patients with celiac disease, as well as by ensuring a family history of celiac disease is documented in the EHR. Future efforts should focus on leveraging this technology to increase awareness of family history among patients and providers, as well as on studying the long-term natural history of testing and outcomes among relatives.

References

1. NIH Consensus Development Conference on Celiac Disease. NIH Consens State Sci Statements 2004;21:1–23.
2. Green PH, Cellier C. Celiac disease. N Engl J Med 2007; 357:1731–1743.

3. Lebwohl B, Sanders DS, Green PHR. Coeliac disease. Lancet 2018;391:70–81.
4. McCabe MA, Toughill EH, Parkhill AM, et al. Celiac disease: a medical puzzle. Am J Nurs 2012;112:34–44; quiz 46, 45.
5. Tio M, Cox MR, Eslick GD. Meta-analysis: coeliac disease and the risk of all-cause mortality, any malignancy and lymphoid malignancy. Aliment Pharmacol Ther 2012;35:540–551.
6. Kurppa K, Paavola A, Collin P, et al. Benefits of a gluten-free diet for asymptomatic patients with serologic markers of celiac disease. Gastroenterology 2014;147:610–617 e611.
7. Vilppula A, Kaukinen K, Luostarinen L, et al. Clinical benefit of gluten-free diet in screen-detected older celiac disease patients. BMC Gastroenterol 2011;11:136.
8. Mahadev S, Gardner R, Lewis SK, et al. Quality of life in screen-detected celiac disease patients in the United States. J Clin Gastroenterol 2016;50:393–397.
9. Singh P, Arora S, Lal S, et al. Risk of celiac disease in the first- and second-degree relatives of patients with celiac disease: a systematic review and meta-analysis. Am J Gastroenterol 2015; 110:1539–1548.
10. Rubio-Tapia A, Hill ID, Kelly CP, et al. ACG clinical guidelines: diagnosis and management of celiac disease. Am J Gastroenterol 2013;108:656–676, quiz 677.
11. Hill ID, Fasano A, Guandalini S, et al. NASPGHAN clinical report on the diagnosis and treatment of gluten-related disorders. J Pediatr Gastroenterol Nutr 2016;63:156–165.
12. Polubriaginof F, Vanguri R, Quinnies K, et al. Estimate of disease heritability using 7.4 million familial relationships inferred from electronic health records. Cell 2018. In press.
13. US Preventive Services Task Force, Bibbins-Domingo K, Grossman DC, et al. Screening for celiac disease: US Preventive Services Task Force recommendation statement. JAMA 2017; 317:1252–1257.
14. Lebwohl B, Ludvigsson JF, Green PH. Celiac disease and non-celiac gluten sensitivity. BMJ 2015;351:h4347.
15. Ludvigsson JF, Montgomery SM, Ekbom A, et al. Small-intestinal histopathology and mortality risk in celiac disease. JAMA 2009;302:1171–1178.
16. Reilly NR, Aguilar K, Hassid BG, et al. Celiac disease in normal-weight and overweight children: clinical features and growth outcomes following a gluten-free diet. J Pediatr Gastroenterol Nutr 2011;53:528531.
17. Rampertab SD, Pooran N, Brar P, et al. Trends in the presentation of celiac disease. Am J Med 2006;119:355 e359–314.
18. Solbak NM, Xu JY, Vena JE, et al. Patterns and predictors of adherence to colorectal cancer screening recommendations in Alberta's Tomorrow Project participants stratified by risk. BMC Public Health 2018;18:177.
19. Jemal A, Fedewa SA. Lung cancer screening with low-dose computed tomography in the United States-2010 to 2015. JAMA Oncol 2017;3:1278–1281.
20. Centers for Disease Control and Prevention. Cancer screening–United States, 2010. MMWR Morbid Mortal Wkly Rep 2012;61:41–45.
21. Patwardhan V, Paul S, Corey KE, et al. Hepatocellular carcinoma screening rates vary by etiology of cirrhosis and involvement of gastrointestinal sub-specialists. Dig Dis Sci 2011;56:3316–3322.
22. Berg AO, Baird MA, Botkin JR, et al. National Institutes of Health State-of-the-Science Conference Statement: family history and improving health. Ann Intern Med 2009;151:872–877.
23. Feero WG. Connecting the dots between patient-completed family health history and the electronic health record. J Gen Intern Med 2013;28:1547–1548.
24. Wang Y, Wang L, Rastegar-Mojarad M, et al. Systematic analysis of free-text family history in electronic health record. AMIA Jt Summits Transl Sci Proc 2017;2017:104–113.
25. Polubriaginof F, Tatonetti NP, Vawdrey DK. An assessment of family history information captured in an electronic health record. AMIA Ann Symposium Proc 2015;2015:2035–2042.
26. Chen LM, Farwell WR, Jha AK. Primary care visit duration and quality: does good care take longer? Arch Intern Med 2009; 169:1866–1872.
27. Ross MK, Wei W, Ohno-Machado L. "Big data" and the electronic health record. Yearb Med Inform 2014;9:97–104.
28. Ludvigsson JF, Pathak J, Murphy S, et al. Use of computerized algorithm to identify individuals in need of testing for celiac disease. J Am Med Inform Assoc 2013;20:e306–e310.
29. Murphy DR, Meyer AND, Vaghani V, et al. Development and validation of trigger algorithms to identify delays in diagnostic evaluation of gastroenterological cancer. Clin Gastroenterol Hepatol 2018;16:90–98.
30. Rubio-Tapia A, Van Dyke CT, Lahr BD, et al. Predictors of family risk for celiac disease: a population-based study. Clin Gastroenterol Hepatol 2008;6:983–987.
31. Toftedal P, Nielsen C, Madsen JT, et al. Positive predictive value of serological diagnostic measures in celiac disease. Clin Chem Lab Med 2010;48:685–691.
32. Hashmi MA, Hussain T, Masood N, et al. Accuracy of anti-tissue transglutaminase IgA antibody in the diagnosis of paediatric celiac disease. J Coll Physicians Surg Pak 2016;26:263–266.
33. Krigel A, Turner KO, Makharia GK, et al. Ethnic variations in duodenal villous atrophy consistent with celiac disease in the United States. Clin Gastroenterol Hepatol 2016;14:1105–1111.
34. Tanpowpong P, Broder-Fingert S, Obuch JC, et al. Multicenter study on the value of ICD-9-CM codes for case identification of celiac disease. Ann Epidemiol 2013;23:136–142.

Reprint requests
Address requests for reprints to: Benjamin Lebwohl, MD, MS, Division of Gastroenterology and Hepatology, Columbia University Medical Center/New York-Presbyterian Hospital, 180 Fort Washington Avenue, Suite 936, New York, New York 10032. e-mail: BL114@cumc.columbia.edu; fax: (212) 305-3738.

Conflicts of interest
The authors disclose no conflicts.

Funding
Supported by grants OT3 TR002027, R01 GM107145, and an Irving Scholars Award (N.T.); AHRQ R01HS021816 (F.P., D.K.V.); and the Jill and Daniel Wallen grant (P.H.R.G.).