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### **Epidemiology Publish Ahead of Print**

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Changes in testing for and incidence of celiac disease in the UK: a population-based cohort study

Abbreviated title: Incidence of Celiac disease

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1

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Keywords: celiac disease; incidence; prevalence; trends

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distributed to third parties, but are available from CPRD following acquisition of the appropriate
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#### To the Editor:

The diagnosis rates of celiac disease differ substantially between countries<sup>1</sup>. Intriguingly, there has been recent evidence from Olmstead County, USA, and Finland that in the last 5-10 years incidence has leveled off or even declined<sup>2, 3</sup>. In most populations the prevalence also varies widely, with serologic prevalence from 0% to 1.87% and clinical prevalence from 0.9 to 12.9 per 100000<sup>1</sup>. Understanding of why this variation exists is minimal, yet one of the key aspects governing incidence rates of any disease are factors related to the health system, such as the availability and use of diagnostic tests. We previously reported rising incidence rates of celiac disease<sup>4</sup> from 1990 to 2011 with differences related to socioeconomic deprivation in the UK. Although national guidance on recognition and diagnosis of celiac disease published in 2009<sup>5</sup> suggested widening the patient groups that should be tested for celiac disease, National Health System (NHS) financial constraints could have hindered implementation of these guidelines. Indeed, in the USA researchers have observed that over the period 2000-2010 there was a marked decrease in treated prevalence of many diseases alongside a sustained period of reduced spending on health care<sup>6</sup>.

We used the UK Clinical Practice Research Datalink GOLD (Independent Scientific Advisory Committee approval 16\_130) to estimate the European (EUROSTAT EU-27 plus EFTA 2013 population<sup>7</sup>) age-standardized incidence rates of celiac disease<sup>8</sup> 2005-2015 and the corresponding rates of serologic testing (Anti-Tissue Transglutaminase antibody (TTG) and anti-Endomysial antibody (EMA)) for the disease. We used Joinpoint analysis<sup>9</sup> to examine statistical evidence of changes in the rates of diagnosis and testing during this period. We estimated celiac disease point prevalence based on all contributing patients at 30 June 2015 and estimated incidence rate ratios (IRR) using Poisson regression for testing and incidence rates.

There were 8177 incident cases of celiac diseases diagnosed among 45,539,211 million person-years. The overall incidence rate between 2005 and 2015 was 18 per 100,000 person-years, serological testing rate was 118 per 100,000 person-years, and point prevalence on the 30<sup>th</sup> June 2015 was 0.30% (95% CI 0.30-0.31). Incidence rates of celiac disease were highest in people aged between 60 and 69 years (23 per 100,000 person-years) whereas the rate of serologic testing was highest in those aged 20-29 (233 per 100,000 person-years). For the calendar period 2005-2015 there was an increase in European age-standardized incidence rates from 2005 until 2012 and then a plateau effect (Figure 1). Serologic testing increased and then decreased during the same period (Figure 2). Joinpoint analysis identified that there were changes in the rates of both diagnosis and testing at 2012 (95% CI 2007-2013) and 2011 (95% CI 2010-2013) respectively. The Joinpoint analysis is presented in the table.

In this study we found that European age-standardized rates of diagnosis of celiac disease and serological testing have, since 2011, respectively leveled off and declined, while prevalence increased from  $0.24\%^4$  to 0.3%.

This could be because, since 2010, the UK NHS has been operating under a period of financial austerity. While health funding has been forecast to grow 1.2 per cent in real terms between 2009/10 and 2020/21 this is below the long-term average increase in health spending of approximately 4 per cent a year since the NHS was established in 1948<sup>10</sup>. Alternatively, clinicians based in primary care could be carrying out more targeted use of testing in certain age or at-risk groups, leading to an overall reduction in testing. We may have missed some tests carried out in secondary care as we did not have access to these. We found some evidence that testing did vary by age, disproportionately to disease incidence, in that the highest testing rate was in those aged 20-29 yet the highest incidence rate was in the 60-69 year old group. Finally, it

is possible that following several years of increasing diagnosis rates prior to 2011<sup>4</sup> that the threshold of clinically identifiable celiac disease in the UK has been reached and a steady-state incidence rate obtained.



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Table. Joinpoint analysis for Celiac disease and Serological testing rates.

	Segment Lower Endpoint		Upper	APC	Lower	Upper	Test Statistic Prob >	
			Endpoint		CI	CI	<b>(t)</b>	t
Celiac disease	1	2005	2012	5.0^	3.1	7.1	6.4	0.0
Serology	2	2012	2015	-0.3	-7.2	7.2	-0.1	0.9
	1	2005	2011	15.4^	12.4	18.5	13.4	0.0
	2	2011	2015	-13.9^	-18.3	-9.2	-7.0	0.0

APC – Annual Percentage Change



 $<sup>^{\</sup>wedge}$  - indicates that the APC is significantly different from zero at the alpha = 0.05

## Figure Legends.

Figure 1. European age-standardized incidence rates of celiac disease per 100,000 person-years

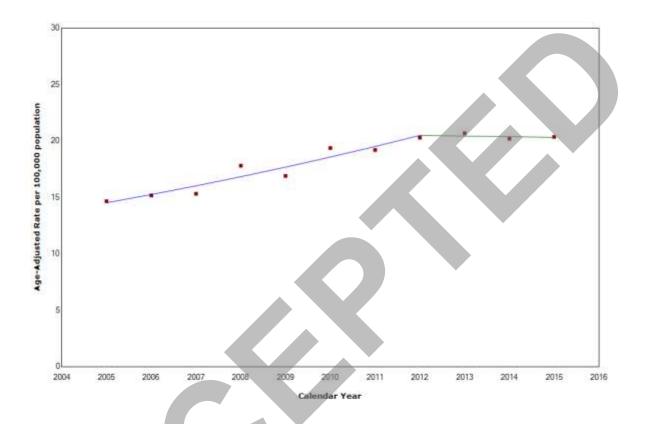


Figure 2. European age-standardized serological testing rates per 100,000 person-years (TTG and EMA) for celiac disease

