

ORIGINAL ARTICLE

GASTROINTESTINAL DISEASES

Escalating incidence of eosinophilic esophagitis in Canton of Vaud, Switzerland, 1993–2013: a population-based study

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Abstract

Background: Eosinophilic esophagitis (EoE) is a chronic, inflammatory disease of the esophagus with a rapidly increasing incidence. However, population-based epidemiologic data on EoE are rare and limited to regions with less than 200 000 inhabitants. We evaluated the incidence and prevalence of EoE over time in Canton of Vaud, Switzerland.

Materials and methods: Canton of Vaud lies in the French-speaking, Western part of Switzerland. As of December 2013, it had a population of 743 317 inhabitants. We contacted all pathology institutes ($n = 6$) in this canton to identify patients that have been diagnosed with esophageal eosinophilia between 1993 and 2013. We then performed a chart review in all adult and pediatric gastroenterology practices to identify patients with EoE.

Results: Of 263 patients with esophageal eosinophilia, a total of 179 fulfilled the diagnostic criteria for EoE. Median diagnostic delay was 4 (IQR 1–9) years. No patient was diagnosed with EoE prior to 2003. Incidence of EoE increased from 0.16/100 000 inhabitants in 2004 to 6.3/100 000 inhabitants in 2013 ($P < 0.001$). The cumulative EoE prevalence in 2013 was 24.1/100 000. The incidence in males was 2.8 times higher (95% CI 2.01–3.88, $P < 0.001$) when compared to that in females. The annual EoE incidence was 10.6 times higher (95%-CI 7.61–14.87, $P < 0.001$) in the period from 2010 to 2013 when compared to that in the period from 1993 to 2009.

Conclusions: The incidence and cumulative prevalence of EoE in Canton of Vaud, Switzerland, has rapidly increased in the past 10 years.

Eosinophilic esophagitis (EoE) has been defined as chronic, inflammatory disorder of the esophagus. This disease is characterized clinically by symptoms related to esophageal

dysfunction and histologically by eosinophil-predominant inflammation (1). EoE is characterized by a male to female ratio ranging from 3 to 4 : 1 and a high sensitization rate to environmental allergens (2–8). Several recent studies have documented that the incidence of EoE is approximately one case per 10 000 inhabitants per year (9, 10). In Westernized countries, a steady increase in incidence of EoE has been observed over the past two decades (9–14). It has been debated whether this observation reflects a true raise in

Abbreviations

EGD, esophagogastroduodenoscopy; EoE, eosinophilic esophagitis; GERD, gastroesophageal reflux disease; HPF, high power field; PPI, proton-pump inhibitors; PPI-REE, proton-pump inhibitor-responsive esophageal eosinophilia.

incidence of EoE or whether it is, among other things, related to an enhanced awareness for EoE by gastroenterologists and pathologists. Most studies addressing this pivotal epidemiological question relied solely on retrospective analyses of pathology or endoscopy databases (2, 3, 15, 16), and data from population-based studies from geographically confined regions remain rare. Our group has recently performed a long-term population-based study in Olten County, Switzerland, a geographically and socioeconomically defined indicator area in the center of the German-speaking part of Switzerland, with approximately 90 000 inhabitants. We observed an increase in EoE incidence (adjusted for the increased number of esophagogastroduodenoscopies [EGD]) over the last 20 years (9). In 2009, we reported on an EoE prevalence of 42.8 per 100 000 persons, corresponding to one patient with EoE in 2336 inhabitants (9). EoE incidence and cumulative prevalence in Olten County might be higher than that in other parts of Switzerland as the two gastroenterologists practicing in this region have an enhanced awareness for EoE and published one of the first EoE patient series (17). Of note, the Western French-speaking part and the Eastern German-speaking part of Switzerland are not only geographically but even more culturally separated due to their different languages. Thus, we performed a population-based study to evaluate the incidence and prevalence of EoE over the last two decades in Canton of Vaud, a French-speaking region in Western Switzerland.

Methods

Canton of Vaud: Population characteristics and healthcare system

Canton of Vaud is situated in the Western part of Switzerland which has about 8 million inhabitants. Canton of Vaud had 593 190 inhabitants in December 1993 and 743 317 inhabitants in December 2013. In December 2013, 32.4% of inhabitants (240 741/743 317) did not hold Swiss passport. Of these foreigners, 73.2% ($n = 176\,300$) came from European Union, 10.7% ($n = 25\,806$) came from non-European Union regions of Europe and Russia, 5.2% ($n = 12\,399$) were from Africa, 5.0% ($n = 12\,141$) were from Asia, 3.4% ($n = 8152$) were from Latin America, 2.2% ($n = 5228$) were from North America, 0.3% ($n = 657$) came from Australia, and 0.02% ($n = 58$) of inhabitants were of unknown or undeclared origin.

According to the 1994 Federal Health Insurance Act, any person living in Switzerland is obliged to purchase a basic health insurance policy. The health insurance provider covers 90% of the medical costs, and the remaining 10% have to be paid by patients themselves.

The gastroenterology service in Canton of Vaud for adult patients is provided by 29 Swiss board-certified gastroenterologists. Of those, nine are working in university hospital (Centre Hospitalier Universitaire Vaudois [CHUV]), and 20 are working in private practice. The majority of gastroenterologists working in private practice are also affiliated with primary or secondary referral centers. The gastroenterology

service for pediatric patients is provided by two board-certified pediatric gastroenterologists at CHUV.

The histopathology service in Canton of Vaud is provided by pathologists working at the Institute of Pathology of CHUV or one of the following five private histopathology institutes: ArgotLab, Aurigen, Institut Pathologie Romand, Promed, and Unilabs.

Patients

The study was approved by the ethics committee of CHUV (study number 329/13). All gastroenterologists and pathologists of Canton of Vaud agreed to participate in this study. Two hundred and sixty-three patients with esophageal eosinophilia, diagnosed between January 1993 and December 2013, were identified by searching the electronic databases of all pathology institutes (Fig. 1). The researchers then visited all gastroenterologists in Canton of Vaud to identify the patients with EoE ($n = 179$). Patients with EoE fulfilled the following published diagnostic criteria: (i) symptoms of esophageal dysfunction, (ii) peak eosinophil count of ≥ 15 /high power field (hpf, magnification 400x) following an 8-week treatment with proton-pump inhibitors (PPI) (single standard or double dose), and (iii) exclusion of other esophageal disorders that might be associated with esophageal eosinophilia (1). Of the 179 patients with EoE, 29 (16.2%) had concomitant gastroesophageal reflux disease (GERD). Eighty-four patients did not fulfill diagnostic criteria for EoE due to the following: 37 patients were diagnosed with GERD, 26 patients did not undergo an 8-week PPI trial, 19 patients were diagnosed with PPI-responsive esophageal eosinophilia (PPI-REE), one patient had achalasia, and one patient suffered from esophageal Crohn's disease. Patients with PPI-REE were excluded given the fact that this entity remains poorly defined and lacks definition of 'clinical and histologic improvement' under PPI treatment (18).

EoE patient records were reviewed. Self-reported atopic diseases/allergies and the length of diagnostic delay, which represents the time from EoE symptom onset until the time

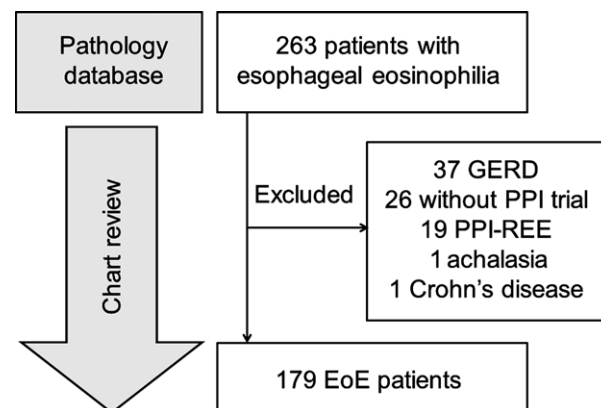


Figure 1 Patient flow. GERD, gastroesophageal reflux disease; PPI-REE, proton-pump inhibitor-responsive esophageal eosinophilia.

of EoE diagnosis, were noted. The endoscopy reports, including pictures, were reviewed and graded according to the recently published endoscopic reference score (19). Peak eosinophil counts were extracted from the histology reports. Participating gastroenterologists provided their numbers of EGD per year since 2002.

Statistical analysis

Data of patients with EoE from Canton of Vaud were entered into an excel sheet (Microsoft excel 2010; Microsoft Corporation, Redmond, WA, USA). The statistical analyses were performed using STATA (version 13.1, College Station, TX, USA). Results of Gaussian numerical data are presented as mean $\pm$ standard deviation (SD) and range, whereas non-Gaussian numerical data are presented as median and interquartile range (comprises the values from the 25th and 75th percentile). Fisher's exact test (two-sided) or the chi-squared test was used to explore associations of categorical data in two independent groups. The Wilcoxon rank sum test was used to explore associations of nonparametric numerical data in two independent groups, and the t-test was used for parametric numerical data. We calculated gender-specific incidence rates using data provided by the Institute of population statistics of Canton of Vaud. To analyze time trends of rates, we used Poisson regression models that model the number of cases with a logarithmic link function and the logarithm of the population figures as an offset variable. The association of risk factors and the length of diagnostic delay (analyzed as continuous variable) was analyzed by means of logistic regressions, in which the dependent (outcome) variable was the length of diagnostic delay. The variables tested as potential risk factors, *that is*, the independent variables, were age at diagnosis (continuous variable), gender (male *versus* female), positive EoE family history (yes *versus* no), and the presence of atopic diseases (yes *versus* no). Each independent variable was first tested individually. Then, all the independent variables with a *P*-value ≤ 0.1 in the one-by-one analysis were entered in a multivariable logistic regression model. A *P*-value < 0.05 was considered statistically significant.

Results

Clinical, endoscopic, and histologic characteristics of diagnosed EoE patients

A total of 179 pediatric and adult patients were diagnosed with EoE in Canton of Vaud between January 1993 and December 2013. Of these, 12 (6.7%) were pediatric patients. The clinical characteristics of patients with EoE at the time of diagnosis are illustrated in Table 1. The mean age at EoE diagnosis was 41 ± 16 years (range 3–81 years). The majority of patients with EoE was male ($n = 130$, 72.6%). At diagnosis, 59% of patients with EoE had known self-reported atopic diseases/allergies, of which rhinoconjunctivitis was the most prominent (29.6%). Concomitant GERD was present in 29 patients (16.2%). Twenty-four patients with EoE

Table 1 Clinical characteristics of patients with EoE in Canton of Vaud

Variable	Patients ($n = 179$)	
	<i>N</i>	%
Age at EoE diagnosis, mean $\pm$ SD (range)	41 ± 16 (3–81)	
Male gender	130	72.6
Positive EoE family history	10	5.6
EoE symptoms at diagnosis (may be in more than 1 category)		
Dysphagia	165	92.2
Food impaction necessitating endoscopic removal	43	24
Thoracic pain, non-swallowing-associated	27	15.1
Heartburn	26	14.5
Swallowing-associated thoracic pain	14	7.8
Weight loss	7	3.9
Allergies		
Known allergies (All)	105	58.7
Allergic rhinoconjunctivitis	53	29.6
Asthma	29	16.2
Allergic rhinoconjunctivitis and asthma	17	9.5
Oral allergy syndrome	18	10.1
Urticaria	6	3.4
Known food allergies	36	20.1

Table 2 Endoscopic and histologic characteristics of the patients with EoE in Canton of Vaud. Peak eosinophil count is reported by median, interquartile range (IQR), and range

Patients ($n = 179$)	
Variable	
Endoscopic features (may be in more than one category)	
White exudates	93 (52%)
Longitudinal furrows	107 (59.8%)
Edema	138 (77.1%)
Corrugated rings	112 (62.6%)
Stricture	65 (36.3%)
Peak eosinophil counts (entire esophagus)	
Median 41, IQR 28–60, range 15–154	
15–30	52 (29.1%)
31–50	53 (29.6%)
>50	74 (41.3%)

(13.4%) underwent esophageal dilation during the diagnostic endoscopy. Dilation was performed in 19 and five patients using through-the-scope balloons and Savary bougies, respectively. Eight patients with EoE (4.5%) underwent dilation before the diagnostic endoscopy (four patients had one, two patients had three dilations, and two patients had five dilations). An esophageal perforation at diagnostic endoscopy was documented in two patients (1.1%).

The endoscopic and histologic characteristics of patients with EoE at the time of diagnosis are shown in Table 2. Edema was the most prevalent endoscopic feature (77.1%), followed by rings, longitudinal furrows, white exudates, and strictures. Strictures were found in 36.3% of patients with a

mean stricture diameter of 9.6 ± 3.3 mm. The median peak eosinophil count was 41 per hpf (IQR 28–60).

Annual incidence rates and prevalence

Annual incidence rates, including gender-specific rates, were calculated and are shown together with the cumulative prevalence in Table 3. In Canton of Vaud, no patient was diagnosed with EoE between 1993, the date of the first comprehensive description of EoE as a distinct disease entity, and 2003 (17). In 2013, the annual incidence was 6.32/100 000 inhabitants, and the cumulative prevalence was 24.08/100 000 persons. The yearly overall and sex-specific EoE incidence rates are shown in Fig. 2. The incidence in males was 2.8 times higher (95%-CI 2.01–3.88, P -value < 0.001) when compared to that in females (Poisson regression). The annual EoE incidence was 10.6 times higher (95%-CI 7.61–14.87, P -value < 0.001) in the period from 2010 to 2013 when compared to that in the period from 1993 to 2009. The annual EoE incidence was 4.0 times higher (95%-CI 2.84–5.56, P -value < 0.001) in the period from 2010 to 2013 when compared to that in the period from 2004 to 2009. Of 29 gastroenterologists, 23 (79.3%) could provide us with their numbers of EGDs they had performed since 2002. A total of 9213 EGDs were performed in 2002 when compared to 11 418 EGDs in 2013. Figure 2 shows that the number of endoscopies per year stayed relatively stable; in contrast with this finding, a rapidly increasing incidence and cumulative prevalence of patients with EoE was noted. As such, the important increase in EoE diagnosis is not explained by the number of EGDs performed in this interval.

Diagnostic delay: length, evolution over time, and risk factor analysis

The median diagnostic delay (time from first symptom onset to EoE diagnosis) was 4 years (IQR 1–9 years, range 0–50 years). The median diagnostic delay of patients presenting with food bolus impaction necessitating endoscopic removal

($n = 43$) was 4 years (IQR 1–8.5 years, range 0–41 years). This period is comparable to the median of 4.5 years (IQR 1–9, range 0–50 years) observed in patients ($n = 136$) that never experienced food bolus impactions necessitating endoscopic removal before the time of EoE diagnosis.

Median diagnostic delay in pediatric patients ($n = 12$) was 2 years (IQR 0–5 years, range 0–9) when compared to that of 4 years (IQR 1–9 years, range 0–50 years) in adult patients ($n = 167$).

The yearly median diagnostic delay is shown in Table S1. The length of diagnostic delay did not change over time ($P = 0.713$, trend test). We further evaluated whether various patient characteristics, such as age at the time of diagnosis, sex, EoE family history, or atopic diseases/allergies, could act as risk factors for the increased length of diagnostic delay (Table S2). No risk factors were identified.

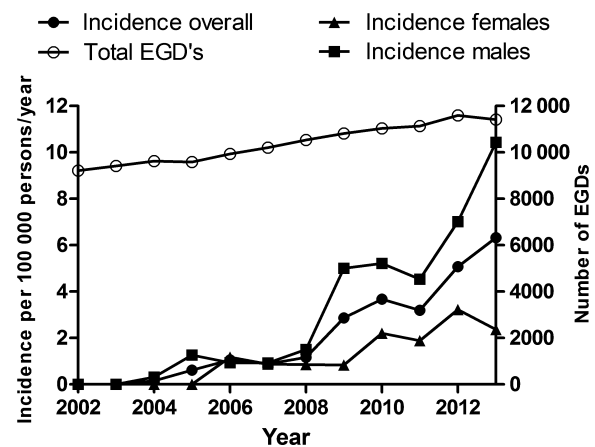


Figure 2 Yearly overall and sex-specific EoE incidence rates per 100 000 inhabitants between 2002 and 2013. Furthermore, the number of EGDs performed in this interval is provided. No patient with EoE was diagnosed in Canton of Vaud between 1993 and 2003.

Table 3 EoE incidence and cumulative prevalence from 1993 to 2013. The incidence is shown per 100 000 inhabitants per year. The cumulative prevalence was calculated per 100 000 inhabitants at the end of the time interval

Year	Patients with EoE	Population in Canton Vaud	Incidence per 100 000	Incidence males per 100 000	Incidence females per 100 000	Prevalence per 100 000	Prevalence: 1 EoE patient per population
1993–2003	0	635 850*	0	0	0	0	0
2004	1	644 097	0.16	0.32	0	0.16	1/644 097
2005	4	650 791	0.61	1.27	0	0.77	1/130 158
2006	7	658 659	1.06	0.94	1.18	1.82	1/54 888
2007	6	668 581	0.89	0.92	0.87	2.69	1/37 143
2008	8	684 922	1.17	1.50	0.85	3.80	1/26 343
2009	20	697 802	2.87	5.0	0.84	6.59	1/15 170
2010	26	708 177	3.67	5.21	2.20	10.17	1/9836
2011	23	721 561	3.19	4.54	1.89	13.17	1/7595
2012	37	729 971	5.07	7.01	3.22	18.08	1/5530
2013	47	743 317	6.32	10.44	2.37	24.08	1/4153

*The population number of Canton of Vaud refers to 2003.

Discussion

Our population-based study from the largest geographically confined region reported to date demonstrates a rapidly increasing incidence and prevalence of EoE during the last decade. Unlike most studies, for which patients were identified using the term 'esophageal eosinophilia' in pathology databases, we additionally conducted an in-depth chart review to identify patients that fulfilled published diagnostic criteria for EoE (1).

Few years ago, our group has already evaluated the epidemiological parameters of EoE in the German-speaking, Eastern part of Switzerland (9). Olten County is an EoE indicator region with approximately 90 000 inhabitants and with a rather low migration rate. Eastern and Western part of Switzerland are quite diverse with respect to language, as well as social and cultural background. In Canton of Vaud, 43.8% of the population are living in cities (defined as community size of >10 000 people) compared to 21.1% in Olten County. As such, the Canton of Vaud is more urban when compared to Olten County. Canton of Vaud has also a higher density of board-certified gastroenterologists ($n = 29$, corresponding to 1 for 25 517 persons) when compared to Olten County ($n = 2$, corresponding to 1 for 45 000 persons). EoE incidence in Canton of Vaud (6.3/100 000 persons) in 2013 was comparable to the one in Olten County (7.4/100 000 persons) observed between 2007 and 2009 (9). In contrast, the cumulative EoE prevalence in Canton of Vaud (24.1/100 000 persons) in 2013 was only half of that in Olten County (42.8/100 000 persons) between 2007 and 2009.

The difference in the cumulative prevalences between Olten County and Canton of Vaud can be explained by the fact that EoE was diagnosed in Olten County starting in 1989, whereas the first EoE patient in Canton of Vaud was diagnosed only in 2004. What are the reasons for this striking difference? The percentage of the non-Swiss population in Canton of Vaud was 32.4% in 2013, which is similar to the 27.6% of foreigners in Olten County. Therefore, the difference in cumulative prevalence cannot be explained by differences in influx of immigrants. Neither did the mildly increasing rate of EGDs performed in this interval explain the important increase in EoE prevalence. However, this difference in prevalence rates can be potentially explained by different degree of EoE awareness between Olten County gastroenterologists, who were among the first to publish on a consecutive EoE patient series, and gastroenterologists and pathologists in Canton of Vaud (17).

How do our data compare to the findings from geographically confined regions in other countries? Our incidence data are similar to the findings of Arias et al., who conducted a study in Castilla-La Mancha, a central region of Spain with a population of approximately 102 000 inhabitants (10). Authors observed a mean annual incidence of 6.4/100 000 persons between 2005 and 2011 (10). However, EoE prevalence observed in Canton of Vaud is approximately half of the one observed by Arias et al. (44.6/100 000 inhabitants) (10). Prasad and coworkers evaluated the EoE incidence and prevalence over the last three decades in Olmsted County, a

geographically confined region in Minnesota (USA) with a population of 120 000 inhabitants (13). Authors found that incidence of EoE increased from 0.35/100 000 inhabitants in the period between 1991 and 1995 to 9.45/100 000 inhabitants in the period between 2001 and 2005. As of January 1, 2006, the EoE prevalence was 55/100 000 persons (13). These prevalence data are very similar to the findings of Spergel et al. who observed an EoE prevalence of 52/100 000 in a large sample from the United States (20). Croese et al. conducted a retrospective observational study to evaluate various epidemiological parameters of EoE in Townsville, Australia (198 000 inhabitants), between 1981 and 2002 (21). Of 31 identified patients with EoE, 19 patients were diagnosed between 2000 and 2001, which gives an average incidence of 4.8/100 000 persons in this 2-year period. The prevalence was 15.6/100 000 persons in 2002.

How do our data compare with studies from other countries that assessed EoE incidence based on endoscopy and histopathology reports? In a cross-sectional study performed by van Rhijn et al. between 1996 and 2010, authors identified patients with 'esophageal eosinophilia' using a nationwide pathology database in the Netherlands (11). Cases were classified according to the diagnosis established by the pathologist, and annual incidence rates were estimated. When searching for the term 'esophageal eosinophilia', 8838 pathology records were identified. Of these, the authors identified 674 records of patients with EoE. Based on that data, authors concluded that EoE incidence increased considerably over the past years, with a peak incidence value of 1.31/100 000 persons in 2010 (11). DeBrosse et al. retrospectively evaluated the epidemiology of pediatric esophageal eosinophilia between 1982 and 1999 in 198 patients with ≥ 15 eos/hpf (12). After correcting for a 40-fold increase in the number of endoscopies during this time period, the proportion of biopsies with ≥ 15 eos/hpf did not change (0.08 in 1982 vs. 0.08 in 1996, $P = 0.9$). The authors concluded that esophageal eosinophilia, at levels consistent with EoE, was present among 30% of patients diagnosed with reflux esophagitis and that the incidence of esophageal eosinophilia did not change over time (12). This finding stands in contrast to our data and the data by van Rhijn (11). Using a national pathology database (Caris Diagnostics, Irving, TX, USA), Kapel et al. identified 363 patients with EoE based on the pathology reports of biopsies sampled during 74 000 EGDs. An EoE prevalence of approximately 0.5% per endoscopy was calculated (3). Dellon et al. evaluated the EoE prevalence in the United States to be 56.7/100 000 persons (22).

To summarize, the observed increase in EoE incidence in Canton of Vaud is in accordance with data from other European countries, Australia, and the United States. The differences in the incidence and prevalence rates may be related to the differences in study design, threshold values for eosinophils per hpf, geographic locations, time frames when the studies were conducted, and awareness levels among gastroenterologists and pathologists.

Our group has recently shown that adult patients with EoE often develop behavioral modifications to living with dysphagia, such as food avoidance, food modification, or

slow eating (23). Such coping strategies can modulate the frequency and severity of dysphagia, experienced by the patients, and can lead to delayed EoE diagnosis. Length of diagnostic delay is associated with the risk of stricture formation and food impaction (24, 25). Median diagnostic delay in our study was 4 years, which is comparable to those observed in German-speaking part of Switzerland, United States, and Australia (9, 21, 26). In EoE patients with acute food bolus impaction seeking medical attention for the first time, the diagnostic delay is exclusively patient related. Median diagnostic delay for this patient subgroup was 4 years, which is equal to the length of diagnostic delay in patients with EoE that did not suffer from bolus impactions necessitating endoscopic removal before the time of EoE diagnosis. Therefore, we can conclude that diagnostic delay, at least in our sample, can be attributed mostly to patients. In fact, many patients show behavioral adaptations to living with dysphagia, such as avoidance of distinct foods, food modification, or slow eating. These strategies can potentially delay referral for diagnostic endoscopy (23). Unfortunately, in accordance with the data from Olten County, we did not observe a decrease in the length of diagnostic delay over time (9). We also could not identify risk factors for the length of diagnostic delay. Given the fact that the lion's share of diagnostic delay is patient related, it would be prudent to establish public awareness programs to reduce the length of this delay.

Our study has several strengths and also some weaknesses. We present the largest population-based study on incidence and prevalence of EoE in a reference population of approximately 740 000 inhabitants. This reference population is roughly 8 times larger than the ones in Olten County and a central region in Spain (9, 10). The study is a population-based one, as all gastroenterologists and pathologists working in Canton of Vaud, collaborated on this project. Patients were not diagnosed based exclusively on pathology or endoscopy databases, but also on a chart review of individual patients. This strategy helped to ensure that the diagnostic criteria according to the published guidelines were fulfilled (1). Identifying patients with esophageal eosinophilia alone in a pathology database without reviewing patient records may lead to biased reporting of EoE incidence and cumulative prevalence. The lack of any patient with EoE diagnosis prior to 2004 in Canton of Vaud is indeed astonishing. We speculate that this might be related to a low EoE awareness among gastroenterologists and pathologists in the 1990s. Another strength is that we took into account the number of upper endoscopies performed between 2002 and 2013. Similar to the data of Olten County, we found that the increase in EoE incidence was not explained by the number of endoscopies (9). A first limitation may be that we did not assess for the number of esophageal biopsies performed. It is possible that EoE is increasingly diagnosed by taking more systematically esophageal samples also from normal esophagus in case of symptomatic patients. A further limitation is that we do not have numbers of patients living in

Canton of Vaud who were diagnosed with EoE outside of this region.

In conclusion, we observed an increase in incidence and cumulative prevalence of EoE in the past 10 years. Given the constant length of diagnostic delay over time, it would be prudent to raise EoE awareness among the general public.

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Author contributions

BG and AMS planned the study. BG, PY, ES, MZ, AR, AN, SRV, CS, AS, and AMS collected, assembled, analyzed, and interpreted the data. BG, ES, AS, and AMS drafted the manuscript. BG, PY, ES, MZ, AR, AN, SRV, CS, AS, and AMS revised the manuscript and approved its final version. AMS supervised the study.

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Conflict of interest

The authors declare that they have no conflicts of interest.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Length of diagnostic delay over time. No change in the length of diagnostic delay was observed over time ($P = 0.713$, trend test).

Table S2. Logistic regression modeling evaluating the length of "diagnostic delay", which is defined as time interval from EoE symptom onset until diagnosis is established.

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Supplementary Table 1: length of diagnostic delay over time. No change in the length of diagnostic delay was observed over time ($p = 0.713$, trend test). Abbreviations: IQR; interquartile range.

Year	Number of patients	Diagnostic delay (years) Median, IQR, range
2004	1	1, 1-1, 1-1
2005	4	5, 2-18, 1-30
2006	7	7, 2-16, 1-20
2007	6	1.5, 1-4, 1-25
2008	8	9.5, 2-13, 0-50
2009	20	4, 2-7, 0-19
2010	26	3, 1-6, 0-25
2011	23	4, 2-10, 0-27
2012	37	5, 1-9, 0-30
2013	47	4.5, 1-8, 0-41

Supplementary Table 2: Logistic regression modeling evaluating the length of “diagnostic delay”, which is defined as time interval from EoE symptom onset until diagnosis is established. The underlined binary item denotes to which specification the Odds Ratio (OR) and Confidence Interval (CI) refer to.

Diagnostic delay from first symptoms to EoE diagnosis			
Item	Univariate logistic regression		
	OR	95%-CI	P-value
Age at diagnosis (years)	0.98	0.95-1.01	0.169
Sex			
- <u>male</u>	0.85	0.28-2.56	0.772
- female	1 (ref)	-	-
Positive EoE family history			
- <u>positive</u>	0.41	0.07-2.33	0.312
- negative	1 (ref)	-	-
Allergies (airborne and/or food allergies)			
- <u>yes</u>	1.96	0.68-5.65	0.214
- no	1 (ref)	-	-