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Original Article

The Changing Epidemiology of Gastroesophageal Reflux Disease: Are Patients Getting Younger?

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Background/Aims
Gastroesophageal reflux disease (GERD) is a common disease globally with increasing prevalence and consequently greater burden on the Healthcare system. Traditionally, GERD has been considered a disease of middle-aged and older people. Since risk factors for GERD affect a growing number of the adult population, concerns have been raised that increasingly younger people may develop GERD. We aim to determine if the proportion of younger patients has increased among the GERD population.

Methods
The incidence of GERD as well as several variables were evaluated during an 11-year period. Explorys was used to evaluate datasets at a "Universal" and Healthcare system in northern Ohio to determine if trends at a local level reflected those at a universal level. GERD patients were classified into 7 age groups (15-19, 20-29, 30-39, 40-49, 50-59, 60-69, and ≥ 70 years).

Results
The proportion of patients with GERD increased in all age groups, except for those who were ≥ 70 years in the universal dataset ($P < 0.001$) and those who were ≥ 60 years in the Healthcare system ($P < 0.001$). The greatest rise was seen in 30-39 years in both datasets ($P < 0.001$). Similarly, the proportion of GERD patients who were using proton pump inhibitors increased in all age groups except for those who were ≥ 70 years in both datasets ($P < 0.001$), with the greatest increase being the group 30-39 years ($P < 0.001$).

Conclusion
Over the last decade, there has been a significant increase in the proportion of younger patients with GERD, especially those within the age range of 30-39 years.
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Key Words
Age; Epidemiology; Gastroesophageal reflux disease; Proton pump inhibitors

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Introduction

Gastroesophageal reflux disease (GERD) is a common disease that can cause troublesome symptoms and have a significant impact on quality of life.[1] GERD is a chronic and highly prevalent disorder. A recent systematic review showed that the prevalence of GERD is 18.1-27.8% in North America, 8.8-25.9% in Europe, 2.5-7.8% in East Asia, 8.7-33.1% in the Middle East, 11.6% in Australia, and 23.0% in South America.[2] The increase in GERD prevalence may be due to multiple factors such as older age, male sex, race, intake of analgesics, consumption of certain types of food and drinks, decrease in the prevalence of *Helicobacter pylori* infection, smoking, family history of GERD, high body mass index (BMI), and limited physical activity. These risk factors are mostly related to a patient's lifestyle.[3-5]

Aging has been consistently associated with an increased risk for GERD symptoms. Some studies have reported that the effects of aging on esophageal and esophagogastric junction mechanophysical properties of patients with GERD may explain the age effect.[6-8] Esophageal peristalsis may decrease, and esophageal acid exposure and anatomical disruption of the esophagogastric junction may increase with aging.[9] In a meta-analysis, the prevalence of GERD symptoms was higher in subjects aged ≥ 50 years (OR, 1.32; 95%, CI, 1.12-1.54) but with significant heterogeneity between studies (I^2 = 91.5%, $P < 0.001$), indicating substantial heterogeneity among study results.[10] In addition, aging was associated with increased hospitalizations for erosive esophagitis and GERD complications.[11] However, in the late 1980s, aging was inversely correlated with hospitalization for esophagitis (OR for > 85 years [65-69 years: the reference], 0.66; 95% CI, 0.65-0.67).[12] This reversal in association of age with erosive esophagitis suggests a cohort effect.

Johnson and Fennerty[13] analyzed 11 945 patients with erosive esophagitis who were enrolled in 5 prospective, randomized, controlled clinical trials. The authors assessed the relationship between age, severe heartburn symptoms, and severe erosive esophagitis. The study demonstrated that severe erosive esophagitis became more prevalent with advancing age. Only 12% of patients aged < 21 years showed severe erosive esophagitis as compared with 37% in those aged > 70 years. The OR of having severe esophagitis increased by 1.17 (95% CI, 1.13-1.20) for each decade of age ($P < 0.001$).

As risk factors for GERD increasingly affect the general population, concerns have been raised that more young individuals will develop GERD and its potential consequences. Thus, the aim of this study is to determine if GERD is becoming more prevalent in younger populations than in older populations by assessing the proportion of patients with GERD in each age group using a population-based data and comparing the results with a major Healthcare system.

Materials and Methods

Patients

A population-based analysis of the Explorys dataset (Explorys Inc, Cleveland, OH, USA; http://www.explorys.com) was performed. Explorys is an aggregate electronic medical record database representing over 54 million patients from 26 institutions throughout the United States of America. De-identified data were obtained using the explore application of the Explorys platform. This placed a Healthcare gateway server behind the firewall of each participating Healthcare institution. The de-identified data were collected through billing inquiries that included diagnosis, findings, procedures, electronic health records, laboratory systems, etc. This was then processed and passed on to a data grid. A web application allowed each Healthcare organization to search and analyze the aggregated, standardized, normalized, and de-identified population level data. All data were de-identified to meet the Health Insurance Portability and Accountability Act (HIPPA) and Health Information Technology for Economic and Clinical Health (HITECH) Act standards. Therefore, this study was deemed not to be human subject research by the Institutional Review Board of the Metro-Health System. Business affiliation agreements are in place between all participating Healthcare systems and Explorys Inc. regarding contribution of electronic health records data and the use of de-identified data. Unified Medical Language Systems (UMLS) ontologies were used to map electronic health records data to facilitate searching and indexing. Diagnosis, findings, and procedures were mapped into the systematized nomenclature of medical-clinical terms (SNOMED-CT) hierarchy. Prescription medication orders were mapped to RxNorm. Laboratory test observations were mapped to logistical observation identifier names and codes (LOINC) established by the Regenstrief Institute. Through the Explorys cohort definition feature, subjects were identified by adding "Diagnosis: Gastroesophageal reflux disease" as the cohort criterion, which was determined by patients' providers. GERD patients were stratified into 7 age groups by years (15-19, 20-29, 30-39, 40-49, 50-59, 60-69, and ≥ 70). Patients younger than aged 15 years were excluded from the analysis. Secular trends of GERD

proportion were assessed for each age group.

Study Design

This was a large nationwide database cohort study using the Explorys dataset. Case identification was carried out using an electronic health search. The diagnosis information was obtained from multiple sources, making it a sensitive tool. The term "gastroesophageal reflux disease" was used in the Explorys search tool. Proportion of GERD as well as several variables such as age, sex, race, BMI, and treatment with a proton pump inhibitor (PPI) were evaluated during an 11-year period from 2006 to 2016. Using Explorys, we examined the universal patient population in the universal dataset and compared it with the patient population of a large Healthcare system in Ohio. Patient demographics, symptoms, associated conditions, and treatments were identified using a search tool. We also stratified patients into the following 5 groups with regard to BMI: underweight (BMI $<$ 18.5 kg/m^2), normal (18.5 kg/m^2 $\leq$ BMI $<$ 25 kg/m^2), overweight (25 kg/m^2 $\leq$ BMI $<$ 30 kg/m^2), obese (BMI 30 kg/m^2 $\leq$ BMI $<$ 40 kg/m^2), and severely obese (BMI $\geq$ 40 kg/m^2). Cell counts in Explorys were rounded to the nearest 10.

Statistical Methods

Most demographic data in this study that were extracted from Explorys were categorical and were thus presented as counts and percentages. Differences across age groups for proportion of GERD and proportion of PPI usage in 2006 compared with 2016 were tested using a 2-way contingency table chi-square test. The Cochran-Armitage test was used to determine if there was a year-by-year trend in the proportion of GERD and PPI usage for the 11-year period from 2006 through 2016. Statistical significance was established at $P < 0.05$ throughout the study. SAS version 9.4 (World Headquarters SAS Institute Inc, Cary, NC, USA) was used to analyze all statistical tests.

Results

Universal Explorys Dataset

Table 1 shows the demographics of GERD patients using the universal Explorys dataset, that the total number of patients diagnosed with GERD in a given year between 2006 and 2016 had increased from 2006 (179 300 patients) to 2014 (1 113 910 patients) but decreased in 2015 (1 113 160 patients) and 2016 (1 032 140 patients). The increase in number of GERD patients represents a growing number of health centers using the Epic electronic medical record and their datasets were incorporated into Explorys universal.

Analysis of GERD diagnosis by age groups revealed that from 2006 to 2016 the proportion of GERD patients over the age 70 ($\geq$ 70) and diagnosed with GERD had significantly decreased (−10.6%, $P < 0.001$) (Fig. 1A), while the younger age groups demonstrated a significant increase in the proportion of GERD patients over the same period of time (15-19: 0.2%, $P < 0.001$; 20-29: 2.4%, $P < 0.001$; 30-39: 3.2%, $P < 0.001$; 40-49: 2.8%, $P < 0.001$; 50-59: 2.5%, $P < 0.001$; 60-69: 0.8%, $P < 0.001$). The greatest increase in the proportion of patients with GERD was noted in the 30-39 years age group (Fig. 2A).

The proportion of patients with GERD by sex has been consistent from 2006 to 2016: 60.0% of the patients with GERD were women, and 40.0% were men. While the majority of the GERD patients were Caucasian, the proportion of Caucasian patients with GERD had increased from 76.1% in 2006 to a peak of 80.7% in 2015, followed by a slight decrease to 80.4% in 2016. African Americans account for the second-highest ethnicity among GERD patients. However, the proportion of GERD patients in this group has decreased over time from 16.5% in 2006 to 11.9% in 2016. The majority of patients with GERD were considered obese (45.4%) or severely obese (30.8%).

When examining PPI usage in patients with GERD by age group, results were similar to distribution of GERD diagnosis (Fig. 3A). The proportion of GERD patients using PPIs has declined significantly in the age group $\geq$ 70 years between 2006 and 2016 (−11.4%, $P < 0.001$), while the proportion of GERD patients using PPIs in the other remaining age groups has increased significantly (15-19 years: 0.2%, $P < 0.001$; 20-29 years: 2.0%, $P < 0.001$; 30-39 years: 3.5%, $P < 0.001$; 40-49 years: 3.5%, $P < 0.001$; 50-59 years: 2.8%, $P < 0.001$; 60-69 years: 0.3%, $P < 0.001$). The highest increase was noted in the 30-39 years age group (Fig. 4A).

Healthcare System

The data collected from patients affiliated with the Northern Ohio Healthcare system showed results similar to the universal dataset. Table 2 demonstrates the demographics of GERD patients at the Healthcare system. The total number of GERD diagnoses in each year had increased 108.0% from 2006 (9110 patients) to 2015 (18 950 patients). In 2016, the total number of patients diagnosed with GERD decreased slightly to 18 460 patients (2.6%). As previously mentioned, the total numbers represent inclusion of new Epic users into the database.

Table 1. Demographics of Gastroesophageal Reflux Disease Patients Using a Universal Explorys Dataset

Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	Trend test	
Total number of GERD	179 300	241 470	299 190	375 110	487 170	602 110	807 900	957 650	1 113 910	1 113 160	1 032 140	z-value	*P*-value
Age (yr, n [%])													
15-19	1200	1540	1920	2570	2900	3610	4920	6340	8440	9050	9170	25.07	< 0.001
	(0.7)	(0.6)	(0.6)	(0.7)	(0.6)	(0.6)	(0.6)	(0.7)	(0.8)	(0.8)	(0.9)		
20-29	3270	4159	6450	9010	12 510	17 710	25 460	33 030	42 400	44 340	43 280	106.04	< 0.001
	(1.8)	(1.7)	(2.2)	(2.4)	(2.6)	(2.9)	(3.2)	(3.5)	(3.8)	(4.0)	(4.2)		
30-39	7820	11120	15 580	20 760	28 260	37 300	52 160	64 340	78 950	81 440	78 480	91.31	< 0.001
	(4.4)	(4.6)	(5.2)	(5.5)	(5.8)	(6.2)	(6.5)	(6.7)	(7.1)	(7.3)	(7.6)		
40-49	15 810	21 600	28 300	36 410	47 980	61 030	84 370	101 980	123 330	125 370	119 800	66.70	< 0.001
	(8.8)	(8.9)	(9.5)	(9.7)	(9.9)	(10.1)	(10.4)	(10.7)	(11.1)	(11.3)	(11.6)		
50-59	28 670	39 180	49 310	62 040	81 670	102 210	139 460	167 670	199 430	202 000	190 600	49.13	< 0.001
	(16.0)	(16.2)	(16.5)	(16.5)	(16.8)	(17.0)	(17.3)	(17.5)	(17.9)	(18.2)	(18.5)		
60-69	38 990	52 580	64 030	80 870	104 850	128 990	174 020	207 490	243 070	247 180	232 140	17.72	< 0.001
	(21.8)	(21.8)	(21.4)	(21.6)	(21.5)	(21.4)	(21.5)	(21.7)	(21.8)	(22.2)	(22.5)		
≥ 70	72 870	96 430	115 620	141 540	182 490	219 110	285 850	326 930	362 370	348 880	310 040	−168.81	< 0.001
	(40.6)	(39.9)	(38.6)	(37.7)	(37.5)	(36.4)	(35.4)	(34.1)	(32.5)	(31.3)	(30.0)		
Sex (male, n [%])	71 310	96 210	119 700	148 100	190 460	235 780	317 490	377 940	441 900	441 050	409 560		
	(39.8)	(39.8)	(40.0)	(39.5)	(39.1)	(39.2)	(39.3)	(39.5)	(39.7)	(39.6)	(39.7)		
Race (n [%])													
Caucasian	136 420	186 920	231 290	293 760	384 950	482 130	648 510	770 180	893 210	897 940	829 430		
	(76.1)	(77.4)	(77.3)	(78.3)	(79.0)	(80.1)	(80.3)	(80.4)	(80.1)	(80.7)	(80.4)		
African American	29 510	34 690	41 990	50 660	65 870	79 130	104 780	115 120	133 320	132 280	122 840		
	(16.5)	(14.4)	(14.0)	(13.5)	(13.5)	(13.1)	(13.0)	(12.0)	(12.0)	(11.9)	(11.9)		
Hispanic/Latino	1110	1700	2390	3260	4460	5500	6850	8200	10 330	11 270	11 380		
	(0.6)	(0.7)	(0.8)	(0.9)	(0.9)	(0.9)	(0.8)	(0.86)	(0.9)	(1.0)	(1.1)		
Asian	1940	2590	3130	4310	5620	7260	9620	14 390	16 260	15 900	14 850		
	(1.1)	(1.1)	(1.0)	(1.1)	(1.2)	(1.2)	(1.2)	(1.5)	(1.5)	(1.4)	(1.4)		
Native American or Alaskan Native	-	-	-	-	-	-	-	-	-	-	-		
Asian/Pacific Islander	-	-	-	-	-	-	-	-	-	-	-		
Unknown Race	26 670	40 640	50 970	60 030	76 840	92 900	115 860	127 790	140 100	140 480	133 180		
	(14.9)	(16.8)	(17.0)	(16.0)	(15.8)	(15.4)	(14.3)	(13.3)	(12.6)	(12.6)	(12.9)		
Other	5250	7120	9490	11450	14620	18440	25930	34230	45780	47520	45930		
	(2.9)	(2.9)	(3.2)	(3.1)	(3.0)	(3.1)	(3.2)	(3.6)	(4.1)	(4.2)	(4.4)		

Table 1. Continued

Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	Trend test	
Total number of GERD	179 300	241 470	299 190	375 110	487 170	602 110	807 900	957 650	1 113 910	1 113 160	1 032 140	z-value	*P*-value
BMI (n [%])													
Severe obesity (BMI ≧ 40 kg/m^2)	8350 (30.1)	12 080 (30.1)	16 430 (30.6)	21 910 (31.1)	30 370 (31.1)	39 680 (31.1)	57 130 (31.1)	69 980 (31.2)	84 130 (31.0)	87 470 (30.7)	83 180 (31.0)		
Obesity (30 ≦ BMI < 40 kg/m^2)	12 230 (44.1)	17 850 (44.5)	23 650 (44.0)	30 970 (43.9)	42 970 (44.0)	56 670 (44.4)	83 970 (45.8)	103 420 (46.2)	126 710 (46.6)	134 850 (47.4)	129 360 (48.3)		
Overweight (25 ≦ BMI < 30 kg/m^2)	2310 (8.3)	3400 (8.5)	4720 (8.8)	6310 (9.0)	8440 (8.6)	10 900 (8.5)	14 860 (8.1)	17 820 (8.0)	22 820 (8.4)	27 800 (9.8)	33 390 (12.5)		
Normal (20 ≦ BMI < 25 kg/m^2)	1450 (5.2)	1900 (4.7)	2530 (4.7)	3270 (4.6)	4870 (5.0)	6330 (5.0)	8370 (4.6)	10 190 (4.5)	12 670 (4.7)	15 380 (5.4)	18 370 (6.9)		
Underweight (BMI < 20 kg/m^2)	530 (1.9)	740 (1.8)	950 (1.8)	1260 (1.8)	1770 (1.8)	2410 (1.9)	3340 (1.8)	4190 (1.9)	5690 (2.1)	7670 (2.7)	10 480 (3.9)		
PPI usage (n)													
Total	117 470	165 810	210 560	265 410	343 550	431 220	584 000	706 240	828 400	831 990	761 910		
15-19 yr	580	770	1020	1330	1460	1860	2560	3470	4680	5000	5060	19.75	< 0.001
20-29 yr	1650	2440	3640	4880	6650	9820	14 590	19 470	25 440	27 240	26 090	85.17	< 0.001
30-39 yr	4160	6370	9310	12 520	16 750	23 030	33 120	42 360	53 290	56 190	53 680	90.29	< 0.001
40-49 yr	9680	13 880	19 030	24 700	32 260	42 280	59 510	73 970	91 120	93 760	88 530	69.13	< 0.001
50-59 yr	18 960	27 290	35 260	44 810	58 890	75 060	102 450	126 490	152 300	155 030	144 190	45.36	< 0.001
60-69 yr	27 230	38 270	47 480	60 760	78 420	97 790	132 380	160 230	189 290	192 840	178 840	8.45	< 0.001
≧ 70 yr	50 750	70 120	86 480	106 110	136 680	166 030	219 040	256 440	285 750	275 790	242 560	−150.21	< 0.001

GERD, gastroesophageal reflux disease; BMI, body mass index; PPI, proton pump inhibitor.

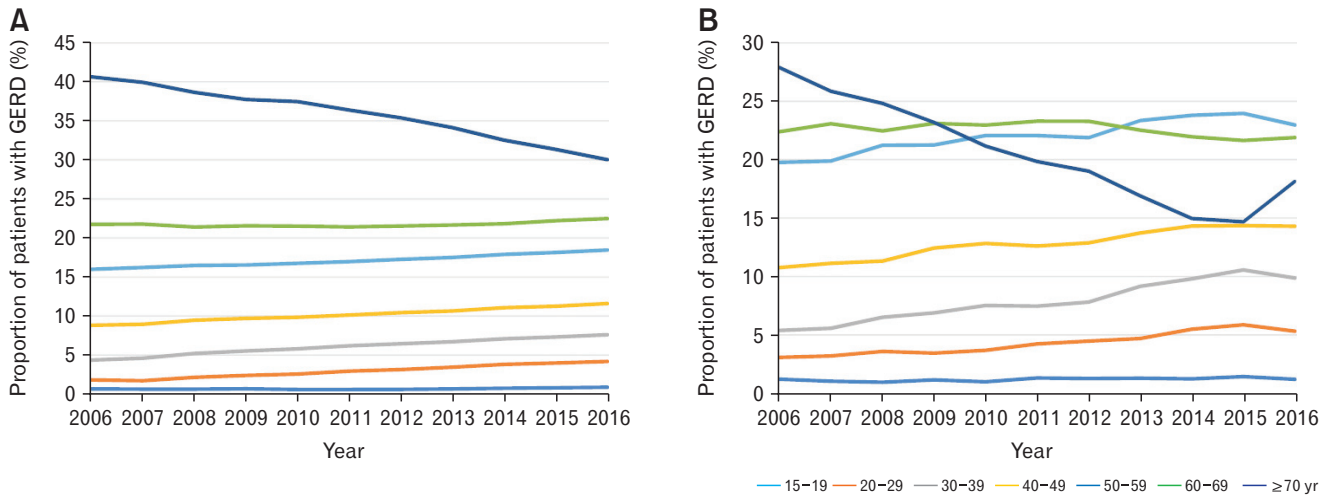

Figure 1. The proportion of patients with gastroesophageal reflux disease (GERD) by age group between 2006 and 2016 using universal Explorys dataset (A) and Healthcare system dataset (B).

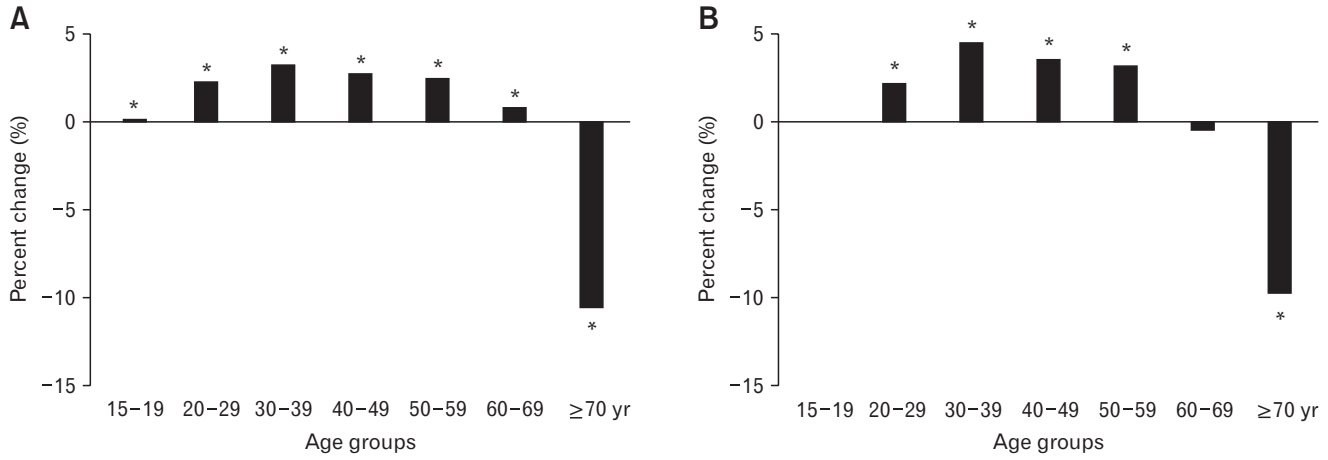

Figure 2. Percent of change in the proportion of patients with gastroesophageal reflux disease (GERD) between 2006 and 2016 using universal Explorys dataset (A) and Healthcare system dataset (B). *$P < 0.001$.

The proportion of patients with GERD by sex has been fairly consistent. When viewing GERD diagnoses in a given year, the proportion ranged from 63.0% to 66.9% for women and from 33.0% to 37.1% for men. Most patients diagnosed with GERD are Caucasian, followed by African Americans, which is similar to that seen in the Universal dataset. The Healthcare system dataset had a population of Native Americans/Alaskan Natives (0.1-0.3%) and Asian/Pacific Islanders (0.1-0.2%). However, Native Americans/Alaskan Natives or Asian/Pacific Islanders were not mentioned in the Universal dataset due to their very small population size relative to the other ethnicities who composed the GERD population. There was no clear trend in GERD incidence by race. While the Universal dataset showed that most patients diagnosed with GERD were obese (44.0-48.0%), the Healthcare system data showed that most patients were severely obese (45.0-49.0%).

The proportion of patients with GERD was also analyzed, and it was found that most patients were aged ≥ 70 years (Fig. 1B). As with the Universal dataset, the proportion of patients diagnosed with GERD in a given year who are aged ≥ 70 years has been decreasing from 2006 to 2016. In addition, the proportion of patients with GERD diagnosis who were aged ≥ 70 years dropped significantly by 9.7% ($P < 0.001$). The proportion of patients with GERD in the 60-69 years age group demonstrated a slight decrease (−0.5%, $P = 0.347$). The proportion of patients with GERD in the remaining age groups showed a significant increase (15-19 years: 0.02%, $P = 0.957$; 20-29 years: 2.2%, $P < 0.001$;

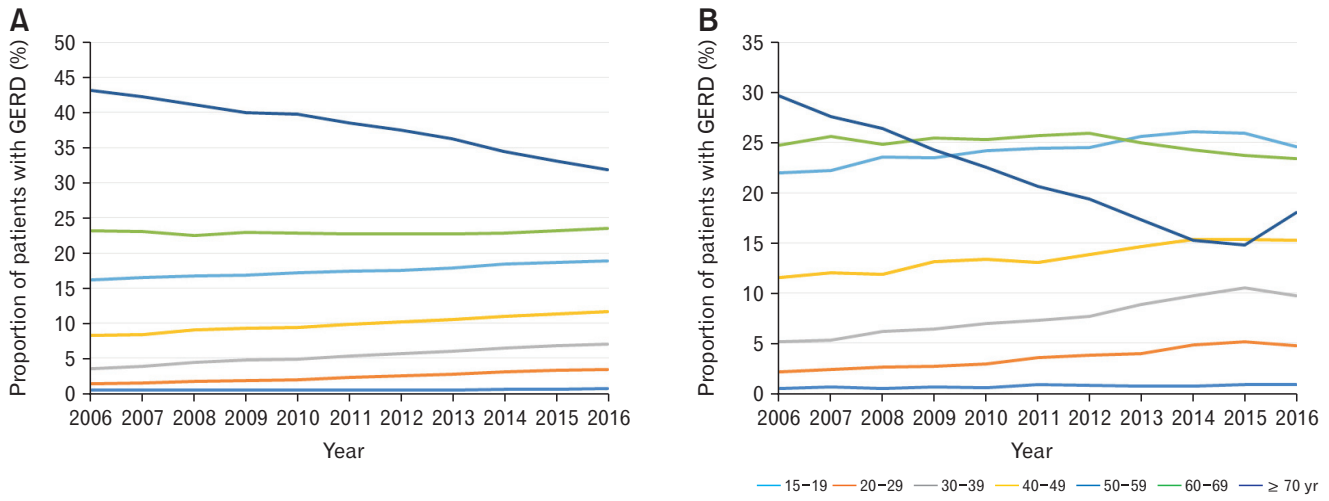

Figure 3. The proportion of gastroesophageal reflux disease (GERD) patients using proton pump inhibitors by age group between 2006 and 2016 using universal Explorys dataset (A) and Healthcare system dataset (B).

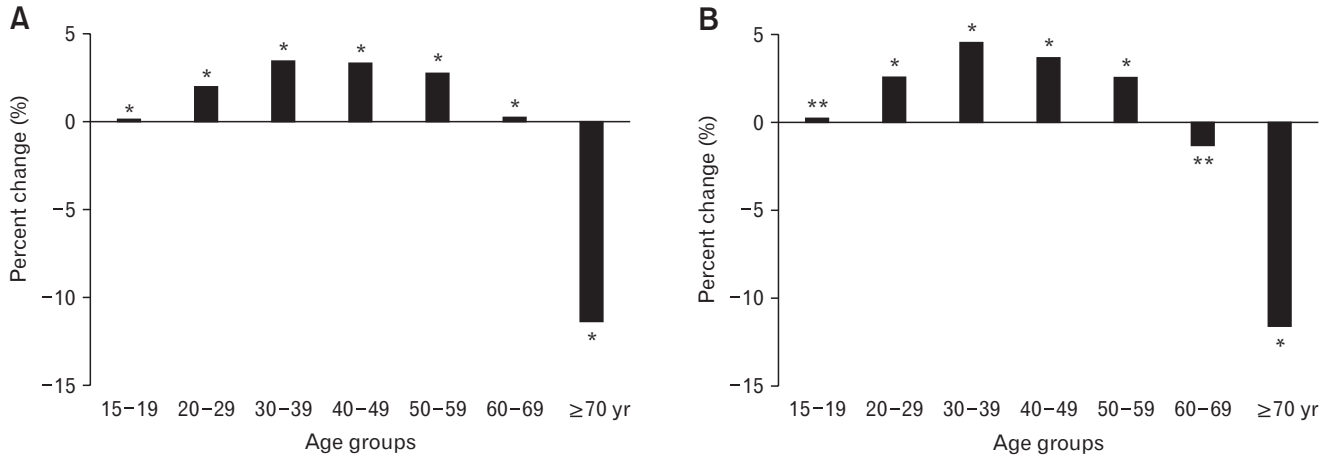

Figure 4. Percent of change in the proportion of gastroesophageal reflux disease patients using proton pump inhibitors between 2006 and 2016 using universal Explorys dataset (A) and Healthcare system dataset (B). *$P < 0.001$, **$P < 0.05$.

30-39 years: 4.5%, $P < 0.001$; 40-49 years: 3.5%, $P < 0.001$; 50-59 years: 2.6%, $P < 0.001$) (Fig. 2B).

When examining PPI usage in GERD patients by age group, the results were also similar to the proportion of patients with GERD (Fig. 3B). The proportion of patients with GERD using PPIs has decreased significantly from 2006 to 2016 in the aged ≥ 70 years (−11.6%, $P < 0.001$) and the aged 60-69 years group (−1.3%, $P = 0.029$). The proportion of patients with GERD who were using PPIs, has increased significantly (aged 15-19: 0.3%, $P = 0.010$; aged 20-29: 2.7%, $P < 0.001$; aged 30-39: 4.6%, $P < 0.001$; aged 40-49: 3.8%, $P < 0.001$; aged 50-59: 2.6%, $P < 0.001$) (Fig. 4B).

Discussion

The present study is a large, population-based cohort study that examined if GERD is becoming more common among younger populations when using trend analysis. In general, the number of patients with GERD in our study has increased over time. However, the observed numerical increase in patients in the dataset represents an increase in the number of registered institutions in Explorys.

Our study showed that the proportion of patients with GERD has increased in all age groups, with the exception of those who

Table 2. Demographics of Gastroesophageal Reflux Disease Patients Using Northern Ohio Healthcare System

Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	z-value	*P*-value
Total number of GERD	9110	9710	10 600	11 340	12 240	13 010	14 990	17 050	18 580	18 950	18 460		
Age (yr, n [%])													
15-19	110	100	100	130	120	170	190	220	230	270	220	3.03	0.003
	(1.2)	(1.0)	(0.9)	(1.1)	(1.0)	(1.3)	(1.3)	(1.3)	(1.2)	(1.4)	(1.2)		
20-29	280	310	380	390	450	550	670	800	1020	1110	980	16.67	< 0.001
	(3.1)	(3.2)	(3.6)	(3.4)	(3.7)	(4.2)	(4.5)	(4.7)	(5.5)	(5.9)	(5.3)		
30-39	490	540	690	780	920	970	1170	1560	1820	2000	1820	22.86	< 0.001
	(5.4)	(5.6)	(6.5)	(6.9)	(7.5)	(7.5)	(7.8)	(9.2)	(9.8)	(10.6)	(9.9)		
40-49	980	1080	1200	1410	1570	1640	1930	2340	2660	2720	2640	13.54	< 0.001
	(10.8)	(11.1)	(11.3)	(12.4)	(12.8)	(12.6)	(12.9)	(13.7)	(14.3)	(14.4)	(14.3)		
50-59	1800	1930	2250	2410	2700	2870	3280	3980	4420	4540	4240	11.24	< 0.001
	(19.8)	(19.9)	(21.2)	(21.3)	(22.1)	(22.1)	(21.9)	(23.3)	(23.8)	(24.0)	(23.0)		
60-69	2040	2260	2380	2620	2810	3030	3490	3840	4080	4100	4040	−3.68	< 0.001
	(22.4)	(23.1)	(22.5)	(23.1)	(23.3)	(23.3)	(23.3)	(22.5)	(22.0)	(21.6)	(21.9)		
≥ 70	2540	1130	2630	2630	2590	2580	2850	2880	2780	2780	3350	−23.13	< 0.001
	(27.9)	(11.6)	(24.8)	(23.2)	(21.2)	(19.8)	(19.0)	(16.9)	(15.0)	(14.7)	(18.1)		
Sex (male, n [%])	3070	3230	3650	3870	4330	4490	5310	6140	6800	6920	6840		
	(33.7)	(33.3)	(34.4)	(34.1)	(35.4)	(34.5)	(35.4)	(36.0)	(36.6)	(36.5)	(37.1)		
Race (n [%])													
Caucasian	4440	4750	5270	5540	5990	6450	7210	7990	8690	8860	9330		
	(48.7)	(48.9)	(49.7)	(48.9)	(48.9)	(49.6)	(48.1)	(46.9)	(46.8)	(46.8)	(50.1)		
African American	3260	3460	3730	4020	4310	4650	5080	5830	6460	6560	6160		
	(35.8)	(35.6)	(35.2)	(35.4)	(35.2)	(35.7)	(33.9)	(34.2)	(34.8)	(34.6)	(33.4)		
Hispanic/Latino	-	-	-	-	-	-	-	-	-	-	-		
Asian	80	90	90	120	130	170	170	230	300	340	320		
	(0.9)	(0.9)	(0.8)	(1.1)	(1.1)	(1.3)	(1.1)	(1.3)	(1.6)	(1.8)	(1.7)		
Native American or Alaskan Native	30	20	30	30	30	30	40	50	50	50	60		
	(0.3)	(0.2)	(0.3)	(0.3)	(0.2)	(0.2)	(0.3)	(0.3)	(0.3)	(0.3)	(0.3)		
Asian/Pacific Islander	-	10	10	10	-	20	20	10	30	30	20		
		(0.1)	(0.1)	(0.1)		(0.2)	(0.1)	(0.1)	(0.2)	(0.2)	(0.1)		
Unknown Race	690	780	880	1060	1230	1390	1520	1600	1880	2050	2070		
	(7.6)	(8.0)	(8.3)	(9.3)	(10.0)	(10.7)	(10.1)	(9.4)	(10.1)	(10.8)	(11.2)		
Other	-	-	-	-	-	-	-	-	-	-	-		

Table 2. Continued

Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	z-value	*P*-value
Total number of GERD	9110	9710	10 600	11 340	12 240	13 010	14 990	17 050	18 580	18 950	18 460		
BMI (n [%])													
Severe obesity (BMI ≧ 40 kg/m^2)	460 (47.4)	520 (47.7)	590 (46.1)	710 (48.3)	780 (47.9)	850 (45.5)	1110 (48.1)	1360 (47.9)	1540 (48.0)	1660 (47.8)	1540 (49.0)		
Obesity (30 ≦ BMI < 40 kg/m^2)	300 (30.9)	350 (32.1)	410 (32.0)	470 (32.0)	530 (32.5)	620 (33.2)	750 (32.5)	950 (33.5)	1050 (32.7)	1190 (34.3)	1090 (34.6)		
Overweight (25 ≦ BMI < 30 kg/m^2)	50 (5.2)	50 (4.6)	60 (4.7)	70 (4.8)	100 (6.1)	110 (5.9)	130 (5.6)	160 (5.6)	190 (5.9)	220 (6.3)	230 (7.3)		
Normal (20 ≦ BMI < 25 kg/m^2)	30 (3.1)	30 (2.8)	40 (3.1)	50 (3.4)	50 (3.1)	60 (3.2)	70 (3.0)	80 (2.8)	100 (3.1)	120 (3.5)	120 (3.8)		
Underweight (BMI < 20 kg/m^2)	20 (2.1)	20 (1.8)	30 (2.3)	30 (2.0)	40 (2.5)	30 (1.6)	40 (1.7)	50 (1.8)	60 (1.9)	90 (2.6)	70 (2.2)		
PPI usage (n)													
Total	7550	8050	8750	9310	9920	10 550	11 640	13 130	14 620	15 240	15 310		
15-19 yr	40	50	40	60	60	90	90	100	110	140	130	4.68	< 0.001
20-29 yr	160	190	230	250	290	380	440	520	710	790	730	18.27	< 0.001
30-39 yr	390	430	540	600	690	770	890	1160	1420	1600	1490	22.00	< 0.001
40-49 yr	870	970	1040	1220	1330	1380	1610	1920	2250	2340	2340	13.17	< 0.001
50-59 yr	1660	1790	2060	2190	2400	2580	2850	3360	3810	3950	3760	8.53	< 0.001
60-69 yr	1870	2060	2170	2370	2510	2710	3020	3280	3550	3620	3590	−4.49	< 0.001
≧ 70 yr	2240	2220	2310	2260	2240	2180	2260	2280	2230	2260	2760	−37.86	< 0.001

GERD, gastroesophageal reflux disease; BMI, body mass index; PPI, proton pump inhibitor.

were aged ≥ 70 years in both the universal and Healthcare system datasets. In the system dataset, it was also found that the proportion of patients diagnosed with GERD has been decreasing in those who are aged ≥ 60 years.

GERD has been considered to be a disease of middle aged and older subjects. One study demonstrated that the prevalence of gastroesophageal reflux symptoms was significantly higher in subjects aged ≥ 50 years as compared with those who were aged < 50 years (OR, 1.32; 95% CI, 1.12-1.54; $P < 0.001$).[10] In a population-based cohort study from Norway, participants were evaluated for the degree of their GERD symptoms during the past 12 months. The study demonstrated that the incidence of GERD-related symptoms increased with age.[14] Despite the results of our study, the age groups 60-70 years and ≥ 70 years remained the largest as compared with all other age groups (as has been shown by the aforementioned studies).

In our study, however, the greatest rise in the proportion of patients with GERD diagnosis was seen in young adults aged 30-39 years in both datasets during the last decade. These results clearly suggest that younger subjects are more exposed today to risk factors for GERD development as compared with 10 years ago. In addition, it appears that risk factors for GERD continue to affect a growing number of the adult population—but specifically younger subjects, with resulting in early development of GERD. In a population-based study, more than 30.0% of heartburn sufferers reported reduced work productivity, with younger age being associated with these findings.[15] Another retrospective study demonstrated that reflux esophagitis is present in 28.7% of all patients between the ages of 1 month and 20 years who underwent an upper endoscopy, which is a dramatic increase over the past 14 years.[16] Interestingly, several studies have demonstrated that erosive reflux disease symptoms, such as heartburn and regurgitation, decrease in severity with aging.[6,13,17,18]

An important finding of our study was the general characteristic of GERD patients who were primarily obese or severely obese, older women, and Caucasian. These findings are consistent with several epidemiological studies, suggesting that GERD is more common in overweight/obese subjects, Caucasians, and older women.[19] While erosive esophagitis and Barrett's esophagus (the more severe presentations of GERD) are more common in overweight/obese subjects, Caucasians, and older males, most GERD patients have nonerosive reflux disease (NERD), which is primarily a female disease explaining the results of our study.[20] NERD accounts for 60-70% of the GERD patients.[21]

In our study, the proportion of GERD patients using PPIs fell significantly in those who were over 70 years old in the universal dataset. In contrast, the proportion of GERD patients using PPIs has significantly increased in the other age groups, with the greatest increase being in the 30-39 years old group. Both trends closely follow the incidence trends of GERD in the same age groups. While PPI consumption remains high, with Americans spending more than 10 billion dollars per year for the different PPIs, concerns have been raised about the possible development of side effects. Based on our study results, more GERD patients are starting on chronic PPI treatment at a younger age, which may potentially increase the likelihood of long-term adverse events such as chronic kidney disease, osteoporosis, gastrointestinal infection, pneumonia, and others.[22]

Our study has several limitations that need to be discussed. The results are based on the Explorys dataset, which originates from 26 major Healthcare systems and 360 hospitals overall. This vast dataset is de-identified and thus may not reveal regional or individual hospital trends. Contributions to the dataset originate from many hospitals around the country, but this may not truly represent the diverse Healthcare system in the United States. Furthermore, the diagnosis of GERD was based on the term "Diagnosis: gastroesophageal reflux disease" as the cohort criterion without clarifying the severity of symptoms. Thus, we could not determine the relationship between severity of GERD and age. Consequently, it is assumed that GERD was diagnosed based on endoscopic findings or patient symptoms. In addition, Explorys is susceptible to limited documentation by physicians, which can lead to error in data collection and confound analysis.

In conclusion, GERD remains predominantly a disease of the middle aged and elderly with a higher proportion among Caucasians and females. However, there has been a significant increase in the proportion of patients with GERD in the younger age groups. Support for our findings comes from the proportion of patients with GERD who were using PPIs in our patient population. Our study suggests that physicians should be more aware that the proportion of young adults with GERD has been increasing continuously. It is also possible—although not evaluated in our study—that the proportion of young adults among patients with erosive esophagitis or Barrett's esophagus has been increasing as well. The ramifications of the aforementioned trend remain to be elucidated.

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