Proton pump inhibitor prescribing patterns in the United Kingdom: a primary care database study.

Running title: Proton pump inhibitor prescribing patterns in the UK

Authors:
Fatmah Othman, Timothy R Card, Colin J Crooks

Authors' affiliation: Division of Epidemiology and Public Health, The University of Nottingham

Corresponding Author Fatmah Othman
Division of Epidemiology and Public Health, The University of Nottingham, Clinical Sciences Building 2, Nottingham City Hospital, NG5 1PB, UK

msxfo1@nottingham.ac.uk

t: +44 (0) 115 8231376

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KEY POINTS:

- The prevalence of PPI use in the UK general population is high and still increasing.
- The majority of patients only use PPIs short term, with only 26% using them long-term.
- Clear attempts to step down long-term use were identified in two fifths of the patients, so there remain further opportunities for reducing the cost and side effects of PPI use through improving adherence to recommended withdrawal strategies.

COMPETING INTERESTS:

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Abstract:

Purpose: To determine the prevalence and pattern of proton pump inhibitor (PPI) prescription, and the practices employed to reduce PPI use in the UK general population.

Method: The UK's Clinical Practice Research Database was used to identify individuals who were issued with ≥1 PPI prescription during the period 1990-2014. Point and period prevalence of PPI use were estimated annually. Additionally, new users of PPI therapy who had five years of follow-up data were included in a cohort analysis to describe patterns of cessation and duration of PPI use.

Results: Both the period and point prevalence of PPI use increased between 1990 and 2014 (period prevalence increased from 0.2% to 15.0% and point from 0.03 % to 7.7%). A total of 596,334 new users of PPI therapy in the cohort study received 8,784,272 prescriptions. Of these, 26.7% used PPI therapy long-term (≥1 year continuously) while 3.9% remained on PPI therapy for five years. Clear attempts to step down dose were identified in 39.9% of long-term users while this was 47% in patients whose initial indication did not mandate long-term use.

Conclusion: A considerable increase in PPI use was observed in UK general practice. 60% of long-term PPI users did not have an attempt to discontinue or step down. Considerable opportunities may therefore exist to reduce the cost and side effects of PPI use through improving adherence to recommended withdrawal strategies.

INTRODUCTION

The introduction of proton pump inhibitors (PPIs) has revolutionised the management of acid-related gastrointestinal disorders[1]. In the United Kingdom (UK), 11,126 thousand prescriptions for PPIs were dispensed in 2000[2], and this increased to 43,127 thousand in 2011[3]. Although the expenditure on PPIs has decreased in the UK since 2006 as a result of government efforts to encourage the use of low-cost generic PPIs[4,5], there has still been an overall increase in the total number of PPI prescriptions dispensed[4]. For instance, in 2010, PPIs became one of the top 20 drugs with the greatest net ingredient cost in the UK[4].

The importance of reducing any overuse of PPIs is not limited to the associated costs, but also to the risks of taking the drugs on a long-term basis[6]. As PPIs have become commonly used for long-term maintenance, concerns have been raised about the safety of such use [6]. Studies have showed that PPI use is associated with malabsorption of vitamins and minerals[7,8], an increased risk of infections, such as pneumonia[9] and enteric infection[10], and an increased fracture risk[11,12]. These potential side effects can be minimized through appropriate prescription practices in terms of stepping down the dose or stopping long-term treatment altogether.

As a consequence of this dramatic increase in PPI use and the associated potential risks, clinical guidelines in the UK have recommended rationing the use of the PPI in the primary care setting, either by stepping down the dose or stopping treatment all together[13]. However, very few research studies have examined the extent to which the clinical guidelines are being followed in the UK [14–19]. The aim of this study was to determine the prevalence of PPI use and assess the practices employed to reduce PPI use in the general UK population. It

is anticipated that research of this nature will help to inform future attempts to moderate the use of PPIs.

METHODS

Study type and data source

We conducted an observational study with repeated cross-sectional analyses to estimate the prevalence of PPI use annually and a cohort design to describe the patterns of PPI utilization by using data from the UK Clinical Practice Research Datalink (CPRD)[20]. CPRD is a large database drawn from the computerised records of primary care practices throughout the UK and encompassing a representative sample of around 6% of UK population [21–23]. The CPRD comprises data about patients' medical diagnoses, GPs' prescriptions, investigations, hospital referrals and discharges, together with basic demographic information. The information on prescriptions includes their issue dates, the drug prescribed, numeric daily dose, daily quantity and the number of packs/pack size prescribed. Many studies have validated CPRD for use in pharmacoepidemiological research[21,24].

Study population

We studied adult patients with at least one month of prospective records after either the date of their current registration or the date after the practice became "up to standard" (UTS) on CPRD[21] whichever was the latest, and an "acceptable" registration status as defined by CPRD[21] between 1st Jan 1990 and 31st December 2014. This population formed our denominator for studies of prevalence. Patients who received ≥1 PPI prescription(BNF 1.3.5 [25]) were classified as exposed subjects in the study (i.e. the numerator).

Prescription duration

The earliest PPI prescription for each patient was considered their index date. Prescription duration was taken as the number of treatment days recorded by the GP, or calculated from the prescribed quantity and numeric daily dose prescribed. If information on both was

missing, the individual median duration was imputed. The duration was recalculated if the calculated prescription duration was less than or equal to seven days assuming that the prescription quantity was referring to the number of individual product packs prescribed.

Prescribing patterns

To describe the prescribing practices of long-term PPI use in general practice in term of discontinuation, stepping down or switching to histamine 2 receptor antagonists (H2RA), we identified new PPI therapy users i.e. patients with at least 12 months of registration on CPRD prior to their index date who had ≥ 5 years of prospective follow-up data. We

The NICE guidelines[13] were used to determine what constitutes expected long-term PPI use within this study. PPIs are used for the short-term management in conditions such as dyspepsia, gastro-oesophageal reflux disease (GORD), and gastric and duodenal ulcers. Long-term PPI therapy is often prescribed to prevent recurrence of GORD complications, and as prophylactic therapy to prevent peptic ulcers in patients who are co-prescribed non-steroidal anti-inflammatory (NSAID) therapy[13].

Exposure to PPIs was considered to begin on the date of a prescription for them and end after its calculated duration unless another prescription was issued ≤30 days after this date in which case we considered exposure continuous. We refer to one set of continuous prescriptions as one course. Courses were classified as short (<12 months) or long (≥12 months), this time period being chosen as 12 months is the minimum frequency with which NICE recommends that these prescriptions should be reviewed and stopped or stepped down if possible. Individuals receiving exclusively short courses were classified as short-term users while individuals who received at least one long course were classified as long-term users even if their records contained other short courses.

Discontinuation (no subsequent PPI prescription issued within 30 days after the end of the previous one) was categorized as temporary (patients subsequently re-prescribed PPI) or permanent (no further prescriptions received up to the end of the patient's follow-up). A step down of PPI therapy was defined as a reduction in daily dose of the subsequent PPI prescription. If a following prescription was for a different PPI, the dose was converted to an equivalent dose based on the recommended dosing in the BNF[25]. A successful step down was defined as maintaining the stepped down dose for 12 months from the step down date. Lastly, a switch to H2RA medication was defined as receiving H2RA prescription within one month before or after discontinuation or stepping down attempt.

Covariates

We abstracted data on patients' age at the index date (in 10-year age bands), gender, and socioeconomic status (derived through linking CPRD to the Index of Multiple Deprivation (IMD) 2007). For each course, the potential indications as specified in the BNF [25] were identified by the presence of relevant Read codes on the first prescription date of a course, or within 30 days before and 12 month after that date. We considered prevention and treatment of NSAID-associated ulcer the indication if NSAID prescription date fell on the same date as the PPI prescription. Potential indications were then classified into 8 categories (supplementary Table1) and missing initial indication was recorded in a separate category.

Statistical analysis

Prevalence of PPI use

For each year we calculated the period prevalence by dividing the number of patients who received at least one PPI prescription during that year by the corresponding mid-year adult population of the CPRD. We also calculated annual point prevalence as the number of

patients with an ongoing PPI prescription on 30th June divided by the corresponding mid-year population. We stratified these prevalence estimates by gender and age (calculated on June 30th and grouped into 10 years age bands).

Patterns of PPI use

The baseline patient characteristics and the use of PPIs among new users were described as proportions of age bands, genders and quintiles of IMD (to represent socioeconomic status). We calculated the percentage of patients who continued their first PPI course, from the index date to the end of five years of follow-up during the study period.

Kaplan Meier survival curves were constructed among all new PPI patients to graphically describe: 1) time to discontinuation (permanent or temporary) of the first PPI course during the five years follow-up, 2) time to permanent discontinuation of all PPI therapy during the five years follow-up. Time to discontinuation of the first PPI course was calculated from the index date to the first PPI course's end date. Time to permanent discontinuation was calculated from the index date to the end date of the last PPI course that each patient received during the follow-up period.

The proportions of patients, who stepped down, or substituted PPIs, were calculated for long-term users as NICE guidelines[13] recommends reviewing long-term PPI user on an annual basis at a minimum. To determine successful step down attempts accurately patients were required to have a 12 month window after the step down date. The analysis of successful step down attempts was therefore limited to patients who had stepdown attempts within the first 4 years of the follow-up to allow adequate follow up within the final year of the cohort. We repeated this analysis restricted to patients who started PPI therapy as long-term and whose indication might not suggest an ongoing need for long-term PPI use,

136 therefore patients with recorded indication of complicated GORD, NSAID-associated ulcers
137 prophylaxis or reducing the degradation of pancreatic enzyme supplements were excluded.

138 Analyses were performed using STATA 12 (Stata Corp, College Station, Texas).

RESULTS

Prevalence of prescribing

We identified 31,956,396 PPI prescriptions in 1,828,141 adult patients during the study period. The point and period prevalence of PPI increased between 1990 and 2014 (Figure 1-a) and it varied substantially by age group (Figure 1-b). The point prevalence of PPI use was similar between males and females, increasing during the study period from 0.04% in 1990 to 7.05% in 2014 in males, and from 0.03% in 1990 to 8.35% in 2014 in females. The female to male prevalence ratio of PPI use was 1.14 (95% confidence intervals (CI) 1.12-1.17) from 1990 to 2014.

Prescribing patterns

During the study period, 596,334 new users of PPI therapy with at least five years of follow-up data were identified. Their mean age was 54.2 years (Standard Deviation SD: 16.3) and 55% were females. They received a total of 8,784,272 prescriptions and 26.5% had one PPI prescription recorded. The median duration for all PPI prescriptions was 28 days (interquartile range (IQR) 18-56 days).

Individual prescriptions were combined to create 1,708,513 PPI courses. The median duration of all courses was 55 days (IQR 28-125 days) and there were a median of 2 courses per patient (IQR 1-4 courses). Patients received prescriptions for enough PPI to cover 96.69% (95%CI 96.68-96.71) of days in these courses.

1,505,758 (88.1%) of the courses were categorised as short courses and 202,755(11.8%) were categorised as long courses with median durations of 28 days (IQR 28-79 days) and 805 days (IQR 526-1345 days) for short and long courses respectively. 73.2% of the cohort received exclusively short courses with a mean age of 51.6years (SD 16.3 years), and 26.7%

received at least one long course with a mean age of 61.2years (SD 14.3 years)(Table 1). Within this cohort, 230,766 patients (38.7%) had only one PPI course, and 365,568 (61.3%) patients had multiple courses. Around 16.3% and 11.4% of patients remained continuously on PPI therapy for 6 and 12 months from their index date, respectively. At the end of 5 years of follow-up, 23,607 (3.9%) patients had remained on PPI continuously from the index date.

Prescription indications

Initially, 365,481 PPI courses (21.3%) had no coded indication for PPI prescription. This fell to 14.0% after assuming prescriptions concurrent with NSAID prescriptions were intended for gastro-protection. Dyspepsia was the most frequent recorded indication (Table2).

Discontinuation, step-down, and substitution

Figure 2 shows the proportion of patients who discontinued the first PPI course (Figure 2-A), and patients who permanently discontinued all PPI courses (Figure 2-B). When considering only long-term PPI patients, 25% had temporarily discontinued their therapy at one year and three months after starting their long-term PPI course, 50% at one year and seven months and by two years and three months 75% had temporarily discontinued their long term PPI course. Of those discontinuing, 9,557 (9%) received a prescription for H2RA within one month before or after this occurred.

Of the 159,259 patients who received long term PPIs, 63,640 (39.9%) had an attempt to step down their PPI dose (Table3). Of these 6,388 (10%) had received an H2RA prescription within one month before or after stepping down PPI dose.

Of 59,734 patients in whom the initial indication for PPI prescription did not suggest a recognised need for PPI use to be prolonged, un-complicated GORD was the most frequent

recorded indication and 39,164 (65.5%) discontinued PPI therapy (temporarily or permanently). For those patients who temporarily discontinued their PPI therapy the median time to this was 3 years and 3 months after starting their PPI course. In those using PPI long term without recognised indication for such use a step down attempt was identified in 47% (Table4).

DISCUSSION

Summary

This study describes the pattern of PPI prescription in UK general practice in terms of its prevalence and the practices employed to reduce long-term use. The proportion of the population using PPIs within each year increased from 0.2% in 1990 to 15.0% in 2014. Of those new PPI users who had five years of follow up available, 26.7% used PPI therapy for more than one year, and 3.9% remained on PPI therapy for five full years. Clear attempts to step down long-term use were identified in about 39%, and 8.7% of long-term users received a H2RA prescription around the time they attempted to step down and/or discontinue their use of PPI. Amongst patients whose initial PPI prescription indication did not necessarily warrant long term PPI use, 47% had attempts to step down their PPI dose.

Comparison with previous work

Our findings pertaining to the prevalence of PPI use in the early years of our study were consistent with the findings of earlier studies involving general practice in the UK[14,16,18,26] in addition, our result revealed that the use of PPI has continued to rise. These trends are not limited to the UK: similar increases in prescription rates have been observed in the United States[27], Australia[28], and many European countries. This widespread increase supports the evidence that PPI prescriptions remain highly prevalent in many healthcare systems despite the extensive literature that indicates overprescribing PPI in both the primary and secondary care setting[29,30].

In this study, the proportion of patients who were on long-term PPI (26%) was higher than that reported in previous studies[16–18], which have reported rates of long-term PPI usage between 0.05% and 4.4%, according to varying definitions of long-term use. Studies have

212 shown that repeat prescription practices account for approximately 32 to 81% of the total
213 cost of prescribed drugs[31]. The continuous increase in PPI use, specifically the increase in the
214 proportion of long-term users, may therefore have important cost implications despite the
215 availability of low-cost PPI.

216 PPIs provide effective symptomatic relief for patients who suffer from dyspepsia
217 symptoms. However, while clinical guidelines suggest the use of PPI therapy over short
218 durations to treat dyspepsia symptoms[13], it seems that PPIs had been prescribed as a form
219 of maintenance therapy without specific underlying cause. Our study revealed that dyspepsia
220 symptoms were the initial indication in 23% of long-term PPI courses. However, as most
221 patients on first presentation in primary care will not have a final endoscopic diagnosis, it is
222 inevitable that the GPs will have recorded less-specific indications in subjects who had other
223 underlying diagnoses. Our results concur with those of several studies that have reported
224 that the majority of patients on PPI therapy are prescribed PPI for the purpose of relieving
225 symptoms without any other clear indications[32,33]. In addition, although its clinical relevance
226 is unproven, it has been proposed that rebound acid hypersecretion following PPI therapy
227 withdrawal may help perpetuate the use of PPIs in patients with uncertain indications or who
228 have received them for symptomatic relief of relatively mild symptoms for more than six
229 weeks [34]. The issue of appropriateness in terms of prescription practices has been discussed
230 in existing literature[29,35,36]. Despite this, PPIs are still being administered to patients for a
231 variety of complaints that are not known to be acid-induced and over a long-term basis.

232 In the view of the emerging concerns regarding adverse events from long-term PPI
233 use, clinical guidelines[13] have encouraged GPs to use PPIs carefully and to continually review
234 long-term patients to try to step down or stop treatment. Our results suggest that GPs are

actively attempting to reduce PPI use by stepping down and substituting alternative medication. Previous studies[36–39] reported discontinuation rates that differed from those identified in our study; however, these can be explained by variations in the study population and the discontinuation strategies employed[38]. Reports regarding the outcomes of step-down therapy have been conflicting[40,41]. For example, one study reported that more than half of the patients involved in the study remained asymptomatic after the step down[41] while another reported that 19% of patients whose PPI therapy was stepped down experienced relapsed symptoms and resumed PPI use[40]. In our study, 60% of the long-term PPI users maintained lower doses for more than one year. However, while we identified an appreciable proportion of long-term PPI users who could potentially reduce the use of the drug, we were unable to find evidence of such attempts in a large proportion of those individuals. Non-adherence to the step down therapy, therefore, allows the maintenance of inappropriate PPI prescription which may sustains overuse of PPIs.

Strengths and limitations

Our study used data from a large database of UK primary care records which has been extensively used and validated for pharmacoepidemiological research[21,24]. The population in our study is therefore representative of the general practice population of the UK to whom our results should be generalizable[21]. The large sample size has allowed us to stratify our analyses by age groups and gender, and to show trends in PPI use over time. It has also provided us with adequate power to identify the relatively small proportion of patients who took PPIs on a long-term basis and describe the management of their prescriptions.

Weaknesses in our study include that we may have underestimated PPI use since neither hospital prescriptions nor over the counter (OTC) use are captured in the data. However,

since secondary care initiated PPI treatment will often be continued by GPs afterwards[35], and prescribed PPI use continued to rise after they became available OTC [42] we think it unlikely that this has led to massive underestimation. Additionally, we focused on long-term users who would be the most likely to obtain their prescriptions from their GPs. Furthermore, the period of PPI exposure for those who took PPI intermittently may have been underestimated, since the calculation of the prescription duration was based on the assumption that the dispensed prescription was consumed as directed. Indeed, CPRD only contains information about the prescriptions of medications; as such, it is not possible to assess whether patients actually collected or consumed the prescribed medication. In addition, our definition of a successful stepdown may underestimate the proportion of patients whose long-term PPI therapy was stepped down but then required a smaller increase in dose lower than the initial dose. However, including this in our definition only identified an additional 997 patients (an additional1.5% of attempted step downs) so for clarity we retained our initial stricter definition. Furthermore, our method of estimating successful step down attempts within the initial 4 years of follow-up would not have led to a substantial underestimation, as it is expected that long-term patients should have been offered a step down attempt at least within the first year of their continuous use of PPI therapy.

CONCLUSION:

During the study period, a considerable increase in the administration of PPI prescriptions was observed in UK general practice. The majority of patients use PPIs on a short-term basis with 26% of the identified use long term. Our results suggest that GPs are actively attempting to decrease the use of PPI by stepping down and discontinuing prescriptions; however, this is not universally practised, nor is it always successful when attempted. If the cost and potential risks of the continuing increase of PPI are to be minimised, a proactive clinical review and adherence to the guidelines is likely to be required.

Ethical approval:

This study was approved by the Independent Scientific Advisory Committee (ISAC) with CPRD number 13_214, and 13-214Mn.

CONTRIBUTORS:

TC & CC supervised FO in conducting this study .TC proposed the original idea. All authors were involved in the study design and concept, and interpretation of results. FO analysed the data set and wrote the initial manuscript draft. TC &CC critically reviewed and edited the drafts of the manuscript. All authors approved the submitted final version. All authors had full access to all of the data and can take responsibility for the integrity of the data and the accuracy of the data analysis.

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Tables and figures:

Table 1: Descriptive characteristics of new users of proton pump inhibitor (PPI) therapy with ≥ 5 years of follow-up data(patients with exclusively short-term courses and patients with at least one long-term course), and the duration (in days) for the first short and long courses.

	Total number		Patients with exclusively short course			Patients with at least one long course in their records		
Patients characteristics	N=596,334		N=437,075		Duration of first short course	N=159,259		Duration of first long course
		%	Number	%	Median(IQR)	Number	%	Median(IQR)
Age								
18-30	50,318	8.4	46,683	92.7	28(28-28)	3,635	7.2	705(484-1172)
31-40	83,579	14.1	72,475	86.7	28(28-49)	11,104	13.2	769(502-1314)
41-50	113,746	19.1	91,721	80.6	28(28-56)	22,025	19.3	816(524-1403)
51-60	120,553	20.3	86,466	71.7	28(28-56)	34,087	28.2	876(544-1491)
61-70	115,470	19.4	73,854	63.9	28(28-56)	41,616	36.0	935(568-1568)
71-80	80,968	13.6	48,034	59.3	28(28-56)	32,934	40.6	978(582-1610)
>80	27,997	4.7	15,216	54.3	28(28-59)	12,781	45.6	1014(592-1656)
Gender								
Male	262,765	44.0	190,947	72.6	28(28-56)	71,818	27.3	920(559-1556)
Female	333,569	55.9	246,128	73.7	28(28-56)	87,441	26.2	882(546-1496)
Index of Multiple Deprivation** (quintiles)								
Unavailable	263,562	44.2	191,426	72.6	28(28-56)	72,136	27.3	905(553-1530)
1(least deprived)	75,711	12.7	57,276	75.6	28(28-56)	18,435	24.3	865(538-1467)
2	78,619	13.1	57,893	73.6	28(28-56)	20,726	26.3	894(550-1512)
3	66,880	11.2	48,987	73.2	28(28-56)	17,893	26.7	905(555-1532)
4	64,654	10.8	47,256	73.0	28(28-56)	17,398	26.9	914(561-1535)
5(most deprived)	46,908	7.8	34,237	72.9	28(28-53)	12,671	27.0	908(557-1574)

IQR=interquartile range

** Socioeconomic status is based on Index of multiple deprivations (IMD) and figures are percent of the people who have available deprivation status

Table 2: Recorded indication for all proton pump inhibitor(PPI)courses(all short courses in exclusively short-term PPI users and all long courses in patients with at least one long-term PPI course).

	Total number N=596,334		Patient with exclusively short courses N=437,075		Patients who had at least one long-term course N=159,259	
Indication category	All PPI courses 1,708,513	%*	Short PPI courses 1,158,705	%*	Long PPI courses 202,755	%*
Dyspepsia	612,842	35.8	452,651	39.0	47,086	23.2
un-complicated GORD	495,288	28.9	309,204	26.6	70,485	34.7
NSAID prophylaxis	132,426	7.7	90,380	7.8	17,926	8.8
Gastritis &duodenitis	125,300	7.3	73,089	6.3	23,037	11.3
peptic ulcer below oesophagus	51,137	2.9	27,871	2.4	10,356	5.1
Helicobacter therapy	24,466	1.4	18,755	1.6	1,581	0.7
GORD complicated	13,146	0.7	5,464	0.4	2,935	1.4
Reduction of pancreatic enzyme degradation	3,450	0.2	1,924	0.1	560	0.2
missing	250,458	14.0	179,367	15.4	28,789	14.2

* column percentage; GORD= Gastro-oesophageal reflux disease; NSAID nonsteroidal anti-inflammatory drugs

Table 3: Numbers and percentages of long-term proton pump inhibitor (PPI) users who attempted a step down in dose, were successful at 12 months, and were prescribed histamin2 receptor antagonists (H2RA) by age, time, and indication.

	Patients with at least one long PPI course	Number of patients who had step down to lower PPI dose		Number of patients who maintained lower dose after step down attempt for 12 months**		Number of patients who received H2RA substitution at time of step down and /or discontinuation	
		Number	%*	Number	%	Number	%*
	159,259	63,640	39.9	36,006	60.5	13,954	8.7
Age group							
18-30	3,632	1,559	42.9	695	47.7	315	8.6
31-40	11,095	4,774	43.0	2,344	52.5	910	8.2
41-50	22,001	9,127	41.4	4,720	55.5	1,568	7.1
51-60	34,040	14,037	41.2	7,777	59.5	2,611	7.6
61-70	42,822	17,205	40.2	9,892	61.5	4,042	9.4
71-80	32,917	12,503	37.9	7,766	66.3	3,271	9.9
>80	12,752	4,435	34.7	2,812	67.9	1,237	9.7
Time when GP attempt to step down							
2 month		25,240	39.6	18,536	73.5	3,986	15.7
6 month		14,414	22.6	8,152	57.7	1,722	11.9
12 month		9,171	14.4	3,819	45.7	6,295	6.0
More than 12 month		14,815	23.2	5,474	46.8	1,951	13.1
Indication							
GORD un-complicated	55,450	26,402	47.6	14,674	59.2	6,125	11.0
Dyspepsia	37,011	14,897	40.2	8,802	63.2	3,203	8.6
Gastritis &duodenitis	18,383	7,889	42.9	3,656	50.3	1,968	10.7
NSAID prophylaxis	13,695	3,591	26.2	2,575	75.9	537	3.9
peptic ulcer below oesophagus	8,188	3,838	46.8	2,306	63.6	780	9.5
GORD complicated	2,209	675	30.5	380	60.8	124	5.6
Helicobacter therapy	1,257	444	35.3	238	57.0	99	7.8
Reduction of pancreatic enzyme degradation	416	129	31.0	59	48.7	28	6.7
missing	22,650	5,775	25.5	3,316	62.2	1,090	4.8

GORD=Gastro-oesophageal reflux disease; NSAID= non-steroidal anti-inflammatory drugs
H2RA=Histamine 2 Receptor antagonist

*percentages were calculated from the total number of long-PPI patients

** percentages were calculated from the number of step down patients who stepped down within the first 4 years of follow-up and successfully stepped down for 12 months(number of patients (59,458))

Table 4 : Numbers and percentages of long-term proton pump inhibitor (PPI) users who attempted a step down in dose, were successful at 12 months, and were prescribed histamin2 receptor antagonists (H2RA) by age, time, and indication. Analysis restricted to indications unsuitable for step down.

	Patients with at least one long proton pump inhibitor course	Number of patients who had step down to lower PPI dose		Number of patients who maintained lower dose after step down attempt for 12 months**		Number of patients who received H2RA substitution at time of step down and /or discontinuation	
		Number	%*	Number	%	Number	%*
	59,734	28,113	47.0	16,907	61.5	5,567	9.3
Age group							
18-30	1,075	569	52.9	282	50.2	105	9.7
31-40	3,586	1,912	53.3	969	51.4	299	8.3
41-50	7,648	3,783	49.4	2,110	56.8	593	7.7
51-60	12,417	6,063	48.8	3,519	59.2	1,003	8.0
61-70	16,347	7,675	46.9	4,679	62.4	1,603	9.8
71-80	13,254	5,902	44.5	3,870	67.4	1,413	10.6
>80	5,407	2,209	40.8	1,478	69.0	551	10.1
Time when GP attempt to step-down							
2 month		11,602	41.2	8,323	71.7	2,019	17.4
6 month		6,922	24.6	4,157	60.0	2,339	6.0
12 month		3,407	12.1	1,683	49.4	433	12.7
More than 12 month		6,182	21.9	2,744	49.5	776	12.5
Indication							
GORD un-complicated	22,173	12,290	55.4	7,290	60.4	2,524	11.3
Dyspepsia	13,686	6,426	46.9	4,116	65.5	1,268	9.2
Gastritis &duodenitis	7,761	3,731	48.0	1,948	53.5	791	10.1
peptic ulcer below oesophagus	4,126	2,101	50.9	1,343	65.4	396	9.6
Helicobacter therapy	402	192	47.0	111	59.0	35	8.7
missing	11,586	3,373	29.1	2,099	64.5	553	4.7

GORD=Gastro-oesophageal reflux disease; H2RA=Histamine 2 Receptor antagonist

* percentages were calculated from the total number of long-PPI patients

** percentages were calculated from the number of step down patients who stepped down within the first 4 years of follow-up and successfully stepped down for 12 months(number of patients (27,473))