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Original article

Prevalence of long-term oral glucocorticoid prescriptions in the UK over the past 20 years

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Abstract

Objective. To assess trends in long-term (i.e. $\geqslant$3 months) oral glucocorticoid (GC) prescriptions over the past 20 years.

Methods. Data of UK adult patients registered between January 1989 and December 2008 with general practices contributing to The Health Improvement Network (THIN) database were obtained. The annual prevalence of long-term oral GC prescriptions was assessed in the whole population and specifically in people with RA, PMR/GCA, asthma, chronic obstructive pulmonary disease (COPD), Crohn's disease and ulcerative colitis (UC). Trends over the 20-year period were estimated using sex- and age-adjusted Poisson regression models.

Results. During the 26 035 154 person-years of follow-up, an average of 0.75% (95% CI 0.74, 0.75) of the study population was prescribed long-term oral GC therapy at any time point. This rose from 0.59% (0.52, 0.67) in 1989 to 0.79% (0.78, 0.80) in 2008. Long-term prescriptions significantly increased in patients with RA [from 10.3% (8.7, 11.9) to 13.6% (12.9, 14.2)] and PMR/GCA [from 57.6% (53.3, 62.0) to 66.5% (65.2, 67.7)], decreased in patients with asthma, COPD and Crohn's disease and remained stable in patients with UC. However, when only incident cases were considered, we found a decreased use of GCs in patients with RA and UC [odds ratio 0.97 (95% CI 0.96, 0.97) and 0.94 (95% CI 0.93, 0.96) per increasing year, respectively].

Conclusion. Over the past 20 years, long-term oral GC prescriptions have increased by 34%. Patients newly diagnosed with RA, Crohn's disease or UC are, however, less likely to receive long-term GC prescriptions than patients with a long past medical history of the disease, suggesting changes in physicians' practice.

Key words: Glucocorticoids, Prevalence, Population-based.

CLINICAL SCIENCE

Introduction

The earliest reports of the efficacy of compound E (i.e. cortisone) in RA were published in the late 1940s [1, 2]. Since then, glucocorticoids (GCs) have been the cornerstone for the treatment of immunological, neoplastic and allergic diseases, but their adverse effects can counter their beneficial effects and can cause concerns about their long-term use. However, in a community-based study published in 1996, 303 (0.5%) out of 65 786 patients received long-term systemic GCs, the most common indications being RA (23%), PMR (22%) and asthma/chronic obstructive pulmonary disease (COPD) (19%) [3]. There are no longitudinal data on prescribing trends of GCs over time and the indications for long-term prescriptions of the drug. Moreover, the availability for some diseases of more targeted therapies (e.g. anti-TNF) could have led to different patterns of GC use.

We aimed to investigate: (i) the overall prevalence of long-term prescriptions of oral GC therapy in the general population and its trend over a 20-year period; and (ii) the pattern of use in prevalent and incident cases of RA, PMR/GCA, asthma, COPD, Crohn's disease and ulcerative colitis (UC).

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Material and methods

Data source: The Health Improvement Network

Approximately 98% of the UK population is registered with a general practitioner [4]. The Health Improvement Network (THIN) is a database of electronic medical records from 429 general practices (GPs) across the UK. Participating general practitioners systematically and prospectively retrieve and record on their computer the clinical information of patients, including demographics data, diagnoses and prescriptions, thus providing a longitudinal medical record for each patient. Both consultations and prescribing data recorded in THIN are representative of those across the UK [5]. Prospective data collection in THIN began in September 2002; however, in many practices, electronic records were used as early as 1987 and these data are included in THIN. THIN has been validated by previous audit and independent studies that have demonstrated a high level of completeness of clinical diagnostic and prescribing data [5–10]. In order to ensure good-quality data and to avoid biases in disease occurrence or prescriptions, we defined our study population using a range of quality indicators (e.g. acceptable mortality reporting) that have been well established and clearly defined elsewhere [5, 11]. We excluded data entered in the first 6 months following registration with the GP as this could represent retrospective recording of a past history rather than a new episode of a problem [12].

GC prescriptions and study population

Each drug is encrypted using multilex codes and is associated with information from the British National Formulary [13]. We selected all the codes for oral GCs, i.e. prednisolone, prednisone, hydrocortisone, dexamethasone, triamcinolone, betamethasone, methylprednisolone and deflazacort. We identified all people aged $\geqslant$18 years who received at least one oral GC prescription and we included data from January 1989 to December 2008. For multiple consecutive prescriptions, the treatment time was taken as the time from the first to the last GC prescription plus the duration of the last prescription. Patients who received a new oral GC prescription after a period of at least 3 months without any other GC prescriptions were considered to have started a new treatment course. A long-term prescription of GCs was defined as a treatment lasting at least 3 months [3, 14].

Identification of underlying diseases

All diagnoses and symptoms are recorded using the Read classification system [15]. Indication for oral GC treatment was obtained by reviewing the medical diagnosis recorded on the same date as treatment was started. If no medical diagnosis was recorded on this date, we searched for relevant chronic conditions recorded closest to when the prescription was issued, up to 2 years before or 1 year after. We then focused our analysis on six diseases, i.e. RA, PMR/GCA, asthma, COPD, Crohn's disease and UC. We chose to study these diseases for three reasons. First, because they frequently require GC therapies. Secondly, to assess the use of GCs in diseases for which new therapies such as anti-TNF are licensed (e.g. RA, Crohn's disease and UC) and compare this with diseases where this is not the case (e.g. PMR/GCA). Lastly, we wanted to compare diseases for which national recommendations regarding GC use are available (e.g. asthma or COPD) with those where this is not so (e.g. PMR/GCA). We defined the start of the disease as the first entry in the clinical notes if it started after the person entered the cohort or as the date of entry in the cohort if the disease was already in progress at that time. Primary care records rarely have an indication of whether a disease resolves. Therefore, we defined the end of the disease as 5 years after the last recorded event or prescription (up to end date) for RA, asthma, COPD, Crohn's disease and UC and 3 years after the start of the disease for PMR/GCA [16–18]. We chose to define an arbitrary disease end date as some of these diseases may be cured (e.g. UC after surgery) and because we felt it was unlikely that a patient would have been affected by a disease such as RA, Crohn's disease or COPD without having had any medical event or prescription related to the condition for $>$5 years. This cut-off, however, had little effect on the denominators as few individuals were followed up $>$5 years after their last record or prescription related to the disease. Due to low number of patients with and/or receiving long-term GC therapy for less common conditions such as Crohn's disease or UC in 1989 and 1990, our analyses started in 1991.

Statistical analysis

Prevalence of prescriptions of oral GCs in the whole population according to calendar time was estimated by dividing the total duration of short-term (i.e. $<$3 months) or long-term oral GCs by the total duration of follow-up. The prevalence of long-term prescriptions issued for each of the six diseases of interest was determined by dividing the number of person-years with the condition receiving long-term GC therapy by the total number of person-years with the condition. We used Poisson regression models adjusted for calendar year, sex and age and weighted by the number of person-time present in a given year and the full population in each calendar year to predict the risks of receiving long-term GC therapy by year and by underlying disease and to assess variations over the 20-year period. We found an interaction between age and sex and, therefore, stratified our analyses by sex. The Kaplan–Meier survival function was used to assess the median duration of treatment according to its year of initiation. The proportion of patients starting a long-term GC course for a given disease during each calendar year was assessed by dividing the number of courses of long-term GC therapy initiated during this year by the number of patients with the disease present in the cohort at the mid-point (June 30) of this year. Poisson regression models stratified on sex and adjusted on age were used to assess variations of these proportions over time. Continuous variables are described by median and

25–75th percentile values. Categorical variables are described as proportions and 95% CI. Means were weighted by the amount of person-time present in a given year. All tests were two-sided, with $P < 0.05$ considered statistically significant. Stata, version 11.0, 2009 (Statacorp, College Station, TX, USA) was used for all analyses. The study has been approved by UCL THIN steering committee and by the Cegedim Strategic Data scientific review board.

Results

Description of long-term GC use

The study population consisted of 4 518 753 adult patients representing 26 035 154 person-years of follow-up. Among them, 384 897 patients were prescribed oral GCs and 102 132 [women: 59.3%, median age at first long-term GC prescription recorded in THIN: 67.4 (54.0–76.8) years] of these people received 167 886 long-term treatments. Prednisolone was the most frequently prescribed (92.3% of long-term prescriptions) followed by dexamethasone (3.5%), hydrocortisone (3.3%), betamethasone (0.5%) and prednisone (0.2%). The median daily dosage of prednisolone equivalent over the follow-up was 7.5 (5.0–11.3) mg and the median duration was 215 (126–490) days [*vs*, respectively, 30 (15–39) mg and 9 (6–10) days for treatments ⩽3 months]. Over a period of 20 years, asthma, PMR/GCA and COPD were the most frequent indications for long-term GC therapy (Table 1).

Table 1 Indications for long-term prescriptions of oral GCs over time

	1990–91	1998–99	2007–08
Asthma, *n* (%)	805 (20.7)	2916 (18.3)	5756 (18.7)
PMR/GCA, *n* (%)	541 (13.9)	2415 (15.2)	4080 (13.2)
COPD, *n* (%)	406 (10.4)	1498 (9.4)	4155 (13.4)
RA, *n* (%)	226 (5.9)	1071 (6.7)	1268 (4.1)
Neoplasms, *n* (%)	158 (4.1)	545 (3.4)	1929 (6.2)
Eczema/atopic dermatitis/pruritis, *n* (%)	142 (3.6)	457 (2.9)	1048 (3.4)
Other dermatosis, *n* (%)	101 (2.6)	539 (3.4)	1101 (3.6)
Crohn's disease, *n* (%)	65 (1.7)	343 (2.2)	463 (1.5)
UC, *n* (%)	55 (1.4)	312 (2.0)	551 (1.8)
Transplantation, *n* (%)	44 (1.1)	181 (1.1)	302 (1.0)
CTD, *n* (%)	54 (1.4)	254 (1.6)	359 (1.2)
Addison's disease, *n* (%)	29 (0.7)	79 (0.5)	152 (0.5)
Other vasculitis, *n* (%)	17 (0.4)	142 (0.9)	245 (0.8)
Myasthenia gravis, *n* (%)	21 (0.5)	61 (0.4)	110 (0.4)
Sarcoidosis, *n* (%)	20 (0.5)	155 (0.9)	232 (0.7)
Renal diseases[a], *n* (%)	16 (0.4)	63 (0.4)	112 (0.4)
Other auto-immune diseases[b], *n* (%)	4 (0.1)	26 (0.2)	116 (0.4)
Others[c], *n* (%)	494 (12.7)	2091 (13.2)	4410 (14.3)
Unknown, *n* (%)	698 (17.9)	2758 (17.3)	4458 (14.4)
Total, *n* (%)	3896 (100)	15 906 (100)	30 847 (100)

[a]Nephrotic syndrome, GN and acute interstitial nephritis. [b]For example, autoimmune hepatitis, autoimmune haemolytic anaemia and ITP. [c]For example, myalgia unspecified, idiopathic fibrosis alveolitis, general aches and pains, and multiple sclerosis.

Prevalence of long-term GC use

GCs were prescribed over 220 195 person-years, of which 194 065 person-years were long-term treatment. Over the 20 years, the mean prevalence of oral GC prescriptions was 0.85% (95% CI 0.84, 0.85) for all types of GC therapies and 0.75% (0.74, 0.75) for long-term therapies (Fig. 1). For long-term prescriptions, this was the lowest in 1989 [0.59% (0.52, 0.67)] and highest in 2008 [0.79% (0.78, 0.80)]. Over the whole period, long-term prescriptions were significantly more commonly issued to women rather than men but increased significantly both in women and men (Fig. 1). The lowest prevalence [0.08% (0.07, 0.09)] was observed in men aged 18–29 years and the highest [3.05% (3.01, 3.09)] in women aged 80–90 years.

Prevalence of long-term GC use in six diseases of interest

Over the study period, the mean prevalence of the six diseases in the UK population was 0.53% (0.52, 0.54) for RA, 0.21% (0.21, 0.22) for PMR/GCA (0.87% in people >50 years), 8.58% (8.13, 9.02) for asthma, 1.65% (1.54, 1.76) for COPD, 0.17% (0.16, 0.18) for Crohn's disease and 0.23% (0.22, 0.24) for UC. Prevalence of asthma, COPD, Crohn's disease and UC increased over time. The overall prevalence of long-term oral GC prescriptions was 13.3% (12.8, 13.8) in patients with RA, 62.4% (60.7, 64.1) in patients with PMR/GCA, 1.3% (1.1, 1.4) in patients with asthma, 3.7% (3.6, 3.9) in patients with COPD, 6.9% (6.1, 7.6) in patients with Crohn's disease and 4.5% (4.3, 4.7) in patients with UC (Fig. 2).

Over the study period, prevalence of long-term GC prescriptions was significantly greater in women than in men with PMR/GCA [odds ratio (OR) 1.68 (95% CI 1.61, 1.74)] or asthma [OR 1.17 (95% CI 1.14, 1.20)], whereas it was lower in women than in men with Crohn's disease [OR 0.75 (95% CI 0.69, 0.81)] or UC [OR 0.71 (95% CI 0.65, 0.76)]. There was no significant difference in prescription issued to women and men with RA or COPD. The

Fig. 1 Prevalence of oral GC prescriptions according to year and sex.

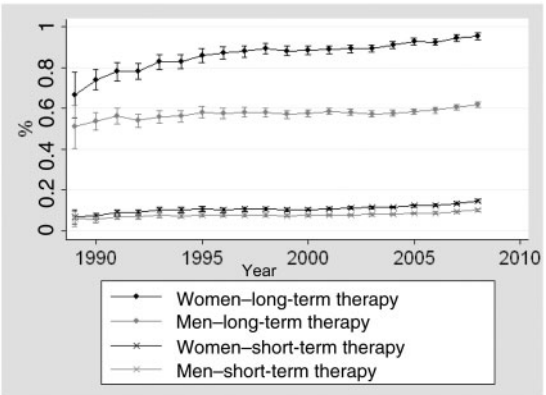


FIG. 2 Prevalence of long-term oral GC prescriptions according to underlying disease and sex.

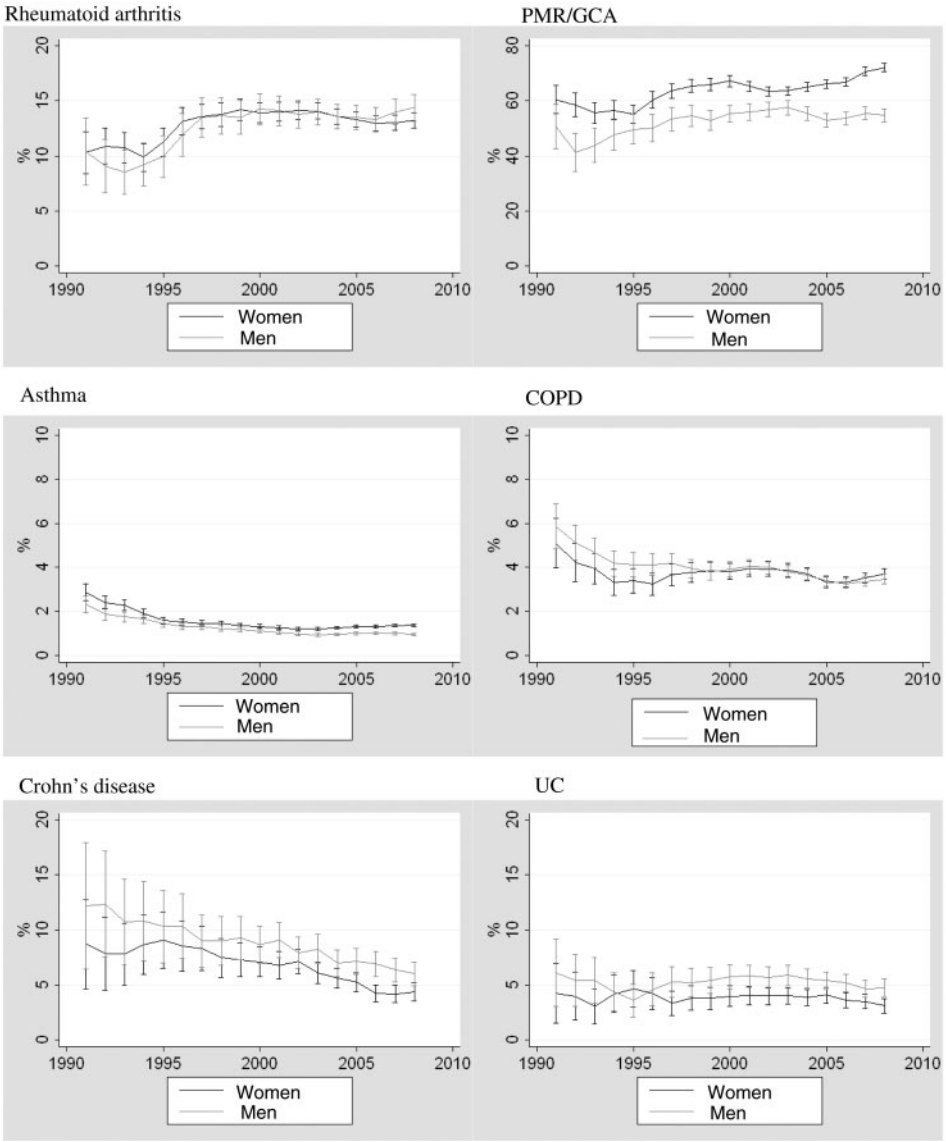


TABLE 2 Prevalence of long-term GC prescriptions per increasing calendar year

	All cases				Incident cases			
	Women		Men		Women		Men	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
RA	1.01 (1.00, 1.01)	0.02	1.01 (1.01, 1.02)	<0.001	0.96 (0.95, 0.97)	<0.001	0.99 (0.98, 1.00)	0.01
PMR/GCA	1.03 (1.03, 1.04)	<0.001	1.01 (1.00, 1.02)	0.04	1.01 (1.00, 1.01)	0.007	1.00 (0.98, 1.00)	0.11
Asthma	0.97 (0.97, 0.98)	<0.001	0.96 (0.95, 0.96)	<0.001	0.98 (0.97, 0.98)	<0.001	0.96 (0.95, 0.97)	<0.001
COPD	0.99 (0.99, 1.00)	0.02	0.98 (0.97, 0.98)	<0.001	0.98 (0.97, 0.99)	<0.001	0.95 (0.95, 0.96)	<0.001
Crohn's disease	0.94 (0.93, 0.96)	<0.001	0.96 (0.94, 0.97)	<0.001	0.91 (0.89, 0.93)	<0.001	0.90 (0.88, 0.92)	<0.001
UC	0.99 (0.97, 1.01)	0.12	1.00 (0.98, 1.01)	0.61	0.93 (0.91, 0.95)	<0.001	0.95 (0.93, 0.97)	<0.001

Table 3 Median duration (in days) of long-term oral GC prescriptions according to year of initiation

	RA		PMR/GCA		Asthma		COPD		Crohn's disease		UC	
	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men
1991	338 (208–1666)	333 (243–2141)	406 (199–860)	371 (199–883)	178 (116–436)	175 (117–430)	268 (135–980)	340 (143–1080)	350 (172–848)	264 (136–450)	145 (110–222)	464 (133–1003)
1995	926 (372–2625)	541 (227–1396)	413 (215–897)	375 (231–707)	157 (111–279)	175 (119–307)	187 (128–483)	238 (132–513)	177 (118–301)	385 (182–1063)	192 (139–413)	184 (143–358)
2000	437 (227–1376)	452 (225–1500)	423 (213–761)	396 (195–684)	166 (117–346)	173 (115–375)	219 (130–661)	219 (136–522)	210 (121–583)	206 (120–464)	183 (119–397)	229 (150–431)
2005	467 (174–1349)	549 (216– .)	446 (226–898)	397 (235–707)	160 (114–311)	162 (113–305)	177 (118–331)	176 (120–386)	160 (118–266)	180 (125–324)	150 (115–249)	173 (113–308)
P-value	<0.001	0.01	<0.001	0.01	0.37	0.05	<0.001	<0.001	0.002	0.01	0.10	0.008

Results are presented as median (Q1–Q3 interquartile range).

prevalence of long-term GC prescriptions significantly decreased in both sexes in patients with asthma, COPD and Crohn's disease, but increased in those with RA or PMR/GCA and remained stable in patients with UC (Table 2). However, taking into account only incident cases (i.e. patients with a first record of the disease after their entry in the cohort), the prevalence decreased in patients with RA and UC (Table 2).

Overall, the median duration of long-term GC prescriptions did not differ between men and women with RA, asthma or COPD, whereas it was 45.4 (28.4–62.4) days longer and 44.2 (−83.1 to −5.3) days shorter for women compared with men with PMR/GCA and Crohn's disease, respectively. Women with UC tended to be treated with shorter courses [−22.6 (−53.0–7.8) days] than men (Table 3). Over time, it decreased in patients with COPD and Crohn's disease and increased in patients with PMR/GCA. Meanwhile, the proportion of patients starting long-term GC therapy by calendar year did not increase for any of the six diseases, but decreased significantly in patients with asthma and Crohn's disease (Fig. 3).

Discussion

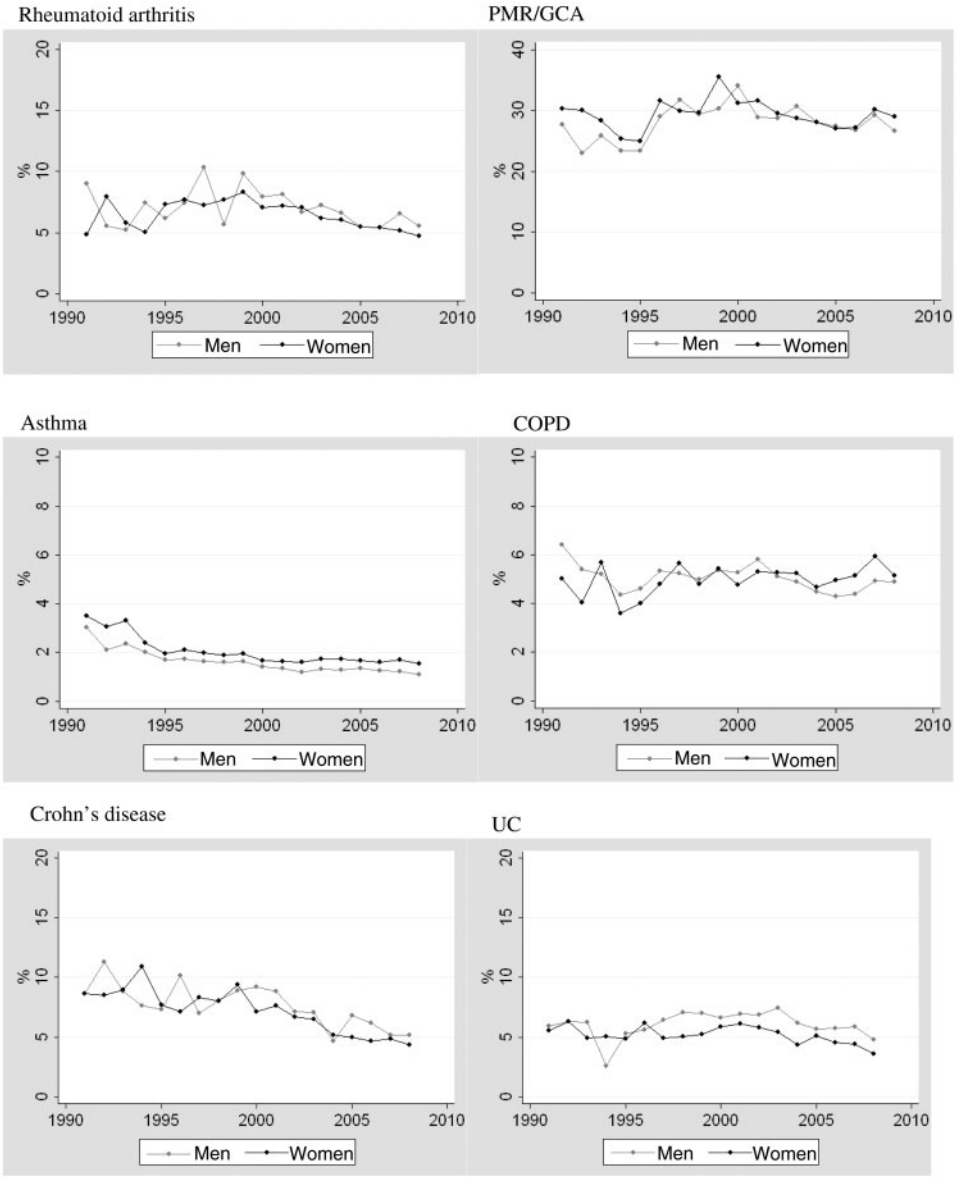
We found that prescribing of long-term GCs is high and increased by nearly 34% between 1989 and 2008. The likelihood of being prescribed long-term systemic GC therapy was related to sex, age and the underlying disease. The increase in the prevalence of use during the 20-year period of our study could be explained by: (i) an increasing duration of long-term prescriptions for some diseases such as RA and PMR/GCA; and (ii) an increase in the prevalence of some common disease frequently requiring long-term therapy with GCs such as asthma or COPD. The proportion of patients starting long-term GC therapy by calendar year did not increase over time for any of the six conditions studied.

Although oral GCs have been used for >60 years, there are limited data on their prescription in the general population. Only one cross-sectional survey published in 1996 has reported data on long-term therapy [3] and another study has reported on total prescriptions of GCs with no specific data on long-term use [19]. Our results on the overall and specifically long-term GC use compare favourably with the data reported in these studies.

We observed very different patterns of use of GC therapy between men and women unlike those previously reported [19]. Women with PMR/GCA were treated for a longer period and those with Crohn's disease or UC for shorter duration. Such disparities between the sexes have been previously reported for PMR/GCA [20, 21], but it is unclear whether this is explained by a different course of the disease or by different patterns of GC tolerance between the sexes.

Our results on the overall prevalence of the six diseases of interest and the increase in prevalence of asthma, COPD, Crohn's disease and UC compare well with other studies conducted on similar populations [22–31].

FIG. 3 Percentage of patients starting long-term GC therapy by calendar year.



Over time, different trends of long-term GC prescriptions were observed for these diseases. Following national clinical recommendations, fewer people with asthma were prescribed long-term GC therapies and people with COPD were treated with shorter therapies [32, 33]. The decrease in long-term GC prescriptions in patients with Crohn's disease may be explained by an increase in the use of immunomodulator and infliximab [34]. The increase in GC prescribing in patients with RA and PMR/GCA was explained by the increase in duration of therapy rather than an increase in the proportion of people treated, which remained stable over time. This may have been favoured by the recent demonstration of the disease-modifying effects (e.g. anti-erosive effects and remission rate) of GCs in RA [35, 36].

In the UK, anti-TNF therapies such as infliximab have been licensed from 1999 for Crohn's disease, 2000 for RA and 2005 for UC. In our population-based cohort, it is unclear whether the availability of these new drugs, which are prescribed in a small proportion of patients [34, 37], has had a large impact on the prescription of GCs in people with these diseases. However, for these diseases, we found that long-term GC prescriptions for incident cases was lower than for both prevalent and incident cases, highlighting a change in physicians' practices over time.

Our study has several strengths, including the use of population-based, unselected population of patients with a wide range of diseases, the inclusion of all adult age groups and the coverage of a 20-year period. However,

there are some limitations, potential inaccuracies in prescription information being the first one. For instance, quite often GCs are prescribed in a higher starting dose and then tapered down. A high daily dosage may be put on the prescription, patients being asked orally to progressively decrease the dosage, depending on their health status. In this case, although, for example, the computer records may indicate that a person was prescribed 40 mg GCs for 2 months, in reality the patient may have used the drug for 4 months in a tapering dose regimen. Although this may have led to an underestimate of the prevalence of long-term GC use, it would not have impacted on the trends over time. Further, it may be suggested that prescriptions written by specialists may not have been recorded by general practitioners. However, within the context of the UK national health system, all therapies even if initiated by specialist must be prescribed in the long term by general practitioners. Lastly, for each GC course, we defined the time on GCs as the time between the first and the last prescription plus the duration of the last prescription. Thus, we assumed that the patients had been taking GCs constantly between these two prescriptions. However, because of adherence issues or because of partial remission of the disease they might have stopped taking GCs during that time. The second potential limitation may be inaccuracies in the validity of diagnostic in the data set. Indeed, although diagnostic information recorded in THIN or other equivalent GP database has been previously validated [5–10], in particular in the field of pulmonary or rheumatological diseases [38, 39], some concerns have been raised about the quality of reporting of the validations [40]. However, the prevalence rates of the six diseases under investigation in this study are consistent with that reported in other populations [22–31], suggesting good validity of the diagnoses on THIN. Thirdly, changes in the data collection system (e.g. introduction of the quality of outcome framework) have occurred within the study period. It is probable that these changes may have impacted on the level of recording of asthma and COPD diagnosis (as these are specific areas of the quality outcomes framework focus). However, the prescription issued through the electronic medical records would not have changed and it has been shown that the minor discrepancies observed between prescription issues on THIN and national dispensing data have remained consistent over time [41].

Although long-term GC therapies are associated with high morbidity, financial cost (mainly due to their adverse events), many patients' concerns and a lower quality of life compared with other treatments [42–46], the overall increasing prevalence of their use over time confirms that they remain a cornerstone for many diseases, in spite of the newly developed efficient alternatives. While prescriptions for certain conditions such as asthma and COPD are decreasing, endorsing the fact that the national recommendations have possibly been appropriately applied, the prevalence of long-term GC use in other diseases such as RA and PMR/GCA is increasing. Further work is needed on the prescribing practices of long-term GCs for these conditions by primary and secondary care practitioners.

Rheumatology key messages

- The prevalence of long-term GC prescriptions increased by nearly 34% between 1989 and 2008.
- Variations observed over time depended on the underlying diseases.
- Physicians' practices regarding long-term GC prescriptions changed over time.

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References

1 Hench PS, Kendall EC, Slocumb CH, Polley HF. The effect of a hormone of the adrenal cortex (17-hydroxy-11-dehydrocorticosterone; compound E) and of pituitary adrenocorticotropic hormone on rheumatoid arthritis. Mayo Clin Proc 1949;24:181–97.

2 Hench PS, Kendall EC, Slocumb CH, Polley HF. Adrenocortical hormone in arthritis: preliminary report. Ann Rheum Dis 1949;8:97–104.

3 Walsh LJ, Wong CA, Pringle M, Tattersfield AE. Use of oral corticosteroids in the community and the prevention of secondary osteoporosis: a cross sectional study. Br Med J 1996;313:344–6.

4 Lis Y, Mann RD. The VAMP research multi-purpose database in the U.K. J Clin Epidemiol 1995;48:431–43.

5 EPIC. THIN data from EPIC: a guide for researchers. London: EPIC, 2007 http://www.epic-uk.org/ (20 September 2010 date last accessed).

6 Bourke A, Dattani H, Robinson M. Feasibility study and methodology to create a quality-evaluated database of primary care data. Inform Prim Care 2004;12:171–7.

7 Lewis JD, Schinnar R, Bilker WB, Wang X, Strom BL. Validation studies of The Health Improvement Network (THIN) database for pharmacoepidemiology research. Pharmacoepidemiol Drug Saf 2007;16:393–401.

8 Ruigómez A, Martín-Merino E, Rodríguez LA. Validation of ischemic cerebrovascular diagnoses in The Health Improvement Network (THIN). Pharmacoepidemiol Drug Saf 2010;19:579–85.

9 Lo Re V 3rd, Haynes K, Forde KA, Localio AR, Schinnar R, Lewis JD. Validity of The Health Improvement Network (THIN) for epidemiologic studies of hepatitis C virus infection. Pharmacoepidemiol Drug Saf 2009;18:807–14.

10 Meal A, Leonardi-Bee J, Smith C, Hubbard R, Bath-Hextall F. Validation of THIN data for non-melanoma skin cancer. Qual Prim Care 2008;16:49–52.

11 Maguire A, Blak BT, Thompson M. The importance of defining periods of complete mortality reporting for research using automated data from primary care. Pharmacoepidemiol Drug Saf 2009;18:76–83.

12 Lewis JD, Bilker WB, Weinstein RB, Strom BL. The relationship between time since registration and measured incidence rates in the General Practice Research Database. Pharmacoepidemiol Drug Saf 2005;14:443–51.

13 British National Formulary. http://bnf.org/bnf/ (20 September 2010, date last accessed).

14 Fardet L, Flahault A, Kettaneh A *et al*. Corticosteroid-induced clinical adverse events: frequency, risk factors and patient's opinion. Br J Dermatol 2007;157:142–8.

15 Chisholm J. The Read clinical classification. Br Med J 1990;300:1092.

16 Bahlas S, Ramos-Remus C, Davis P. Clinical outcome of 149 patients with polymyalgia rheumatica and giant cell arteritis. J Rheumatol 1998;25:99–104.

17 Delecoeuillerie G, Joly P, Cohen de Lara A, Paolaggi JB. Polymyalgia rheumatica and temporal arteritis: a retrospective analysis of prognostic features and different corticosteroid regimens (11 year survey of 210 patients). Ann Rheum Dis 1988;47:733–9.

18 Ayoub WT, Franklin CM, Torretti D. Polymyalgia rheumatica. Duration of therapy and long-term outcome. Am J Med 1985;79:309–15.

19 van Staa TP, Leufkens HG, Abenhaim L, Begaud B, Zhang B, Cooper C. Use of oral corticosteroids in the United Kingdom. Q J Med 2000;93:105–11.

20 Barraclough K, Liddell WG, du Toit J *et al*. Polymyalgia rheumatica in primary care: a cohort study of the diagnostic criteria and outcome. Fam Pract 2008;25:328–33.

21 Cimmino MA, Parodi M, Caporali R, Montecucco C. Is the course of steroid-treated polymyalgia rheumatica more severe in women? Ann N Y Acad Sci 2006;1069:315–21.

22 Simpson CR, Sheikh A. Trends in the epidemiology of asthma in England: a national study of 333,294 patients. J R Soc Med 2010;103:98–106.

23 Upton MN, McConnachie A, McSharry C *et al*. Intergenerational 20 year trends in the prevalence of asthma and hay fever in adults: the Midspan family study surveys of parents and offspring. Br Med J 2008;321:88–92.

24 Soriano JB, Maier WC, Egger P *et al*. Recent trends in physician diagnosed COPD in women and men in the UK. Thorax 2000;55:789–94.

25 Symmons D, Turner G, Webb R *et al*. The prevalence of rheumatoid arthritis in the United Kingdom: new estimates for a new century. Rheumatology 2002;41:793–800.

26 Spector TD, Hart DJ, Powell RJ. Prevalence of rheumatoid arthritis and rheumatoid factor in women: evidence for a secular decline. Ann Rheum Dis 1993;52:254–7.

27 Bernatsky S, Joseph L, Pineau CA *et al*. Polymyalgia rheumatica prevalence in a population-based sample. Arthritis Rheum 2009;61:1264–7.

28 Salvarani C, Gabriel SE, O'Fallon WM, Hunder GG. Epidemiology of polymyalgia rheumatica in Olmsted County, Minnesota, 1970–1991. Arthritis Rheum 1995;38:369–73.

29 Stone MA, Mayberry JF, Baker R. Prevalence and management of inflammatory bowel disease: a cross-sectional study from central England. Eur J Gastroenterol Hepatol 2003;15:1275–80.

30 Armitage E, Drummond HE, Wilson DC, Ghosh S. Increasing incidence of both juvenile-onset Crohn's disease and ulcerative colitis in Scotland. Eur J Gastroenterol Hepatol 2001;13:1439–47.

31 Rubin GP, Hungin AP, Kelly PJ, Ling J. Inflammatory bowel disease: epidemiology and management in an English general practice population. Aliment Pharmacol Ther 2000;14:1553–9.

32 Guidelines on the Management of Asthma. Statement by the British Thoracic Society, the Brit. Paediatric Association, the Research Unit of the Royal College of Physicians of London, the King's Fund Centre, the National Asthma Campaign, the Royal College of General Practitioners, the General Practitioners in Asthma Group, the Brit. Assoc. of Accident and Emergency Medicine, and the Brit. Paediatric Respiratory Group. Thorax 1993;48(2 Suppl):S1–24.

33 Chronic Obstructive Pulmonary Disease (COPD). Clinical Guideline. www.nice.org.uk/article.asp?a=91784 (date last accessed 12 May 2010).

34 Herrinton LJ, Liu L, Fireman B *et al*. Time trends in therapies and outcomes for adult inflammatory bowel disease, Northern California, 1998–2005. Gastroenterology 2009;137:502–11.

35 Graudal N, Jürgens G. Similar effects of disease-modifying antirheumatic drugs, glucocorticoids, and biologic agents on radiographic progression in rheumatoid arthritis: meta-analysis of 70 randomized placebo-controlled or drug-controlled studies, including 112 comparisons. Arthritis Rheum 2010;62:2852–63.

36 Kirwan JR, Bijlsma JW, Boers M, Shea BJ. Effects of glucocorticoids on radiological progression in rheumatoid arthritis. Cochrane Database Syst Rev 2007;(1):CD006356.

37 Grijalva CG, Chung CP, Stein CM, Mitchel EF Jr, Griffin MR. Changing patterns of medication use in patients with rheumatoid arthritis in a Medicaid population. Rheumatology 2008;47:1061–4.

38 Hansell A, Hollowell J, Nichols T, McNiece R, Strachan D. Use of the general practice research database (GPRD) for respiratory epidemiology: a comparison with the 4th morbidity survey in general practice (MSGP4). Thorax 1999;54:413–9.

39 Thomas SL, Edwards CJ, Smeeth L, Cooper C, Hall AJ. How accurate are diagnoses for rheumatoid arthritis and

juvenile idiopathic arthritis in the general practice research database? Arthritis Rheum 2008;59:1314–21.

40 Herrett E, Thomas SL, Schoonen WM, Smeeth L, Hall AJ. Validation and validity of diagnoses in the general practice research database: a systematic review. Br J Clin Pharmacol 2010;69:4–14.

41 Langley TE, Szatkowski L, Gibson J *et al*. Validation of The Health Improvement Network (THIN) primary care database for monitoring prescriptions for smoking cessation medications. Pharmacoepidemiol Drug Saf 2010;19:586–90.

42 Pisu M, James N, Sampsel S, Saag KG. The cost of glucocorticoid-associated adverse events in rheumatoid arthritis. Rheumatology 2005;44:781–8.

43 Hoes JN, Jacobs JW, Verstappen SM, Bijlsma JW, Van der Heijden GJ. Adverse events of low- to medium-dose oral glucocorticoids in inflammatory diseases: a meta-analysis. Ann Rheum Dis 2009;68:1833–8.

44 Morrison E, Crosbie D, Capell HA. Attitude of rheumatoid arthritis patients to treatment with oral corticosteroids. Rheumatology 2003;42:1247–50.

45 Cullen G, Kelly E, Murray FE. Patients' knowledge of adverse reactions to current medications. Br J Clin Pharmacol 2006;62:232–6.

46 Bernklev T, Jahnsen J, Schulz T *et al*. Course of disease, drug treatment and health-related quality of life in patients with inflammatory bowel disease 5 years after initial diagnosis. Eur J Gastroenterol Hepatol 2005;17:1037–45.