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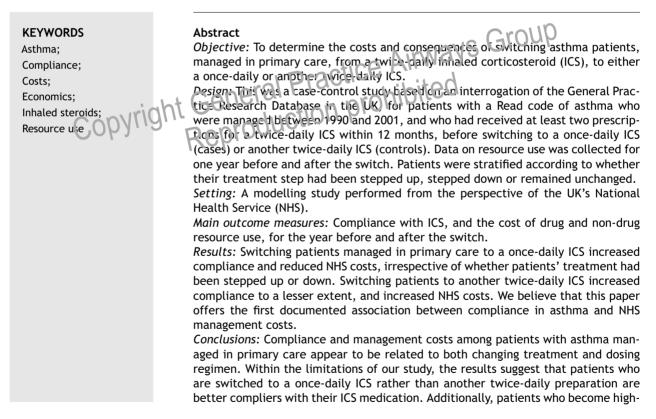
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Switching asthma patients to a once-daily inhaled steroid improves compliance and reduces healthcare costs

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compliers after being switched to a once-daily ICS incur lower management costs than patients who become high-compliers after being switched to another twice-daily ICS. These findings should now be investigated further under more controlled conditions. © 2005 General Practice Airways Group. Published by Elsevier Ltd. All rights reserved.

Introduction

Improving compliance with anti-asthma medication is central to improving clinical and economic outcomes for the 5% of people aged between 20 and 44 years and the 10% of children who suffer from the disease [1]. However, it has been estimated previously that only 40% of asthma patients are compliant with their medication over five weeks; half the patients in one study underused their medication and 10% overused their inhaler [2]. In another study, compliance declined from 51% during the first week of treatment to less than 30% after 10 weeks [3]. Non-compliance does not always lead to disease exacerbation. Nevertheless, enhancing compliance is clearly central to improving clinical and economic outcomes in general practice.

Treatment complexity is considered one of the best predictors of compliance [4]. When introduced in the mid-1970s, patients used ICS treatment three or four times daily. During the 1980s most patients followed a twice-daily regimen [5]. Today, increasing evidence suggests that ICs treatment alle in UResource utilisation ates symptoms and enhances quality of life when given once-daily, especially in patients with mildto-moderate asthma [6]. We have previously reported that compliance improves when patients switch from a twice-daily to a once-daily ICS [7].

These studies are part of a growing and compelling body of evidence suggesting that reducing the number of daily doses of ICS frequently improves symptom control, adherence, quality of life, patient satisfaction and costs, across several disease areas [8]. In an analysis of 76 studies that used electronic monitoring, compliance was 79% with once-daily dosing regimens, compared to 65% and 51% with three- and four-times daily dosing, respectively [9].

Asthma accounts for between 1-2% of total healthcare expenditure across industrialised countries [10]. Exacerbations of the illness associated with non-compliance can result in hospital admissions and bed occupancy [11,12]. Despite this heavy toll, to the best of our knowledge no previous study has documented an association between improved compliance in asthma, and costs of management, from the perspective of the UK's NHS.

Against this background, we compared the costs and consequences of switching asthma patients managed in primary care from a twice-daily inhaled corticosteroid (ICS) to either a once-daily or another twice-daily ICS from the perspective of the UK's NHS. Patients were stratified according to whether their GP or nurse moved their drug treatment step up or down, or whether it remained unchanged after the switch.

Methods

Study design

This was a retrospective, case-control design study of asthma patients (n = 222) who were managed in primary care between 1990 and 2001, who had received at least two prescriptions for a twice-daily ICS within the 12 months before switching to a oncedaily ICD (cases; n = 104) or another twice-daily ICS Ccontrols; n = 118)

The study used compliance rates and quantitative healthcare resource-utilisation estimates obtained from the General Practice Research Database (GPRD), which contains more than 30 million patient years of data [13]. GPRD is the world's largest computerised database of anonymised longitudinal clinical records from over 300 general practices. All relevant Read and OXMIS codes and products were used for the search, and included, but were not limited to, H33xxx, 493xxx, 663xxx and 90Jxxx for asthma attacks and monitoring, and 879xxx for assessing patients' treatment step.

Patients' use of the following resources was estimated from the database: drug prescriptions; GP surgery visits; GP-initiated tests; GP domiciliary visits; outpatient visits; and hospital admissions. Resource use was collected for one year before and after the switch. Systematic assumptions were made with respect to poor coding of hospital utilisation pertaining to asthma treatment. Events and prescriptions recorded around the time of hospital admission were used as a marker for hospital resource use.

Cases and controls were matched according to: age at switch; gender; location of general practice; compliance level; treatment step; co-morbidities (i.e. the incidence of bronchitis, chronic obstructive pulmonary disease (COPD) and respiratory infections); and duration of asthma medication.

Data analysis

Patients were stratified according to whether their drug regimen had been stepped up, stepped down, or remained unchanged after the switch. Treatment step was assessed by analysing a patient's asthmarelated medication in the year before and after the switch, based on dose, regimen, number of drugs and corresponding drug class.

Differences in drug and non-drug resource use between cases and controls were tested for statistical significance using a 'goodness-to-fit' Chi-square test, whereby the mean annual amount of resource use, and number of scrips, were weighted according to the number of patients in each group. Differences in patients' age were tested using a Mann Whitney U-test.

Annual resource use and prescribed medication in the year before and after the switch was costed at 2001/02 prices using unit costs obtained from published sources [14–16], from the perspective of General Practic the UK's National Health Service (NHS).

Compliance

ICS compliance was assessed for the year before and after switching by comparing the theoretical and actual duration of the prescription. This was achieved by using the time between prescription issues for inhaled corticosteroids as a proxy for compliance, taking into account prescription size and dosage instruction as previously described [7]. Patients were stratified into three bands:

- High: ICS compliance between 71% and 100%.
- Medium: ICS compliance between 31% and 70%.
- Low: ICS compliance between 0% and 30%.

Ethics approval

Approval for this study was obtained from the GPRD's Scientific and Ethical Advisory Group.

Results

The cases and controls were well matched as shown in Table 1, with no significant differences between the two groups in respect of matching criteria. It is noteworthy that 29% of cases switched to a differ-

| Table 1 Patient demographics. | | | | | |
|--|-----------------------------------|-----------------------------------|--|--|--|
| | Cases | Controls | | | |
| Total number of patients | 104 | 118 | | | |
| Male (%) | 50 | 47 | | | |
| Female (%) | 50 | 53 | | | |
| Age (years) | $\textbf{30.4} \pm \textbf{25.7}$ | $\textbf{27.2} \pm \textbf{26.6}$ | | | |
| Time on treatment before switch (months) | 46 ± 25.2 | 39 ± 27.6 | | | |
| Proportion switching to the same/different inhaled steroid | | | | | |
| Same (%) | 71 | 0 | | | |
| Different (%) Incidence of co-morbidities (year before switch) | 29 | 100 | | | |
| Bronchitis | 7.7% | 8.5% | | | |
| COPD | 2.9% | 1.7% | | | |
| Respiratory infection Incidence of co-morbidities (year after switch) | 31.7% | 35.6% | | | |
| Bronchitis | 1.0% | 5.1% | | | |
| COPD | 6.8% | 1.7% | | | |
| Respiratory injection | 28.8% | 21.2% | | | |

er tICS while the other 71% of cases switched from a twice-daily to a once-daily formulation of the same drug.

Respiratory infections were the primary comorbidity for both groups. 32% of cases and 36% of controls experienced an infection before the switch, and after the switch this decreased to 29% and 22% respectively.

Compliance

Compliance improved significantly among cases whose drug treatment was stepped up in the year after the switch, with a 67% increase in the proportion of high-complying patients. Similarly, there was a 55% increase in the proportion of highcompliant controls in the year after the switch (see Table 2). However, there were no significant differences in compliance between cases and controls in the year after the switch.

There were no significant differences in compliance among cases whose drug treatment remained unchanged in the year after the switch. However, compliance among controls improved significantly, with a 55% increase in the proportion of mediumcompliers and a 36% decrease in the proportion of low-compliers in the year after the switch. More-

| | Percentage of patients in a compliance band in the year before the switch | | Percentage of patients in a compliance band in the year after the switch | | |
|----------------|---|--------------|--|--------------|--|
| | Cases (%) | Controls (%) | Cases (%) | Controls (%) | |
| Treatment step | ped up | | | | |
| High | 37.1* | 37.7** | 62.9* | 58.5** | |
| Medium | 45.7 | 45.3 | 22.9 | 32.1 | |
| Low | 17.1 | 17.0 | 14.3 | 9.4 | |
| Treatment unch | anged | | | | |
| High | 63.3 | 61.1 | 70.0*** | 55.6*** | |
| Medium | 20.0 | 22.2**** | 23.3 | 38.9**** | |
| Low | 16.7 | 16.7**** | 6.7 | 5.6**** | |
| Treatment step | ped down | | | | |
| High | 61.5 | 61.7 | 69.2 | 66.0 | |
| Medium | 25.6 | 25.5 | 20.5 | 25.5 | |
| Low | 12.8 | 12.8 | 10.3 | 8.5 | |

 Table 2
 Compliance distribution stratified by treatment step

p < 0.001.

*** *p* < 0.05. **** p < 0.005.

******p* < 0.005.

over, there were significantly more high-compliers among cases than controls in the year after the resource costs and at 11% increase in drug costs. Genera switch (Table 2).

There were no significant differences among patients whose drug treatment was stepped low, in the year after the switch.

Healthcare resource use and corresponding costs

Patients whose drug treatment was stepped up

Resource use among patients whose drug treatment was stepped up is shown in Table 3. There were minimal differences between cases and controls before and after the switch in any of the compliance bands. Most notably, non-drug healthcare resource use did not differ between cases and controls, in corresponding compliance bands, in the years before or after the switch. However, highcompliant cases (p < 0.001) and controls (p < 0.01) made more GP visits than patients in the mediumand low-compliance bands in the year before the switch. Additionally, after the switch, cases in the high-compliance band received fewer (p < 0.005), and low-compliers received more (p < 0.01), prescriptions for inhaled steroids than controls. All other prescribing patterns were comparable (Fig. 1).

The total cost of managing high-compliant cases decreased by 14% in the year after switching (from

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£690 to £596), reflecting a 31% decline in non-drug The total cost of managing controls increased by 67% after switching (from £480 to £801), due to increases of 161% and 14% in medication and in nondrug resource costs, respectively (Fig. 2).

The total annual cost of managing mediumcompliant cases and controls increased by 30% (from £382 to £495) and 14% (from £301 to £342) respectively, after the switch. This was due to increases in drug costs of 85% (cases) and 27% (controls), as well as higher costs of non-drug resource use by 8% (cases) and 1% (controls).

The total annual cost of managing low-compliers increased by 170% (from ± 154 to ± 415) among cases and decreased by 30% (from £175 to £125) among controls after the switch. This was due to a 179% and 159% increase in drug and non-drug resource costs, respectively, among cases in the year after the switch, compared to a 24% increase in drug costs and a 47% decrease in non-drug resource costs among controls.

Patients whose drug treatment step remained unchanged

Resource use among patients whose drug treatment remained unchanged is shown in Table 3. There were minimal differences between cases and controls before and after the switch in any of the compliance bands. Most notably, non-drug health-

^{**} *p* < 0.05.

| | Resource use per patient | | | | | | | | | |
|--------------------------|--------------------------|------------------|----------|------------------------|-------------------|---------|---------------------|-----------------|-------|--|
| | High compliance band | | | Medium compliance band | | | Low compliance band | | | |
| | Case | Control | р | Case | Control | р | Case | Control | р | |
| Patients whose drug trea | | | l up | | | | | | | |
| Before switch | (<i>n</i> = 13) | (n = 20) | | (<i>n</i> = 16) | (n = 24) | | (n=6) | (n = 9) | | |
| GP visits | 14.69 | 10.65 | ns | 7.56 | 8.00 | ns | 4.17 | 6.22 | ns | |
| Hospital admissions | 0.08 | 0.00 | n/a | 0.00 | 0.00 | n/a | 0.00 | 0.00 | n/a | |
| Outpatient visits | 0.85 | 0.50 | ns | 1.13 | 0.75 | ns | 1.33 | 1.22 | ns | |
| GP-initiated tests | 0.00 | 0.00 | n/a | 0.13 | 0.46 | n/a | 0.00 | 0.33 | n/a | |
| GP domiciliary visits | 0.08 | 0.00 | n/a | 0.00 | 0.08 | n/a | 0.00 | 0.22 | n/a | |
| After switch | (n = 22) | (<i>n</i> = 31) | | (<i>n</i> = 8) | (<i>n</i> = 17) | | (<i>n</i> = 5) | (<i>n</i> = 5) | | |
| GP visits | 10.95 | 13.81 | ns | 8.75 [′] | 8.35 ⁽ | ns | 10.80 | 3.80 | ns | |
| Hospital admissions | 0.05 | 0.03 | n/a | 0.00 | 0.00 | n/a | 0.00 | 0.00 | n/a | |
| Outpatient visits | 1.18 | 1.52 | ns | 0.25 | 0.41 | ns | 0.40 | 0.80 | ns | |
| GP-initiated tests | 0.18 | 0.29 | n/a | 0.13 | 0.41 | n/a | 0.00 | 0.00 | n/a | |
| GP domiciliary visits | 0.00 | 0.00 | n/a | 0.00 | 0.00 | n/a | 0.00 | 0.00 | n/a | |
| Patients whose treatme | nt step re | mained un | changed | | | | | | | |
| Before switch | (<i>n</i> = 19) | (<i>n</i> = 11) | en angea | (<i>n</i> = 6) | (n = 4) | | (<i>n</i> = 5) | (<i>n</i> = 3) | | |
| GP visits | 8.68 | 10.82 | ns | 7.50 | 12.50 | ns | 4.60 | 14.67 | ns | |
| Hospital admissions | 0.05 | 0.05 | n/a | 0.00 | 0.00 | n/a | 0.20 | 0.00 | n/a | |
| Outpatient visits | 0.89 | 0.91 | ns | 0.17 | 0.00 | ns | 1.60 | 0.11 | ns | |
| GP-initiated tests | 0.21 | 0.09 | n/a | 0.00 | 2.00 | n/a | 0.00 | 0.67 | n/a | |
| GP domiciliary visits | 0.00 | 0.00 | n/a | 0.00 | 0.00 | n/aavis | 0.00 | 0.33 | n/a | |
| After switch | (<i>n</i> = 21) | (<i>n</i> = 10) | | (n = 7) | e=All | Ways | (n = 2) | (<i>n</i> = 1) | | |
| GP visits | 8.48 | 12.40 | ns P | (ä.Glu | 13.29 | ins d | 4.00 | 1.00 | ns | |
| Hospital admissions | 0,05 | 20000 | r.7a | 0.00 | 6.29 | 11EO | 0.00 | 0.00 | n/a | |
| Outpatient visits | 0.03 | J.40 | ns ti | O PAN | 1.57 | ns | 0.00 | 0.00 | ns | |
| GP-initiated tests | 0.00 | 0.40 | n/a Cl | 0.43 | 1.57 | n/a | 0.00 | 0.00 | n/a | |
| GP domicitiary visits | 0.00 F | | n/a | 0.00 | 0.00 | n/a | 0.00 | 0.00 | n/a | |
| Patients whose drug trea | 1 | | l down | | | | | | | |
| Before switch | (n = 24) | (n = 29) | | (<i>n</i> = 10) | (<i>n</i> = 12) | | (<i>n</i> = 5) | (<i>n</i> = 6) | | |
| GP visits | 13.25 | 12.28 | ns | 6.20 | 11.92 | ns | 5.20 | 10.33 | ns | |
| Hospital admissions | 0.04 | 0.00 | n/a | 0.00 | 0.00 | n/a | 0.00 | 0.00 | n/a | |
| Outpatient visits | 1.13 | 0.55 | ns | 0.10 | 0.75 | <0.01 | 0.20 | 1.17 | ns | |
| GP-initiated tests | 0.17 | 0.07 | n/a | 0.10 | 1.00 | n/a | 0.00 | 1.83 | n/a | |
| GP domiciliary visits | 0.04 | 0.07 | n/a | 0.00 | 0.00 | n/a | 0.00 | 0.67 | n/a | |
| After switch | (<i>n</i> = 27) | (<i>n</i> = 31) | | (<i>n</i> = 8) | (<i>n</i> = 12) | | (n = 4) | (n=4) | | |
| GP visits | 10.44 | 12.94 | ns | 7.00 | 7.92 | ns | 3.00 | 3.50 | ns | |
| Hospital admissions | 0.07 | 0.00 | n/a | 0.00 | 0.25 | n/a | 0.00 | 0.00 | n/a | |
| Outpatient visits | 0.93 | 0.42 | ns | 0.63 | 0.92 | ns | 0.00 | 1.00 | ns | |
| GP-initiated tests | 0.75 | 0.42 | n/a | 0.03 | 0.00 | n/a | 0.00 | 0.25 | n/a | |
| GP domiciliary visits | 0.00 | 0.13 | n/a | 0.00 | 0.00 | n/a | 0.00 | 0.23 | n/a | |
| Gr donnentiary visits | 0.00 | 0.19 | n/α | 0.00 | 0.00 | πα | 0.00 | 0.00 | 11/ 0 | |

 Table 3
 Mean resource use, stratified by compliance and treatment step.

care resource use did not differ between cases and controls in corresponding compliance bands in the years before or after the switch, and there was no significant change within the groups as a result of the switch. However, after the switch, high-compliant cases received fewer prescriptions for oral steroids (p < 0.05) and xanthines (p < 0.05) than controls, although use of the former declined among controls (p < 0.05). All other prescribing patterns were comparable (Fig. 3).

The total cost of managing high-compliant cases decreased by 6% in the year after switching (from ± 563 to ± 528), due to decreases of 13% and 2% in drug and non-drug resource costs, respectively. However, the total cost of managing controls increased by 40% after switching (from ± 473 to ± 654), due to a 55% increase in medication costs and a 27% increase in non-drug resource costs (Fig. 4).

Furthermore, the total cost of managing medium-compliant cases decreased by 2% after the

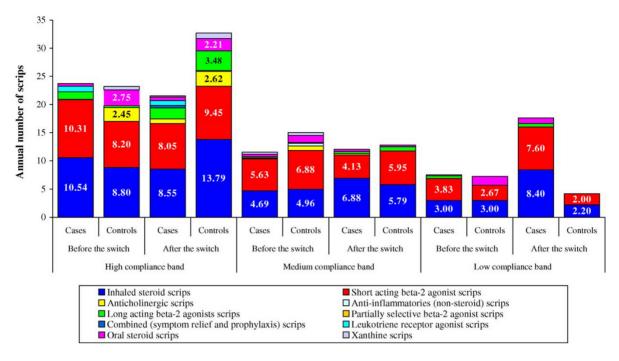


Figure 1 Annual number of prescriptions for patients whose drug treatment was stepped up.

switch (from ± 521 to ± 511). Non-drug costs declined by 49% but drug costs rose by 263%. The cost of managing medium-compliant controls increased by 31% after the switch from ± 472 to ± 618) due to an 8% decrease in drug costs and a 64% increase in non-crug costs. The cost of managing low-compliant cases increased by 74% in the

year after the switch (from ± 262 to ± 457), due to a 63% decrease in non-drug resource costs and a 449% increase in arug costs. This compared to an 88% decrease in the cost of managing low-compliant controls (from ± 343 to ± 41) due to decreases of 54% and 94% in drug and non-drug costs, respectively.

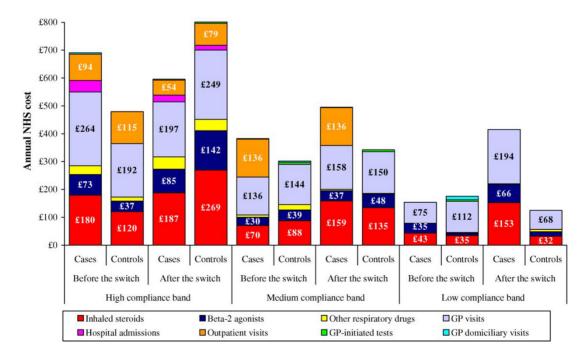


Figure 2 Mean NHS cost of resource use for patients whose drug treatment was stepped up.

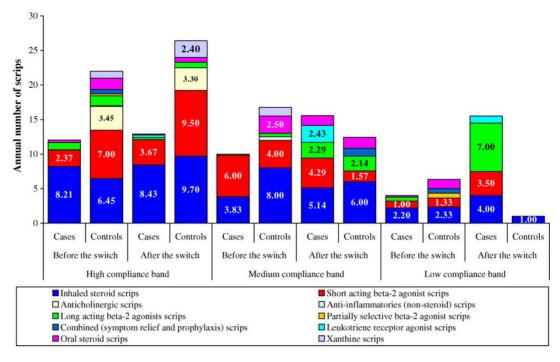


Figure 3 Annual number of prescriptions for patients whose drug treatment step remained unchanged.

Patients whose drug treatment was stepped down

Resource use among patients whose drug treatment of was stepped down is shown in Table 3. There were minimal differences between cases and controls before and after the switch in any of the compliance

bands. Most notably, non-drug healthcare resource use did not differ between cases and controls in corresponding compliance bands in the years before or after the switch (except for the number of outpatient visits among medium-compliers in the year before the switch), and there was no sig-

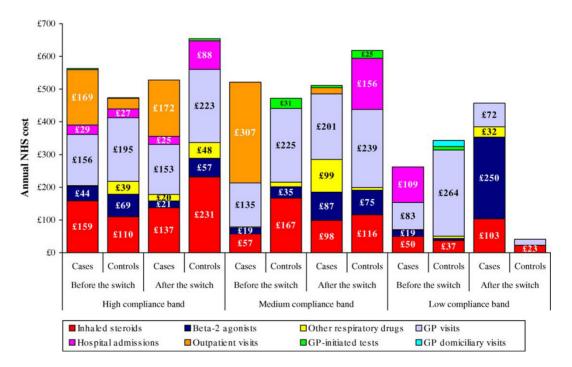


Figure 4 Mean NHS cost of resource use for patients whose drug treatment step was unchanged.

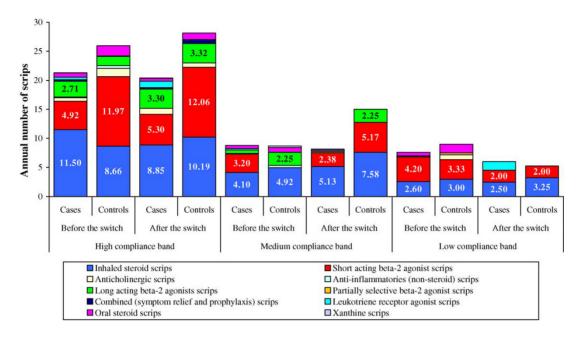


Figure 5 Annual number of prescriptions for patients whose drug treatment was stepped down.

nificant change within the groups as a result of the switch. However, high-compliant cases received fewer (p < 0.01) prescriptions for short-acting beta-2 agonists in both years compared to controls. High-compliant cases also received more (p < 0, 0)leukotriene prescriptions than controls in the year after the switch Medium-compliant cases received fewer (p < 0.05) inhaled steroid prescriptions during the year after the switch than controls. All other prescribing patterns were comparable (Fig. 5).

The total cost of managing high-compliant cases decreased by 23% in the year after switching (from \pm 774 to \pm 597), due to a reduction of 17% and 27% in drug and non-drug resource costs, respectively. The total cost of managing controls increased by 41% after the switch (from \pounds 509 to \pounds 717), due to increases of 38% and 44% in drug and non-drug resource costs (Fig. 6).

The total annual cost of managing mediumcompliant cases and controls increased by 31% (from £292 to £384) and 19% (from £423 to £479) respectively, after the switch. This was due to increases in drug costs of 10% (cases) and 13% (controls) and non-drug resource use costs of 41% and 23%, respectively. Furthermore, the total annual cost of managing low-compliant cases increased by 24% after the switch (from ± 159 to ± 197), due to a 119% increase in drug costs and a 42% decrease in non-drug resource costs. The annual cost of managing comparable controls decreased by 52% (from ± 288 to ± 139), due to a 73% decrease in non-drug resource costs and a 102% increase in drug costs (Fig. 6).

Discussion

Group The costs ci healthcare have assumed increasing innertance in recent years, and this has been reflected in the demod for studies that are cognisant of the likely economic impact of an intervention, as well as its potential clinical benefits. By stratifying patients according to their treatment step, our analysis found that proportionally more patients become high-compliers for less NHS cost when their treatment is stepped up or down, by switching to a once-daily inhaled steroid rather than another twice-daily preparation.

We previously reported that compliance was significantly improved when patients switch from taking a twice-daily to a once-daily inhaled steroid [7]. Additionally, once-daily inhaled steroids have been shown to improve compliance due to the easy, burden-free dosing regimen [17]. Patients have solely to decide at what point during the day they should administer their medication. Research suggests afternoons or evenings to be most effective [5]. Apart from these studies, our literature review found very few other studies assessing the economic impact of switching from a twice-daily to a once-daily inhaled steroid.

Patients whose drug treatment was stepped up

In this study, compliance was found to be comparable between cases and controls whose treatment

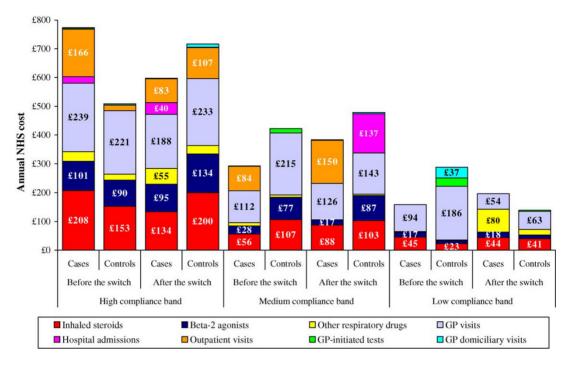


Figure 6 Mean NHS cost of resource use for patients whose drug treatment was stepped up.

was stepped up in the year after the switch. Moving up a step may underscore to a patient that their asthma was poorly controlled. The number of HCS prescriptions decreased for high-complian cases in the year after the switch, leading in a significant difference (see Fig. 1) between the number of ICS prescriptions for cases and controls in the high-compliance band. Evidence suggests that increasing medication improves patients' symptoms and quality of life, and that poor inhaler technique resulting in a lower respirable dose of ICS can be managed efficiently by stepping patients up [4]. Hence, both could enhance compliance. The reduction in ICS prescriptions for high-compliant cases could suggest that stepping asthma patients up in their treatment has improved their symptoms and quality of life.

The study further illustrates that when treatment is stepped up, the cost of managing highcompliant cases after being switched to a oncedaily ICS is less than that of managing highcompliant controls after they have been switched to another twice-daily ICS. Cases in the highcompliance band made fewer GP visits and received less ICS prescriptions in the year after the switch, resulting in a 14% decrease in the cost of managing these patients. However, comparable controls made more GP visits and received more ICS prescriptions, thus increasing management costs by 67%. A reduction in costs associated with simpler dosing regimens has been reported in other studies [8].

Patients whose drug treatment step remained unchanged

Proportionally more cases whose treatment step remained unchanged in the year after the switch became high-compliers compared to controls. However, proportionally more controls became medium-compliers in the year after the switch. These changes in compliance were associated with a decrease in the cost of managing high-compliant cases, and an increase in the costs of managing high- and medium-compliant controls. This suggests that compliance improves if treatment regimens are simplified, a finding consistent with several other studies [6,9,18,19]. Patients continuing with a twice-daily dosing regimen may have less motivation and willingness to comply with treatment than those following a once-daily regimen [12].

Patients whose drug treatment was stepped down

Compliance among cases and controls was found to be comparable in the year after the switch for those whose treatment was stepped down. Highcompliant cases received fewer ICS prescriptions in the year after the switch, and fewer than their matched controls. They also received fewer prescriptions for short-acting beta-2 agonists in the year after the switch, but more prescriptions for leukotrienes. Furthermore, these changes in prescription quantities for the latter two preparations were significantly different to the prescription changes for high-compliant controls (see Fig. 5). Additionally, high-compliant cases made fewer GP visits, but more outpatient visits, in the year after the switch compared to high-compliant controls whose treatment was stepped down.

The differences between high-compliant cases and controls when treatment is stepped down showed in the costs of managing these patients in the year after the switch. Cases in the highcompliance band incurred a decrease in management costs (23%), as compared to high-compliant controls whose management costs increased by 31%. This resulted in the reduced costs of managing high-compliant cases after switching to a oncedaily ICS, as compared to the cost of managing highcompliant controls after they had been switched to another twice-daily ICS.

These findings add to existing evidence suggesting that the aim of asthma management is to increase and maintain a high level of compliance, in order to achieve maximum asthma control with the lowest possible dose of ICS.

Study limitations

This study employed a case control design in order to make comparisons between switching patients from a twice-daily inhaled stervid to a once-daily regimen or to another twice-daily inhaled steroid, in terms of resource use and compliance with ICS. This design resulted in small numbers of patients eligible for analysis. Nevertheless, we believe this paper offers the first documented association between improved compliance in asthma and NHS management costs. Notwithstanding this, our study is subject to a number of limitations.

This was a retrospective, observational study and GPs may have had a multiplicity of reasons for changing treatment. Patients were not randomised to treatment, and patients may have had numerous reasons for altered behaviour which may relate only marginally to altered treatment. The study relies on surrogate markers of compliance, rather than direct measures. Moreover, the analysis does not disentangle other factors employed by physicians in general practice that might influence compliance, such as clinical feedback [3] or motivational models [20]. Neither does the study consider the impact of different devices available for delivering the ICS dose. The analysis was unable to consider under- or over recording of asthma-related resource use, and systematic assumptions were made with respect to asthma resource utilisation in the presence of poor coding and the absence of clinical expertise. Additionally, the potential for some patients in the data set to have COPD, misdiagnosed as asthma, cannot be eliminated. GPs and nurses are still less confident about diagnosing COPD as compared to asthma [21]; hence, informed decisions with regard to misdiagnosis could not be made.

Cases and controls were matched according to age, gender, location of general practice, compliance level, treatment step, co-morbidities, and duration of asthma medication, at the time of switching. However, patients were not matched according to baseline use of healthcare resources, as this potentially could have reduced the already small numbers. Nevertheless, our analysis found that there were no significant differences in resource use between cases and controls in the year before the switch, except for outpatient visits among mediumcompliers whose treatment was stepped down after the switch.

Despite these limitations, the data contained within the GPRD, whilst retrospective, reflect clinical practice on a large number of patients without the selection biases associated with inclusion criteria that may arise in intervention studies [13]. Hence, this study represents patients' management innaturalistic general practice, rather than an artificial clinical tria in which patients may alter their compliance by being aware that they could be assessed. As a result, we believe our findings support the notion that compliance and management costs are related to both changing treatment and dosing regimen. These findings should now be investigated further under more controlled conditions.

Conclusion

Compliance and management costs among patients with asthma managed in primary care appear to be related to both changing treatment and dosing regimen. Within the limitations of our study, the results suggest that patients who are switched to a oncedaily ICS rather than another twice-daily preparation are better compliers with their ICS medication. Additionally, patients who become high-compliers after being switched to a once-daily ICS incur lower management costs than patients who become highcompliers after being switched to another twicedaily ICS. We hope that our findings can help reduce the clinical and economic toll arising from poorly controlled, poorly-compliant asthma patients.

Conflict of interest statement

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