Impact of pharmaceutical representative visits on GPs’ drug preferences

Jens Søndergaarda,b, Kirstin Vacha, Jakob Kragstrupa and Morten Andersen a


Background. Pharmaceutical representative visits are believed to have substantial impact, but the effects on prescribing patterns have not been systematically evaluated.

Objective. This study investigates how pharmaceutical sales representative visits influenced physicians’ company-specific drug preferences and prevalence of steroid prescribing.

Methods. Observational cohort study in Funen County, Denmark, including 165 general practices visited 832 times by pharmaceutical representatives and 54 080 patients treated with asthma drugs. Visits were conducted from 2001 to 2003. Our main outcome measures were (i) company-specific drug preferences measured as the proportion of dispensings of the promoted drug among all dispensings of fixed combinations of inhaled corticosteroid and long-acting β2-agonists and (ii) the proportion of patients receiving repeated β2-agonist dispensings who were treated with inhaled steroids.

Results. The first visit had a statistically significant effect on the GPs’ drug preference in favour of the marketed drug [odds ratio (OR), 2.39; 95% confidence interval (CI), 1.72–3.32]. The effect on drug preference increased further after the second visit (OR, 1.51; 95% CI, 1.19–1.93), while there was no significant change after the third visit (OR, 1.06; 95% CI, 0.94–1.20). Pharmaceutical sales representative visits did not influence the overall treatment pattern with inhaled steroids (OR, 1.01; 95% CI, 0.97–1.06).

Conclusions. Pharmaceutical sales representative visits markedly increased the market share of the promoted drug, but only the two first visits had significant impact. Visits had no significant impact on GPs’ overall prescribing of inhaled steroids.

Keywords. Prescribing, epidemiology, family medicine, practice management.

Introduction

The frequent interaction between GPs and pharmaceutical companies has been a matter of debate in numerous publications.1–5 This interaction extends from companies’ financial support for research and medical education to their provision of up-to-date treatment details and educational material targeted at patients and doctors. In such interaction, pharmaceutical sales representatives constitute one of the most expensive and extensively used resources for dissemination of information to GPs.

Pharmaceutical sales representatives often visit GPs in their clinic. Many GPs have a positive attitude towards their interactions with drug companies6 and pharmaceutical representatives’ promotional visits are seen as an efficient source of drug information that may be difficult to obtain otherwise, e.g. information about new treatment principles. It has been claimed that such contacts can lead to irrational prescribing, but there may also be beneficial effects from the interaction7–9 and research so far has not focused on whether the promotional visits can improve the visited physicians’ practice patterns. Inhaled steroids are recommended for the treatment of asthma and COPD and it is well known that contrary to the recommendations, many patients are not being treated with inhaled steroids.10–12 Hence, when pharmaceutical companies promote new inhaled
steroids, their activities may have a positive impact on the physicians’ inclination to prescribe these medications in general and thus to increase the proportion of patients treated with inhaled steroids. It appears that educational outreach visiting can often change behaviour.\textsuperscript{13–15} One study has even attempted to use an industry-inspired approach to influence prescribing practice.\textsuperscript{16} However, the effects of pharmaceutical representative visits on physicians’ treatment patterns have not been evaluated in a large-scale cohort study using proprietary data from a drug company.

The present study investigated the effects of pharmaceutical sales representatives’ promotional visits in primary care. Our objective was to analyse how the promotional visits affected treatment patterns including preferences for the promoted drug and the prevalence of treatment with inhaled steroids.

Methods

We performed a retrospective cohort study in Funen County, Denmark, including 165 practices with 398,909 registered patients. We used information from the pharmaceutical company AstraZeneca’s marketing database and health care databases.

The pharmaceutical representatives’ promotional visits were conducted during 27 months between 2 April 2001 and 2 July 2003 in conformity with the company’s normal marketing approach. The visits promoted prescribing of Symbicort Turbuhaler (in some countries known as Turbuhaler), a fixed combination of inhaled corticosteroid and long-acting \( \beta_2 \)-agonist (budesonide and formoterol). The present observational study was planned after July 2003.

Health care databases

The Danish health care system is a tax-funded state system with universal, free and equal access to health care services. The regional health administration is responsible for the provision of health care services and for drug reimbursement. Approximately 97\% of the population is registered with a general practice.

Data on practices and patient demographics were retrieved from the health administration and linked to the marketing data using the practice registration number. GPs in group practices share the same registration number. After the visits had been conducted, but before the data analyses took place, all the GPs were informed about our study and offered to be excluded from analyses, which two wished to be. Among the remaining 191 practices in the county, 16 were excluded due to incomplete follow-up and 10 were excluded because they were conducting a clinical trial on Symbicort. In the remaining 165 practices (273 GPs), 101 were solo practices that had a median of 1513 patients (range, 472–2498 patients) and 64 were group practices (two to seven GPs) who had a median of 3361 patients (range, 1492–9251 patients).

The Odense Pharmacoepidemiological Database maintained by the University of Southern Denmark contains information on all reimbursed drugs sold by pharmacies in the County of Funen.\textsuperscript{17,18} For each drug dispensing, the following information is recorded: patient identity including sex and date of birth, date of drug purchase, number of packages purchased, brand name, strength, form, Anatomical Therapeutic Chemical classification code,\textsuperscript{19} volume in defined daily doses and the practice registration number of the prescriber. Indication for treatment and dosage instructions were not recorded. Asthma drugs were all reimbursed in a general scheme covering all patients.

The pharmaceutical representatives had reported information to AstraZeneca’s database on every promotional outreach visit. From the database, we retrieved information on date of each visit and identity of the visited GP. During the study period, 141 practices received a total of 832 representative visits. The median time from marketing of the promoted drug to the first visit was 59 days (range, 0–708 days, interquartile range, 31–136 days). The practices visited received a median of five visits (maximum 19, interquartile range, 3–8).

Table 1 reports practice characteristics, number of registered patients and number of users of asthma drugs included in the study. The study was approved by the Danish Data Protection Agency.

Outcome measures

To assess the effects of the pharmaceutical sales representatives’ visits, dispensings of drugs after each visit were compared with dispensings before the visit.

The impact on the GPs’ company-specific drug preferences was evaluated using the proportion of

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Included practices and patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of practices</td>
<td>165</td>
</tr>
<tr>
<td>No. of GPs</td>
<td>273</td>
</tr>
<tr>
<td>Solo practices</td>
<td>101</td>
</tr>
<tr>
<td>Mean no. of GPs per group practice (SD)</td>
<td>2.7 (1.1)</td>
</tr>
<tr>
<td>Mean no. of registered patients per practice (SD)</td>
<td>2417 (1574)</td>
</tr>
<tr>
<td>Total no. of registered patients\textsuperscript{a}</td>
<td>398,909</td>
</tr>
<tr>
<td>Use of any asthma drug</td>
<td></td>
</tr>
<tr>
<td>No. of patients</td>
<td>54,080</td>
</tr>
<tr>
<td>No. of dispensings</td>
<td>491,511</td>
</tr>
<tr>
<td>Use of fixed combination of inhaled long-acting ( \beta_2 )-agonist and corticosteroid</td>
<td></td>
</tr>
<tr>
<td>No. of patients</td>
<td>5188</td>
</tr>
<tr>
<td>No. of dispensings</td>
<td>34,108</td>
</tr>
<tr>
<td>Repeated use of inhaled ( \beta_2 )-agonist\textsuperscript{b}</td>
<td></td>
</tr>
<tr>
<td>No. of patients</td>
<td>22,514</td>
</tr>
<tr>
<td>No. of dispensings</td>
<td>297,489</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Mean for observation period.

\textsuperscript{b} Dispensing of an inhaled \( \beta_2 \)-agonist (including fixed combinations with anticholinergics or corticosteroids) during the observation period and at least one other time during the preceding 365 days.
Symbicort dispensings among all dispensings of fixed-combination inhaled corticosteroid and long-acting β₂-agonist drugs.

International recommendations for asthma treatment emphasize the relevance of preventive treatment with inhaled corticosteroids, even for mild asthma. Furthermore, inhaled steroids are indicated for many COPD patients. We assume that the promotion of fixed combinations with inhaled steroids could lead to an overall increase in the proportion of users of inhaled steroids. We wanted an accurate measure of the prevalence of inhaled steroid prescribing that could capture changes in patient treatment status at each new prescription. We used as denominator all patients receiving repeated inhaled β₂-agonist dispensings, i.e. dispensings to persons with at least one other dispensing during the preceding 365 days. Fixed combinations of inhaled β₂-agonists with anticholinergics or corticosteroids were included. The numerator was the number of patients treated with inhaled steroids, i.e. patients who had purchased inhaled steroids including fixed combinations at any time during the preceding 365 days.

Data analysis
We analysed dispensing of the promoted drug between the two alternatives and steroid use preceding inhaled β₂-agonist dispensings as binary outcomes by means of logistic regression. The reference category was dispensing before the first representative visit. We used random effects regression models that took into account that patients were nested within practices and that the same patient could occur more than once in the analysis. Analyses were done in a stepwise manner, evaluating each model refinement by likelihood ratio tests ($P < 0.05$) and checking for collinearity. In the first, simple model we compared dispensing before the first visit with dispensing after this event. We adjusted for effects of calendar time. We added interaction variables reflecting possible changes in the effect of the first visit with time, both the time from marketing until the first visit and the time since the first visit as continuous variables. We subsequently added a variable for the second visit and the interaction between this and the time between the first and second visit. We proceeded adding variables for the following visits in a similar way. We controlled for calendar time effects using indicator variables for 3-month periods. The adjustment for time as a continuous variable gave similar results but led to multi-collinearity with the time interaction effects in the analysis of drug preference.

We investigated a possible device preference effect, i.e. an increased probability of prescribing the promoted drug to patients already using inhaled β₂-agonists or inhaled steroids with the same inhalation device (Turbuhaler). For this purpose, we employed a variable that, for each dispensing of a fixed-combination corticosteroid and long-acting β₂-agonist, indicated if the patient had used other types of asthma drugs with the Turbuhaler device during the preceding 365 days. Estimates of representative visit and time effects were virtually unchanged, demonstrating no confounding effect. Restricting the analysis to dispensings in patients with either previous use or no previous use of the same device also led to no substantial changes in visit or time effects, and we could thus rule out significant effect modification.

In the analysis of inhaled steroid use, we also adjusted for age, sex and average inhaled β₂-agonist dose. We performed all analyses as both random effect models and fixed effect models (conditional logistic regression) and the results were comparable. We further analysed solo and group practices separately, and, finally, we excluded practices never visited during the observation period. The findings of these supplementary analyses were compatible with those of the main analysis including all practices. Data were analysed using Stata software, release 9.2 (StataCorp, College Station, TX).

Results
The GPs’ preference for the promoted drug rose from 15% before the first visit to 28% after the third visit whereafter it stabilized (Table 2). The preference proportion rose with time both before and after the first visit (Fig. 1). Table 3 shows that the first visit had a significant effect with an odds ratio (OR) of 2.39 [95% confidence interval (CI), 1.72–3.32]. This effect declined with time since marketing (OR, 0.95; 95% CI, 0.92–0.97). The second visit also had a significant additional effect (OR, 1.51; 95% CI, 1.19–1.93) that depended on the time between the visits (OR, 0.95; 95% CI, 0.93–0.98). Because of collinearity, it was not possible to include interactions with time after the second visit. Additional effects of the third and following visits were not significant and did not improve the fit of the model. The promoted drug was chosen in 42% of dispensings to patients already using another inhaled asthma drug with the same device compared to 17% of dispensings to patients without previous use of the device. Thus, there was a clear device preference (OR, 3.63; 95% CI, 3.43–3.86).

We observed an apparent increase with the number of visits in the proportion of inhaled β₂-agonist dispensings given to users of inhaled steroids (Table 2). An increase over time was, however, seen both for dispensings before and after the first visit: from 74% at baseline to 78% after 27 months (Fig. 2). Regression analysis accordingly found a statistically significant time effect, but no effect of promotional visits on steroid prescribing when adjusting for the time trend (Table 3).
Discussion

The main finding was that pharmaceutical outreach visits had a significant impact on GPs’ drug preferences, but there was no additional effect from conducting more than two visits. The representative visits did not influence the overall prescribing of inhaled steroids.

The results should be considered in relation to potential strengths and weaknesses of the study’s design. The study uses proprietary data from one drug company, which is unique in the literature. The effect on drug preferences seems to be reliable. Because data were based on a highly valid and complete register covering all prescribed asthma drugs, bias caused by self-reporting was avoided. Neither the GPs nor the representatives were informed in advance about our study, and awareness of being monitored could therefore not influence the GPs’ prescribing patterns. Further, only two of the practices in the county requested to be withdrawn from the analysis. In our analyses, we aimed to separate effects of representative visits from other influences by taking into account calendar time and device preference. After adjusting for these possible confounders, a substantial and significant effect of the two first representative visits remained. Furthermore, subgroup analyses demonstrated no important changes in results. Finally, the effect of promotional visits could in part be caused by representatives selecting practices with a higher probability of adopting the promoted drug. Although we have controlled for the time until first visit, a selection effect cannot be excluded. The County of Funen is comparable to the general Danish population and health system characteristics, including GPs. The prevalence of asthma medicine use is similar to that of the rest of Denmark. To what extent our results are generalizable to other countries is uncertain. However, we have no reason to believe that the mechanisms the pharmaceutical representatives apply in order to promote their products have a markedly different impact on other countries’ GPs.

The observed lack of impact on overall use of inhaled steroids should be interpreted with caution. Firstly, in view of the statistical precision, our study results could reflect either a small increase or a small decrease in total steroid use. The number of dispensings of the fixed combination inhaled corticosteroid is small relative to the total number of repeated dispensions of inhaled \( \beta_2 \)-agonists (Table 2). An increase in the use of fixed-combination steroid would therefore only lead to a small increase in the overall proportion of steroid users. Secondly, a ‘ceiling effect’ should be considered. If there is no place for improvement, even the best intervention appears to be ineffective and in our study, most of the \( \beta_2 \)-agonist users

<table>
<thead>
<tr>
<th>Number of visits</th>
<th>Number of practices observed</th>
<th>Dispensings of the promoted drug</th>
<th>All dispensings of fixed combination of inhaled corticosteroid and long-acting ( \beta_2 )-agonist</th>
<th>Promoted drug (%)</th>
<th>Use of inhaled corticosteroid</th>
<th>Repeated dispensings of inhaled ( \beta_2 )-agonists</th>
<th>Use of inhaled corticosteroid (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>165</td>
<td>1025</td>
<td>6668</td>
<td>15.4</td>
<td>41 307</td>
<td>54 188</td>
<td>76.2</td>
</tr>
<tr>
<td>1</td>
<td>141</td>
<td>901</td>
<td>4834</td>
<td>18.6</td>
<td>25 018</td>
<td>32 894</td>
<td>76.1</td>
</tr>
<tr>
<td>2</td>
<td>125</td>
<td>1144</td>
<td>4709</td>
<td>24.3</td>
<td>17 383</td>
<td>22 596</td>
<td>76.9</td>
</tr>
<tr>
<td>3</td>
<td>113</td>
<td>1175</td>
<td>4227</td>
<td>27.8</td>
<td>10 848</td>
<td>14 198</td>
<td>76.4</td>
</tr>
<tr>
<td>4</td>
<td>97</td>
<td>916</td>
<td>2940</td>
<td>31.2</td>
<td>9938</td>
<td>12 870</td>
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<tr>
<td>5</td>
<td>82</td>
<td>755</td>
<td>2539</td>
<td>29.7</td>
<td>11 533</td>
<td>14 680</td>
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<tr>
<td>6</td>
<td>68</td>
<td>728</td>
<td>2247</td>
<td>32.4</td>
<td>8117</td>
<td>10 022</td>
<td>81.0</td>
</tr>
<tr>
<td>7–9</td>
<td>50</td>
<td>1150</td>
<td>3555</td>
<td>32.3</td>
<td>11 383</td>
<td>14 278</td>
<td>78.6</td>
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<tr>
<td>&gt;10</td>
<td>27</td>
<td>772</td>
<td>2389</td>
<td>32.3</td>
<td>8117</td>
<td>10 022</td>
<td>81.0</td>
</tr>
</tbody>
</table>

*Dispensing of an inhaled corticosteroid including fixed combinations within 365 days before dispensing of an inhaled \( \beta_2 \)-agonist.

*Dispensing of an inhaled \( \beta_2 \)-agonist (including fixed combinations with anticholinergics or corticosteroids) during the observation period and at least one other time during the preceding 365 days.

Figure 1  Preference for the marketed drug before and after the first pharmaceutical representative visit. Percentage of dispensings of the marketed drug among all dispensings of fixed combinations of inhaled long-acting \( \beta_2 \)-agonist and corticosteroid as 3-month averages. Time after marketing in months.
(approximately 75%) were already being treated with inhaled corticosteroids. Thirdly, some patients may have switched from non-combination inhaled steroids to the fixed-combination products, thus not changing the proportion of steroid users.

We could not distinguish between individual GPs in group practices. Not all GPs in a visited practice may have participated in the meetings with the pharmaceutical representatives. Our results therefore reflect a mixture of the visited GPs’ and their colleagues’ prescribing patterns, and they accordingly underestimate the effects of the promotional visits. We obtained information on the marketing visits from only one of the two companies that sell fixed combinations of inhaled long-acting β₂-agonists and corticosteroids and the results would therefore also be underestimated in the case that the competing firm’s drug marketing efforts also affected drug preferences. We used the dispensings as a proxy for the GPs’ prescribing patterns. Some patients may have received a prescription for an asthma drug, but never redeemed it. However, in general, the non-redeption rate seems to be low for asthma drugs.21

Interactions between drug industry and GPs have frequently been discussed and most articles focus on whether pharmaceutical industry marketing entails sub-optimal or harmful prescribing patterns. The industry’s role in improving care has received much less attention.1,4,22 Our study did confirm that representatives had significant impact on GPs’ drug choice, but the additional gain from conducting more than two promotional visits is minimal or non-existing. The latter could reflect the fact that the novelty value of presenting a recently marketed drug plays an important role. However, several mechanisms may be responsible for the effects of the drug company’s promotional visits and it may not

### Table 3

<table>
<thead>
<tr>
<th>Representative visits</th>
<th>Choice of promoted drug&lt;sup&gt;h&lt;/sup&gt;</th>
<th>Use of inhaled corticosteroid&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unadjusted&lt;sup&gt;d&lt;/sup&gt;</td>
<td>Adjusted&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td>No visits</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>First visit</td>
<td>2.35 (1.70–3.26)</td>
<td>2.39 (1.72–3.32)</td>
</tr>
<tr>
<td>Time until first visit&lt;sup&gt;f&lt;/sup&gt;</td>
<td>0.95 (0.92–0.98)</td>
<td>0.95 (0.92–0.97)</td>
</tr>
<tr>
<td>Time since first visit&lt;sup&gt;f&lt;/sup&gt;</td>
<td>1.50 (1.18–1.90)</td>
<td>1.51 (1.19–1.93)</td>
</tr>
<tr>
<td>Second visit</td>
<td>1.50 (1.18–1.90)</td>
<td>1.51 (1.19–1.93)</td>
</tr>
<tr>
<td>Time between first and second visit&lt;sup&gt;f&lt;/sup&gt;</td>
<td>0.96 (0.93–0.99)</td>
<td>0.95 (0.93–0.98)</td>
</tr>
<tr>
<td>Third visit&lt;sup&gt;g&lt;/sup&gt;</td>
<td>1.07 (0.95–1.20)</td>
<td>1.06 (0.94–1.20)</td>
</tr>
<tr>
<td>Time since marketing&lt;sup&gt;h&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Months 1–3</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Months 13–15</td>
<td>2.50 (2.00–3.12)</td>
<td>2.61 (2.08–3.29)</td>
</tr>
<tr>
<td>Months 25–27</td>
<td>3.72 (2.76–5.01)</td>
<td>3.93 (2.89–5.35)</td>
</tr>
<tr>
<td>Previous use of device&lt;sup&gt;i&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>3.63 (3.43–3.86)</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup>Random effects logistic regression model with cumulative effect of visits.

<sup>b</sup>Among all dispensions of fixed combination of inhaled corticosteroid and long-acting β₂-agonist.

<sup>c</sup>Within 365 days before repeated dispensings of inhaled β₂-agonists.

<sup>d</sup>Only time variables included.

<sup>e</sup>Adjusted for previous use of device.

<sup>f</sup>Interaction between respective visits and time as continuous variable (months).

<sup>g</sup>No significant effect of subsequent visits and no improvement in model fit (likelihood ratio test).

<sup>h</sup>Adjustment for calendar time effect in 3-month periods, only two periods reported.

<sup>i</sup>Dispensing of other types of asthma drugs with the same device as the marketed drug during the preceding 365 days.

<sup>j</sup>Adjusted for patients’ age, sex and average dosage of inhaled β₂-agonists.

![Figure 2: Treatment with inhaled corticosteroid before and after the first pharmaceutical representative visit. Percentage treated with inhaled steroids including fixed combinations among patients repeatedly receiving inhaled β₂-agonists. Time after marketing of the promoted fixed combination of inhaled budesonide and formoterol in months](https://academic.oup.com/fampra/article-abstract/26/3/204/510492/590x595)
be possible to determine to which extent the effects observed were attributable to different components of the ‘promotional package’. The first representative visit has a greater effect if it is conducted close to the time of marketing, and the effect of the visit gradually wears off. Further, there is a considerable increase over time in preference for the promoted drug even if practices are not visited. This indicates that the largest effect would be achieved by conducting two visits with a relatively short interval early after the drug is marketed.

Conclusions

In conclusion, pharmaceutical sales representative visits markedly increased the market share of the promoted drug, but only the two first visits had significant impact. Visits had no significant impact on GPs’ overall prescribing of inhaled steroids.

Acknowledgements

AstraZeneca is thanked for showing courage by disclosing information that pharmaceutical companies normally regard as confidential.

Declaration

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References