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Primary care physicians’ adoption of new drugs is not associated with their clinical interests: A pharmacoepidemiologic study

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Abstract
Objectives. Increasing drug expenditures call for better understanding of the reasons behind individual general practitioners’ (GPs’) prescribing decisions. The aim was to analyse associations between GPs’ clinical interests and their preference for new drugs.

Design. Historical cohort study using population-based prescription data and data collected by postal questionnaire.

Setting and subjects. A total of 68 single-handed GPs in the County of Funen, Denmark. Main outcome measures. GPs’ preferences for two new (2004) drug groups (selective cyclo-oxygenase-2 inhibitors and angiotensin-II antagonists) were analysed. The preference was defined as the percentage of patients receiving a new drug among first-time users of either the new drug or an older alternative. The GPs’ preference proportion was modelled using linear regression analysis. Data from a questionnaire on GPs’ interest in corresponding clinical areas (musculoskeletal diseases and hypertension, respectively), continuing medical education (CME) activities, and previous employment were the independent variables.

Results. The adjusted mean difference in preference for new drugs between GPs with high and low interest in each of the two clinical areas was 0.4% (95% CI –2.0% to 2.8%), and –2.2% (–15.0% to 10.7%), respectively. Only current CME activities in the area of hypertension were significantly associated with GPs’ preference for new drugs (adjusted mean difference 17.9% (95% CI 5.8% to 30.0%).

Conclusion. No clear association between GPs’ self-rated clinical interest and their prescribing of new drugs was found.

Key Words: Drug utilization, general practice, pharmacoepidemiology, questionnaires

General practitioners’ (GPs’) prescribing of new drugs may have a considerable impact on health care expenditures and quality of care [1,2]. While some new drugs represent important therapeutic improvements, many are not clearly superior to older and less expensive alternatives [3,4]. Often interventions have been launched in order to optimize physicians’ choice among new and old therapeutic alternatives. However, randomized controlled trials evaluating interventions targeting inappropriate prescribing have only rarely demonstrated an impact [4–6]. Effective interventions should be based on comprehensive insight into the mechanisms that influence GPs’ choice of drug [7,8]. Traditional intervention strategies, such as the dissemination of guidelines, address all physicians. Ideally, they should be directed at those GPs who are “in most need” of being influenced, but knowledge of key characteristics associated with prescribing of new drugs is currently limited [9,10]. For example, a GP’s willingness to prescribe new drugs in one therapeutic group seems unrelated to previous prescribing of the same group and also unrelated to the use of new drugs in other therapeutic drug groups [11,12].

Since previous studies have failed to explain sufficiently how and why physicians prescribe new drugs as they do, we suggest exploring more personal physician characteristics. It has been demonstrated that there are no or only weak associations between adoption of new drugs and the physicians’ age and sex [13–16], hence other explanations should be sought. It has been hypothesized that GPs are inclined to prescribe new drugs in clinical areas in which they have a clinical interest [17–19]. Therefore, we aimed to analyse associations between GPs’ clinical interests and their preference for new drugs.
General practitioners’ (GPs’) adoption of new drugs may influence health care quality and expenses.

- Contrary to our hypothesis we found no association between physicians’ self-rated clinical interests and their prescribing of new drugs.

### Material and methods

This study was carried out in the Danish County of Funen (~470,000 inhabitants) in 2004 and comprised data from a mailed questionnaire to GPs and from a prescription register. We chose to study prescribing in two clinical areas: musculoskeletal diseases and hypertension. As new drugs we included the class of selective cyclo-oxygenase-2 (COX-2) inhibitors and angiotensin-II antagonists (AT-II) (Table I). COX-2 inhibitors selectively inhibit cyclo-oxygenase-2 and it was believed that these drugs would be effective therapy for painful conditions and in contrast to the traditional non-steroidal anti-inflamatory drugs (NSAIDs) would prove safer for the gastrointestinal (GI) tract by “sparring” the COX-1 inhibition of protective prostaglandins. AT-IIs selectively block the angiotensin II receptor in contrast to the older alternative, the ACE inhibitors, that work earlier in the cascade and often have cough as a side effect.

### The questionnaire

In December 2004, we sent a questionnaire focused on clinical interests to all GPs in the county (n = 326). The questionnaire was part of a survey of GPs’ demands and preferences for continuing medical education (CME). It was sent by mail together with a covering letter explaining the survey briefly but not disclosing that the data would also be used to study adoption of new drugs. A prepaid reply envelope was enclosed. Non-responders were followed up after two and five weeks. The questionnaire had been pilot tested with GPs in another county (County of Northern Jutland) and minor linguistic modifications were subsequently made. For each clinical area, the GPs were asked to indicate their level of clinical interest on a four-grade rating scale (from 1 = very low to 4 = very high) in musculoskeletal diseases and hypertension. The doctors were also asked to indicate on a scale from 1 to 4 their perceived need for CME and to indicate current CME activities defined as whether in 2004 they had attended CME activities relevant to the clinical area or whether they planned to attend any in 2005. Finally, they were asked to indicate whether, prior to becoming a GP, they had been employed in hospital departments of cardiology and rheumatology. As an incentive to answer the questionnaire, all GPs participated in a lottery where the prizes comprised minor diagnostic equipments.

### Databases

The Odense University Pharmacoepidemiologic Database (OPED) comprises information on all prescriptions redeemed at pharmacies in the County of Funen since 1992 [20]. Information includes date of redemption, the identity of the prescribing unit (general practice, specialist, or hospital department), the patient’s identity, age, and gender, the brand, the Anatomical Therapeutic Chemical classification code, and the quantity of the drug prescribed.

The Danish healthcare system is a tax-funded state system following the principle of universal, free, and equal access to healthcare services from hospitals and physicians outside hospitals [1]. Most drugs are partly reimbursed by the national health services (NHS) and the GPs can freely prescribe any of the studied drugs. Approximately 97% of the Danish population is listed with a GP and the NHS keeps records of the patients’ identity, age, and gender. The Danish Data Protection Agency approved the study. According to the Regional Research Ethics

### Table I. Clinical areas studied and corresponding new and old drugs.

<table>
<thead>
<tr>
<th>Clinical area</th>
<th>New drugs</th>
<th>Old drug alternatives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Musculoskeletal diseases</td>
<td>Selective cyclo-oxygenase-2 inhibitors: celecoxib, etoricoxib, rofecoxib</td>
<td>Other non-steroidal anti-inflammatory drugs: aceclofenac, dexibuprofen, diclofenac, etodolac, flurbiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, lornoxicam, meloxicam, nabumetone, naproxen, phenylbutazone, piroxicam, sulindac, tenoxicam, tiaprofenic acid, tolfenamic acid</td>
</tr>
<tr>
<td></td>
<td>Reimbursement date: 5 December 1994</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>Angiotensin-II receptor antagonists: candesartan, eprosartan, irbesartan, losartan, telmisartan, valsartan</td>
<td>Angiotensin-converting enzyme inhibitors: captopril, benazepril, enalapril, fosinopril, lisinopril, moexipril, perindopril, quinapril, ramipril, trandolapril</td>
</tr>
<tr>
<td></td>
<td>Reimbursement date: 24 January 2000</td>
<td></td>
</tr>
</tbody>
</table>
Committee, no ethical approval is necessary for this kind of register study.

Variables

For GPs working in group practices, the OPED cannot identify the individual physician’s prescribing. Therefore, only data for GPs in single-handed practices were included in this study. For each clinical area, we quantified each GP’s preference for new drugs in 2004 by the preference proportion. This was defined as the percentage of patients receiving a new drug within the respective class among first-time users of either the new or an old drug (see Table I). First-time (incident) users were patients who had purchased neither a new nor an old drug during the 365 days preceding their first purchase in the study period. We standardized the preference proportion according to age and sex by means of direct standardization to the total population of users of new and old drugs.

Analyses

For each drug group, we modelled the preference proportion as a function of GPs’ clinical interest in the corresponding clinical area (i.e. the group of selective COX-2 inhibitors and the clinical area musculoskeletal diseases) using linear regression.

First, we undertook univariate regression analysis using the independent variable self-rated clinical interest dichotomized into GPs with “low clinical interest” (scores 1 and 2) and “high clinical interest” (scores 3 and 4). With respect to clinical interest in musculoskeletal diseases, only six GPs fell into the low interest group. Here, the lowest three levels (scores 1–3) were combined in the analysis. The regression coefficient of the dichotomized interest variable corresponds to the mean difference in preference proportion between the two “interest groups”. Since perceived need for CME, current CME activities, and previous hospital employment may also influence GPs’ choice of drugs, these were included in the analyses and the adjusted mean difference calculated using multivariate regression. Finally, we repeated the analyses using self-rated clinical interest and perceived need for CME as continuous variables (from 1 to 4).

Stata version 8.2 was used for statistical analyses. P-values of less than 0.05 were considered statistically significant.

Results

There were 95 single-handed practitioners. Among these, 18 did not respond and nine declined participation. This left 68 GPs (72%) for analyses. The GPs’ age, gender, mean prescribing rates, and variation index (defined as the ratio between the 90% and the 10% percentiles) were similar among responders and non-responders. Table II gives the distribution of answers to the questionnaire.

There was no statistically significant association between GPs’ self-reported “clinical interest” and their preference for new drugs in the same clinical area for either of the two drug groups (Table III). This was the case when using univariate analysis and after adjustment for “perceived need for CME”, “CME activities”, and “previous hospital employment”.

Among the four independent variables, only “CME activities” was statistically significantly associated with GPs’ preference for new drugs and the association was significant only for the clinical area hypertension (and the prescribing of angiotensin-II antagonists) (see Table III). The adjusted mean difference was 17.9 (95% CI: 5.8% to 30.0%).

Discussion

Little, if any, of the variation in the GPs’ preference for new drugs could be attributed to the level of their

<table>
<thead>
<tr>
<th>Variables</th>
<th>Clinical area</th>
<th>Very high</th>
<th>High</th>
<th>Low</th>
<th>Very low</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-rated clinical interest</td>
<td>Musculoskeletal diseases</td>
<td>19 (27)</td>
<td>42 (62)</td>
<td>6 (9)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>11 (16)</td>
<td>40 (59)</td>
<td>17 (25)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Perceived need for continuing medical education</td>
<td>Musculoskeletal diseases</td>
<td>2 (3)</td>
<td>37 (54)</td>
<td>24 (35)</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1 (1)</td>
<td>12 (18)</td>
<td>46 (68)</td>
<td>4 (6)</td>
<td></td>
</tr>
<tr>
<td>Current continuing medical education activities</td>
<td>Musculoskeletal diseases</td>
<td>44 (65)</td>
<td>24 (35)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>46 (68)</td>
<td>22 (32)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous hospital employment</td>
<td>Rheumatology</td>
<td>15 (22)</td>
<td>53 (78)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiology</td>
<td>15 (22)</td>
<td>53 (78)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table III. General practitioners’ preference for two new drug groups (n = 68) in corresponding clinical areas, quantified by the preference proportion (PP).

<table>
<thead>
<tr>
<th>Clinical area</th>
<th>Musculoskeletal diseases</th>
<th>Hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Independent variables</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Self-rated clinical interest Low</td>
<td>5.1 (2.3–7.4)</td>
<td>27.6 (6.2–33.6)</td>
</tr>
<tr>
<td>Mean difference (95% CI)</td>
<td>0.8 (–1.5–3.0)</td>
<td>–1.3 (–14.7–12.1)</td>
</tr>
<tr>
<td>Adjusted mean difference (95% CI)</td>
<td>0.4 (–2.0–2.8)</td>
<td>–2.2 (–15.0–10.7)</td>
</tr>
<tr>
<td>High</td>
<td>5.9 (2.6–8.2)</td>
<td>26.3 (9.0–36.5)</td>
</tr>
<tr>
<td>Mean difference (95% CI)</td>
<td>–1.3 (–14.7–12.1)</td>
<td>–2.2 (–15.0–10.7)</td>
</tr>
<tr>
<td>Adjusted mean difference (95% CI)</td>
<td>–1.3 (–14.7–12.1)</td>
<td>–2.2 (–15.0–10.7)</td>
</tr>
<tr>
<td>Perceived need for continuing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>medical education Low</td>
<td>5.4 (1.7–8.7)</td>
<td>26.8 (6.9–36.5)</td>
</tr>
<tr>
<td>Mean difference (95% CI)</td>
<td>–0.1 (–2.1–2.0)</td>
<td>–0.9 (–16.0–14.3)</td>
</tr>
<tr>
<td>Adjusted mean difference (95% CI)</td>
<td>–0.2 (–2.3–1.9)</td>
<td>–0.3 (–14.9–10.7)</td>
</tr>
<tr>
<td>High</td>
<td>5.3 (2.4–6.8)</td>
<td>25.9 (8.7–37.6)</td>
</tr>
<tr>
<td>Mean difference (95% CI)</td>
<td>26.8 (6.9–36.5)</td>
<td>25.9 (8.7–37.6)</td>
</tr>
<tr>
<td>Adjusted mean difference (95% CI)</td>
<td>26.8 (6.9–36.5)</td>
<td>25.9 (8.7–37.6)</td>
</tr>
<tr>
<td>Current continuing medical</td>
<td></td>
<td></td>
</tr>
<tr>
<td>education activities No</td>
<td>4.4 (2.3–6.0)</td>
<td>14.2 (0.0–19.2)</td>
</tr>
<tr>
<td>Mean difference (95% CI)</td>
<td>5.9 (2.0–8.8)</td>
<td>32.4 (10.9–51.9)</td>
</tr>
<tr>
<td>Adjusted mean difference (95% CI)</td>
<td>1.5 (–0.6–3.6)</td>
<td>18.2 (6.5–29.9)</td>
</tr>
<tr>
<td>Yes</td>
<td>5.6 (2.3–7.7)</td>
<td>25.3 (6.7–35.8)</td>
</tr>
<tr>
<td>Mean difference (95% CI)</td>
<td>1.6 (–0.5–3.8)</td>
<td>17.9 (5.8–30.0)</td>
</tr>
<tr>
<td>Adjusted mean difference (95% CI)</td>
<td>1.6 (–0.5–3.8)</td>
<td>17.9 (5.8–30.0)</td>
</tr>
<tr>
<td>Previous hospital employment No</td>
<td>4.5 (1.5–6.8)</td>
<td>31.4 (9.0–54.1)</td>
</tr>
<tr>
<td>Mean difference (95% CI)</td>
<td>–1.1 (–3.6–1.3)</td>
<td>6.1 (–7.7–20.0)</td>
</tr>
<tr>
<td>Adjusted mean difference (95% CI)</td>
<td>–1.4 (–4.0–1.2)</td>
<td>3.5 (–9.9–16.9)</td>
</tr>
</tbody>
</table>

Notes: 1 Linear regression analysis; 2 p < 0.05.

clinical interests. Although their preferences for new drugs appeared to be associated with CME activities in some clinical areas, the association was not consistent across both classes of drugs.

Recall bias when GPs report on CME activities and previous hospital employment could be a serious concern. However, because GPs only had to remember CME activities over the last year and only had to remember in what type of department they had been employed (not the exact place and duration of employment) recall bias is unlikely to have influenced the results highly. A major strength of our study is the use of reliable, population-based data on GPs’ prescribing [20], which enabled us to accurately measure GPs’ actual prescribing patterns. In Denmark, all prescriptions are registered electronically and health care providers and pharmacists have an economic incentive to provide accurate data. Non-redemption of prescriptions (primary non-compliance) may reduce the data accuracy, but this seems to be a minor problem in Denmark [21].

Statistical power is an important issue when studies do not detect significant association as proposed by the hypothesis. The narrow confidence intervals (see Table III) in our study indicate, however, that we had sufficient power to detect relevant associations. It is noteworthy that among physicians with low as well as among physicians with high interest in a clinical area, their preferences for new drugs varied considerably as indicated by the wide inter-quartile ranges (Table III). This variation indicates that there may be other factors influencing GPs’ choice of drug, thus making it difficult to detect a significant effect of clinical interest per se.

The decline in COX-2 prescribing rates after reports on cardiovascular toxicity is proof that a single issue concerning drug safety may lead to great changes during a short period of time. More generally, however, insight into what factors affect physicians’ prescribing is still lacking. GPs’ choice of prescription drugs may be influenced by patient, physician, and drug characteristics. Patient characteristics may include aspects such as medical condition including diagnosis and sociodemographic variables such as age, sex, and social class [22]. Doctor characteristics may include such aspects as age, sex, attitude towards prescribing of new drugs [19,22], practice style and setting [18,23,24], hospital-initiated prescribing [25], patient pressure [26], pharmaceutical contacts [18], and other attempts at intervention (27). Drug characteristics may be related to price, potential side effects, perceived effectiveness, long-term effects, and likely benefits of the drug [17–19]. With so many different factors likely to influence the GPs’ drug choice, it is conceivable that each factor will have only a moderate impact, which may explain the lack of positive findings in this study. This may particularly be so because interaction between the various factors may hide the impact of each single factor. GPs’ choice of prescription drugs is the result of a complex decision process with an array of potential influences. In other words, we need high-powered studies with a high number of explanatory variables. In order to better tailor interventions, we still lack a
better understanding of the mechanisms underlying drug choice.

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