Author’s response to reviews

Title: Is new drug prescribing in primary care specialist induced?

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Author’s response to reviews: see over
Dear Editor,

Please find enclosed our second adjustments to our manuscript "Linking community pharmacy dispensing data to prescribing data of general practitioners" in response to your reviewers. Below you will find our revisions to the manuscript. Based on the reviewer's comments, modifications were also made to the manuscripts.

Reviewer Jane Robertson

Major compulsory revisions

Comment 1
The reviewer is indeed right that it is likely that there is a difference in specialist influence between drugs that are first in class, and drugs in an existing class. We have not included drugs that are entirely new in class, except maybe Vioxx. We have added the following lines to the discussion in order to address this issue:

The five different new drugs were not chosen randomly but all illustrated different types of new drugs. Salmeterol/fluticasone was seen as an innovation as it combines two existing compounds in one dosing device with a claimed benefit for compliance. Rofecoxib was chosen as a new drug from a new therapeutic class. Although clearly resembling the non-selective NSAIDs, the COX-2 inhibitors were seen as a new class of analgesic at time of marketing. Esomeprazole was chosen a classic example of a me-too drug; showing no benefit over the older drugs. Tiotropium was also chosen as an stepwise innovation because the improved dosing regiment going from 4 times daily to once daily administration. Rosuvastatin was seen as the newest statin on the block that was heavily marketed as the most potent statin available. However, around time of market introduction Rosuvastatin was heavily debated about its safety profile, making it a new drug with high perceived risks. The level of specialist prescribing differs per new drug. Especially for rosvastatin, esomeprazole, and rofecoxib, GP were in most cases the first prescribers. On the other hand, tiotropium and the combination salmeterol/fluticasone were mostly initiated by specialists. This is in line with other studies 8,9,20,21.

Comment 2
All new drugs in the study, as stated in the study design, were fully reimbursed by all health insurance companies in The Netherlands and could be prescribed without any restrictions by both GPs as hospital specialist. In addition, The Netherlands works with a reference based pricing system making the price difference between the different compounds in the therapeutic classes of little importance. For these reasons costs will have little influence on our results. Only in the case of Vioxx the other compounds existed in generic forms. The price differences between the new and generic drugs would have resulted in a lower uptake of the drugs and would not bias our results. For both GPs as hospital specialists the cost issues would be of similar magnitude.

Comment 3
Our pharmacy data did indeed not include information on letter or telephone consultation. We’ve added the following to the Discussion session to highlight this limitation of our data:
Influence of specialists on prescribing practices of GPs may of course go beyond direct influence through prescription of new drugs to patients treated by the GP. It is possible that specialists, or indeed GPs among themselves, influence prescribing through meetings, telephone consultations, letters or otherwise. This type of influence could not be measured in the present study. We feel however that it is unlikely that specialists would promote new drugs without prescribing them themselves. Therefore, we believe that prescribing sequences, as studied here, are a good proxy for the general influence on prescribing habits.

We agree with the reviewer that is important to clarify the differences between the patient level and the GP level analyses in Tables 2 and 3. We have added some lines to the methods and results sections on this.

Comment 4

Minor Essential Revisions
All typos were corrected and grammatical issues addressed. We have adapted the methods section as suggested by the reviewer.

Reviewer Tom Walley

Comment 1
We acknowledge that we only measured the direct influence of the hospital specialist on the prescribing behavior of GPs. It may well be that GPs developed over the years their own special interest in a particular medical therapeutic field, e.g. hypertension or asthma, that made them more willing or confident to try out new agents. We have this comment in our discussion to highlight this phenomenon:

Also, it may of course be possible that GPs have special interest in certain clinical fields, which makes it more likely that they are among the early adopters of drugs within that field. However, from previous research we found that if a GP is an early prescriber of one new drug, he is very likely to also be an early prescriber of other new drugs, indicating a general willingness to prescribe new drugs rather than a special interest in a certain field. 28

Comment 2
We agree with dr. Walley that the interaction between GPs may be an important factor in the uptake of new drugs in general practice. To address the issue of intercolleague advising about new drugs, as describe by previous research we have added the following sentence to the discussion:

Influence of specialists on prescribing practices of GPs may of course go beyond direct influence through prescription of new drugs to patients treated by the GP. It is possible that specialists, or indeed GPs among themselves, influence prescribing through meetings, telephone consultations, letters or otherwise. This type of influence could not be measured in the present study. We feel however that it is unlikely that specialists would promote new drugs without prescribing them themselves. Therefore, we believe that prescribing sequences, as studied here, are a good proxy for the general influence on prescribing habits.
Comment 3
The point mentioned by the reviewer is an interesting research question. We know from previous work that receiving pharmaceutical representatives is an important determinant for prescribing new drugs rapidly after market introduction. However, it is beyond the scope of our study to estimate the correlation between being an early prescriber of new drugs and having a particular medical interest in a therapeutic area.

Comment 4
The authors are aware of the “gaming” going on between primary and hospital physician. From the data it is not possible to elucidate the magnitude of this phenomenon as the reviewer already mentioned. We also acknowledge the important findings of Prosser et al. and Jacoby et al. but on the other hand also conclude that our findings contradict the idea that the diffusion of newly marketed drugs always follows a two-step model, with medical specialists as the innovators and GPs as the followers. We believe that the “traditional” idea of the two step model is not always the case for most new drugs.