European Journal of Clinical Pharmacology (2019) 75:577–586
https://doi.org/10.1007/s00228-018-02611-y

PHARMACOEPIDEMIOLOGY AND PRESCRIPTION

Effectiveness of an academic detailing intervention in primary care on the prescribing of non-steroidal anti-inflammatory drugs

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Received: 3 September 2018 / Accepted: 10 December 2018 / Published online: 31 December 2018
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Abstract

Purpose The objective of this study was to examine the impact of an academic detailing programme in primary care in Norway on the prescribing rate of diclofenac, naproxen and non-steroidal anti-inflammatory drugs (NSAIDs) in total.

Methods An academic detailing programme was delivered to general practitioners (GPs) in two Norwegian cities. The key message was to avoid diclofenac and COX-2 inhibitors and to use naproxen as the NSAID of choice. We analysed prescription data for 12 months before and after the programme to estimate its impact, using interrupted time series to control for underlying trends, and using the rest of Norway as a comparator. The primary outcome was change in the proportion of the population filling a prescription for diclofenac; secondary outcomes were change in naproxen prescribing and change in total NSAID prescribing.

Results Controlling for baseline trends, and relative to changes in the rest of Norway, there was a statistically significant reduction in the prescribing rate of diclofenac in both cities (− 18% and − 16%, respectively) immediately after the intervention. The impact of the programme on prescribing of diclofenac was maintained by the end of the 12 month follow-up period. An increase in the prescribing of naproxen was observed in both cities. The programme had no impact on the overall rate of prescribing of NSAIDs.

Conclusion Academic detailing was effective in changing the choice of prescribed NSAID amongst Norwegian GPs. Academic detailing is potentially an important method for providing GPs with independent, evidence-based updates on pharmacotherapy to improve prescribing.

Keywords Academic detailing · Continuing medical education · Educational outreach visits · Primary care · Non-steroidal anti-inflammatory drugs · Interrupted time series analysis

Background

Non-steroidal anti-inflammatory drugs (NSAIDs) are amongst the most widely prescribed medicines; however, they have potentially severe side effects and are one of the major reasons for hospital admissions attributed to adverse effects [1, 2]. Several meta-analyses have shown that the cyclooxygenase-2 (COX-2)-selective inhibitors (coxibs) have a higher risk for cardiovascular disease than non-selective NSAIDs [3–5]. Two large meta-analyses published in 2011 and 2013 provided evidence that diclofenac has a similar cardiovascular risk as the coxibs, while naproxen has no or a very

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00228-018-02611-y) contains supplementary material, which is available to authorized users.

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low increase in the risk for cardiovascular adverse effects [4, 6]. As a consequence, the European Medicines Agency published new safety advice for diclofenac in June 2013 [7], an advice that was reiterated by the Norwegian Medicines Agency (NOMA) [8].

At that time, diclofenac was the most commonly prescribed NSAID in Norway. More than 15% of the Norwegian population filled at least one prescription for an oral NSAID (anatomical therapeutic chemical classification system (ATC) codes M01AA–M01AH) in 2013, and almost 60% of these used diclofenac [9]. NOMA and other Norwegian health authorities informed prescribers of the new guidelines for diclofenac, using direct communication, adverts in the *Journal of The Norwegian Medical Association*, warnings in the online version of the Norwegian Pharmaceutical Product Compendium (Felleskatalogen) and automatic reminders ("pop-ups") in the general practitioners' prescribing tools. Those interventions had some impact, and from 2013 to 2014, the prescribing rate of diclofenac in Norway was reduced by 11.0% [9].

Still, with a high rate of prescribing of diclofenac, the knowledge about the unfavourable cardiovascular risk profile of diclofenac did not seem to have been sufficiently translated into a change in prescribing. We therefore implemented an academic detailing intervention to discuss the risk/benefit profile of NSAIDs with primary care doctors.

The basis of academic detailing is a face-to-face interactive conversation by a trained health professional ("academic detailer") in a one-to-one setting with the prescriber in the prescriber's workplace [10, 11]. These one-to-one visits have been shown to be more effective than group meetings as a behaviour change intervention [12, 13]. Previous studies have also shown that academic detailing has been effective in changing prescribing of NSAIDs [12, 14, 15].

The objective of this study was to evaluate if the academic detailing programme in Norwegian primary care had an impact on the prescribing rate of diclofenac, naproxen and NSAIDs in total.

Methods

The academic detailing campaign

Experienced pharmacists and consultants in clinical pharmacology, who were trained in academic detailing, conducted the visits. A total of seven academic detailers (four pharmacists and three consultants in clinical pharmacology) participated in the study. All academic detailers were employed at a governmentally funded public hospital. A four-page brochure was developed based on updated evidence, and this brochure was used as the basis for a 20-min one-to-one visit in the general practitioner's office. Our advice did not consider cost of the individual drugs, but was only based on an evaluation of the risk for adverse effects, assuming equal therapeutic effects. The brochure focused on the general side effects of NSAIDs, and the key message was to avoid selective COX-2 inhibitors and diclofenac, and to use naproxen as the NSAID of choice (see Box 1).

We invited all general practitioners (GPs) in two Norwegian cities, Tromsø and Trondheim, to participate. In Trondheim, 180 GPs were invited, and 162 received a visit (90%). In Tromsø, 67 GPs were invited, and 51 received a visit (76%). Visits were conducted during March through May 2015. After the visits, all GPs received an electronic survey with questions to evaluate their experience with the visit. In total, 169 of the 213 GPs visited (79%) completed this questionnaire.

Data sources and outcomes

As we did not have access to actual prescribing data from the GPs, we used data from the Norwegian Prescription Database (NorPD) as a proxy of prescribing. This database contains all prescriptions that are being dispensed from Norwegian pharmacies. In this article, we will use the term "prescribing" in relation to the data from NorPD. We retrieved the number of NSAID prescriptions dispensed per month in the intervention cities Trondheim (population 184,900 in January 2015) and Tromsø (population 72,681 in January 2015) for a total of 25 months (March 2014–March 2016). We used population census data [9] to estimate the rate of monthly prescribing in the 12 months before and after the start of the intervention.

Our primary outcome was change in prescription rate (i.e. number of prescriptions per 1000 inhabitants per month) of diclofenac (ATC codes: M01AB05 and M01AB55). Secondary outcomes were change in prescription rate of naproxen (ATC codes: M01AE02 and M01AE51) and change in prescription rate of NSAIDs (ATC codes: M01AA–M01AH) in total.

As comparators, we used two cities similarly sized as the intervention cities: Bergen (population 275,112 in January

Box 1 Key messages of the academic detailing programme

- Avoid using selective COX-2 inhibitors and diclofenac. Use naproxen for shortest possible time and, if needed, with a proton pump inhibitor
- Older patients and persons with increased risk of cardiovascular disease, with reduced kidney function, and those using angiotensin-converting enzyme inhibitors, angiotensin receptor blockers or diuretics, are at particular risk
- For patients with soft tissue injuries or pain in superficial joints like in the hands, knees or ankles, topical use of an NSAID gel is a good alternative
- Many patients will benefit from paracetamol in monotherapy or as add-on therapy

2015) as a comparator for Trondheim and Bodø (population 50,185 in January 2015) as a comparator for Tromsø. We also used the whole country of Norway, excluding the intervention cities Trondheim and Tromsø (population 4,705,790 in January 2015), as a second comparator for both intervention cities.

Statistical methods

We used an interrupted time series design to evaluate the impact of the academic detailing programme. This quasi-experimental design is frequently used when evaluating longitudinal effects of interventions, as it distinguishes the effect of the intervention from change that would have happened in the absence of the intervention [16]. We used segmented regression models to fit a least squares regression line to each segment before and after the intervention, assuming a linear relationship between time and rate of prescribing within each segment [17]. We tested for non-linearity by regressing time on rate of prescribing and examining the residuals for unusual patterns, to ensure suitability of the modelling technique [18].

We used multiple group comparisons in the segmented regression models to compare the intervention cities with the control groups [19]. We examined differences in baseline level and trend between the intervention and control cities, and for all analyses, we present unadjusted effect sizes and those adjusted for changes in comparator cities.

All analyses were conducted using Stata/IC 14.1. We used the "acttest" in Stata to test for the presence of autocorrelation (i.e. similarity between observations as a function of the time lag between them) and used the "lag()" specification to correctly account for any significant autocorrelation, and estimated the coefficients with Newey-West standards errors [19]. This was done as ordinary least squares regression assumes that the error terms are uncorrelated, and ignoring autocorrelation may overestimate the effects of an intervention [17]. We did not include a lag period, as one would expect an immediate intervention effect, owing to the nature of NSAIDs prescribing. Baseline was defined as March 2014. For the analyses, the intervention month was defined as March 2015.

P values < 0.05 were considered statistically significant. Differences in levels and slopes are presented as estimates with 95% confidence intervals (CIs).

Results

The principal results of the diclofenac prescribing before and after the intervention are presented in Table 1 and Fig. 1, and the corresponding results for the naproxen prescribing are presented in Table 2 and Fig. 2.

Diclofenac prescribing—Trondheim

Unadjusted results

In Trondheim, the baseline rate of diclofenac prescribing was 9.23/1000 inhabitants (Table 1). Following the intervention, the intercept change was − 1.30/1000 inhabitants (95% CI − 2.51 to − 0.08, $p = 0.038$) representing a drop in prescribing after the intervention of 1.3 prescriptions per 1000 inhabitants over a month. There was no statistically significant change in the slope following the intervention, and the impact of the intervention was maintained at the end of the follow-up period (Fig. 1a).

Results adjusted for changes in the comparator groups

At baseline, there was a very slight difference in the rate of diclofenac prescribing between Trondheim and the comparator city, Bergen (Table 1), without any difference between the pre-intervention slopes. While there was no significant difference in the pre-intervention level of prescribing between Trondheim and the rest of Norway, there was a slight but statistically significant difference in the pre-intervention slopes. Controlling for baseline trends, and relative to Bergen, there was a significant decrease in prescribing of diclofenac in the month immediately after the intervention in Trondheim (− 1.42/1000 inhabitants, 95% CI − 2.22 to − 0.62, $p < 0.001$). A similar effect size was seen when using the rest of Norway as a comparator (− 1.40/1000 inhabitants, 95% CI − 2.22 to − 0.58, $p < 0.001$), which represents a relative reduction in prescribing of diclofenac of 18% in Trondheim after the intervention compared to the rest of Norway. There was no significant difference in slopes between Trondheim and either Bergen or the rest of Norway after the intervention, meaning that the immediate effect of the reduction in prescribing of diclofenac was maintained during the follow-up period.

Diclofenac prescribing—Tromsø

Unadjusted results

In Tromsø, the baseline rate of diclofenac prescribing was 7.14/1000 inhabitants (Table 1). Following the intervention, the intercept change was − 1.02/1000 inhabitants (95% CI − 1.6 to − 0.43, $p < 0.01$), i.e. a drop of 1.02 prescriptions per 1000 inhabitants over a month. There was a statistically significant reduction in the slope after the intervention (Table 1), as the rate of prescribing of

Table 1 Effect estimates of the academic detailing programme on prescribing rate of diclofenac

Prescribing of diclofenac/1000 inhabitants per month	Trondheim			Tromsø		
	Prescribing rate/1000 inhabitants per month	95% CI	*p* value	Prescribing rate/1000 inhabitants per month	95% CI	*p* value
Unadjusted effect size						
Baseline prescribing in the intervention group	9.23	8.54 to 9.91		7.14	6.68 to 7.60	
Intervention level change (unadjusted)	− 1.30	− 2.51 to − 0.08	$p = 0.038$	− 1.02	− 1.60 to − 0.43	$p < 0.01$
Intervention slope change (unadjusted)	− 0.02	− 0.16 to 0.12	$p = 0.770$	− 0.13	− 0.22 to − 0.04	$p < 0.01$
Adjusted for change in control group A[a]						
Difference in level between intervention and control A prior to intervention	− 0.57	− 1.13 to − 0.01	$p = 0.047$	− 3.23	− 4.55 to − 1.91	$p < 0.001$
Difference in slope between intervention and control A prior to intervention	− 0.08	− 0.17 to 0.01	$p = 0.063$	0.13	−0.07 to 0.34	$p = 0.188$
Between group (intervention–control A) difference in level after intervention	− 1.42	− 2.22 to − 0.62	$p < 0.001$	− 2.06	− 4.05 to − 0.07	$P = 0.040$
Between group (intervention–control A) difference in slope after intervention	+ 0.03	− 0.08 to 0.14	$p = 0.617$	− 0.10	− 0.34 to 0.15	$p = 0.447$
Adjusted for change in control group B[b]						
Difference in level between intervention and control B prior to intervention	− 0.44	− 1.00 to 0.12	$p = 0.117$	− 2.52	− 3.11 to − 1.94	$p < 0.001$
Difference in slope between intervention and control B prior to intervention	− 0.09	− 0.18 to − 0.00	$p = 0.041$	0.06	− 0.03 to 0.15	$p = 0.203$
Between group (intervention–control B) difference in level after intervention	− 1.40	− 2.22 to − 0.58	$p < 0.001$	− 1.12	− 1.88 to − 0.35	$p < 0.01$
Between group (intervention–control B) difference in slope after intervention	+ 0.02	− 0.10 to 0.14	$p = 0.746$	− 0.09	− 0.22 to 0.04	$p = 0.180$

[a] Control group A: Bergen for Trondheim; Bodø for Tromsø

[b] Control group B: The rest of Norway (excluding Trondheim and Tromsø)

diclofenac increased the year prior to the intervention, while it decreased after the intervention. The impact of the intervention was maintained at the end of the follow-up period (Fig. 1b).

Results adjusted for changes in the comparator groups

In Tromsø, the rate of diclofenac prescribing at baseline was significantly lower than in the comparator city, Bodø, and in the rest of Norway. Comparing for baseline trends and relative to Bodø, there was a significant decrease in prescribing of diclofenac the month immediately after the intervention (Table 1). Comparing Tromsø with the rest of Norway, the adjusted effect size of the intervention was − 1.12/1000 inhabitants (95% CI − 1.88 to − 0.35) representing an immediate reduction in prescribing of diclofenac of 16% in Tromsø compared to the rest of Norway. There was no significant difference in slopes between Tromsø and either Bodø or the rest of Norway after the intervention, meaning that the immediate effect of the reduction in prescribing of diclofenac was maintained during the follow-up period.

Naproxen prescribing

Unadjusted results

At baseline, the rates of naproxen prescribing were 4.30/1000 inhabitants in Trondheim and 3.95/1000 inhabitants in Tromsø (Table 2). Following the intervention, the unadjusted intercept change in Trondheim was 1.81/1000 inhabitants (95% CI 0.72 to 2.86 $p < 0.0001$) representing an increase in prescribing in the month after the intervention of 1.8 prescriptions per 1000 inhabitants (Fig. 2a). There was no statistically significant monthly change in the pre-post trend (Table 2). The unadjusted intercept change in Tromsø was 1.61/1000 inhabitants (95% CI 0.97 to 2.25, $p < 0.0001$) (Fig. 2b). There was a statistically significant monthly increase in the pre-post trend, as the rate of prescribing of naproxen was decreasing prior to the intervention (Fig. 2b).

Results adjusted for changes in the comparator groups

In Trondheim, controlling for baseline trends and relative to the rest of Norway, the intercept change

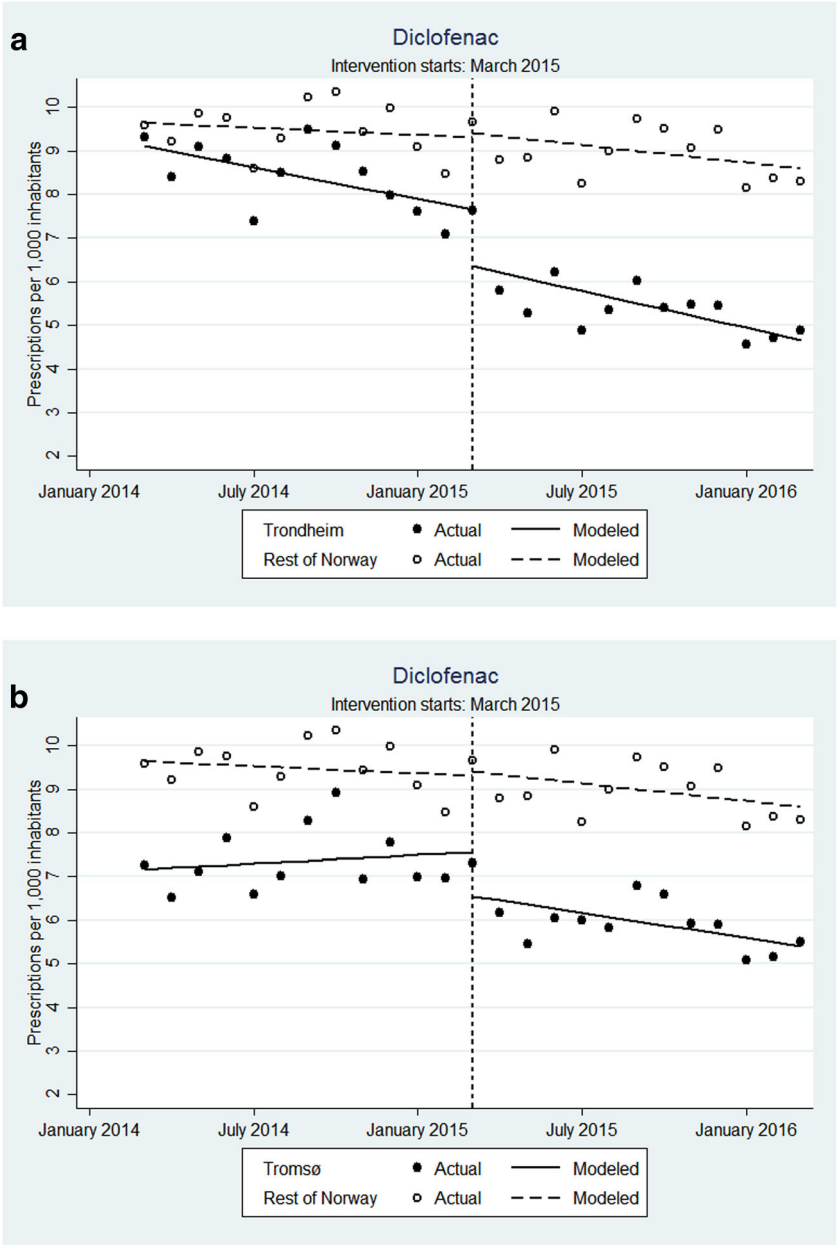

Fig. 1 Actual and modelled diclofenac prescribing. Rate of prescribing of diclofenac in **a** Trondheim, **b** Tromsø and the rest of Norway for 12 months before and after the intervention of an academic detailing programme targeting General Practitioners in Trondheim and Tromsø. Regression with Newey-West standard errors—lag(12)

immediately following the intervention was 1.53/1000 inhabitants (95% CI 0.81 to 2.25, $p < 0.0001$), a relative increase of 24%. In Tromsø, the adjusted intercept change was 1.33/1000 inhabitants (95% CI 0.56 to 2.09, $p < 0.001$), an increase of 41%. Both effect sizes were smaller than those seen with the unadjusted analysis, as prescribing of naproxen was also increasing in the rest of the country during this time (Fig. 2).

Total NSAID prescribing

The baseline rate of prescribing of all NSAIDs was similar in Trondheim (20.3/1000 inhabitants) and Tromsø (20.8/1000 inhabitants), and lower than that seen in the rest of Norway (23.8/1000 inhabitants). Following the intervention, there were no significant changes in levels or trends in either of the intervention areas or the comparators. (See Supplemental Fig. 1).

Discussion

This academic detailing programme caused a marked effect on changing prescribing from diclofenac to naproxen, but the overall prescribing of NSAIDs did not change. The effects on diclofenac prescribing were similar in Trondheim (− 1.40/1000 inhabitants, 18% reduction) and Tromsø (− 1.12/1000

Table 2 Effect estimates of the academic detailing programme on prescribing rate of naproxen

Prescribing of naproxen/1000 inhabitants per month	Trondheim			Tromsø		
	Prescribing rate/1000 inhabitants per month	95% CI	*p* value	Prescribing rate/1000 inhabitants per month	95% CI	*p* value
Unadjusted effect size						
Baseline prescribing in the intervention group	4.30	4.00 to 4.60		3.95	3.77 to 4.12	
Intervention level change (unadjusted)	1.81	0.72 to 2.86	$p < 0.0001$	1.61	0.97 to 2.25	$p < 0.001$
Intervention slope change (unadjusted)	− 0.03	− 0.20 to 0.05	$p = 0.586$	0.13	0.01 to 0.25	$p = 0.033$
Adjusted for change in control group A[a]						
Difference in level between intervention and control A prior to intervention	0.77	0.43 to 1.11	$p < 0.0001$	− 1.02	−1.65 to − 0.39	$p < 0.01$
Difference in slope between intervention and control A prior to intervention	0.12	0.06 to 0.17	$p < 0.0001$	− 0.02	− 0.12 to 0.07	$p = 0.621$
Between group (intervention–control A) difference in level after intervention	1.58	0.90 to 2.26	$p < 0.0001$	1.30	0.42 to 2.17	$p < 0.001$
Between group (intervention–control A) difference in slope after intervention	− 0.05	− 0.18 to 0.07	$p = 0.389$	0.09	− 0.11 to 0.29	$p = 0.363$
Adjusted for change in control group B[b]						
Difference in **level** between intervention and control B prior to intervention	0.29	− 0.10 to 0.68	$p = 0.143$	− 0.07	− 0.41 to 0.28	$p = 0.703$
Difference in **slope** between intervention and control B prior to intervention	0.10	0.03 to 0.16	$p < 0.01$	− 0.06	− 0.12 to 0.01	$p = 0.080$
Between group (intervention–control B) difference in level after intervention	1.53	0.81 to 2.25	$p < 0.001$	1.33	0.56 to 2.09	$p < 0.001$
Between group (intervention–control B) difference in slope after intervention	− 0.05	− 0.19 to 0.08	$p = 0.423$	0.11	− 0.05 to 0.26	$p = 0.163$

[a] Control group A: Bergen for Trondheim; Bodø for Tromsø

[b] Control group B: The rest of Norway (excluding Trondheim and Tromsø)

inhabitants, 16% reduction), when adjusted for any changes in the rest of Norway. The effects on naproxen prescribing were + 1.53/1000 inhabitants (24% increase) in Trondheim and + 1.33/1000 inhabitants (41% increase) in Tromsø when adjusted for any changes in the rest of Norway. The relative increase in Tromsø was higher owing to the lower rate of prescribing at baseline. For both diclofenac and naproxen, the effect of the intervention was immediate and changes were sustained by the end of the 12-month follow-up period. The results can be interpreted to assume that prescribers switched from diclofenac to naproxen, given that there was no overall change in the prescribing of total NSAIDs during this period.

The decline in use of diclofenac in Norway preceded the intervention, with a 3.6% reduction from 2014 to 2015 [9] and continued in the follow-up period as illustrated in Fig. 1. This can probably be attributed to increased knowledge of the adverse effects of diclofenac amongst prescribers due to the general information provided by the regulatory authorities. The larger decrease in the use of diclofenac in the intervention cities indicates that academic detailing is an effective way of updating prescribers, even when presenting information that already has been given via more traditional ways of communication. The change in level of prescribing at the time of intervention in both Trondheim and Tromsø indicates that there was an immediate effect of the intervention. With interventions for changing prescribing there is sometimes an immediate effect that wanes after time. The lack of statistically significant difference in slope between the intervention areas and the comparators show that the effect of the intervention was sustained 12 months later.

The main message in our campaign was considered quite clear and simple. At the same time, as use of one drug (diclofenac) was discouraged, we presented an alternative with similar therapeutic effect and indications (naproxen). This is an easy change for the prescriber, as he or she could follow our advice, and still offer the patient an oral NSAID prescription. Although the campaign also gave general warnings about the use of systemic NSAIDs, the total prescribing rate of NSAIDs did not change. The reasons for the lack of reduction in total prescription rate of NSAIDs are unclear. One reason could be that it is easier for the GP to switch to a similar drug with a more favourable side effect profile (i.e. naproxen)

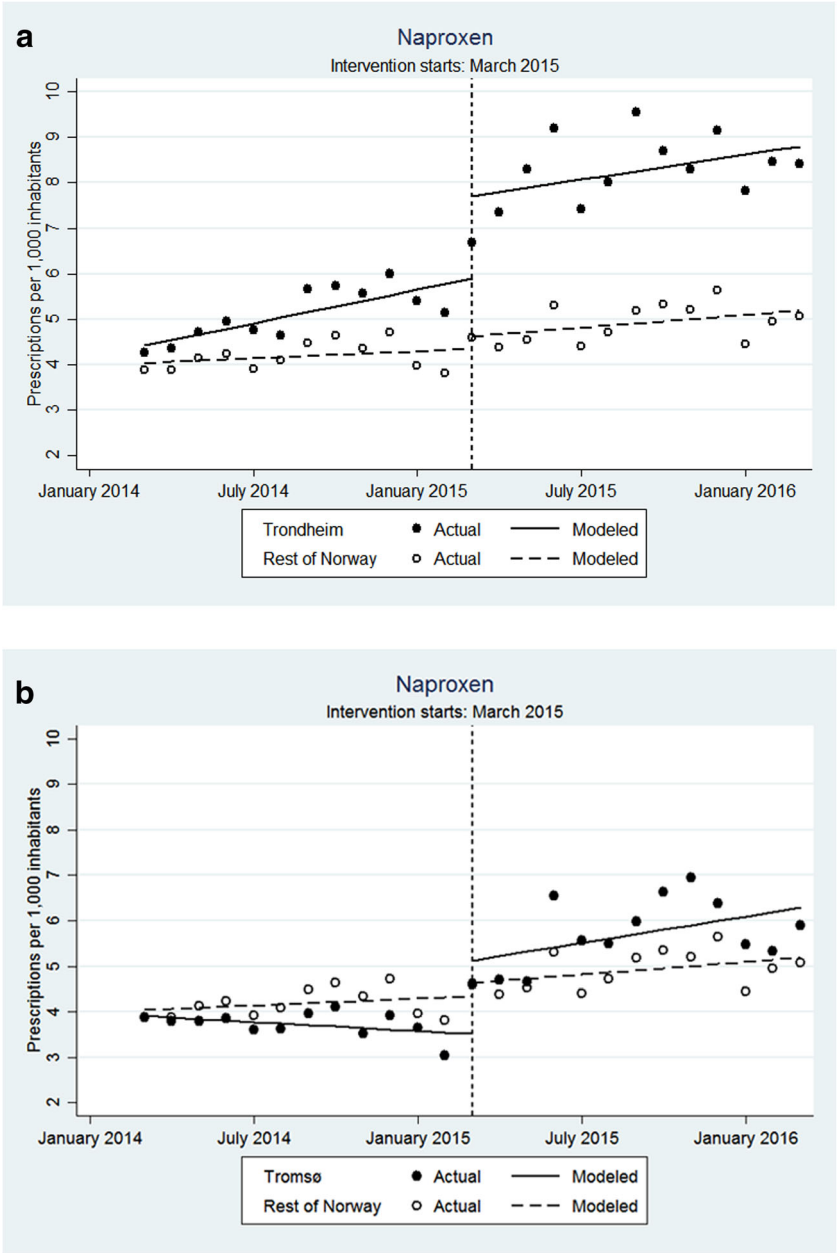

Fig. 2 Actual and modelled naproxen prescribing. Rate of prescribing of naproxen in **a** Trondheim, **b** Tromsø and the rest of Norway for 12 months before and after the intervention of an academic detailing programme targeting General Practitioners in Trondheim and Tromsø. Regression with Newey-West standard errors—lag(12) (Fig. 2a), lag(4) (Fig. 2b)

than to stop or reduce prescribing. Another reason could be that the campaign focused on the differences between diclofenac and naproxen, and that the general warnings on use of NSAIDs, particularly for elderly patients, were not communicated clearly enough, even though this was one of the key messages. As we did not have access to individual prescribing rates, we could not evaluate if there was a reduction in the total prescribing rate for NSAIDs in elderly patients.

Previous studies have shown that academic detailing, both alone or when combined with other interventions, has consistent and small, but potentially important, effects on prescribing [20]. There are few published studies specific to the prescribing of NSAIDs. A study from Scotland found that clinical outreach as part of a complex intervention reduced the proportion of high-risk prescribing of NSAIDs [21]. A recently published study conducted in Belgium found a 19% increased odds for being reimbursed for a recommended NSAID amongst those reimbursed for any NSAID, but no significant impact on related outcomes after academic detailing on prescribing of recommended NSAIDs in osteoarthritis. Their analyses led them to the same conclusions as ours, i.e. that an advice to change the prescribed drug to a similar but safer drug is more easily accepted than an advice to reduce overall prescribing [15]. A study from Spain compared changes in prescribing of NSAIDs both after one-to-one and group sessions. Both study groups improved their prescribing as measured on an indicator

scale compared to a control group, and although the improvement was quite small, it was about threefold higher after one-to-one meetings than after group sessions (6.5% vs 2.4%) [12]. An Australian study also showed a reduction in both prescribing (− 9%) of NSAIDs and hospitalisation for upper gastrointestinal tract ulcerations after an academic detailing programme on NSAIDs [14]. All those studies differ from ours in both design and outcomes, but the results from our study confirm earlier findings that academic detailing is effective in improving the quality of NSAID prescribing.

There is a lack of a clear consensus about how academic detailing is best performed [22–24]. Literature reviews have found large variations both in the results from academic detailing programs and how the interventions are performed [20, 22, 24]. One review found that the average visit duration was nearly 90 min, while 60-min visits were most common [22]. In our intervention, the visits had an average duration of 24 min. The relatively shorttime consumption, chosen to correspond to the length of one patient consultation in general practice in Norway, makes the intervention easier to accept for the GPs, who in Norway are paid per consultation. The participating GPs were not compensated to accept the visit, so it was important to keep the duration of the visit to a minimum. The relatively short visits also reduced the labour-intensiveness of the intervention, a common barrier to academic detailing [22]. Our study shows that a shorter visit may be sufficient to facilitate change, at least for campaigns with a clear and simple message that is easy to adhere to. This finding is similar to that in the Belgian study cited above, where the time frame was 15–20 min [15].

Our academic detailing programme was well received by the participating GPs. Amongst those responding to the electronic questionnaire sent to them after the visit, 90% considered that academic detailing was a suitable method for producer-independent, evidence-based information. In addition, 91% of responders answered that it was likely or very likely that they would change their prescribing of NSAIDs after the visit. These results indicate that the academic detailers had high credibility and that the GPs trusted the validity of the key messages.

A major strength of our study is the application of segmented regression in interrupted time series. We used recently published recommendations on how to use rigour in the conduct and reporting of interrupted time series analyses in drug utilisation studies [18], and applied a systematic approach to minimise the likelihood of potential biases overestimating the effect size [19]. A criticism of interrupted time series analysis is that it is not possible to disentangle the impact of co-interventions; however, including control groups with physicians who would also be exposed to the same co-interventions adds strength to our analysis and validity of our findings [19]. Co-interventions were national and would be expected to affect the two intervention cities and the rest of Norway in a similar way, so it is unlikely that co-interventions would add to the differences between the groups.

As a prescription in Norway is valid for a period of 365 days, the full effect of an intervention on filling data from pharmacies would be somewhat delayed, even though we expect that the effect of new NSAID prescriptions from the physicians would take place immediately after the academic detailing visit. Nevertheless, we assume this delay to be shorter for NSAIDs, which are mainly used for acute conditions, using non-reiterated prescriptions, than drugs used for typically chronic diseases like hypertension and hypercholesterolemia. To be conservative in our approach, we decided not to include a lag period in our analyses; in fact, including a lag period could in principle tends to increase the effect of an intervention.

Finding a suitable comparator in interrupted time series regression is difficult and requires that there were no significant differences between the intervention groups and comparators in terms of baseline levels and slopes. Our predefined plan was to use Bergen as a comparator for Trondheim, and Bodø for Tromsø. However, neither cities served as an ideal comparator, owing to the slight (but significant) differences in the rate of prescribing and/or slopes before the intervention. Therefore, we primarily present our effect estimates adjusted for changes seen in the rest of Norway, although we also present data according to our original plan, adjusted for changes in the two comparator cities.

A limitation of our study is that we did not have actual prescribing data. We used filled prescriptions at pharmacies, retrieved from the NorPD, as a measure of prescribing. We, however, believe that this is a reliable measure of total prescribing, as most patients would be expected to fill their prescription, particularly related to drugs for the treatment of painful conditions. Moreover, there is no reason to expect a difference in the percentage of prescriptions being filled based on which NSAID was being prescribed. It should also be mentioned that although the use of coxibs was discouraged in the campaign (Box 1), we did not analyse prescribing trends for this subgroup separately. The reason for this decision was that the total sales of coxibs in Norway already before the campaign was so low that a further reduction could not be expected; therefore, the aim with the recommendation to avoid coxibs was to prevent a shift from diclofenac to coxibs. Another limitation is that the data from NorPD includes all filled prescriptions, including prescriptions from GPs as well as from other prescribers, e.g. specialists working in hospitals or having their own practice. Our campaign only targeted GPs, and we would not expect other physicians to change their prescribing. Additionally, we were not able to restrict the analysis to those GPs that received the intervention. We visited 90% of all GPs in Trondheim and 76% of all GPs in Tromsø. Both these factors would, however, lead to an underestimation of the impact of the intervention. Similarly, as we were unable to identify individual prescribing trends, we could not examine *which* components of the intervention or which characteristics of the participating GPs that specifically correlated with the prescribing changes. Finally, it is a weakness that we

were not able to calculate the exact cost of the programme and to evaluate the cost-effectiveness of our intervention. Thus, we cannot compare it with cost-effectiveness of other interventions.

Conclusion

We conclude that academic detailing was found to be an effective method to change the choice of prescribed NSAID amongst GPs, being a potentially important method for providing GPs with independent, evidence-based updates on pharmacotherapy to improve prescribing.

Authors' contributions HCL, RD and OS conceived the study and accessed the data. EH conducted the analyses and wrote the methods and the results with contributions from HCL. HCL took lead authorship of the paper with contributions from EH, RD and OS. All authors have approved the final version of the manuscript.

Funding The study is partly funded by a grant from The Norwegian Directorate of Health (NOK 400 000). It, however, had no role in the study design, data collection, analysis, interpretation of results or writing the manuscript.

Compliance with ethical standards

Ethics approval and consent to participate As no individual data from patients or GPs was collected during the study, there was no need for consent to participate.

Conflict of interest HCL and RD were involved in planning the AD programme and were part of the group performing the visits. HCL, RD and OS are employed at the department where the AD programme was managed.

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