Impact of guidance publication on primary care prescribing rates of simple analgesia: an interrupted time series analysis in England

Reichel Hannah; Stanbrook Rhian; Johnson Hans; Proto William; Shantikumar Mary; Bakhshi Pooja; Hillman Sarah; Todkill Dan; Shantikumar Saran

DOI: https://doi.org/10.3399/bjgp20X714101

To access the most recent version of this article, please click the DOI URL in the line above.

Received 09 April 2020
Revised 24 August 2020
Accepted 25 August 2020

© 2020 The Author(s). This is an Open Access article distributed under the terms of the Creative Commons Attribution 4.0 License (http://creativecommons.org/licenses/by/4.0/). Published by British Journal of General Practice. For editorial process and policies, see: https://bjgp.org/authors/bjgp-editorial-process-and-policies

When citing this article please include the DOI provided above.
Impact of guidance publication on primary care prescribing rates of simple analgesia: an interrupted time series analysis in England

Hannah Reichel, MBioSci 1
Rhian Stanbrook, MB BChir, MRCGP 2
Hans Johnson, MRes 3
William Proto, PhD, MPH 1
Mary Shantikumar, MBChB, MRCGP 4
Pooja Bakhshi, MBChB, DTMH 5
Sarah Hillman, PhD, MRCGP 1
Dan Todkill, MBChB, MPH 1
Saran Shantikumar, MBChB, PhD 1

1 Warwick Medical School, University of Warwick, Coventry, UK.
2 Medwyn Surgery, Surrey, UK
3 Bristol Medical School, University of Bristol, Bristol, UK
4 Central Surgery, Rugby, UK
5 Health Education West Midlands, Birmingham, UK

Correspondence to:
Dr S Shantikumar, Clinical Lecturer in Public Health
Room B163, Warwick Medical School, University of Warwick, Coventry, UK. CV4 7AL
Email: saran.shantikumar@warwick.ac.uk

Abstract Word Count: 248 words
Manuscript Word Count: 2584 words (excl. abstract, figures and references)
Abstract

Background
In March 2018, NHS England published guidance for Clinical Commissioning Groups (CCGs; NHS bodies that commission health services for local areas) to encourage implementation of policy to reduce primary care prescriptions of over-the-counter medications, including simple analgesia.

Aims
To investigate: the impact of guidance publication on prescribing rates of simple analgesia (oral paracetamol, oral ibuprofen and topical non-steroidal anti-inflammatory drugs [NSAIDS]) in primary care; CCG implementation intentions; and whether it has created a health inequality based on socioeconomic status.

Design and Setting
Interrupted time series analysis of primary care prescribing data in England.

Methods
Practice-level prescribing data from January 2015 to March 2019 were obtained from NHS Digital. Interrupted time series analyses assessed the association of guidance publication with prescribing rates. The association between practice-level prescribing rates and Index of Multiple Deprivation score (a marker of socioeconomic deprivation) before and after publication was quantified using multivariable Poisson regression. Freedom of information requests were submitted to all CCGs.

Results
There was a 4% reduction in prescribing of simple analgesia following guidance publication (adjusted incidence rate ratio [aIRR] 0.96, 95% CI 0.92-0.99, p=0.027), adjusting for underlying time trend and seasonality. Practice-level prescribing rates were greater in more deprived areas. There was considerable diversity across CCGs in whether or how they chose to implement the guidance.

Conclusion
Guidance publication was associated with a small reduction in the prescribing rates of simple analgesia across England, without evidence of creating an additional health inequality. Careful implementation by CCGs would be required to optimise cost-saving to the NHS.

Keywords
Analgesia, general practice, interrupted time series analysis, prescriptions
How this fits in

As part of a medication optimisation strategy, in March 2018 NHS England published guidance for Clinical Commissioning Groups (CCGs; NHS bodies that commission health services for local areas) that included a list of medications that were available over-the-counter and that should not be routinely prescribed by general practitioners in the NHS. Specifically examining simple analgesia, specifically paracetamol and ibuprofen, we found only a small reduction in national prescribing rates following publication of the guidance. Information collected through Freedom of Information requests to CCGs found a diverse approach as to how the guidance would be implemented, with some areas having no plans for implementation. The findings suggest that guidance publication alone had little benefit in reducing prescribing rates. Careful implementation would be required to achieve the full potential cost-saving benefit of the guidance to the NHS, although care needs to be taken to ensure that implementation does not result in a health inequality with the requirement for patients to purchase medication items themselves.
Introduction

In light of the current funding deficit in the NHS, it is imperative that spending is made more efficient – a sentiment acknowledged by the NHS Long Term Plan published in 2019. One key area for improvement that has been previously identified is medication optimisation – ensuring medicines are both clinically effective and cost-effective. Pharmaceutical spending is a common source of financial strain on healthcare systems worldwide, and is one of the highest NHS expenditures, second only to staffing. NHS England published guidance in March 2018 specifying medications that should not be routinely prescribed in primary care, including items that are available for purchase over the counter (see Methods). Whilst this guidance allows for a nationally coordinated response, the decision to implement it as a policy, as well as the choice of implementation strategies, lies with Clinical Commissioning Groups (CCGs) – statutory regional NHS bodies that are responsible for the planning and commissioning of healthcare services for their local area.

Prior to publication of this guidance, stakeholder consultation revealed a fear that implementation could perpetuate health inequalities given the consequent need for people to purchase some medications themselves over the counter, which some individuals may not be able to do. Subgroups thought to be at particular risk were the disabled, the elderly, those of lower socioeconomic status or those who have a limited capacity for self-care.

The estimated annual spend across the NHS on simple analgesia for minor conditions associated with pain, discomfort or fever is £38 million, or around 7% of total spending on OTC medication in the year prior to 2017. The recent NHS England guidance suggests that people should be encouraged to supply their own OTC analgesics for minor conditions such as colds, earache, teething pain and self-limiting musculoskeletal pain, including those who would normally be exempt from paying the usual prescription charge in England, such as those aged under 16 or over 60 years, pregnant women, individuals on income support and those with one of a specified list of medical conditions. Patients in England pay a fixed per-item prescription charge, which does not necessarily cover the total cost.
incurred by the NHS in prescribing these medications. However, for those exempt from paying prescription charges, a requirement to purchase their own OTC medications will result in a personal cost.

The aim of this study is to evaluate the impact of publication of the March 2018 NHS England guidance on primary care prescribing of simple analgesia available over the counter: paracetamol tablets and suspensions; ibuprofen tablets and suspensions, and topical non-steroidal anti-inflammatory drugs, as identified in the guidance. Specifically we (1) explore whether there has been a change in the prescribing rates of simple analgesia since the publication of the guidance; (2) assess whether there is any evidence the guidance has resulted in a health inequality by socioeconomic deprivation; and (3) explore the extent to which individual CCGs have considered and implemented this guidance.
Methods

Description of the Guidance

NHS England published the document “Conditions for which over the counter items should not routinely be prescribed in primary care: Guidance for CCGs” in March 2018\(^5\). Aimed at Clinical Commissioning Groups, this guidance includes items that can be purchased over the counter (OTC), often at a lower personal cost than that which would be incurred by the NHS in part due to additional administrative and dispensing costs, as well as medications which lack robust evidence for clinical effectiveness. Some drug classes are subject to specific exceptions where they may justifiably be prescribed; for example, it is suggested that vitamins are not prescribed except where there is a medically diagnosed deficiency, osteoporosis or malnutrition. The guidance also provides a list of “general exceptions” – criteria where the guidance need not apply and OTC medication may be prescribed by the primary care physician. These include where patients are prescribed an OTC medication for long-term conditions (such as chronic arthritis), where patients have complex medical issues (such as immunosuppression), or where an OTC medication is being prescribed for an unlicensed indication.

Data Sources

Primary care prescribing data in England are published by NHS Digital (https://digital.nhs.uk) on a monthly basis, detailing the number of items, quantity and cost of NHS prescriptions dispensed in the community by individual primary care practices\(^9\). Monthly datasets were downloaded from January 2015 to March 2019 (up to 12 months after the publication of the NHS England guidance – hereby also referred to as the intervention).

A list of British National Formulary (BNF) codes was curated for each of the simple analgesics mentioned in the NHS England policy (Supplementary Box 1)\(^10\). Specifically, this included paracetamol
tablets (up to 500mg), paracetamol suspensions, ibuprofen tablets (up to 400mg), ibuprofen suspensions, and topical non-steroidal anti-inflammatory drugs (NSAIDs), and excluded opioid medications. Branded and generic medications were included. Prescription-only medications, and those combined with other drugs (such as co-codamol) were excluded. The monthly prescribing datasets were filtered, by BNF code, to include only simple analgesia.

The number of items of simple analgesia prescribed by each practice every month was aggregated. Information on age/sex-stratified practice list sizes, published quarterly by NHS Digital\textsuperscript{11}, were retrieved to calculate the monthly prescribing rate per 1000 patients. Practice-level socioeconomic deprivation data, as quantified by the Index of Multiple Deprivation (IMD) score\textsuperscript{12}, were retrieved from Public Health England\textsuperscript{13}, recoded as quintiles, and linked to prescribing data as previously described\textsuperscript{14}.

**Interrupted Time Series Analysis**

To elicit an effect of the intervention on primary care prescribing, interrupted time series analyses (ITSA\textsc{s}) were conducted using segmented Poisson regression, with the number of items prescribed per month as the dependent variable, using the total GP-registered population as an offset variable to model rates\textsuperscript{15}. The ITSA model include month as a linear variable to model for an underlying linear time trend (with month in the dataset labelled from 1 to 51, for the 51 monthly prescribing datasets used), and the intervention as a dummy variable, coded “0” for the pre-intervention period and “1” for the post-intervention period. A second (“adjusted”) model additionally accounted for seasonality in the underlying prescribing rates, using a harmonic term based on the month of the year and using two sine/cosine pairs per 12-month period\textsuperscript{15,16}. Initial analyses suggested overdispersion of the data, so a quasi-Poisson model was used. It was hypothesised that the intervention would result in a level (step) change in the outcome, given how widely the NHS England guidance was reported at the time of publication\textsuperscript{17,18}. Any changes in linear trend after this point would likely be affected by how well the guidance was subsequently implemented, so we did not include an analysis of this in our model. For
this analysis, the pre-intervention time period was from January 2015 to March 2018, and the post-intervention time period was from April 2018 to March 2019. There were no documented missing data in the NHS Digital prescribing or practice list size data, and no sensitivity analyses were conducted.

**Association with Deprivation**

The association between practice-level IMD score and annual simple analgesia prescribing rates, 12 months before and after the intervention, was tested using univariate and multivariable Poisson regression, the latter adjusted for the practice proportion of males, proportion of over-65s, and practice list size, as we have previously found practice age and sex distribution and practice list size to be confounders for practice-level prescribing of other medications. Poisson regression analyses are presented as unadjusted or adjusted incidence rate ratios (IRRs), comparing the relative rate of prescribing in each IMD score quintile with practices in quintile 1 as the reference group (the least deprived quintile). To visualise geographic disparity in prescribing rates, CCG-level prescribing was stratified by deciles and plotted on a choropleth map, with the use of CCG boundary shapefiles published by the Office for National Statistics. For this analysis, the pre-intervention time period was from April 2017 to March 2018 and the post-intervention time period was from April 2018 to March 2019.

A $p$ value < 0.05 was considered statistically significant. All data were analysed, and all plots generated, using the software R (v3.5.3). The template R script is available at [https://github.com/sirsazofduck/2020ReichelH](https://github.com/sirsazofduck/2020ReichelH). No ethical approval was required as all data used are publicly available, and there is no published protocol for this study.

**Freedom of Information Requests**
A Freedom of Information (FOI) request was submitted to all 191 CCGs (as of April 2019) to request information concerning their level of consideration and implementation of the NHS England policy and the prescribing of analgesics available over-the-counter (see Supplementary Box 2 for the full list of questions). As there was considerable diversity in the methods and strength of implementation (from “position statements” to local guideline development, with or without additional education or incentives), as well as in the timing of implementation (which in some cases occurred before the publication of the national guidance), we were not able to examine whether or not the strength of implementation was associated with the magnitude of the level or trend of change of prescribing rates. A qualitative analysis of the CCG responses is outside the scope of the current study and will be conducted separately.
Results

Trends in Prescribing Rates

Data from 7914 practices were included across the study period, covering ~120 million prescriptions for oral paracetamol, oral ibuprofen and topical NSAIDs. When considering all medication groups together, there was a reduction in the number of items prescribed per 1000 registered patients per month by GPs in England since the introduction of the NHS England guidance in March 2018 (the intervention; crude prescribing rates 42.3 [before intervention] versus 35.5 [after intervention] per 1000 patients per month). After adjusting for an underlying linear decline in prescribing rates over time and seasonality, the intervention was associated with a 4.4% level change reduction in prescribing rates (adjusted IRR [aIRR] 0.956, 95% CI 0.919-0.995, p=0.027, Figure 1). The time- and season-adjusted prescribing rates reduced from 38.5 to 36.6 prescriptions per 1000 per month from the month before to the month after the intervention.

The ITSAs for each of the subgroups of simple analgesia showed similar trajectories, with all except ibuprofen tablets/capsule demonstrating a small statistically significant reduction in prescribing rates following the intervention, after accounting for the underlying long-term linear time trend and seasonality (Table 1). The greatest level change was seen in ibuprofen suspensions (13.2% reduction in prescribing rate, aIRR 0.868, 95% CI 0.758-0.993, p=0.045), and no level change was seen in ibuprofen tablets and capsules (aIRR 0.991, 95% CI 0.931-1.055). The time series for all individual medication groups can be found in Supplementary Figure 1.

Of all medication groups analysed, the rate of prescriptions for all but topical NSAIDs had begun to decrease prior to both the date the guidance was published and the related consultation period (Supplementary Figure 1). Indeed, the rate of topical NSAID prescriptions was steadily increasing. Following the intervention, the immediate level change reduction was not sustained, and prescribing has continued to rise again (Figure 2). The average actual spend on simple analgesia per 1000 patients for the 12-month period after the intervention was £98, compared to £123 in the 12 months prior to
the intervention. It is not possible to separate how much of this is attributable to the intervention rather than to the underlying time trend. However, using the previous 12 months as a baseline, the 4.4% reduction in prescribing associated with the intervention equates to an approximate additional reduction of £5.40 per 1000 patients, or ~£320,000 saving to the NHS across England for the year.

**Association of Prescribing with Deprivation**

In the 12 months before the intervention, there was a higher rate of prescribing of simple analgesia in more deprived practices (329 items per 1000 registered patients in the least deprived decile vs. 612 in the most deprived decile; 709 or 710 practices per decile). In the 12 months after the intervention, this association persisted (Figure 3), although there was a general reduction in prescribing rates across all deciles (Supplementary Table 1A).

In a multivariable Poisson regression analysis, in the 12 months before the intervention, the rate of prescribing of simple analgesia was around 2.5 times higher in practices in the most deprived quintile compared to those in the least deprived quintile (aIRR 2.44, 95% CI 2.33-2.57). Similar differences were found in the 12 months after the intervention (aIRR 2.42, 95% CI 2.30-2.56, for the most vs. least deprived quintile, Supplementary Table 1B). The geographical variation of prescribing rates by CCG is shows in Supplementary Figure 2.
Guidance Implementation by Clinical Commissioning Groups

Freedom of Information requests were submitted to all 191 CCGs (Supplementary Box 2). Of these, 170 (89%) had a formulary for use by primary care prescribers. 172 (90%) CCGs claimed to have given consideration to the NHS England guidance, with 86 (45%) confirming that they had developed their own policy regarding simple analgesia prescribing (28 had a policy before March 2018). A further 68 (36%) released a “position statement” or directly replicated the NHS England guidance, with 18 (9%) others suggesting that a CCG-specific policy was currently under development.

Relevant education for prescribers had been provided by 120 (62%) CCGs. A wide variety of strategies had been used, the most common being: electronic or written communications; meetings to discuss the policy; and training sessions (including e-learning). Financial incentivisation is being used by 55 (28%) CCGs, with 26 (13%) indicating plans to enforce the guidance.
Discussion

Summary

NHS England published guidance for CCGs in March 2018 to encourage primary care prescribers to rationalise the prescription of medications that were also available for purchase over the counter. Focusing on the impact on simple analgesia prescribing, we found that the intervention resulted in a significant additional reduction in prescribing rates after accounting for the underlying long-term decline in prescribing and seasonal variation. However, the magnitude of reduction varied with different analgesics, being the highest for suspension ibuprofen. The reasons for this are unclear.

Perhaps individuals with short-term self-care conditions that the NHS England guidance targets are more likely to be prescribed suspension ibuprofen (e.g. children with acute febrile illness). Formulations that are more likely to be used for longer-term pain management, for example tablets or capsules, may continue to be prescribed in line with the guidance if for such indications and thus prescribing rates would reduce by a lesser degree than other formulations, such as suspensions, that may be less likely to be prescribed for long-term pain management. This could also partly explain the different (increasing) prescribing profiles seen for topical NSAIDs – a prescription for this formulation may be more likely sought for longer-term pain management. There is also the possibility that willingness of patients to purchase simple analgesia over the counter is inversely proportional to the personal cost incurred. Topical NSAIDs are usually more expensive over-the-counter than tablet or capsule formulations, therefore prescribers may be more willing to provide a script, especially if a patient qualifies for free prescriptions. However, the underlying reasons for this unusual trend require further exploration.

On exploring whether there was any change in the socioeconomic gradient of prescribing before and after publication of the guidance, we found no evidence to suggest a widening of the existing inequality of prescribing rates by Index of Multiple Deprivation score decile. Finally, through Freedom
of Information requests, we found CCGs were employing a range of approaches for implementing the guidance, from no implementation to policy development and education.

Given the disparity in when and how CCGs implemented this guidance, we were unable to examine the effect of implementation measures. However, it is unlikely that CCG implementation resulted in the rapid level change in prescribing found in this study. The wide publicity surrounding the guidance publication may have resulted in immediate modification of prescribing behaviours. Indeed, publicity of guidance and publications have been previously noted to be associated with changes in prescribing, although it is difficult to attribute causation\textsuperscript{21,22}.

**Comparison with Existing Literature**

The pre-intervention trend of declining prescribing rates of simple analgesia suggests prior influencing factors. NHS “111” services may have had some impact. In England, the “111” telephone service provides medical advice and signposting to appropriate services. By suggesting treatment plans or pharmacy services, the “111” service may reduce need for patients to seek prescriptions from their GP, and data from the service suggest the frequency of calls taken has increased by ~25% between 2015 and 2019\textsuperscript{25}.

Despite prior concerns around health inequalities, we found no change in the relationship between practice-level socioeconomic deprivation and prescribing rates of simple analgesia before and after the intervention. This may in part be due to the general exceptions clause in the guidance, with the higher prescribing rate seen in more deprived practices reflecting a higher prevalence of chronic conditions that require simple analgesia\textsuperscript{26}. In practice, the requirement for patients to buy simple analgesia themselves risks the least well-off or vulnerable in society being unable to purchase or access required medication. We cannot exclude the creation of such inequality by this guidance based on the results of our analysis. Furthermore, health inequalities can occur in domains other than deprivation level, such as by ethnicity, and these were not considered in our analysis of aggregate
practice-level data. There is also a risk that shifting purchasing responsibility to patients results in additional inappropriate use of OTC simple analgesics. Indeed, inappropriate use has been described to be a risk of OTC NSAID purchasing, with gaps identified in consumer knowledge\textsuperscript{27,28}, and it is possible that such outcomes are associated with deprivation.

In addition to the finding that many CCGs were replicating the NHS England guidance as policy, or developing their own, some had used or considered additional strategies for implementation, including education, financial incentives and enforcement. A systematic review found that educational interventions improved prescribing competency in both medical and non-medical prescribers\textsuperscript{29}. Despite some evidence for their effect\textsuperscript{30-32}, some have questioned whether the introduction of incentivisation or enforcement may impact the delivery of proper and ethical care\textsuperscript{33,34}. This notion is particularly concerning here as there are genuine exceptions whereby the prescribing of OTC medications is justified. In addition, it may also leave GPs in breach of their General Medical Services contracts to refuse to prescribe medications outside of the guidance\textsuperscript{35}. As our analysis did not compare linear prescribing trend changes before and after guidance publication, we are unable to make inferences around the effectiveness of different forms of implementation.

**Strengths and Limitations**

The strengths of this study include the inclusion of primary care prescribing across England, with a long lead-in duration before the studied intervention. The analysis of individual CCG implementation measures provides evidence of heterogeneity in actions across the country, and this is an area where further work is required.

There are limitations in the presented study. We used aggregated practice-level prescribing data, so it was not possible to determine the indications for prescriptions. The deprivation analyses were not adjusted for confounders other than age, sex and practice list size. Individual patient data would be required to identify and account for other factors which may drive prescribing, such as the presence
of chronic disease, the incidence of acute febrile illness, and the overall age distribution of the registered patients. Furthermore, the deprivation analyses required the assumption that each practice only had a single deprivation score. Individual-level data analyses are required to confirm whether or not patients from more deprived backgrounds are not disadvantaged by the guidance. A second limitation surrounds the use of ITSA in general; that the level changes in prescribing rates seen may not have been secondary to the publication of the NHS England guidance but rather to other factors. However, most of the level changes seen were statistically significant and the new guidance was widely publicised, so it is possible this influenced prescribing behaviours. Thirdly, we, could not ascertain whether the form of CCG implementation influenced prescribing rates.

Implications for Research and Practice

Further work is required to identify which CCG implementation measures bring about the greatest impact on prescribing behaviour. Ultimately, while promoting self-care and the use of alternative healthcare avenues may play a key role in medicines optimisation, mere publication of guidance on prescribing restrictions may only result in a modest cost-saving to the NHS. CCGs play a key role in ensuring effective implementation, and the value and potential harms of such implementation – including any detrimental effects on the doctor-patient relationship – will need to be the focus of future work.
Additional Information

Funding

SH and SS are funded by National Institute of Health Research (NIHR) Clinical Lectureships. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the UK’s Department of Health and Social Care. No specific funding was sought for the presented analysis.

Ethical Approval

Not required – this study used publicly available data only.

Competing Interests

None declared
References

2. NHS. The NHS Long Term Plan. 2019. NHS.
Figure 1. Adjusted model of prescribing rates of all simple analgesia.

Seasonal model of primary care prescribing rates per 1000 registered patients across England for all simple analgesia considered (ibuprofen/paracetamol tablets, capsules and suspensions, and topical NSAIDs), from January 2015 to March 2019. Red line shows the predicted trend based on the seasonally adjusted regression model; green line shows the deseasonalised trend. Grey box represents the post-intervention period (after March 2018).
Figure 2. Seasonally adjusted model of prescribing rates of topical NSAIDs.

Seasonal model of primary care prescribing rates per 1000 registered patients across England for topical NSAIDs, from January 2015 to March 2019. Red line shows the predicted trend based on the seasonally adjusted regression model; green line shows the desesasonalised trend. Grey box represents the post-intervention period (after March 2018).
Figure 3. Average practice prescribing rates of simple analgesia by deprivation decile.

Upper panel is pre-intervention; lower panel is post-intervention. Deprivation deciles stratified according to practice Index of Multiple Deprivation (IMD) score. Prescribing rates given as number of items of simple analgesia prescribed per 1000 registered patients over a 12-month period. Error bars show the 95% confidence intervals.
Table 1. Effect of the intervention on prescribing rates of simple analgesia.

For all, and for each subgroup of, simple analgesia, the percentage reduction in prescribing rates associated with the intervention is given for the time- and seasonally-adjusted model, along with the IRR/aIRR and 95% confidence intervals. The slope coefficients for the linear trends before and after the intervention are shown (as change in prescribing rate per 1000 registered patients per month).

(aIRR = adjusted incidence rate ratio; CI = confidence interval)

<table>
<thead>
<tr>
<th>Medication Group</th>
<th>% reduction</th>
<th>aIRR (95% CI)</th>
<th>p value</th>
<th>pre-intervention slope (by month)</th>
<th>post-intervention slope (by month)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All simple analgesia</td>
<td>4.4%</td>
<td>0.956 (0.919, 0.995)</td>
<td>* 0.027</td>
<td>-0.22</td>
<td>-0.18</td>
</tr>
<tr>
<td>Paracetamol tablets/capsules</td>
<td>3.9%</td>
<td>0.961 (0.925, 0.999)</td>
<td>* 0.05</td>
<td>-0.15</td>
<td>-0.12</td>
</tr>
<tr>
<td>Paracetamol suspensions</td>
<td>9.3%</td>
<td>0.907 (0.827, 0.995)</td>
<td>* 0.045</td>
<td>-0.02</td>
<td>-0.02</td>
</tr>
<tr>
<td>Ibuprofen tablets/capsules</td>
<td>0.9%</td>
<td>0.991 (0.931, 1.055)</td>
<td>0.772</td>
<td>-0.06</td>
<td>-0.04</td>
</tr>
<tr>
<td>Ibuprofen suspension</td>
<td>13.2%</td>
<td>0.868 (0.758, 0.993)</td>
<td>* 0.045</td>
<td>-0.01</td>
<td>-0.01</td>
</tr>
<tr>
<td>Topical NSAIDs</td>
<td>9.0%</td>
<td>0.910 (0.873, 0.948)</td>
<td>* &lt; 0.001</td>
<td>0.03</td>
<td>0.03</td>
</tr>
</tbody>
</table>