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Low-value pharmaceutical care among Dutch general practitioners: a retrospective cohort study

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Abstract

Background: Low-value pharmaceutical care exists in general practice. However, the extent among Dutch general practitioners (GPs) remains unknown.

Aim: To assess the prevalence of low-value pharmaceutical care among Dutch GPs.

Design and Setting: Retrospective cohort study using patient record data.

Method: We examined the prevalence of three types of pharmaceutical care, topical antibiotics for conjunctivitis, benzodiazepines for non-specific lower back pain (LBP), and chronic acid reducing medication (ARM) prescriptions, prescribed by GPs between 2016-2019. Multilevel logistic regression analysis was performed to assess prescribing variation and the influence of patient characteristics on receiving a low-value prescription.

Results: Large variation in prevalence and practice variation was observed among the examined types of low-value pharmaceutical GP care. Between 53%-61% of patients received an inappropriate antibiotics prescription for conjunctivitis, around 3% of LBP patients received an inappropriate benzodiazepine prescription and 88% received an inappropriate chronic ARM prescription during the years examined. The odds of receiving an inappropriate antibiotic or benzodiazepine prescription increased with age ($p<0.01$), but decreased for chronic inappropriate ARM prescriptions ($p<0.01$). Gender affected only the odds of receiving a non-indicated chronic ARM, with men being at higher risk ($p<0.05$). The odds for receiving an inappropriate ARM also increased with neighbourhood socio-economic status ($p<0.05$). Increasing practice size also decreased the odds of inappropriate antibiotic and benzodiazepine prescriptions ($p<0.01$).

Conclusion: Our results show that the prevalence of low-value pharmaceutical GP care varies among the clinical problems examined. Significant variation in inappropriate prescribing exists between different types of pharmaceutical care - and GP practices.

Keywords: Medical Overuse, Inappropriate Prescribing, General Practitioners, General practice

How this fits in:

The extent of low-value prescribing among Dutch General Practitioners (GPs) is largely unknown. Obtaining insight into the prevalence of low-value care is an essential first step in the process of improving the quality of care. In close collaboration with the Dutch College of General Practitioners, we assessed three types of low-value GP pharmaceutical care. This information could be used to design a campaign, nationally or locally, in order to improve guideline consistent prescribing behaviour.

Introduction

Low-value care, defined as care that is unlikely to benefit the patient given the potential harm, cost, available alternatives and patient preferences, is considered one of the most complex problems in modern healthcare. [1, 2] In an effort to support clinicians in their daily practice, professional bodies, such as the Dutch College of General Practitioners (NHG), have published more than 120 evidence-based clinical practice guidelines. [3] However, despite the wide distribution and promotion of these guidelines, studies show that adherence among Dutch general practitioners (GPs) could be improved. [4-10] Up to one third of Dutch GP pharmaceutical prescriptions could be of low-value [6]. International studies show that low-value GP prescribing is also common outside of the Netherlands. [2, 11-17]

Obtaining insight into the prevalence of low-value prescribing is an essential first step in improving practice. [18] Although some assessments of low-value prescribing among Dutch GPs exist, these are outdated and conducted using data that are not nationally representative. [4, 19-21] We therefore aimed to quantify the prevalence and variation in low-value pharmaceutical treatments among GPs by using national medical records data. We selected three recommendations from the set of GP guidelines that clearly emphasise that physicians should refrain from prescribing medication except when specific indications are met (box 1 contains a detailed description of the rationale behind the selection, and supplementary box 1 an description of the operationalization of each recommendation):

1. The prescription of local antibiotics for an infectious conjunctivitis. [22]
2. The prescription of benzodiazepines in the treatment of non-specific lower back pain (LBP). [23]
3. The chronic prescription or continuation of acid-reducing medication (ARM). [24]

Through quantification of these prescribing practices, we hope to obtain a clearer view of low-value prescribing among GPs in the Netherlands. This is a first step in addressing the specific issue of low-

value GP prescribing. In addition to both the prevalence and the variation in prescribing behaviour, we were interested in the characteristics of patients associated with low-value prescribing.

Methods

Design and database

We conducted a retrospective cohort study with data derived from the Nivel Primary Care Database (Nivel-PCD). The Nivel-PCD contains care data routinely collected from electronic medical records from GPs throughout the Netherlands. The data were obtained from 529 GP practices, representing approximately 2 million registered patients. [25] The sample was shown to be representative for the total population of Dutch primary care practices. [26-28] The database contains longitudinal information regarding patient characteristics such as age, gender, GP consultations, diagnoses, and drug prescriptions. Diagnoses are recorded using the International Classification of Primary Care version 1 (ICPC-1). Prescriptions are recorded using the Anatomical Therapeutic Chemical classification system (ATC). This study was approved by the relevant governance bodies of the Nivel-PCD (nr. NZR00320.001).

Cohort selection

For each low-value care examined, patients with relevant episodes were extracted from the Nivel-PCD. Next, the prescription files for each type of pharmaceutical care were filtered for prescriptions associated with relevant ICPC codes. The resulting selection was then used in our analysis.

Supplementary box 1 contains an overview of the ATC and ICPC codes used to define the patient population for each of the recommendations. We only included GP practices in our analysis for which sufficient prescription data of high quality were available between 2016 and 2019. GP practices had to meet the following criteria to be included in our analysis: 1) At least 85% of the prescriptions were encoded with a valid ATC code; 2) A minimum of 46 weeks of prescription data had to be present and; 3) A minimum of 500 patients per practice should be present in the data.

Data analyses

Our assessments were performed using a patient-indication lens, as described by Chalmers et al. [29] Meaning we only included patients with a specific indication in our denominators. Our primary outcome is the percentages of patients, with an indication, who received a low-value prescription at least once. Analysis was performed using STATA 16 [30]. Data visualisation was carried out using R-V3.6.3. [31] and the R-package ggplot2. [32]

Practice variation

Variation among GP practices was assessed through multilevel logistic regression analysis over 2019, with random effects on the practice level. Before performance of multilevel logistic regression, variance inflation factors (VIF) were calculated to test for collinearity among the included variables. In order to prevent the standard errors of the (multilevel) regression coefficients becoming too large, GP practices with fewer than five cases of low-value prescribing, or fewer than 30 patients with a relevant indication for the type of care examined, were excluded from the analysis. Intraclass correlation coefficients (ICC) were calculated to assess variation in low-value prescribing between GP practices. [33] C-statistics were calculated for models with, and without, a random effect for the level of the practice. Suggesting that the models with an random intercept for the level of practice have more predictive accuracy. The difference between both C-statistics was used as a measure for variation among GP practices. Additionally, we have also assessed whether or not a significant correlation exists between the prescription rates of the three types of low-value pharmaceutical care over 2019. Correlations were assessed using the Pearson correlation coefficient for normally distributed variables and the Spearman correlation coefficient for non-normally distributed variables. Normality was assessed using both density plots and the Shapiro-Wilk test (supplementary table 2).

Case mix variables

The following patient variables were included in our models in order to assess their influence on the odds of receiving low-value care: age, gender, and neighbourhood socio-economic status (SES).

These case mix variables were selected based on previous research indicating that these factors affect the amount of care patients require, receive, and have access to. [34-38] SES scores from 2017 were derived from the Dutch Institute for Social Research (SCP). [39] Patients were assigned to one of five categories (lowest, below average, average, above average, highest) based on quintiles. In addition to these patient characteristics, the number of patients registered at each GP practice was also included in our analysis and categorised as a small, medium or large practice, based on the division of each population into tertiles (supplementary table 5 contains the tertile boundaries).

Results

Table 1 and figure 1 provide a summary of the study results. Patients with an episode of infectious conjunctivitis were regularly prescribed local antibiotics without appropriate indication. The proportion of patients inappropriately prescribed antibiotics decreased from 61% to 53% between 2016 and 2019. The chronic use of ARMs without an appropriate indication was highly prevalent. Between 2016 and 2019, around 88% of patients with a chronic ARM prescription lacked an appropriate indication. The prescription of benzodiazepines for LBP without indication remained around 3% over the four years. A more detailed table is presented in supplementary table 1.

Variation on the practice level

Figure 2 shows the prevalence of low-value prescribing among GP practices during 2019. We observed large variation in the proportion of patients receiving at least one non-indicated prescription for antibiotics for conjunctivitis (figure 2A). This varied between 0 and 90.3% (median: 52.8%). Benzodiazepines were prescribed largely in line with the guidelines, showing limited variation. Between 0 and 11% (median: 3.0%) of the LBP patients at each of the included GP practices received an inappropriate prescription. ARMs were prescribed chronically without an appropriate indication, in between 79% and 97% of the GP practices included (median: 88%). Comparison of the rates of non-indicated prescription of the three low-value pharmaceutical GP care across practices only revealed a significant weak positive correlation (correlation coefficient: 0.17) between the rate

of low-value antibiotic and low-value benzodiazepine prescriptions (supplementary table 2). No other significant correlations were identified. Supplementary table 3 contains an overview of the rates of low-value care for each of the examined types of care across practices in 2019. After adjusting for case mix variables, the ICCs on the practice level for each of the prescriptions for low-value care ranged from 5.55% to 10.24% (Table 2). Analysis of the VIF factors revealed that little or no collinearity exists among the variables included in our analysis (supplementary table 4). The C-statistics of the models with a random effect on the practice level were significantly higher for all three types of low-value GP care examined, compared to the models without random effect. Supplementary table 5 presents an overview of the contribution of each case mix variable to the final model.

Patient characteristics associated with receiving low-value prescriptions

The inappropriate prescription of antibiotics for conjunctivitis, and benzodiazepine for non-specific LBP, showed a significant increase in odds with increasing age ($p < 0.05$, supplementary table 5). Conversely, patients were less likely to receive an inappropriate chronic prescription of ARMs with increasing age. Gender and SES significantly affected ($p < 0.05$) the odds of receiving a non-indicated chronic ARM prescription. Women were slightly less prone to receiving a non-indicated chronic ARM prescription. Patients showed significantly increased odds of receiving an inappropriate ARM with increasing SES. Furthermore, SES had only a small significant increase in odds of receiving an inappropriate antibiotic for conjunctivitis, when comparing the average SES with the lowest category. The size of the GP practice significantly affected the odds of receiving any of the three types of low-value care examined. In general, larger GP practices are less prone to providing any of the three types of low-value care compared to smaller ones. Only in cases of the chronic ARM use, it appeared that medium-sized practices did not significantly differ in odds from the smaller ones (Figure 3).

Discussion

Summary

Our study shows that the prescription of low-value pharmaceutical GP care varies depending upon the clinical problem. Inappropriate prescriptions of both antibiotics for conjunctivitis and ARMs are highly prevalent, while the proportion of patients with LBP receiving a benzodiazepine is small. Large variation in pharmaceutical treatment was found for the prescription of a non-indicated antibiotic for conjunctivitis, whereas limited variation was found in the prescription of non-indicated benzodiazepines or chronic ARM prescriptions. Our analysis of correlation among the practices over 2019 only revealed a significant weak positive correlation between the rate of low-value antibiotic and benzodiazepine prescriptions. The odds of a patient receiving either of the three low-value treatments are significantly affected by age. Men were found to have significantly higher odds of receiving a non-indicated chronic ARM prescription compared to women, while the odds of patients receiving an inappropriate ARM significantly increased with increasing neighbourhood SES. Apart from ARMs, SES only showed a small significant increase in the odds of receiving an inappropriate antibiotic for conjunctivitis, when comparing the average with the lowest category. The odds of receiving an inappropriate antibiotic or benzodiazepine significantly decreased as the size of the GP practice increased. ARMs also showed a similar decrease as the size of the GP practice increased. However, this was only found to be significant in cases of the largest practice sizes.

Strengths and limitations

A strength of this study is that low-value care among Dutch GPs was assessed of patients receiving an inappropriate prescription among using routinely collected, nationally representative, data over four consecutive years. Furthermore, the use of high quality and complete clinical data made it possible to distinguish appropriate from inappropriate care.

Our study has some limitations. First, there is an inherent uncertainty in identifying whether a prescription is of low-value. Recommendations contain terms that do not map directly to data

variables, while diagnosis and procedure codes may not precisely identify patients for whom care is of low-value. For example, the recommendations regarding conjunctivitis and ARMs were not described with enough detail or required variables which are absent in the data to distinguish appropriate from inappropriate prescribing. The recommendation regarding conjunctivitis requires us to identify patients with conjunctivitis caused by a banal pathogen, and who are at high-risk. The information required to distinguish the cause of an episode of conjunctivitis is not recorded within the Nivel-PCD, and therefore not available in the data used. We also could not identify patients whom were at high risk, since the recommendation and the guideline did not provide sufficient detail on the definition of the high-risk population, to be able to distinguish them (if the information was available). Our assessment therefore could be an overestimate. However, we do not expect these factors to have a major effect on our assessment outcome, since conjunctivitis is most commonly caused by a banal pathogen. [40] Furthermore, in our analysis of chronic ARM prescriptions, the guideline states that gastro-protection using an non-selective NSAID is justified if a patient is using a high dosage of a NSAID. However, information regarding the dosage of the prescribed NSAIDs was not present within the data used. We therefore could not include these requirements in our assessment. Our assessments might therefore under, or over, estimate the magnitude of the problem. Secondly, we could not identify patients suffering from chronic heartburn, while we only had access to diagnosis established within the years examined. Patients diagnosed with heartburn outside of this period could therefore not be identified. Also, heartburn is often only present for a short period of time, until ARMs are prescribed. The prescription of ARMs often resolve the patients' complaints resulting in removal of the diagnosis from the patients' medical records, making it difficult to define chronic heartburn. For similar reasons, we did not have access to practice and physician characteristics, which could explain variation in prescribing behaviour between GP practices, for example, the number of physicians and their age or sex. [41-43] Thirdly, both the antibiotic and benzodiazepine recommendations are directly linked to specific diagnoses, thereby making their assessment relatively straightforward. However this is not the case for the

recommendation of chronic ARMs use, which makes its assessment difficult and more uncertain in comparison to the other recommendations. Finally, our final logistic models reported moderate C-statistics. This suggests that these models are unsuitable for predicting, reliably, the risk of patients receiving either of the low-value GP prescriptions. Receiving low-value GP care could have been influenced by other patient or GP characteristics that are not available in the data. [44]

Comparison with existing literature

Previous studies from Australia, the US, and the Netherlands reported between 60% and 80% of patients with infectious conjunctivitis received a non-indicated antibiotics prescription, which is higher compared to our assessment outcome. [20, 45, 46] The differences between the assessments could be explained by differences in the data sources, study designs and populations included. For example, Shekhawat et al. used a patient-indication lens and included all GPs in their analysis, while Cherry et al. included only patients who visited GP registrars in their sample resulting in distinct assessment denominators and outcomes. [45, 46]

Our assessment of non-indicated prescribing of benzodiazepines for non-specific LBP shows that Dutch GPs mostly adhere to professional guidelines. Only 3% of patients received an inappropriate prescription, which is lower compared to the findings of recent studies from the US. [47, 48] Agarwal et al. reported that 8.5% of patients with back or chronic pain received a benzodiazepine prescription. [47] Furthermore, Azad et al., reported that 11.5% of US patients new to opioids with LBP, received a benzodiazepine within 12 months of their diagnosis. [48] However, it is difficult to compare these assessments with our study as patient-population lenses were used in the US studies, while our study applied a patient-indication lens resulting in different denominators being used. [15, 29]

We did not identify any assessments regarding non-indicated chronic ARM use within the literature as most studies focus solely on chronic Proton Pump Inhibitor (PPI) use. However, since only approximately 3.5% of all ARM prescriptions in our assessment did not concern PPIs, we feel our

assessment closely resembles those that solely focus on PPIs. Our assessment shows that the non-indicated chronic use of ARMs is highly prevalent in the Netherlands. However, this is only slightly higher compared to what is reported in international literature. According to recent literature between 30% to 80% of PPI prescriptions have no appropriate indication. [49-55] Again, these high levels of variation could be explained by differences in population characteristics, study design – such as the inclusion of all ARMs – and setting. Furthermore, unlike other studies, we did not limit our assessment to a specified population; such as the elderly [51, 56]. According to Dutch and international guidelines, the elderly have more indications justifying the use of a PPI which might have affected the prevalences reported.

The high amount of inappropriate antibiotic prescriptions could be explained by GPs experiencing patient pressure to provide low-value care. Previous research, shows that patient pressure and the GP's need to maintain a good patient-physician relationship, could induce inappropriate prescribing. [57] Furthermore, the low-level of inappropriate benzodiazepine prescriptions could be explained by a long-term policy, promoting cautious prescribing of benzodiazepines due to their addictive properties. Finally, the high prevalence of inappropriate chronic ARM prescriptions could be due to their reputation, at least, for being harmless. ARMs, in contrast to antibiotics and benzodiazepines, are commonly sold over-the-counter at most drugstores in the Netherlands. We therefore expect that our assessment is most likely an underestimate, since we were not able to capture all chronic ARM users in this study, thereby missing non-prescription ARM in our assessment.

The implications for research and/or practice

Our assessment of three low-value pharmaceutical GP prescriptions demonstrates that both antibiotics for conjunctivitis, and the chronic use of ARM, are prescribed inappropriately with no indication that this will greatly decline over time. This suggests a joint national effort is required to change prescribing behaviour. For such an effort, detailed insight into the views of patients and prescribers, and the barriers and facilitators for the withdrawal of inappropriate medication –

deprescribing – is required in order to design a tailor-made deprescribing strategy. Furthermore, our observation that little to no correlation exists between the low-value prescription rates of the three types of low-value pharmaceutical care within practices, suggests that the problem of low-value pharmaceutical GP care cannot be addressed through a single deprescribing strategy. But rather requires deprescribing strategies that are tailor-made to the type of pharmaceutical care that one aims to address. The assessment methods from this study could be used to monitor changes resulting from any following interventions. Furthermore, the knowledge of potential patient characteristics that are associated with the increased odds of receiving any of the low-value prescriptions examined could provide some focus for policy interventions.

Conclusions

Our research shows that low-value pharmaceutical care is prevalent among Dutch GPs, but its prevalence varies depending on the clinical problem. Between 2016 and 2019, many patients received an inappropriate antibiotic or chronic ARM prescription. Benzodiazepines for LBP are generally prescribed in line with the guidelines. Among the three types of low-value pharmaceutical care, large variation between GP practices and general variation in prescribing were observed. These insights could help in designing a national campaign in order to change this behaviour.

Additional information

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Ethical approval

The research ethics committee of the Radboud University Nijmegen Medical Center has judged our research proposal and concluded that the abovementioned study does not fall within the remit of the Medical Research Involving Human Subjects Act (WMO) (dossier number: 2020-6322).

Competing interests

None to declared.

Acknowledgements

None to declare.

Data accessibility

Data is available upon request and under conditions of Nivel-PCD.

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Boxes, figures and tables.

Box 1: Rationale behind the recommendations selected.

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1. *The prescription of local antibiotics for an infectious conjunctivitis.* [22] A Dutch study from 2007 showed that up to 80% of conjunctivitis episodes were inappropriately treated with a topical antibiotic. [20] The indications for prescribing an antibiotic for conjunctivitis have not changed since then. One study from the USA showed that the number of conjunctivitis diagnoses has increased between 2005 and 2014 and the percentage of low-value antibiotic prescriptions slightly decreased from 18.3% to 17.2%. [46] It would be interesting to see whether the prevalence of antibiotic description in the Netherlands has also changed over time.
2. *The prescription of benzodiazepines in the treatment of non-specific lower back pain.* [23] Lower back pain is one of the most prevalent conditions in general practice. [58] Its treatment, however, is complex. [59] Studies indicate that both inappropriate imaging [11, 12, 60, 61] and prescribing of opioids [59, 62, 63] are highly prevalent. However, there is a lack of information about the prevalence of inappropriate prescribing for LBP in the Netherlands.
3. *The chronic prescription or continuation of acid-reducing medication (ARM) without indication.* [24] Inappropriate prescription of ARM, predominantly Proton Pump Inhibitors (PPIs), has been shown to be an international problem. [49-54] However, the extent of this problem in the Netherlands is unknown.

Supplementary box 1 contains a detailed description of how each recommendations was operationalized and the used definitions.

Figure 1: Estimates of the prevalence of patients receiving one of three types of low-value care.

Figure 2: Proportion of patients of each practice who received each of the low-value prescriptions for care at least once during 2019. The practice numbers do not directly correlate to the practice numbers as provided in supplementary table 3.

Figure 3: Adjusted odds ratios and confidence intervals associated with patient characteristics for all three types of low-value GP care. The asterisk indicates the reference categories.

Table 1: overview of assessment outcomes

1. Do not prescribe a local antibiotic for an infectious conjunctivitis due to a banal pathogen, unless for a high-risk patient.								
	2016		2017		2018		2019	
<i>No. of practices included</i>	316		329		296		346	
<i>No. of patients with (at least) one episode of conjunctivitis (denominator)</i>	17.332		18.076		15.345		17.994	
	Total no.	% of total	Total no.	% of total	Total no.	% of total	Total no.	% of total
<i>No. of patients whom received appropriate treatment</i>	6.778	39,11	7.339	40,6	6.789	44,24	8.472	47,08
<i>No. of patients with no clear indication for their antibiotic prescription (numerator)</i>	10.554	60,89	10.737	59,4	8.556	55,76	9.522	52,92
2. Do not prescribe benzodiazepines in patients with non-specific lower back pain								
	2016		2017		2018		2019	
<i>No. of practices included</i>	313		328		296		346	
<i>No. of patients with (at least) one episode of lower back pain (denominator)</i>	99.262		105.641		94.685		111.703	
	Total no.	% of total	Total no.	% of total	Total no.	% of total	Total no.	% of total
<i>No. of patients whom did not receive a benzodiazepine or received one for a different indication</i>	95.909	96,62	101.922	96,48	91.742	96,89	108.441	97,08
<i>No. of patients with no clear indication for benzodiazepine use (numerator)</i>	3.353	3,38	3.719	3,52	2.943	3,11	3.262	2,92
3. Do not chronically prescribe or continue acid-reducing medication, without proper indication								
	2016		2017		2018		2019	
<i>No. of practices included</i>	284		276		250		245	
<i>No. of patients with chronic prescription of ARM (denominator)</i>	100.319		105.043		93.053		91.563	
	Total no.	% of total	Total no.	% of total	Total no.	% of total	Total no.	% of total
<i>No. of patients with an indication for chronic ARM use</i>	12.931	12,89	11.941	11,37	11.334	12,18	11.174	12,20
<i>No. of patients with no clear indication for chronic ARM use (numerator)</i>	87.388	87,11	93.102	88,63	81.719	87,82	80.389	87,80

Table 2: overview of model characteristics; Intraclass correlation coefficient (ICC); Confidence Intervals (CIs)

Recommendation	ICC practice (and 95% CIs)	C-statistic model with random effect practice (and 95% CIs)	C-statistic model without random effect practice (and 95% CIs)
1. Do not prescribe a local antibiotic for an infectious conjunctivitis due to a banal pathogen, unless for a high-risk patient.	0.08 (0.06 - 0.11)	0.65 (0.64 - 0.66)	0.54 (0.53 - 0.55)
2. Do not prescribe benzodiazepines in patients with non-specific lower back pain	0.10 (0.07 - 0.15)	0.67 (0.66 - 0.68)	0.59 (0.58 - 0.60)
3. Do not prescribe or continue acid-reducing medication, without proper indication	0.06 (0.03 - 0.09)	0.72 (0.71 - 0.72)	0.70 (0.69 - 0.70)

Figure 1: Estimates of the prevalence of patients receiving one of three types of low-value care.

338x338mm (300 x 300 DPI)

Figure 2: Proportion of patients of each practice who received each of the low-value prescriptions for care at least once during 2019.

317x254mm (300 x 300 DPI)

Figure 3: Adjusted odds ratios and confidence intervals associated with patient characteristics for all three types of low-value GP care. The asterisk indicates the reference categories.

177x254mm (300 x 300 DPI)