New medicines in primary care

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General discussion

New medicines can have advantages in terms of morbidity, longevity and quality of life [1,2]. However, the use of new medicines can also involve negative aspects, including safety risks and increasing healthcare costs [3,4]. Rational use of new medicines in primary care is therefore important to maintain quality of care and prevent increasing healthcare costs. The overall aim of this thesis was to gain insight into the perspectives and practices of healthcare professionals in primary care towards new medicines, focusing on the assessment criteria of new medicines, factors that are associated with the decision of individual healthcare professionals to prescribe new medicines and the actual prescription patterns of new medicines in primary care.

MAIN FINDINGS FROM THIS THESIS

Assessment criteria

Chapter 2 of this thesis focused on healthcare professionals' preferences for outcomes and minimal clinically important differences (MCIDs) used in the evaluation of new medicines in relation to the standards used by registration authorities and professional organisations. With questionnaires, the preferred endpoints and MCIDs for chronic obstructive pulmonary disease (COPD) and type 2 diabetes mellitus (T2DM) by a sample of Dutch healthcare professionals, including general practitioners, pharmacists and practice nurses, were investigated. As for COPD (**2.1**), the preferred endpoints by healthcare professionals corresponded to the clinical endpoints which the European Medicines Agency (EMA) uses for the evaluation of new medicines. However, healthcare professionals preferred higher MCIDs for dyspnea and health status than currently used by the EMA, meaning that healthcare professionals were more strict in defining clinical relevance on these endpoints than the registration authority. This stricter view on what is considered a clinically relevant difference was also seen for assessment criteria for new T2DM medicines (**2.2**). Compared to the professional organisation that developed the Dutch T2DM guideline, healthcare professionals had a stricter view on the importance of the outcomes HbA1c and hospital admissions and the MCIDs for mortality and other hypoglycemia. An additional finding of this study was that healthcare professionals experienced difficulties estimating the desired relative risk measures. A substantial part of the respondents had no opinion or did not answer the questions about MCIDs and the wide range of answers given indicated interpretation difficulties of especially relative outcome measures.

Factors impacting decision-making

Chapter 3 of this thesis focused on internal and external factors that are associated with the decision of individual healthcare professionals to prescribe new medicines. In focus

group discussions with primary care practitioners, the reasons for the prescription of new, non-recommended insulins were investigated (**3.1**). Non-adherence to prescription guidelines was largely driven by argumentation in the domain of attitudes, with lack of agreement with the guideline recommendations and different interpretation of evidence as most prominent perspectives. External factors, including patients' abilities to use the insulin as instructed, contradictory guidelines, continuation of prescriptions from other healthcare professionals and marketing by pharmaceutical companies were also impacting the decision to prescribe new insulins. The impact of the pharmaceutical industry was further investigated in **3.2**, focusing on the persuasion strategies present in 69 unique direct marketing materials from pharmaceutical companies, collected by general practices in the Netherlands. All seven persuasion strategies defined by Cialdini [5] and one newly identified strategy, namely emotional pressure, were present in the materials, with liking, emotional pressure and authority as the most prominent strategies. The presence of eight different persuasion strategies indicates that pharmaceutical companies use a wide range of strategies to influence the attitudes of healthcare professionals towards prescribing their (new) medicines and that healthcare professionals should become more aware of these attempts to influence their prescription behaviour.

Prescription of new medicines

Chapter 4 of this thesis focused on prescription patterns of new medicines in Dutch general practices. In retrospective cohort studies with data from Nivel Primary Care Database, the prescription of new insulins, 3 – 5 years after their introduction, and uptake of anticoagulants and incretin-based therapies during 2007 – 2019 were investigated. New insulins (**4.1**) accounted for a median of 21.2% (interquartile range (IQR) = 12.5 – 36.4%) of all insulin prescriptions. Dispensing practices, male patient sex, younger age of patients, and prescriptions for other new blood glucose lowering agents were positively associated with newer insulin prescriptions. On the contrary, patients with prescriptions for metformin or sulphonylurea were less likely to receive a prescription for newer insulins. Large variation between general practices existed, even after correction for differences at patient and practice level. As for direct-acting oral anticoagulants (DOACs) and incretin-based medicines (**4.2**), the uptake patterns were markedly different from each other. For DOACs, the uptake remained very low for a couple of years and then substantially increased. For incretin-based therapies, the uptake steadily increased during the first years of introduction and then stabilized. No correlation was found between the uptake of both new classes of medicines, meaning that early adoption of one type of new medicine could not predict the early adoption of other new medicines.

In this last chapter, the results will be placed in a broader perspective. Two main conclusions derived from this thesis will be further discussed, followed by recommendations based on these conclusions.

THE UPTAKE OF NEW MEDICINES IN PRIMARY CARE IS UNPREDICTABLE

This thesis shows that the uptake of new medicines in primary care is unpredictable and no clear profile of the early adopter of new medicines exists, as we found great differences between the adoption of three different groups of new medicines (**4.1, 4.2**). Also, a large variation between practices exists in the prescription of new medicines in primary care, which cannot be explained by variation in practice and patient characteristics (**4.1**). Finally, early adoption of one group of new medicines could not predict the early adoption of another group of new medicines, although we did find a correlation between new medicines intended for the same condition (**4.1, 4.2**).

Different adoption profiles

Among the three different medicine groups in this thesis, new insulins were rapidly adopted which resulted in more prescriptions than expected based on the guideline recommendations (**4.1**). The adoption of DOACs went slowly in the first years after their introduction, but then rapidly increased (**4.2**). And finally, the incretin-based therapies showed a rapid adoption in the first years, followed by a period of stabilization (**4.2**).

Despite their different adoption profiles, DOACs and incretin-based therapies have in common that their adoption in the Netherlands was generally slower than in other countries [6-9]. Differences in uptake between countries can be explained by, among others, changes in country-specific clinical guidelines, national medicines policies and reimbursement decisions [7]. The exact reason for the relative slow uptake of new medicines in the Netherlands is not known. Contributing factors are, among others, an already good-functioning healthcare system, including the Thrombosis Services, leading to a limited need of new therapies [10], a relative long period between registration and reimbursement [9], a well-functioning system of clinical guidelines of which most general practitioners are adherent to [9,11,12] and multiple initiatives aimed at the stimulation of rational use of new medicines [13,14].

Taken into account the generally slow adoption of new medicines in Dutch primary practice [9,15-17], the popularity of new insulins in Dutch primary care is even more remarkable. Three to five years after their introduction, new insulins accounted for more

than a quarter of all insulin prescriptions in primary care (**4.1**). The popularity of those new insulins shows resemblance with the introduction of the insulin analogues almost 20 years ago. Insulin glargine 100 U/ml and insulin detemir were also rapidly adopted, despite professional organisations recommending other insulins [18-23].

The differences in pace of adoption of newer insulins, DOACs and incretin-based medicines correlate with the relative degree of innovation and the place in therapy. New insulins can be considered less innovative than DOACs and incretin-based medicines. New insulins are examples of structural innovations, meaning that they have the same mode of action as already existing insulins. DOACs and incretin-based medicines are pharmacological innovations that focus on a new therapeutic target [24]. Structural innovations are, compared to pharmacological innovations, associated with fewer uncertainties in the benefit-risk balance, which can explain the rapid adoption of newer insulins compared to DOACs and incretin-based therapies. When comparing the uptake profiles of DOACs and incretin-based medicines, their differences might be explained by their different places in therapy. Incretin-based medicines can be *added* to blood-glucose lowering medicines the patient already uses, while DOACs have to *replace* the existent treatment. The addition of a new medicine might be less troublesome to healthcare professionals than the replacement of a familiar medicine with a new one.

Whether the relative degree of innovation is indeed an explanation for the differences in adoption profiles of the studied and other medicines remains to be elucidated. Differences between the relative degree of innovation and the number of adopters in the first months have been described before. However, it can also be argued that medicines with new acting mechanisms are more likely to be rapidly adopted than me-too medicines, because of their greater potential for therapeutic advantages [25]. More studies towards the possible relation between degree of innovation and uptake are warranted.

Practice variation and associated patient and practice characteristics

In addition to the adoption profiles, we also studied practice variation in the prescription of new medicines and the relation with patient and practice characteristics. We concluded that practice variation was large. No strong predictors at patient or practice level for the early adoption of new medicines in primary care were identified (**4.1**, **4.2**).

Variation between practices is common and not problematic in itself, since patients and practices may differ, which calls for different treatments [26]. However, if the prescription of new medicines was solely based on medical reasons, a more balanced distribution between practices would be expected than we found and which was also

found in previous research. For example, in studies among British general practitioners, 42% of prescriptions for new medicines were initiated by 10% of the physicians [27]. The variation in the prescription of new medicines found in our studies was also large, especially in the first years after introduction. Even after adjustment for differences between patient and practice characteristics, we found a substantial part of the variation at the practice level (**4.1**, **4.2**). We identified some patient and practice characteristics (including dispensing state as practice characteristic and sex, age and former use of medicines as patient characteristics) which were associated with the prescription of new medicines. However, the associations were weak and could not explain the large practice variation in the prescription of new medicines (**4.1**). The lack of strong predictors for the early adoption of new medicines in primary care is confirmed in other studies. A systematic review from 2021 found a broad range of factors affecting the uptake of new medicines, which could be grouped into patient, prescriber, medicine, organisational, and external environment factors [28]. Although many factors have been identified, correlations with the early prescription of new medicines are often weak and differ among studies [24,29,30]. Early prescription of new medicines could not be predicted by a vast set of patient and practice characteristics [29]. The idea of the existence of a general profile of 'the early adopter' is therefore questionable [31,32]. Our studies confirm that early adoption of new medicines is not solely dependent on a vast set of patient and practice characteristics and indicate that other factors are important in the understanding of early adoption profiles of new medicines.

Correlation between uptake of new medicines

In addition to the above-mentioned lack of predictive characteristics for the early adoption of new medicines, we did conclude that early adoption of one group of new medicine could not predict the early adoption of another group of new medicines (**4.2**), although a correlation did exist between the early adoption of new medicines meant for the same condition (**4.1**).

In 2004, Dybdahl et al. demonstrated for four new medicine groups (angiotensin II receptor blockers, triptans, selective cyclo-oxygenase-2 antagonists and esomeprazole) that early adoption of one group of new medicines was poorly associated with adoption of other new medicines [31]. This finding was confirmed in our study, in which we failed to relate the prescription of DOACs to the prescription of incretin-based medicines (**4.2**). Interestingly, we did find an association between the adoption of new medicines meant for the same disease (i.e., dipeptidyl peptidase-4 (DPP-4) inhibitors, glucagon-like peptide-1 (GLP-1) receptor agonists and sodium-glucose co-transporter 2 (SGLT2) inhibitors on one hand and new insulins on another hand) **(4.1**). These differences might be explained by the concept of domain-specific innovation. This concept describes

the tendency of someone to acquire information and new products within a specific product domain [33]. Domain-specific innovation might explain why early prescription of DPP-4 inhibitors, GLP-1 receptor agonists and SGLT2 inhibitors is associated with early prescription of new insulins, but not DOACs. However, whether domain-specific innovation is indeed the explanation for the patterns found in our studies remains to be elucidated. Former studies showed that prescription of new medicines by general practitioners could not be related to previous prescribing of medicines in the same therapeutic class [32] or self-reported therapeutic interests [34]. In other words, affinity with a therapeutic area is no predictor for the early prescription of new medicines in that therapeutic area, which argues against the concept of domain-specific innovation. It can however not be excluded that an association exists between affinity with *innovations* in a therapeutic area and early prescription of new medicines. This gap in understanding calls for further research.

SCIENTIFIC EVIDENCE PLAYS A LIMITED ROLE IN THE DECISION TO PRESCRIBE NEW MEDICINES

The lack of uniformity and explanatory patient and practice characteristics in the uptake of new medicines in primary care raises the question which considerations of healthcare professionals lead to the prescription of new medicines. This thesis shows that the prescription of new medicines is often driven by non-scientific argumentation. First, we concluded that healthcare professionals found it difficult to interpret and estimate realistic benefits and risks of new medicines (**2.1**, **2.2**). Second, we identified individual attitudes of healthcare professionals towards new medicines as the most important factor in the decision to prescribe new medicines. These attitudes were related to argumentation that often lacked scientific rationale, as was also concluded by healthcare professionals themselves (**3.1**). Third, healthcare professionals are constantly exposed to marketing activities from pharmaceutical companies. Those activities are known to stimulate the prescription of new medicine, rather than to stimulate the *rational* prescription of new medicine (**3.2**).

Interpreting benefit-risk balance

A realistic estimation of the desired benefits and risks should be the scientific basis for the decision to prescribe new medicines by healthcare professionals. However, chapter **2.1** and **2.2** show that a balanced estimation of benefits and risks by healthcare professionals is hampered. If a solid scientific basis exists, alignment between preferences for evaluation criteria among healthcare professionals, and between healthcare professionals and official institutions would be expected. However, healthcare

professionals had in general stricter preferences for evaluation criteria and thresholds for clinical relevance of new COPD and T2DM medicines than official organisations (**2.1**, **2.2**). Moreover, large differences also existed *between* healthcare professionals (**2.1**, **2.2**). Finally, healthcare professionals experienced great difficulties in understanding and estimating risk measures, especially relative risk reductions for T2DM medicines (**2.2**). Taken together, those findings illustrate the difficulties healthcare professionals experience in estimating and interpreting realistic effects of new medicines. These difficulties hamper a balanced evaluation of benefits and risks and may lead to unrealistic expectations and even irrational prescription of new medicines.

Different views from healthcare professionals and official organisations on the clinical relevance of new medicines have been described before [35,36]. As already stated in the general introduction, different evaluation domains to assess new medicines exist at various moments. While official institutions rely on scientific evidence to assess quality, the benefit-risk-balance, cost-effectiveness and additional therapeutic value at population level, an individual healthcare professional has to evaluate what is the best option for an individual patient. Individual considerations can differ from considerations at population level. It has been shown before that decisions in daily practice might be more influenced by short term outcomes at the patient level, while clinical guidelines and regulatory agencies particularly focus on long term outcomes and population level [37,38]. Considering what is best for a patient is of course good clinical practice, as long as it is based on realistic expectations. However, our studies, together with previous research also show that healthcare professionals find it hard to estimate and interpret realistic benefits and harms of medicines [39,40].

Whether the interpretation differences in realistic outcomes and improvements on these outcomes found in our studies led to over- or underestimation of benefits and risks of new medicines was not investigated. Theoretically, both situations are possible, as indicated in the example below.

According to chapter 2.1: healthcare professionals prefer an MCID of 11 points for SGRQ. The MCID used by registration authorities is 4 units. A new COPD medicine improves the SGRQ with 5 units. The EMA therefore concludes that this medicine gives a clinically relevant improvement of health related quality of life.
***Healthcare professional 1** is really interested in new COPD medicines and studies the original clinical study and evaluation by the EMA. She notices that the improvement on SGRQ is 5 units, which she thinks is not clinically relevant. The healthcare professional concludes the new COPD medicine gives no clinically relevant improvement according to her own standards and decides not to prescribe the new COPD medicine to her patients.*
***Healthcare professional 2** reads a short article about the new COPD medicine, stating 'clinically relevant improvement of health related quality of life according to the EMA'. The healthcare professional concludes the new COPD medicine gives a clinically relevant improvement according to an official institution and decides to prescribe the new medicine to her patients. She is unaware that the medicine does not meet her own expectations of clinical relevance, which is set at 11 points.*

Although not investigated in our studies, situation two seems most plausible. General practitioners have been shown to acquire information about new medicines in an opportunistic way, rather than based on active searches of new medicine information [41]. Moreover, the expected consequence, namely the overestimation of benefits is also confirmed in a systematic review towards expectations of clinicians towards treatments, screening and tests. Based on 48 studies, of which 20 focused on treatments, the authors concluded that clinicians rarely had accurate expectations of benefits or harms of medicinal interventions. Both over- and underestimation was present, although benefits were mostly overestimated and harms underestimated. This therapeutic illusion or unjustified enthusiasm could lead to inappropriate use of interventions [42]. The different views of healthcare professionals and registration authorities towards benefits and risks of new medicines have also been described in a study performed by the EMA. They concluded that better communication about benefits and risks of medicines is necessary, given the divergent views and perspectives [43].

Importance of attitude

The attitudes of healthcare professionals play an important role in the decision to prescribe new insulins. Those attitudes markedly differed between professionals and were made up of different argumentation, which often lacked scientific rationale (**3.1**). Previous studies towards reasons for guideline non-adherence have confirmed the importance of individual attitudes of healthcare professionals [11,44]. Specifically for the prescription of new medicines, individual beliefs of healthcare professionals have been related to early prescription, rather than objective evaluation of the literature [30]. In addition, the decision to prescribe new medicines is prone to the mode of exposure to pharmacological information and social influences [41]. The prescription of new, non-guideline recommended new medicines seems therefore mostly dependent on individual choices of healthcare professionals, rather than on robust scientific evidence.

Interestingly, the argumentation used by healthcare professionals to justify the use of new medicines was not only challenged by current scientific evidence, but also by other healthcare professionals. Moreover, some healthcare professionals also tended to challenge their own argumentation (**3.1**). While this might raise even more questions about the sustainability of argumentation, it also indicates that prescription of new medicines can become more aligned and rational by stimulating independent interprofessional communication and discussion. The importance of interprofessional communication has also been shown before. Pharmacotherapy audit meetings (PTAMs), in which general practitioners and community pharmacists exchange information and views about pharmacotherapy with the aim of improving the prescribing and dispensing of medicines, have been shown to be associated with rational use of medicine. Previous

studies have demonstrated that healthcare professionals participating in high-quality PTAMs are less likely to prescribe new medicines [45]. Moreover, participating in PTAMs contributes to the overall quality and cost-effectiveness of prescribing, especially if the quality level of PTAM is high [46-48]. PTAMs are therefore considered as an important setting to stimulate the rational use of (new) medicines [49]. In order to reduce the practice variation caused by non-scientific argumentation, interprofessional communication might play an important role.

Pharmaceutical industry

The rationality in the prescription of new medicines is further complicated by the presence and activities of companies with commercial interests in the use of new medicines. In our study, we found that healthcare professionals mentioned marketing activities of pharmaceutical companies as reason for the prescription of new medicines (**3.1**). In addition, we found that marketing materials from pharmaceutical companies made use of multiple persuasion strategies to create a positive attitude towards new medicines (**3.2**).

The pharmaceutical industry has been known for decades to try to persuade healthcare professionals to prescribe their new medicines. In this thesis, only marketing materials were studied. But even in this small part of all marketing activities, multiple persuasion strategies were identified. Adding those results to former demonstrated lack of educational value in marketing materials [50-52], it becomes clear that these materials have little to do with scientific rationale in the decision to prescribe new medicines. Numerous studies have shown that any form of interference by the pharmaceutical industry can lead to more prescriptions for new medicines. Investigated interventions include among others promotional literature [53,54], commercial medicine information from sales representatives [55], gifts from pharmaceutical companies [56] and pharmaceutical sales representatives [57] or a combination of activities [52,58]. Moreover, marketing activities have also been associated with nonrational prescription behaviour [59] and restriction of marketing activities is associated with reductions in prescription of new medicines [60]. Healthcare professionals themselves also acknowledged the influence of marketing activities from pharmaceutical companies on their behaviour (**3.1**). However, studies also proof that most healthcare professionals still underestimate their vulnerability to marketing, thinking they themselves are not affected by marketing activities [5,54,58]. It can therefore be concluded that marketing activities from pharmaceutical companies contribute to non-scientific argumentation to prescribe new medicines. Restriction of marketing activities and awareness of persuasion strategies can contribute to more rational prescription of new medicines.

IMPLICATIONS FOR INITIATIVES AIMED AT THE RATIONAL USE OF MEDICINES

The unpredictability of uptake of new medicines and limited role of scientific evidence in the decision to prescribe new medicines urge for initiatives to continuously stimulate the rational use of new medicines. The stimulation of rational use of new medicines should start with the education of aspirant healthcare professionals. Education about how to evaluate benefits and risks of new medicines, and how pharmaceutical companies try to influence decision-making should be part of educational programmes of all healthcare professionals. In addition to the education of aspirant healthcare professionals, initiatives directed at practicing healthcare professionals are also warranted. In the Netherlands, the programme 'MedicijnBalans' of the Dutch Institute for the Rational Use of Medicine (IRUM) is set up by the Ministry of Health, Wellbeing and Sports to stimulate the rational use of new medicines by healthcare professionals. MedicijnBalans provides unbiased information about new medicines and stimulates the discussion about the added value of new medicines before their uptake in guidelines. Several lessons, aimed at MedicijnBalans and equivalent interventions to stimulate the rational use of new medicines, can be derived from this thesis:

1. **Gain insight into the considerations, context and perspectives for every medicine group individually, before developing interventions**.

This thesis clearly shows that no general profile of early adoption of new medicine exists and that considerations and contexts regarding new medicines differ between different therapeutical classes. In order to develop interventions to stimulate the rational use of a certain class of new medicines, insight in the attitudes and external factors influencing prescription behaviour is essential. Those findings cannot just be extrapolated from one medicine group to another.

2. **Communicate clearly about the expected benefits and risks of new medicines**.

This thesis shows that expectations of new medicines by healthcare professionals do not necessarily align with those by official organisations. The interpretation of – most notably – relative risk measures and terms like 'clinical relevance' differs and can lead to overestimation or underestimation of the benefits and risks of new medicines. Transparency and clear communication about the expected benefits and risks, avoiding the use of relative risk measures and multi-interpretable terminology are essential in the unbiased information about new medicines. The need of clear communication does apply to all organisations who communicate about (new) medicines, including

registration authorities, Health Technology Assessment (HTA) bodies, education institutes and professional organisations.

3. **Stimulate communication among healthcare professionals**.

This thesis showed that healthcare professionals were willing to discuss viewpoints and the differences in argumentation. In order to stimulate the rational use of new medicines, interprofessional communication, for example in PTAMs, might help to minimize practice variation and prevent unrealistic expectations of new medicines.

4. **Pay attention to the persuasion strategies of the pharmaceutical industry**.

This thesis shows that multiple persuasion strategies are present in only a small subset of marketing activities from pharmaceutical companies. Initiatives aimed at the rational use of new medicine should be aware of these mechanisms, both to prevent themselves from being influenced and to educate healthcare professionals about these mechanisms. Initiatives to stimulate the rational use of new medicines could also make use of the same mechanisms, to persuade healthcare professionals to the rational use of medicine.

IMPLICATIONS FOR FURTHER RESEARCH

In addition to the conclusions and recommendations drawn from this thesis, the findings have also resulted in directions for further research. To obtain more insight in the perspectives and practices of primary care healthcare professionals related to new medicines, more research is warranted.

The first finding calling for further investigation is whether the general principle of domain-specific innovation applies to the prescription of new medicines. Our finding that the prescription of new diabetes medicines was associated with the prescription of new insulins but not DOACs implicates that the general concept of domain-specific innovation also applies to the prescription of new medicines. This hypothesis warrants further investigation. Further research could focus on associations between the prescriptions of other new medicines in the same therapeutic areas, but also on the relation between non-pharmacological innovations (for example new medical devices) and prescription of new medicines in the same therapeutic area.

A second direction for further research includes the stricter views on endpoints and MCIDs for the evaluation of new medicines by healthcare professionals. Whether this also results in stricter definition of clinical relevance of new medicines cannot be concluded from this thesis, since different medicine groups, years and samples of healthcare professionals are investigated among the studies. It is therefore not known whether these stricter views of evaluation criteria also result in stricter views of the clinical relevance of the new medicines. Future research has to determine how healthcare professionals evaluate the clinical benefit of new medicines, how their assessment relates to that of official institutions and whether an association exists between the definition of evaluation criteria for clinical relevance and ultimate evaluation of clinical relevance of new medicines.

Third, the persuasion strategies used by pharmaceutical industries calls for further studies. To date, it is not known to which extent these strategies affect healthcare professionals. From former studies, it is known that these persuasion strategies activate automatic decision-making processes. To which degree these strategies also affect attitudes and behaviour of healthcare professionals remains to be elucidated. Further research could focus on the impact of these different persuasion strategies on attitudes towards new medicines and prescription behaviour of healthcare professionals.

Overall, this thesis makes clear that initiatives aimed at the rational use of medicines are warranted and offers some lessons for these initiatives. Further research should investigate the impact of these initiatives and confirm whether these initiatives indeed stimulate the rational use of new medicines.

CONCLUSION

Healthcare professionals are, compared to official institutions, in general more strict in defining clinical relevance of new medicines. The attitude of healthcare professionals towards new medicines is an important factor in the decision to prescribe new medicines, and the prescription of new medicines markedly differs between general practices. The unpredictability in the uptake of new medicines and limited role of scientific evidence in decisions to prescribe new medicines indicate room for improvement. Therefore, initiatives to continuously stimulate the rational use of new medicines in primary care are warranted, to ensure that new medicines are prescribed to patients who need them and withheld from patients who do not.

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