Improving antimicrobial prescription in primary care: a multi-dimensional approach to antimicrobial resistance

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Chapter 7

Discussion

Aim

The aim of this thesis was to examine the impact and quality of antimicrobial prescribing in primary care, and to determine the extent to which the quality of antimicrobial prescribing can be improved. This chapter discusses the main findings of this thesis per aim. A discussion of methodological considerations, recommendations concerning how to incorporate the main findings into AMS interventions, as well as future perspectives, is included in this chapter.

Main findings of the research in this thesis

An important finding, described in **chapter 2,** was that the impact of antimicrobial prescriptions originating in primary care may be much greater than previously assumed. The main determinants associated with inappropriateness of antimicrobial prescription, using the framework in **chapter 3,** were found to be 1) presence of comorbidity, 2) the view of many primary care physicians that their approach to antimicrobial prescribing is not responsible for AMR, 3) diagnostic uncertainty, and 4) the supposed expectations of patients regarding antimicrobial prescription. The studies in **chapters 2** and **3** were conducted with international data and the studies in **chapters 4** to **6** with data from The Netherlands .

In **chapter 4** we found that fewer antimicrobials were prescribed to patients during a SARS-CoV-2 episode compared to patients during influenza or influenza-like infection in four other influenza seasons**.** In **chapter 5**, rates for completeness and correctness of antibiotic allergy registrations were 0% and 29.3%, respectively. Perceived barriers to improved antibiotic allergy registration included insufficient knowledge, lack of priority, limitations of registration features in electronic medical records (EMR), fear of medical liability and patients interpreting side effects as allergies. In **chapter 6** we describe the overprescribing of antimicrobials for RTIs and of macrolides. Factors associated with more appropriate antimicrobial prescribing were a Moroccan migration background of the patient and a smaller primary care practice size, which we consider a proxy for sufficient consultation time and continuity of care by the same GP.

Impact of antimicrobial prescribing in primary care

The impact of antimicrobial prescribing in primary care on the development of AMR has not been previously established at country level. As already discussed in detail in the introduction, one could reasonably argue that the impact of primary care on AMR is likely to be low, as narrow-spectrum penicillins are presumably chosen for early disease stages. Results in **chapter 4** underline the necessity of actually assessing impact, as our study showed that some GPs believe that antimicrobial prescribing in primary care does not contribute to the development of AMR (1, 2) and that only hospital and veterinary care are responsible for AMR development. Analysis of antimicrobial prescriptions in **chapter 2** showed that these prescriptions are not primarily confined to narrow-spectrum penicillins, with proportions of penicillin prescriptions ranging from as low as 29% up to 65% in the 12 European countries included in the study. These findings were confirmed in **chapter 6,** where we found that penicillins represent only 44% of antimicrobial prescriptions in Dutch primary care. Furthermore, 11% of all antimicrobial prescriptions were for macrolides, a broad-spectrum antimicrobial, and 77.2% of these prescriptions were not first or second choice antimicrobials as defined in guidelines.

In **chapter 2** we used the antibiotic spectrum index (ASI), a proxy indicator for antimicrobial selection pressure, to assess the impact of antimicrobial prescribing in primary care. The ASI incorporates the volume of antimicrobials used as well as their activity against microorganisms, expressed as an index number representing the spectrum of microorganisms susceptible to that drug (3). This is a novel method to assess the impact of antimicrobial prescribing. The common method is to assess volumes using defined daily doses (DDD). A major advantage of the ASI compared to DDD is the incorporation of an antimicrobial activity spectrum. In our analysis we found a better correlation between ASI and the prevalence of AMR compared to DDD. Between 80-90% of the cumulative ASI in a country originates from antimicrobial prescriptions in primary care, demonstrating that the impact of primary care on antimicrobial selection pressure is much larger than previously assumed.

Our findings are supported by previous studies. A review of 243 studies showed a positive association between the volume of antimicrobial consumption in a country and the prevalence of AMR (4). Another review (n=24 studies) showed that antimicrobial prescriptions for individuals with a UTI in primary care lead to development of AMR to that antimicrobial, which may persist for up to 12 months (5). Compared to previous studies, ours was the first to use ASI to measure impact on antimicrobial selection pressure at the country level.

The high proportion of ASI generated in primary care highlights the central role of primary care in increasing AMR. The unexpectedly low proportion of penicillins and relatively high proportion of inappropriately prescribed macrolides show that antimicrobial prescribing in primary care is not confined to relatively harmless antimicrobials. These results underline the need to include primary care in nationwide AMS programs, and a better appreciation of the impact on AMR will raise awareness among GPs, whose knowledge and awareness will be crucial to the successful implementation of AMS interventions in primary care.

Quality of antimicrobial prescribing in primary care

Role of the patient

Patients play a crucial role in the decision to prescribe antimicrobials, as outlined in **chapters 3 to 6.** The systematic literature review in **chapter 3** identified several patient-related factors, including past experiences leading to expectations of antimicrobial prescription, high expectations of antimicrobial effectiveness, and requests for antimicrobial drugs without justification. Previous literature found an important interaction between patient and GP: the often unverified GP assumption that a patient's wish for an antimicrobial prescription was the reason for their visit (6-9). In fact, patients may visit their GP for a variety of other reasons, such as reassurance (10-12). In **chapter 6** we describe how patients with a Turkish, Surinamese and Dutch-Caribbean migration background were more often prescribed antimicrobial medications considered inappropriate compared to patients with a Dutch or Moroccan background. We assume these patterns are due to cultural differences and/or GP expectations regarding a patient's wish for an antimicrobial prescription. For these groups, it is therefore important to establish whether GPs have unverified expectations regarding a patient's wish for an antimicrobial prescription.

Several studies have explored the reasons underlying antimicrobial overprescribing for RTIs, which we found in **chapter 6**. The studies examined the beliefs, needs and perspectives of patients receiving antimicrobials for RTIs. A Dutch study by Duijn et al. compared patient and GP perspectives on RTIs through questionnaires. Patients placed more emphasis on the seriousness of symptoms, the need to consult a GP, the need to prescribe antimicrobials and the assumption that antimicrobials hasten recovery. By contrast, GPs place more emphasis on the self-limiting character of respiratory tract symptoms and on the side effects of antimicrobials (13). Another Dutch study based on an online questionnaire among 1,248 patients showed that 48% believed antimicrobials are effective in treating a viral infection (14). Encouragingly, around 92%

of patients felt that decisions regarding antimicrobial prescription are the physician's responsibility and that AMR can develop with use of antimicrobials. A German study with a similar design found that, among the 1,076 responders, circa 30% thought that antimicrobials help in case of a cold or flu and 25% thought that antimicrobials are effective against a virus (15). Although most patients with RTI symptoms visit their GP for reassurance and/or physical examination and not for an antimicrobial prescription (10-12), this belief may nonetheless lead to more antibiotic prescription. The results of our studies as described in this thesis, as well as studies by van Duijn et al., Cals et al. and Faber et al., emphasize the importance of effective communication directed to the needs and beliefs of patients (13-15).

Role of general practitioners

A GP's decision to prescribe an antimicrobial should be primarily based on clinical aspects such as severity, type and location of infection as well as expected course and risk of complications. However, the decision is as well influenced by non-clinical determinants such as diagnostic uncertainty, larger practice size, GPs' unverified assumptions regarding patient wishes for an antimicrobial prescription, or an inability to effectively negotiate or explain antimicrobial use. These factors were all observed in the studies described in **chapters 3 to 6**.

Diagnostic uncertainty was identified as an important determinant in **chapters 4 and 6**. Up to 40% of antimicrobial prescriptions for an RTI were not in accordance with primary care guidelines (**chapter 6**). This overprescribing may be partly due to diagnostic uncertainty, as the diagnosis, severity and individual patient risk for a severe RTI course are often uncertain in daily practice. This means that it is not always clear beforehand which patients with an RTI will benefit from an antimicrobial prescription. As shown in **chapter 4**, reducing diagnostic uncertainty may lead to fewer antimicrobial prescriptions. This was illustrated by the reduction in antimicrobial prescriptions for COVID-19 infections compared with influenza-like infections, which was most likely attributable to active testing for SARS-CoV-2 during the COVID-19 pandemic, while testing for influenza virus during influenza seasons is generally lacking. In cases of SARS-CoV-2 infection it was usually obvious to both the patient and the GP that a virus caused the symptoms and an antimicrobial prescription was unnecessary.

Our results showed that the context in which GPs work influences antimicrobial prescribing. A larger practice size was related to relatively more inappropriate antimicrobial prescribing in **chapters 3 and 6**. A scoping review published by Al-Azzawi et al. has examined antimicrobial prescribing in primary care, with a focus on context (practice location, size and GP decision making) and how these factors influence decisions such as antimicrobial treatment (16). The authors of this review concluded that context has a profound impact on the decision to prescribe an antimicrobial and that this is not a “simple” decision.

Another important behavioural aspect is the ability of a GP to communicate, explain and negotiate effectively concerning antimicrobials and disease course (**chapter 3).** This was illustrated in a Danish study which explored the effect of empathy on the rate of antimicrobial prescription (17). GPs showing high empathy prescribed less penicillins compared to GPs showing less empathy. According to the authors, high empathy GPs may prescribe less penicillin because they take more time to explain and meet the patient’s fears and expectations, as well as evaluating antimicrobial choices in their community with reference to local resistance patterns. High empathy GPs may be better at identifying patient’s concerns and expectations and may be better able to contextualize the patient’s infection in the community (17).

This thesis and previous studies have shown that antimicrobial prescribing in primary care is not always based on clinical aspects alone, but also involves nonclinical determinants such as practice size and an ability to communicate effectively. Patients, as well as a GP’s practice context, influence GP behaviour up to a point, but the GP ultimately decides whether to prescribe an antibiotic. This is suggested in a Dutch report, which showed large variation in the number of antimicrobial prescriptions per primary care practice (18). This variation was partly due to differences in encountered infections per practice, patient populations, and factors such as comorbidity, patient age and practice size (19-21), but these differences did not fully explain variance between practices. Practice variation is therefore likely due to differences in style of work, which in turn influences a GP’s decision to prescribe an antimicrobial.

Room for improvement in antimicrobial prescribing

We found significantly higher antimicrobial prescription rates during influenza infections compared to during SARS-CoV-2 infections (**chapter 4**), which was remarkable considering the very similar RTI caused by the two viruses. Both virus types cause a generally self-limiting disease, although both carry a risk of bacterial superinfection and a severe course, potentially leading to hospital admission or even death (22, 23). As previously described, an explanation for differences in prescription rates may have been the influence of SARS-CoV-2 diagnostic testing on decision making. One could therefore reasonably argue that testing for influenza will reduce antimicrobial prescriptions.

A study in the United Kingdom has shown that an influenza point-of-care (POC) test is feasible in primary care (24). A Dutch study concluded that an influenza POC test might contribute to a more precise diagnosis of RTIs (25). Two primary care cohort studies showed that the number of antimicrobial prescriptions is lower if patients with influenza-like symptoms are tested for influenza (26, 27). A randomized clinical trial has been suggested as a way to determine whether influenza POC tests are effective in lowering antimicrobial prescriptions for RTIs which is currently underway (28).

An important finding of this thesis, described in **chapter 6**, was that approximately 40% of antimicrobial prescriptions for an RTI can be considered inappropriate, a proportion similar to other Dutch studies (29, 30). While at first glance there appears to be room for a 40% improvement, there are valid reasons to prescribe an antimicrobial despite guideline recommendations. For example, GP familiarity with their patients and their medical history, as previous similar infections may have had an unexpectedly severe course that required antimicrobial treatment. Another factor when deciding to prescribe an antimicrobial is diagnostic uncertainty regarding RTIs, a problem that will persist as long as reliable tests are unavailable. One strategy to lower diagnostic uncertainty could be the use of prediction models, although these are still based on signs and symptoms, themselves subject to diagnostic uncertainty. Adding CRP testing may make a modest contribution to reducing uncertainty (31). However, we can conclude that reducing presumed inappropriate antimicrobial prescribing for RTIs will be a significant challenge.

In addition to the decision concerning whether to prescribe antimicrobials, we applied two approaches to examine factors influencing the choice between various antimicrobials: antibiotic allergy registrations, as discussed in **chapter 5,** and a simpler dosing scheme, as discussed in **chapter 6**.

Registration of antibiotic allergies may lead to avoidable prescribing of broad-spectrum antimicrobials, as discussed in detail in the introduction (32-38). GPs play a pivotal role in registering allergies and assessing antibiotic allergy registrations as part of their role as gatekeeper in the healthcare system. As described in **chapter 5**, many aspects of antibiotic allergy registration could be improved. All registrations lacked additional contextual information essential to determining the accuracy of registrations, such as the symptoms of an allergic reaction. Adding this information could theoretically lead to a reduction of up to 90% in antimicrobial antibiotic allergy registrations. For instance, one reported intervention in a hospital removed 50% of antibiotic allergy registrations simply by taking a medical history (39). A similar reduction of redundant allergy registrations in primary care is likely to be possible.

However, retrieving additional contextual information that should accompany any allergy registration will be a challenge and will often be impractical due to lack of GP time. Removal of incorrect interpretations of allergy registrations would help considerably in improving the quality of antimicrobial prescriptions, as 1st choice and/or narrow-spectrum antibiotics will be prescribed relatively more often.

Another finding from **chapter 5** was that GPs need a better understanding of antimicrobial allergies in order to be able to accurately assess possible allergic reactions and verify existing antibiotic allergy registrations. This could be initially promoted through education of primary care teams involved in registration, thus increasing knowledge and awareness. Verifying existing antibiotic allergy registrations can be effective in lowering the number of antibiotic allergy registrations.

Another observed problem was difficulty in entering or removing an antibiotic allergy registration in an EMR. Removing registrations is particularly difficult, as due to technical communication issues between different EMRs deleted registrations tend to reappear if not completely removed. When an allergic reaction is entered into any EMR in any domain, registrations in The Netherlands are centralized in a national hub [“landelijk schakelpunt” (LSP)] and subsequently communicated to other EMRs. Removal of the original allergy registration is required to achieve removal of the LSP registration and subsequent removal from other EMRs.

A substantial proportion of macrolides are prescribed to patients despite being neither the first nor second choice in guidelines, as described in **chapter 6**. This finding is corroborated by another Dutch study (40) and should be considered serious overprescription of macrolides to patients. A hypothesized explanation is the simpler dosing scheme of macrolides compared with many first or second choice antimicrobials. Some macrolides need only be taken once a day for only three days, whereas penicillin, for example, must be taken 3 to 4 times a day for 5 or more days. GPs assume that a lower burden for the patient may improve compliance. Indeed, as discussed in **chapter 6,** most macrolides were prescribed for children under the age of 5 years, for whom compliance can be a problem. However, there are no studies confirming our hypothesis. In addition, children in that age group have virtually no contraindications for the use of penicillins. Other explanations might be availability or deliverability, or may relate to the presumed causative microorganisms that justify macrolide treatment. This relative overprescription of macrolides should nevertheless be discouraged, as macrolides generally have a broader antibacterial spectrum compared to penicillin and consequently increase the risk of AMR. One can reasonably argue that a substantial proportion of these prescriptions could be avoided.

Antimicrobial stewardship interventions in primary care

Earlier sections described determinants that affect the quality of antimicrobial prescribing and what might be improved in primary care. This section is dedicated to how these results might be integrated into existing AMS interventions to improve the quality of antimicrobial prescribing. When implementing (more) effective AMS interventions, several aspects have to be considered: combined AMS interventions are more effective than a single intervention (41), active rather than passive implementation is most effective (42), and multilevel barriers and facilitators of AMS uptake should be identified before implementation of an AMS intervention (43).

Improving the patient experience

As described earlier, patients often have more diverse needs and beliefs about RTIs than GPs assume. Effective interventions should incorporate these needs and beliefs. Patients sometimes express the wish for an antimicrobial prescription without a medical reason. This wish or need can nevertheless be fulfilled through delayed antimicrobial prescribing, a scenario in which a GP prescribes an antimicrobial but persuades the patient to postpone its use until symptoms worsen or become too prolonged. Studies have found that patients with an RTI or UTI may be willing to postpone antimicrobial use (44, 45).

For a variety of RTIs this delayed antimicrobial prescribing strategy was found to be safe compared to direct antimicrobial prescribing (46), and no difference in patient satisfaction was found between the two strategies. A meta-analysis has shown that delayed antimicrobial prescribing is safe for most patients, even in a higher risk group (47), and no difference was seen in RTI complication rates or patient satisfaction. Delayed prescribing may reduce consultation rates compared to no antimicrobial prescribing, and postponing an antimicrobial prescription for UTIs reduced antimicrobial prescriptions by 63% (48). However, postponing an antimicrobial prescription for a UTI was associated with higher risk of incomplete recovery (OR 3.0 95% CI: 1.65 - 5.47) or a complicated UTI (OR 5.63 95% CI: 2.29-13.87) (48). Both can still be treated effectively and no urosepsis cases were reported in the review.

Patients often consult a GP for a physical examination or seek reassurance when nothing is seriously wrong (10-12). The actual need of the patient at that moment is reassurance, which can be fulfilled via other communication channels such as eHealth (e-mail and online consults). During the COVID-19 pandemic, the telehealth approach used for RTI consults satisfied patients (49, 50). Patients need easy access to reliable information, and Thuisarts.nl has been shown to be a safe and effective online platform that can inform and reassure patients (51).

Assisting General Practitioners

Diagnostic uncertainty is a major determinant of inappropriate antimicrobial prescribing. In the case of an RTI this can be addressed through use of the C-reactive protein point-of-care (CRP-POC) test. When a GP is in doubt, a CRP-POC test can be used to discriminate between an uncomplicated versus complicated RTI. Use of this test has proven effective in lowering the number of antimicrobial prescriptions (52-56).

Antimicrobial overprescribing for RTIs and overprescribing of macrolides can be tackled using several interventions. For example, GP communication training on RTIs (57), GP education and a feedback session on antimicrobial prescribing were all effective in reducing prescriptions (41, 58-63). Feedback sessions may provide insight concerning the number of antimicrobial prescriptions a GP writes and their impact on antimicrobial resistance, which may in turn encourage a physician to reflect on his or her antimicrobial prescription habits.

Large practice size and GPs failing to verify assumptions about a patient wanting an antimicrobial prescription were the main determinants associated with more inappropriate antimicrobial prescribing in **chapters 3 and 6**. The latter factor is the most likely explanation of higher inappropriate antibiotic prescribing for patients with a Turkish, Surinamese and Dutch-Caribbean background (**chapter 6**). This illustrates the benefits of efficient communication skills and having sufficient time to communicate with patients.

Methodological considerations

The outcomes and interpretation of the studies described here should be viewed in the context of the strengths and limitations of each study. The studies described in **chapters 3, 4, 5 and 6** used routinely collected healthcare data. In **chapter 6,** a large healthcare registry was combined with a large registry containing data on social-economic determinants. A limitation of this approach is that health records are not primarily designed for research purposes, which can result in missing data as not all required information is systematically recorded. Missing data can lead to registration bias, causing either under - and over-registration. However, as the healthcare registries used in **chapter 4, 5 and 6** contained very large amounts of data, any registration bias was probably diluted and unlikely to affect the results of our studies. Regarding strengths, the use of routinely collected healthcare data for medical research has many advantages, providing relatively easy access to rich, ecologically valid, longitudinal data from large populations (64). It reflects daily practice and combining two different registries at the patient level makes it possible to examine new causal associations.

A second methodological consideration is the use of proxy indicators as in **chapters 2 and 6**. Proxy indicators, such as ASI or size of a primary care practice can be used where it is not possible to extract the desired endpoint variable, in these cases antimicrobial selection pressure and time per patient visit, respectively, from available healthcare registries. Advantages of these proxy indicators are their availability, reproducibility and measurability compared to the desired endpoints. A disadvantage, however, is the somewhat simplified representation of reality.

A third methodological consideration is the context in which the studies took place. The main country of research in this thesis was The Netherlands, which differs from other European countries in a variety of ways. For example, the number of antimicrobial prescriptions in The Netherlands is lower compared to most European countries (65), which could be due to the fact that GPs in The Netherlands are both well informed and constrained by restrictive guidelines, leading to prudent antimicrobial prescribing. Consequently, AMR prevalence is lower compared to most other European countries (65). If AMR prevalence in a country is low, GPs already tend to prescribe narrow-spectrum antimicrobials, helping maintain the low prevalence of AMR. GPs in The Netherlands function as gatekeepers in the healthcare system and all inhabitants are registered with only one primary care centre. Both of these contextual factors help lower the number of antimicrobial prescriptions (66).

Despite the relatively lower number of antimicrobial prescriptions and low prevalence of AMR in The Netherlands, it is reasonable to generalize the results from **chapters 2, 3, 4 and 6** to other countries, as for example the high number of seemingly inappropriate antimicrobial prescriptions for RTIs described in **chapter 6** reflects results of many previous studies in other countries (67-70). Our study underlines the fact that inappropriate antimicrobial prescriptions for RTIs may be high, even in a country with a low overall antimicrobial prescription rate. Despite the low overall rate of antimicrobial prescription there is still room for improvement in The Netherlands, which could act as a reference point for other countries. Furthermore, our findings on specific migrant backgrounds may be reproducible in other European countries, although these findings may need to be reconfirmed in their specific context.

Future perspectives

The overarching goal of this thesis was to find starting points to improve the prescribing of antimicrobials to slow down the unavoidable increasing prevalence of AMR. The results from this thesis showed that antimicrobial prescribing in Dutch primary care can generally be considered as prudent. Dutch GPs tend to follow the recommendations provided by the guidelines (**chapter 6**), resulting in a lower prescription rate in primary care when compared to many other European countries (65). However, there is still room for improvement as can be deducted from the results of the studies described in **chapter 5** and **6**. Here we found that there is an overprescribing of antimicrobial therapy for RTIs and that there is an overuse of macrolides. In addition, the incorrect registrations of antibiotic allergies lead to avoidable prescription of broad-spectrum instead of low-spectrum antimicrobials. It is clear that these elements need to be improved.

An extra challenge in primary care regarding AMR is formed by epidemiological changes in the Dutch population, such as aging and the therewith increasing number of co-morbidities. Both are associated with antimicrobial overprescribing (**chapter 3** and **6**) and will probably lead to more antimicrobial use in the long-term with the risk of an increasing AMR prevalence. This makes the previously described need for improvement and continuation of already prudent antimicrobial prescribing practices even more important.

The aging population and increasing number of comorbidities will increase patients need to consult a GP for RTI symptoms as they seek reassurance (10-12). This need can not only be addressed through consultation in a primary care practice, as GPS are already experiencing to be overloaded with work. To address this need, other ways of communicating with and informing of patients has to be researched and implemented. For example, mass media campaigns informing patients on the self-limiting character of RTIs and interactive websites or smartphone apps informing patients when they have contact the primary care.

Another aspect regarding interventions, they have to focus on patient groups who visit a primary care practice more often and use more antimicrobials, as current interventions are mostly 'one size fits all'. There is a need for tailored made interventions as shown in this thesis. For example, compared with other migrants groups, patients with a Turkish, Surinamese and Dutch-Caribbean background were more often prescribed inappropriate antimicrobials (**chapter 6**). This finding highlights our current lack of knowledge concerning the influence of migrant and cultural background on antimicrobial prescribing in primary care. Qualitative research, such as focus groups or interviews, is needed to further explore and explain these findings.

Another future challenge is the expected increasing AMR prevalence. More treatment failure with small spectrum antimicrobials will probably occur, leading to more broad spectrum antimicrobials prescriptions. This cascade requires up-to-date and more proactive surveillance of antimicrobial use and resistance in primary care. In addition, this surveillance can be part of the pandemic preparedness as shown in **chapter 4**. If there is an increase in antimicrobial use, specifically broad-spectrum, or an increase in resistant bacteria groups, intervention aimed at these developments can be implemented immediately. For example, through adjustments in national guidelines, messages in newsletters of national organisations or by pharmacotherapy education. Artificial Intelligence (AI) or Big Data can contribute to this surveillance. **Chapter 6** showed that Big Data is applicable for analysis of antibiotic use. By use of these resources new relevant associations between antibiotic prescriptions and migrant groups were discovered. The use of AI in surveillance not only in the analysis of antimicrobial prescribing behaviour, but also in the support of prescribing process itself, is the next step to be investigated in this regard.

Conclusion

The aim of this thesis was to examine the impact and different elements of antimicrobial prescribing in primary care, and to define the extent to which the quality of antimicrobial prescribing can be improved. These goals were selected in light of our ultimate aim, which is to prevent a further increase in the prevalence of AMR. This can be achieved by, among others, improving the quality of antimicrobial prescribing in primary care. As antimicrobial prescribing in primary care is influenced by numerous varied factors this thesis took a multi-dimensional approach, with each study addressing a different dimension of AMR in primary care.

A important finding was that primary care may have a much larger impact on the development of AMR than previously assumed. Important determinants of this impact were diagnostic uncertainty, inability to effectively negotiate or explain antimicrobial use, as well as the assumption that patients expect an antimicrobial. Considerable improvements in antimicrobial prescribing in primary care can be achieved for RTIs, macrolide prescription and for patients with a specific migrant or cultural background (Turkish, Dutch-Caribbean, Surinamese). The registration of antimicrobial allergies could be improved through better education of GPs to increase awareness and knowledge, by verifying existing antibiotic allergy registrations and through easier registration in the EMR. These improvements would help lower the number of antibiotic allergy registrations and therefore increase prescribing of first choice antimicrobials instead of second choice (broad-spectrum) antimicrobials.

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