IMAGINE - IMproving Adherence to Guidelines in Infectious diseases through Nudging and Education

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CHAPTER 10

Summary of main findings, general discussion and future directions

GUIDELINE ADHERENCE IN ANTIBIOTIC PRESCRIBING AND INFECTION CONTROL

Antibiotic resistance describes the ability of bacteria to withstand the effects of our antibiotics. The problem of antibiotic resistance is growing and has been named one of the biggest challenges facing twenty-first century medicine. It is not an overstatement to say that most of modern medicine hinges on the effectiveness of antibiotics: without them, a large part of medicine (e.g. surgery, chemotherapy) becomes impossible. The biggest threat is that everyday infections may eventually become untreatable; preventing development and further dissemination of antibiotic resistance is therefore of the utmost importance.

Two factors greatly influence dissemination: firstly, the (unnecessary) use of antibiotics, and secondly, transmission, for example from person to person. Efforts directed at the first factor aim to prevent development of resistance by promoting prudent use of antibiotics. These interventions are collectively known as antimicrobial stewardship. The key to the second factor lies in prevention, through infection control measures such as hand hygiene.[1] Although the connection between these two factors seems evident (if you prevent infections, you will prevent the need for antibiotics), they are rarely viewed as two sides of the same coin; efforts to promote antimicrobial stewardship and efforts to promote infection control are remarkably disconnected.

In January 2014, the Amsterdam UMC, location VUmc, in Amsterdam, The Netherlands, initiated the Commission on Infection prevention and Antibiotics (CIA). The aim of this new commission was to combat antibiotic resistance by combining efforts to tackle both of these factors. To aid antibiotic prescribing and infection prevention, a lot has been invested in national and local guidelines. Unfortunately, adherence to these guidelines is notoriously poor: hand hygiene is often inadequate and inappropriate prescribing of antibiotics remains frequent, despite decades of trying to achieve improvement.[2,3] The most important question therefore was: how can we promote adherence to these guidelines? This question is addressed in part I of this thesis.

PART I – Behavioural interventions

It is increasingly recognized that improving guideline adherence requires behaviour change. Safety culture is one of the factors that seems to play an important role in achieving this.[4,5] The importance of culture in hospital units became evident during one of the CIA's projects, in which we launched an extensive hospital-wide campaign to improve adherence to hand hygiene guidelines (also known as compliance). We performed a before-after trial to measure whether compliance had improved after the campaign and found great differences between hospital units in how much improvement had been achieved. In the qualitative investigation of safety culture that followed, we found that units with high levels of safety culture had improved their compliance, while units with lower levels of safety culture had not **(chapter 2)**. This suggests that strengthening safety culture before implementing interventions (for example through team building exercises) could aid in achieving the behaviour change that is needed for improved guideline adherence.

Although guidelines are meant to support healthcare workers' decision-making, they can be perceived as a way of 'being told what to do', which can make them counterproductive. A second important factor in achieving behaviour change is therefore involving stakeholders to prevent this sense of being ordered around. Structured group processes such as participatory action research, nominal group technique, and root cause analysis can be used to generate ideas, reach consensus, and engage group members in problem solving.[6,7] In another CIA project, we applied this approach to promote adherence to hospital dress code. Identifying causes for non-compliance and involving all stakeholders in the development of interventions to target these causes, led to improved adherence **(chapter 3)**. These results strengthen previous findings that have shown that involving members of the target audience and addressing their barriers is essential in order to achieve behaviour change and improve guideline adherence.[8]

A third possibly useful method to achieve behaviour change is nudging: a friendly push to encourage desired behaviour. When healthcare workers seldom encounter clear problems of infections caused by antibiotic-resistant bacteria, they will consider the odds of transmission negligible, and this will greatly reduce their willingness to adhere to guidelines. This is caused by so-called 'heuristics'. Heuristics are defined as decisional short-cuts which can be useful, as they help us to quickly make judgements or decisions. However, when heuristics lead to cognitive biases, they may confound our judgement and thus influence our behaviour, which can lead to non-compliance. Nudges can address heuristics and cognitive biases and thus encourage certain behaviour. This was previously shown for influenza vaccination among healthcare workers: nudges specifically designed to target heuristics regarding vaccination were able to increase vaccine uptake.[9] In addition, nudges displayed as posters in general practitioners' offices reduced unnecessary antibiotic prescriptions.[10] A systematic review of the literature provided us with several cognitive biases that can play a role in non-compliance with hand hygiene. In a controlled before-after trial, we showed that nudges, based on these cognitive biases and displayed as posters, can increase the use of alcohol-based hand rub when shown next to dispensers **(chapter 4)**.

Nudging could therefore provide an easy, inexpensive measure to support behaviour change strategies and thus promote guideline adherence.

EDUCATING JUNIOR DOCTORS

The 'better to prevent than to cure' approach is also useful in education: teaching certain behaviour from the start is considered more effective than attempting to change behaviour later on. This also applies to educating junior doctors on antibiotic resistance. In Dutch hospitals, junior doctors are responsible for the majority of antibiotic prescriptions and play a key role in infection control, as they have very frequent interactions with patients. Strangely, they are seldom addressed in antimicrobial stewardship interventions, nor taught how to comply with infection prevention measures. At the same time, junior doctors frequently report a lack of knowledge and clinical skills such as prescribing medication, particularly antibiotics.[11,12] Education aimed at guideline adherence in busy daily practice therefore seems needed. E-learning appears to be a valuable method, but to fully benefit from e-learning, more insight is needed into its merits and into ways to maximize its effect. Part II therefore addresses education of medical students and junior doctors on these subjects, with a focus on e-learning as an educational tool.

PART II – E-learning

Although e-learning is increasingly used, little is known on its effectiveness in changing long-term prescribing behaviour.[13-15] We performed a prospective controlled intervention study among VUmc medical students, in which we implemented an e-learning module on antibiotics as a temporary, non-compulsory course for fourth-year students **(chapter 5)**. Students in the intervention group performed better in their prescribing examinations six months later, with higher pass percentages (97% versus 86%) and higher scores. This means that e-learning during a limited period can have long-term impact, and can impact behaviour in a situation that mimics clinical practice.

However, a common downfall in non-obligatory e-learning is suboptimal participation. E-learning requires a lot of motivation, as it is usually non-obligatory and performed individually. This applies even more to postgraduate e-learning, as residents need to combine learning with (often demanding) clinical duties. In a cohort study among residents of four hospitals (two university medical centres, two teaching hospitals), we found that participation in non-obligatory e-learning on antibiotic prescribing was higher in residents with more autonomous motivation **(chapter 6)**. Autonomous motivation is described as motivation that originates from an interest in the subject or an understanding of its importance, as opposed to controlled motivation, which comes from rewards (such as credits).[16] Studies have shown that autonomous motivation is associated with higher study effort in medical students,[17] higher achievements in residents,[18] and more increased participation in continuing education among pharmacists.[19] This means that interventions to increase autonomous motivation could improve e-learning participation. Face-to-face education to explain the importance of the subject preceding e-learning, could enhance autonomous motivation and thus optimize e-learning participation.

Two other important aspects of educating junior doctors are of note. Firstly, timing. In VUmc, we interviewed residents from several specialties and found that junior doctors experience a hectic first few months, during which they are not receptive to (e-)learning. Secondly, while e-learning obviously aims to educate, we ultimately want doctors to put this knowledge into practice, a process that also requires behaviour change. We found that 'nudging', 'creating a social standard', formulating an 'implementation intention' and 'public commitment' are behavioural interventions that are easily incorporated in an e-learning module and are all acceptable to junior doctors **(chapter 7)**. Determining the most opportune moment for e-learning and combining a module with behavioural interventions seems promising to improve junior doctors' antibiotic prescribing and adherence to infection control guidelines.

DESIGNING GUIDELINES

One important question remains: if we aim to promote guideline adherence to prevent further dissemination of antimicrobial resistance, how well are the guidelines themselves designed to do that? In part III, we investigated this for two common guidelines on antibiotic prescribing and infection control.

PART III – Antibiotic stewardship and infection control in guidelines

Guidelines for antibiotic prescribing provide recommendations for empiric treatment of infections. Empiric means that at the time of prescribing, the causative organism and its susceptibility to antibiotics are not yet known, therefore treatment is based on epidemiology: the most common causative pathogens of this type of infection and their susceptibility to antibiotics.[20] Guidelines for empiric treatment are usually adjusted when resistance of the most likely pathogen reaches 10%.[21] This makes sense for 'simple' infections such as urinary tract infections: most are caused by *Escherichia coli*, therefore if *E. coli*'s resistance to the empiric therapy increases, this will affect most patients. However, this approach causes a problem when dealing with infections with many possible causative agents, such as bloodstream infections (BSI). In a multicentre, retrospective cohort study, we investigated Ð4000 patients suspected of BSI. We found that resistance to second-/third-generation cephalosporins (3GC) affected less than 2% of patients suspected of BSI, despite 3GC-resistance among Gram-negatives reaching 20%.

Patients suspected of BSI encompass a large and diverse group; there are many possible causative pathogens, and blood cultures often remain negative.[22] This causes a phenomenon we named 'dilution' of resistance **(chapter 8)**. We additionally found that in these patients, the use of more broad-spectrum antibiotics (i.e. carbapenems or aminoglycosides combination therapies) significantly increased the risk of *Clostridium difficile* infection and acute kidney injury, respectively. In addition, broad-spectrum therapy was deemed superfluous in as many as eight to nine out of ten patients to whom they were prescribed. Although the issues with cut-off percentages for single pathogens have been pointed out before,[22,23] this approach to adaptation of empiric treatment is still common practice. Efforts to improve risk stratification are needed to better guide empiric treatment decisions.[24] However, until then, the practice of adapting empiric therapy based on resistance of the most likely pathogens, without taking into account that this resistance only occurs in a very small proportion of patients suspected of BSI, may lead to high overtreatment rates with an associated increase in important adverse events, and further development of antibiotic resistance. Efforts to promote prudent antibiotic prescribing should therefore also focus on whether guidelines are 'stewardship'-proof, as this is overlooked in current approaches.

An important question in clinical decision making is the treatment and prevention of infections when using medical devices, such as urinary catheters and intravenous lines. It is common to think that timely replacement of such devices may prevent infection, especially when they are in place for longer periods of time. However, as replacement of these devices has several downsides, such as patient discomfort and risk of bleeding, the question of prevention over cure is more complicated. In haematology patients, peripherally inserted central catheters (PICCs) are used for venous access and may remain in situ for weeks or even months. Unfortunately, like other central lines, PICCs are associated with central line-associated bloodstream infection (CLABSI).[25] Previous studies have proposed that bacterial colonization of central lines is non-linear, i.e. that the risk of infection increases with longer indwelling time.[26-28] Under this assumption, routine replacement of PICCs may prevent CLABSI and thus lower the need for antibiotics. In a multicentre cohort study, we assessed 455 PICC episodes in 352 haematology patients, constituting 18977 catheter days. We found that in these patients, the cumulative risk of CLABSI increases slightly during the first 28 days, but does not increase with longer indwelling time thereafter. These findings suggest that routinely replacing PICCs before 28 days, e.g. after 2 weeks, would prolong the period of increased risk, while routine replacement thereafter would not aid in preventing PICC-associated infections in this population **(chapter 9)**.

FUTURE DIRECTIONS

The challenge of antibiotic resistance has many facets, including important behavioural, political and financial aspects. The importance of the latter is painfully portrayed by what has been named the *discovery void*, an ongoing period since 1987, during which no (genuinely) new classes of antibiotics have been developed. To pharmaceutical companies, development of new antibiotics is not of interest: antibiotics are used for a very limited time (typically a few days to a few weeks) and physicians are encouraged to use as little of them as possible, so expected revenues are too low. This means that other incentives (for example from governments) are needed to secure investments in research and development, but these are slow to take form.[29] Therefore, until then, we must preserve what is left of our precious antimicrobial arsenal; prescribing doctors carry the heaviest responsibility in securing their future effectiveness.

Preserving the efficacy of antibiotics forms the cornerstone of antibiotic stewardship programs, which encompass efforts to ensure prudent use. However, as mentioned before, most of these programs disregard a very clear aspect of the antimicrobial resistance challenge. The saying 'an ounce of prevention is worth a pound of cure' most certainly goes for antibiotic resistance: prevent infections, and there will be less need for antibiotics. This has been an important factor underlying this thesis; much of the work was founded on the notion that antibiotic stewardship and infection control are intertwined themes that need a combined approach and can benefit from approaches based on the same concepts. The work presented in this thesis shows that involving the target audience and addressing their barriers is essential to creating successful interventions and consequently achieving behaviour change. This not only applies to the design of new interventions, but perhaps even more so to the implementation of interventions that were developed elsewhere, as these are typically less successful.[30] This failure to implement previously successful interventions is often attributed to the 'not invented here syndrome'. This syndrome causes a negative attitude towards products or knowledge developed in other organizations or disciplines, which leads to its suboptimal utilization or even rejection. Instead of fighting this syndrome, we can utilize its positive counterpart, known as the IKEA-effect. The IKEA-effect causes us to have greater appreciation for our own creations than for items that are identical, but were constructed by someone else.[31,32] Taking existing guidelines or interventions and having healthcare workers shape them to make them their own, can be a powerful tool to generate support and ultimately adherence. In addition, despite our scientific tendency to look for highly successful single interventions, we have shown that it pays to look for seemingly small interventions, such as nudging, that can support other, perhaps more impactful ones.

The concept of nudging relies on the fact that the layout of our surroundings influences how we choose. This means that 'choice architecture', a term coined originally by Thaler and Sunstein,[33] makes it possible to impact decision-making. We all know how attractive products can look when positioned near the supermarket check-out: a layout or 'architecture' that causes us to make impulse buys. Although often criticised as a mere way to trick consumers into buying things they do not really need or want,[34] nudging is also widely used to stimulate healthy behaviour, such as smoking cessation and healthy food choices: descriptive labels that highlight a product's favourable characteristics, such as 'low-fat,' can nudge consumers towards the healthier choice.[35,36]

Nudging of healthcare workers has only recently been addressed in a few studies, in which various kinds of nudges proved successful in influencing physician prescribing behaviour.[10,37-39] Although the exact mechanism has not been clarified, it has been suggested that nudges can also influence behaviour by addressing cognitive biases that underlie someone's non-compliance.[9] Cognitive biases are often caused by 'heuristics'. Described in detail by Tversky and Kahneman, heuristics can be defined as decisional shortcuts which can be useful, as they help us quickly make judgements or decisions.[40] However, when heuristics lead to cognitive biases, they can confound our judgement and thus influence our behaviour. In medical decision making, several cognitive biases and underlying heuristics have been proposed to play a role.[41,42] A striking example is the 'availability heuristic', which describes how we assess the probability of an event by the ease with which we can recall it: the easier an event is to recall, the more likely we consider it to occur.[40] For example, if physicians have just diagnosed a patient with a rare disease, in their next patient, they will consider a diagnosis of that same rare disease much more likely. Conversely, this means that if prevalence of healthcare-associated infections is low, healthcare workers are inclined to believe that the chances of transmitting an infection through lack of hand hygiene are also low, thus leading to non-compliance.[43] A vital feature of nudging is that it makes choosing a preferred option easier, without taking away less fortunate alternatives. Nudging thus preserves professional autonomy, which is integral to improving guideline adherence.[8] It is a strategy not yet commonly used in health care (perhaps also driven by the, not invented here, syndrome), but with enough promising potential to warrant further research.

As virtually all doctors are allowed to prescribe antibiotics, regardless of specialty, experience, or knowledge, it has to be made clear to all (aspiring) doctors that antibiotic resistance is a complex problem, that requires their attention. Unfortunately, education of future prescribers is often overlooked in antibiotic stewardship programs. Prudent use of antibiotics is an integral part of rational medical decision making, and should be approached as such from the beginning of medical training. This includes education on how to handle guidelines: a vital but sometimes neglected aspect of guideline adherence is reasoned deviation from them, which we should actively teach future and junior doctors. An undergraduate to postgraduate continuum that incorporates blended learning (a combination of face-to-face learning and e-learning), explains their responsibility towards preservation of antibiotics,[44] and teaches them how to handle guidelines, is needed to achieve responsible prescribing. To fully benefit from blended learning, future studies should focus on the remaining question whether face-to-face education can enhance participation in e-learning and can thus improve appropriate prescribing.

Rising antibiotic resistance also challenges us when we develop guidelines for empiric antibiotic treatment. Empiric therapy comprises a calculated risk: the risk of empiric undertreatment versus the risk of adverse events due to empiric overtreatment. When considering adaptation of empiric guidelines, we are confronted with an increasingly delicate balance between the two. Although the effects of (unnecessary) treatment with broader-spectrum antibiotics on the development of antibiotic resistance are well-known,[45,46] fear of too narrow empiric treatment usually dominates, and side effects in individual patients are often brushed aside. Our study showed that resistance rates of a subgroup of possible causative pathogens have little impact on the risk of undertreatment, which means that this resistance does not translate well to the individual patient. Efforts to improve risk stratification[24] and decrease time to susceptibility results are therefore much needed to guide future empiric treatment decisions.

Antibiotic resistance is a complex problem and its prevention requires complex interventions. The next step in efforts to prevent further dissemination of antibiotic resistance would be to combine the findings of this thesis, and assess its effect on antibiotic prescribing and infection control in clinical practice during a randomized trial. As junior doctors are often overlooked in stewardship interventions, they should be the target population for further research.

We previously applied the lessons learned from **chapter 7**, in which we assessed the needs of junior doctors regarding education on antibiotic prescribing and infection control, to develop an e-learning module. This module was pilot-tested and evaluated among junior doctors, with input from medical specialists, infectious disease experts, and behavioural and educational experts. It consists of case vignettes, web lectures, and interactive quizzes aimed at junior doctors' needs, and focuses on overcoming perceived barriers. It would be interesting to combine this educational module with several behavioural interventions, such as explicitly formulating a commitment to apply these skills in daily practice,[47] cues that remind participants of their commitment to reinforce its effect and nudge them towards the desired behaviour,[10] and face-to-face explanation of the importance. Most importantly, not the interventions themselves, but the approach to their development is integral to their success; therefore close collaboration with local stewardship programs is paramount to make full use of the IKEA-effect. We would propose to apply this combined intervention in a multicentre, stepped wedge, cluster randomized trial by reviewing appropriateness of antibiotic prescriptions[48] and the occurrence of hospital-acquired infections before and after implementation, to assess the effect on those for whom it matters most: our patients.

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