Improving medical decision making: Stroke prevention in atrial fibrillation
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Chapter 9

General discussion
General discussion

This thesis consists of three parts. In part A of this thesis we investigated guideline adherence to the guideline for atrial fibrillation (AF) of the Dutch College of General Practitioners (NHG) and appraised the guideline to identify barriers to adherence. We found low adherence to the guideline resulting in both over and under treatment. During our appraisal of the guideline we identified several potential improvements for the structure and contents of the guideline. Next we searched the literature and categorized reasons for intentional non-adherence in a systematic review. Reasons for guideline non-adherence were frequent and sometimes valid, pertaining to patient preferences and contra-indications.

Part B presents the main study of this thesis: The Expert-AF trial. We implemented a clinical decision support system (CDSS) to improve adherence to the Dutch NHG AF guideline and evaluated its effectiveness in a cluster randomized trial. We could not show a significant increase in guideline adherence as a result of the implementation of the system. We did, however, identify valuable insights into barriers to usage in a mixed-methods evaluation of the system. In Part C we take a first step towards better prediction of stroke using complex prediction models, and show that these models hold promise for the future of stroke prediction. Chapter 10 contains a summary of each individual chapter.

THE EXPERT-AF TRIAL

To gain insights into real-life performance of interventions, the use of pragmatic trials should be propagated (1). We designed the Expert-AF trial, in which a CDSS for prevention of stroke in patients with AF was tested. We randomized clusters of GPs and offered real-time decision support in a non-obtrusive way. Furthermore, we planned to freeze the GP EHR system when a GP deviated from the advice. This condition was meant to force the GP to explain why he or she deviated from the guideline.

A strength of the Expert-AF project was its pragmatic nature: a multi-domain clinical decision support system implemented in the busy daily practice of the GP. This made it difficult for GPs to establish whether they were randomized in the intervention or the control group. The fact that the Expert-AF project was embedded in a multi-domain CDSS might also have worked against it; it greatly increased the number of alerts presented, which in turn might have resulted in alert fatigue (3).

We were required to work with the vendors of the GP Electronic Health Record (EHR) systems. This proved to be a hurdle, as we weren’t able to implement every feature that we required in a way that we wished. We were, for instance, not allowed to freeze the GP’s EHR system when requiring the GP to enter a reason for deviating from a recommendation, a feature that has shown to increase CDSS effectiveness and could have provided us valuable information about possible shortcomings of the guideline (2).
Furthermore, discontinued support for the CDSS plugin meant that we could not include more GPs in the trial, limiting representativeness of the sample. Despite these limitations, this trial provided us with valuable insights that can guide future designers of clinical decision support systems.

IMPLICATIONS FOR SCIENCE AND PRACTICE

On guidelines
This thesis has shown that guideline adherence in atrial fibrillation is poor (4). However, there are valid reasons to deviate from guidelines and perfect adherence is not desirable, considering the current quality of guidelines (5). Expert opinion and experience often fill in the gaps that guidelines currently leave open, especially in older patients with multimorbidity and a short life expectancy. Although some doctors refer to “cookbook medicine” when discussing guidelines, that doesn’t do justice to the concept of EBM, in which external evidence from properly conducted research should be used in conjunction with clinical experience and expert opinion to provide the best care possible (6). That is by no means cookbook medicine, as the physician and patient ultimately determine the treatment strategy together. Therefore, real-world studies are necessary when studying the proper use of guidelines. This is especially true in that many guidelines have several limitations and cannot be easily applied to complex individual patients (7-9). As it stands, we should accept that perfect guideline adherence is currently unattainable in complex patients. Thus, expert opinion and patient preference should dictate prioritization in cases where guidelines cannot.

On decision support
Healthcare is becoming more complex and demanding (10). Properly implemented guidelines can improve clinical practice (11, 12). Many look to CDSS to improve guideline adherence, but currently these systems cannot fulfill that promise. While some studies have shown the effectiveness of CDSS, mainly in a single-disease setting, many other studies, including our Expert-AF trial, have failed to do so (13, 14). The qualitative evaluation of our trial revealed many important barriers that limited effectiveness of our intervention. These barriers were also identified in similar trials and reviews studying CDSS effectiveness (15-17). The most important barriers we have identified in this thesis relate to lack of time (for the GP), lack of context, and lack of functionality. To remove these barriers, much work is needed. First, we need to address the issue of lack of time and alert fatigue. How can we effectively present the physicians with gaps in current patient care, without overloading them with recommendations during their already busy day (18)? Alert prioritization, customization, and different modes of presenting alerts can be a step
in the right direction. These features will allow the user to prioritize specific disease areas over time and tailor recommendations to personal preferences. This will reduce the number of alerts shown at one time and optimize integration into a personal workflow. To further increase CDSS effectiveness, patients should be involved in prioritization of health issues. Personal Health Records (PHR) and pre-visit questionnaires can be used to inform patients about issues that were detected by the CDDS and allow them to prioritize these issues before meeting with their physician (online or offline) (19).

Realistic, controlled lab tests (including simulation patients), should be used to determine how to implement these features. These lab tests should precede further real-world trials, as implementation in real-world systems may restrict the freedom needed to perform robust trials with reproducible outcomes, throughout different fields of medicine. Results from these simulations can be used to expand on current theoretical frameworks, such as the Two Stream Model (20). Once we have established and confirmed properties of effective CDSS in various simulated clinical settings, we should proceed with real-world trials, based on a solid theoretical framework. Researchers and vendors can use the theoretical knowledge of “what works”, to slowly transform existing systems into platforms that allow implementation of all features that make CDSS effective. Collaboration between international research groups and standardization of research protocols is preferable. This can result in best practices that are more generalizable and allow for distribution of tasks, resulting in better use of research funding.

**On complex prediction models in clinical practice**

Current risk stratification scores are often based on data from old trials, and individual risk factors are subject to interpretation (21). High-quality data should never be wasted, and ideally we would use all relevant data, old and new, global and local, to create the best disease prediction models possible. By “local” data, we mean data that are collected in one region or even in one hospital. These data can be used to fine-tune existing models and can account for geographic differences and local definition of risk factors. Using these locally optimized models can improve risk stratification accuracy (22). The increasing interest in “personalized medicine” (inclusion of, e.g., biomarkers to determine treatment for individual patients and adapting interventions to a complex personalized context) increases the need for complex prediction models that require the computational power of modern computers (23-25). These models allow for the complex non-linear relationships between risk factors and (bio)markers that personalized medicine requires. Studies have shown that stroke prediction in patients with AF can benefit from the incorporation of biomarkers (26-28). Net benefit of anticoagulation in this patient group can be high, but side effects of anticoagulants are severe, making this domain a good candidate for early trials on computerized personal prediction models.
Decision support systems can and should be used to implement personalized medicine through these prediction models, as traditional methods of decision support, such as paper guidelines, will not be able to effectively guide patient-specific medical decision making. Decision support will become more effective using personalized predictions and simultaneously involve patients in the decision-making process.

**FUTURE PERSPECTIVES**

Healthcare complexity and costs will continue to increase: Personalized medicine will make caring for individual patients more complex, aging populations will require more long-term care, expensive new treatments will continue to emerge, and administrative requirements will likely increase. Computerized, locally optimized guidelines will likely play an important role in dealing with these changes. Figure 1 provides an overview of the concepts we mention hereafter, sections are referenced as numbers in square brackets. Standardized guideline development and increased scientific knowledge may result in higher-quality guidelines, and medical societies [1] may start publishing their own “e-guidelines” [4], consisting of decision rules using crisp (unambiguous) definitions of medical terms [29, 30]. Standardized EHR data may allow for continuous [8], real-time feedback loops with primary outcome data that can be used to identify gaps in (e-)guide-
lines and improve prediction of disease and therapy effects (Figure 1). Increased sharing of higher-quality research data [2] may enable learning algorithms for early disease prediction [3] that can be implemented uniformly in EHRs (31). Early patient involvement will allow decision support systems [5] to provide recommendations that are deemed relevant for individual patients. The use of computerized complex prediction models will allow for visualization of patient-specific net benefit (and risks) over time, enabling informed shared decision making [6] and patient-tailored treatment [7]. This may result in more patient-centered care, and (interested) patients should be able to prioritize what gaps in their care plan require the most attention (32). Tight integration with EHR systems may reduce administrative load and allow easier execution of recommendations (33, 34). Natural language processing may allow for more free-flowing documentation of care by healthcare providers, as opposed to the structured documentation they are currently required to perform (35, 36).

Combining these improvements may finally result in fulfilling the long-standing expectations for healthcare IT: supporting and improving care.

**CLOSING THOUGHTS**

The future as described above is certainly attainable, but requires determined action from patients, researchers, healthcare providers, vendors, healthcare organizations, and governments. Until we can accurately process free text notes, healthcare providers and vendors will have to invest in improving the quality of EHR data. Currently, EHR data is often unstructured and not usable for high-quality decision support (37, 38). Governments should require that health data is standardized and accessible. Healthcare providers need to accept that structured documentation of care is required to move forward. EHR vendors should invest in standardizing data that are being collected in their systems using detailed clinical models (39, 40).

In the Netherlands, a small number of EHR providers are active in the market due to risk avoidance and procurement influenced by peers. This potentially limits willingness to make the required lasting changes that are needed for effective decision support. The future of healthcare depends on being able to support healthcare providers in daily practice, and computers are one of the most promising areas in this regard. Only when vendors truly cooperate with researchers, will we be able to implement effective decision support across healthcare.
CONCLUSION

Are guidelines and computers the future of medical decision making? This thesis has shown there is a long road ahead of us before these tools might replace expert opinion and experience. But, seeing the growing (scientific) interest, need, and collaboration on these topics, we can expect them to help us improve care and reduce costs in years to come, by helping us practice evidence-based medicine.
REFERENCES


