Improving medical decision making: Stroke prevention in atrial fibrillation
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Citation for published version (APA):
Chapter 10

English summary
In this thesis we have investigated guideline non-adherence, the implementation of a decision support system to improve adherence and its evaluation. Furthermore, we investigated usage of complex prediction models to improve stroke prediction in patients with atrial fibrillation. Below a brief summary of each chapter is provided.

Chapter 1
In Chapter 1 we introduced the concepts of evidence based medicine (EBM), clinical practice guidelines (CPG), clinical decision support systems and complex prediction models. EBM is the current gold standard for clinical practice, as ideally diagnostic and treatment strategies should be based on a synthesis of empirical studies from groups of patients, as opposed to one physician’s opinion. It implies using the best available evidence, in the form of CPGs, to make decisions in relation to patients’ circumstances and preferences. However, guideline adherence is low throughout medicine: making good use of guidelines requires high-quality evidence, a willing doctor and patient, the right tools, circumstances, and time.

Can we improve guideline adherence by supporting physicians by means of clinical decision support systems? We attempted to answer this question in the field of atrial fibrillation (AF), specifically stroke prevention in AF. Guideline non-adherence is prevalent in this field and the potential for improving patient outcomes is large. Atrial fibrillation is the most common form of cardiac arrhythmia (abnormal heart rhythm). Its prevalence is age-dependent and has increased over the last 30 years due to aging populations and improved diagnostics. It now ranges from 0.7% (age 55-59) to 17.8% (age > 85). Patients with AF are at high risk for stroke, with up to a five-fold risk compared to patients without AF. Oral anticoagulation (OAC), such as warfarin and the new oral anticoagulants (NOACs), can reduce risk of stroke by 60%. Therefore, most patients with AF need to be treated with antithrombotic medication to reduce their risk of stroke. However, adherence to stroke prevention guidelines in AF is poor. This non-adherence is mainly related to underuse of OAC in patients with medium to high stroke risk.

Chapter 2
To determine if guideline non-adherence in AF stroke prevention was an issue in the Netherlands, we investigated general practitioners’ adherence to the Dutch Guideline for Atrial Fibrillation in Chapter 2. Our findings were in line with other national and international studies: adherence was low (43%) and some patient groups were over-treated (31%) and other undertreated (26%). We suspected this low guideline adherence might have been partially due to a lack of knowledge about the guideline. This provides an opportunity to employ clinical decision support systems (CDSS) to increase adherence,
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as these systems can remind and inform the GP about the guideline through notifications in their electronic health records system.

Chapter 3

To gain insight into possible guideline related barriers for adherence, we appraised the Dutch guideline for atrial fibrillation in Chapter 3. We found that guideline adherence might improve by involving more stakeholders (e.g. patients and physicians), standardizing the layout to allow for easier interpretation and clarifying ambiguous terms that hamper the operationalization in electronic systems. The latter will allow for easier implementation of the guidelines in computerized systems such as CDSS. These systems in turn, can support physicians with implementing the guideline.

Chapter 4

We studied reasons why physicians intentionally deviate from guidelines in Chapter 4. We found that, depending on the guideline, there are many valid reasons, as adjudicated by peers, for guideline non-adherence. Reasons often were related to contra-indications (that were not mentioned explicitly in the guideline) or patient preference. The latter seems to agree with our findings in Chapter 3, where more stakeholder involvement would be recommended. Involving more physicians would allow for more extensive documentation of contra-indications, whilst involving patients might improve patient adherence with the guideline.

Chapter 5

In Chapter 5 we described the protocol for our randomized controlled trial for the evaluation of a clinical decision support system in general practice: Expert-AF. It was specifically designed to increase adherence to the atrial fibrillation guideline of the Dutch national College of General Practitioners and support GPs in providing antithrombotic treatment to their patients. We created a plugin for the GP Electronic Health Records system (EHR) together with two vendors. This plugin was displayed on the GP’s screen and could be expanded to show recommendations for the current patient, i.e. the patient file that was open on the screen (figure 1). Clicking on a recommendation opened a larger window with additional details (figure 2). We expected to see an absolute increase of guideline adherence by 10 to 20% in the intervention groups. The study employed a cluster randomized design with three groups, one control group and two intervention groups. Both intervention groups received the same recommendations, but the groups differed on the fact that the second intervention required the GPs to enter a reason to deviate from the recommendation, whereas the third group was not asked for these reasons.
Atrial fibrillation

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Stroke prevention in AF

Clinical Rules

Yearly medication revision

Risk of falling

Figure 1. The notification window in its expanded state, showing three notification items.

Figure 2. The window after clicking on a notification item, containing background information, an actionable recommendation and response buttons to allow the GP to indicate whether they accept (1) or decline (2) the advice (3) close the window (no action).
Chapter 6
The results of the Expert-AF project are described in Chapter 6. The trial ran for 240 days in general practices in Amsterdam South-East. Usage of the system varied greatly between GPs. Some opened almost all of the recommendations, while others did not open more than 3 throughout the trial. Overall, usage was low and declined over time. We were unable to show a significant difference in the increase of guideline adherence between groups: both groups improved by more than 5% compared to baseline adherence. We suspect the simultaneous introduction of a new guideline for AF might have played a part here, as well as the low usage of the system.

Chapter 7
In Chapter 7 we employed a mixed methods evaluation of the reasons for low usage of the Expert-AF system described in the previous chapter. A survey and a focus group revealed the main barriers to usage of our system. These were mainly related to lack of time to follow recommendations, too many alert notifications and limitations of the system’s functionality. Participants in our study acknowledged the potential that CDSSs hold for the future of healthcare, but implementing these systems in daily practice for multiple domains remains challenging. Alert prioritization, user customization, tight EHR integration and strict selection of alerts might improve CDSS effectiveness.

Chapter 8
In Chapter 8, we attempted to improve stroke prediction for patients with atrial fibrillation using logistic regression and neural networks. Currently, the CHA2DS2-VASc is used for stroke prediction in most international guidelines. However, its performance could be improved to allow for more tailored stroke treatment of patients with AF. The prediction models we developed demonstrated we could reduce overtreatment in low risk patients, thus sparing patients from adverse events resulting from antithrombotic medication use. We also concluded that due to the use of ambiguous terms in prediction scores, the future of disease prediction in healthcare may lie in creating locally optimized and validated models using local EHR data. It might be more effective to recreate and validate a prediction model using the local definition of a risk factor, using EHR data, than to and map it to a generic definition.

Chapter 9
In Chapter 9 we reviewed the Expert-AF trial and discussed implications of this thesis for current and future clinical practice and research. 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. However, it was this pragmatic nature that required us 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. 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.

Furthermore, we concluded that perfect guideline adherence is currently not attainable and not desirable due to gaps in guidelines and the many valid reasons physicians have for not adhering to these guidelines completely. Decision support systems can help improve non-adherence that results from other factors than those mentioned, by ensuring physicians are always aware when a guideline is applicable and supporting its implementation. To fulfil this promise, we need more knowledge on “what works” before we continue with more real world trials. We suggest several features that might improve effectiveness of CDSS, but realistic, controlled lab tests (including simulation patients), should be used to determine how to implement these features. This will allow for reproducible results throughout different fields of medicine as opposed to the heterogeneous nature of current real world trials on decision support. 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.

Next, we discussed complex locally optimized prediction models and how these can improve risk stratification accuracy and disease prediction. 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. We conclude that 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.

**Future perspectives**

Healthcare complexity and costs will continue to increase. Proper use of technology is one of the few possible solutions for these growing issues. We discussed the possibilities of properly applied technology in the final section of chapter 9. Briefly, standardized healthcare data could be used to continuously improve e-guidelines, that can be directly integrated into decision support systems. These data can also be used to develop early disease prediction algorithms. Complex computerized prediction models can integrate patient preference with current evidence and allow for informed shared decision making using visualization of personalized risk over time. These improvements may finally result in fulfilling the long-standing expectations for healthcare IT: supporting and improving care.
To reach this goal, all stakeholders should invest in standardizing healthcare data and systems. Researchers and vendors need to collaborate closely to create systems that are effective at supporting medical decision making in modern healthcare.