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To stop or not to stop : deprescribing preventive cardiovascular medication in low-risk general practice patients

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CHAPTER 1

General introduction

GENERAL INTRODUCTION

Approximately 27% of global mortality is caused by cardiovascular disease (CVD).¹ Furthermore, ischemic heart disease is the leading cause of years of life lost, both globally and in the Netherlands.¹ As a result of more effective treatment options and an increase in preventive measures and surveillance, the worldwide age-standardized death rate has decreased with a median percentage of 22 from 1990 onwards, and years of life lost due to CVD have decreased about two- to four-fold.^{1,2} Reduction of hypertension and hypercholesterolemia on a population-level can (cost-)effectively prevented new cases of CVD and death from CVD, resulting in a reduction of Disability Adjusted Life Years (DALYs).^{2,3} Hence, the impact of preventive strategies on reducing CVD is evident. Because of the importance of CVD prevention, many countries have guidelines with recommendations on prevention of CVD in adults with as well as without a history of CVD.⁴⁻¹⁰ Although these guidelines have the same goal, there is no consensus about the screening methods, which prediction models to apply, and what thresholds to use regarding initiation of drug treatment in patients in order to prevent CVD.¹¹ The European Society of Cardiology, for example, recommends to initiate antihypertensive drugs based on a combination of total cardiovascular risk and blood pressure, whereas the guideline from the Centers of Disease Control and Prevention/American Heart Association recommends to start treatment based on a combination of blood pressure level and the presence of chronic kidney disease or diabetes mellitus.¹¹ Medical science continuously investigates the optimal way to prevent CVD in individuals, which is the reason for regular revision and further refinement of guidelines in the area of prevention of CVD.^{5, 6, 12-19}

1. THIS THESIS

This thesis addresses a problem that was raised, predominantly in Dutch general practice, as a result of revisions of guidelines in the area of primary prevention of CVD and that expands into the area of further individualizing preventive interventions during lifetime. This thesis concerns the practical problem of general practitioners (GPs) on how to deal with patients using antihypertensive and/or lipid-lowering drugs (preventive cardiovascular medication) in whom guideline changes, changing insights in risk assessment or changing individual circumstances, result in losing the strict indication for initiation and further use of these drugs.

To illustrate this problem, first the history of the Dutch guidelines in the area of primary prevention of CVD will be discussed. Next, two vignets of patients will be introduced (miss Bremer and mister Aalbers), to exemplify the issues that GPs encounter in general practice. Finally, the aims of the thesis are presented.

2. THE DUTCH SITUATION

In the Netherlands, the first guidelines in the area of primary prevention of CVD were the guidelines "Hypertensie" [Hypertension] and "Cholesterol", launched by the Dutch College of General Practitioners (Nederlands Huisartsen Genootschap, NHG) in 1993. These guidelines recommended opportunistic screening of blood pressure and cholesterol in patients at risk of hypertension, hypercholesterolemia, or patients at increased risk of developing CVD (e.g., in case of diabetes mellitus). Recommendations in these two former guidelines differ from the recommendations in the current Cardiovascular Risk Management (CVRM) guideline with respect to, for example, definition of hypertension, preferred prescribed medications, and thresholds for initiation of medication.

As of 2003, the Dutch hypertension guideline advocated for the assessment of total (or: global) cardiovascular risk, using a 10-year risk of cardiovascular morbidity essentially based on the Framingham Risk Score to evaluate whether drug treatment should be initiated. In 2006, the guidelines on hypertension and on hyperlipidaemia were integrated into one CVRM guideline advocating for the assessment of total (or: global) cardiovascular risk, based on all traditional risk factors. However, the 2006 CVRM guideline refrained from using the Framingham Risk Score, and started using a 10-year risk of CVD morbidity and mortality (10-year CVD risk) score based on the SCORE equation to evaluate drug treatment initiation.²⁰ In the CVRM guideline that was established in 2012, this 10-year CVD risk score was based on the SCORE equation for low-risk European countries and improved for the Dutch population with help of data of the Dutch MORGEN-cohort and a Dutch cohort from the ERGO study.^{4, 16, 21} Five determinants currently define a patient's 10-year CVD risk: systolic blood pressure (range 120 to 180 mmHg), total cholesterol/high-density lipoprotein cholesterol (TC/HDL) ratio (range 4 to 8), age (range 40 to 70 years; 15 years are added to age in the presence of diabetes mellitus or rheumatoid arthritis), sex (male or female), and smoking status (yes or no). In case a patient has a low risk, i.e. 10-year CVD risk <10%, the guideline recommends physicians to discuss lifestyle when necessary. In case a patient has a medium risk, i.e. 10-year CVD risk 10% to 20%, the recommendation for initiation of

drug treatment depends on the presence of additional determinants that could increase CVD risk, such as family history of CVD, physical activity level, body mass index, and kidney function. This means that, if there are no or few risk increasing factors, these medium-risk patients are considered low-risk patients and initiation of drug treatment is not recommended (and vice versa: with many risk increasing factors, drug treatment is recommended). In case a patient has a high risk, i.e. 10-year CVD risk $\geq 20\%$, initiation of drug treatment is recommended under all context circumstances.

2.1. Consequences of a guideline revision for clinical practice

Guideline revisions resulting in different thresholds for initiation of drug treatment compared to previous guidelines, as described above, can have implications for clinical practice. This is because guideline recommendations do not only refer to 'new patients', but also to patients who are already being treated for their specific disease or risk factor(s). However, these implications are often not considered by physicians, policy makers and guideline committees, and most guidelines lack recommendations for physicians on how to deal with the consequences of guideline revisions.²²

In Part 1 of this thesis we describe the effects of the last revision of the Dutch CVRM guideline on a population- and an individual patient-level.

3. ILLUSTRATION OF THE PROBLEM WITH PATIENT CASES

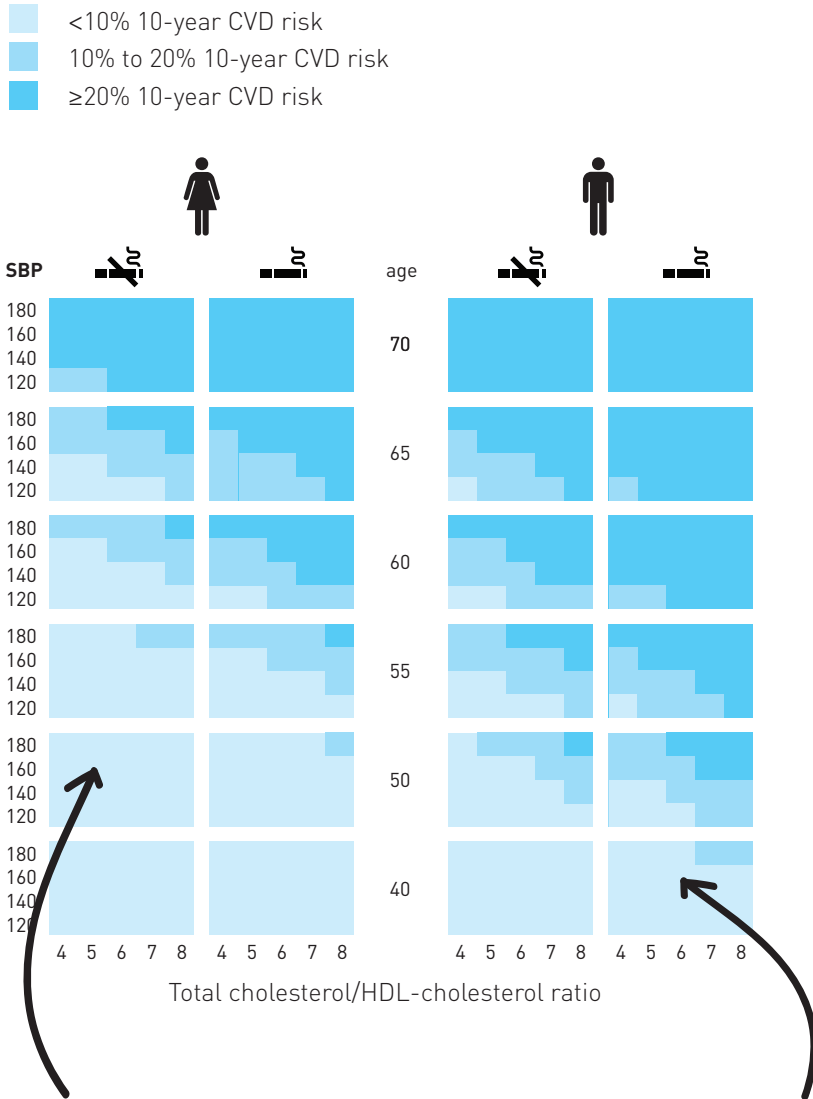
To illustrate the problem that is addressed in this thesis we describe the cases of miss Bremer and mister Aalbers who both did not experience a cardiovascular event and have a low overall CVD risk. They both visit the same GP. The most recent CVRM guideline does not recommend initiation of drug treatment in low-CVD-risk patients such as miss Bremer and mister Aalbers, and drug treatment in low-CVD-risk could be considered as overtreatment. However, they are already using preventive cardiovascular medication, because in earlier days antihypertensive and/or lipid-lowering drugs were prescribed following guidelines that were in force at the time. Both patients present themselves to their GP because of the routine preventive check-up, which is recommended when patients use preventive cardiovascular medication. How should the GP deal with the possible overtreatment in these patients?

Just after the revision of the CVRM guideline, miss Bremer visits her GP for her routine preventive check-up. She is 50 years old and uses an ACE-inhibitor (enalapril 5 mg once daily) for three years now. Her antihypertensive drugs were initiated during a period in which she had headache complaints and a relatively high systolic as well as diastolic blood pressure found repeatedly during consultations in the past (160/90 mmHg). She has never smoked, her TC/HDL ratio is 5, her current systolic blood pressure is 135 mmHg, and she has no additional risk increasing factors (no elevated body mass index, normal kidney function, no family history of CVD, and a good physical activity level). She sees her GP during the yearly preventive check-up. Her headache has faded since, and the general practitioner questions herself whether miss Bremer could stop her antihypertensive drugs.

Just after the revision of the CVRM guideline, mister Aalbers visits his GP for his routine preventive check-up. He is 40 years old and uses antihypertensive and lipid-lowering drugs for two years now (hydrochlorothiazide 12.5 mg, enalapril 5 mg, and simvastatin 40 mg, all once daily). At the time, the GP had advised him to start medication because of his risk factors for developing a cardiovascular disease. He is a smoker, has a TC/HDL ratio of 5 (it was 6 at the time he started his medication), an LDL-cholesterol of 2.4 mmol/L (it was 4.1 mmol/L at the time he started his medication), and his systolic blood pressure is 136 mmHg (it was 155 mmHg at the time he started his medication). Furthermore, he has a body mass index of 37 kg/m², he has a sedentary lifestyle, and his kidney function is 55 ml/min/1.73m². His brother was 48 when he had a heart attack and his mother suffered from a stroke at the age of 62. Mister Aalbers visits his GP and asks her if he could stop his medication because he does not see or feel any benefits of it and dislikes use of medication.

Figure 1 shows miss Bremers' and mister Aalbers' 10-year CVD risk score, based on their pre-treatment levels of blood pressure (miss Bremer), and LDL-cholesterol (mister Aalbers), as if they would currently not be using preventive cardiovascular medication. Because there is a lack of evidence to judge overtreatment and to guide the decision whether or not to deprescribe in these cases, assessing the 10-year CVD risk score as if patients do not use preventive cardiovascular medication is used here to inform the decision-making process.

The general discussion of this thesis will address recommendations for the GP on how to deal with the potential overtreatment in these two patients, based on the findings of the studies discussed in this thesis.



10-year CVD risk score of miss Bremer. Based on her pre-treatment systolic blood pressure level, current cholesterol levels, smoking status, age and sex.

10-year CVD risk score of mister Aalbers. Based on his pre-treatment systolic blood pressure and cholesterol levels, smoking status, age and sex.

Figure 1. 10-year CVD risk score table

3.1. Potentially inappropriate prescribing

As illustrated by the cases of miss Bremer and mister Aalbers, for patients who are already using preventive cardiovascular medication based on former guideline recommendations, a revision of the guideline may question the need to continue preventive cardiovascular medication. In these two low-CVD-risk patients the guideline revision may change the feeling of urgency for treatment in hindsight and potentially results in inappropriate prolonging of prescription, where potential risks of the medication (e.g., side effects) outweigh their potential benefits.²³⁻²⁵

The question whether or not to continue the preventive cardiovascular medication will probably lead to a physician-patient discussion about deprescribing. Deprescribing has been defined as the process of withdrawal (or dose reduction) of medication that became inappropriate following evaluation, supervised by a healthcare professional.²⁶ GPs seem to be reluctant to advise about deprescribing, since evidence to change a supposedly "winning team" is lacking and the impact of deprescribing preventive cardiovascular medication on a low-CVD-risk patient's health actually is unknown. Is it safe to deprescribe? And, if it is safe, should GPs invite all low-CVD-risk patients in a structured way for a deprescribing consultation to discuss whether to withdraw preventive cardiovascular medication? Time and costly efforts should be balanced against the impact of the guideline revision on patients' health to assess whether such a structured deprescribing strategy is an effort that should be made. In Part 2 of this thesis we have investigated the safety, effectiveness, and cost-effectiveness of a structured deprescribing strategy, to evaluate whether active invitations for deprescribing consultations in possibly overtreated, low-CVD-risk patient populations in general practice are recommended.

3.2. The deprescribing consultation

The deprescribing consultation, in which patients like miss Bremer and mister Aalbers discuss with their GP whether or not to withdraw their preventive cardiovascular medication, may play a big role in the (cost-)effectiveness of the overall deprescribing strategy; if none of the patients, as outcome of a shared decision with their GP, would decide to stop the medication, the deprescribing strategy would definitely not be (cost-)effective. Because the (cost-)effectiveness of a structured deprescribing strategy could be highly influenced by the course of the deprescribing consultation, it is worthwhile to find out more about the course of these conversations and what factors have a bearing on its outcome (deprescription or continuation). In addition, knowledge of the factors that play a role in the decision-making process can aid the physician-patient communication in future deprescribing consultations

In Part 3 of this thesis we have discussed the factors influencing the outcome of the deprescribing consultation.

3.3. Predictors of successful deprescribing

Regardless of the risks and benefits of a deprescribing strategy for the total population of low-CVD-risk patients, there will always be individual low-CVD-risk patients that embrace the idea to stop their medication. The other way around, some GPs will always question the necessity of preventive cardiovascular medication in some low-CVD-risk patients. In these cases, information about the patient's individual probability to successfully stop the medication could be helpful in the decision-making process. In addition, this information can be used to screen the electronic medical records of general practices for patients who have a high probability of successful stopping. In Part 3 we have investigated predictors of successful stopping preventive cardiovascular medication.

4. AIMS OF THIS THESIS: SUMMARY

The overall aim of this thesis is to improve cardiovascular preventive care in general practice for low-CVD-risk patients, aged 40 to 70 years, and with a changed indication or without a strict indication for preventive cardiovascular medication.

The aim of Part 1 is to investigate the implications of the revision of the Dutch CVRM guidelines on a population- and an individual patient-level.

Part 2 aims to evaluate the safety, the effectiveness, and the cost-effectiveness, of a structured deprescribing strategy in patients aged 40 to 70 years and using preventive cardiovascular medication, but without a history of CVD and with low risk of future CVD, and (therefore) losing a strict indication for prolonged preventive cardiovascular medication in general practice.

The aim of Part 3 is two-fold. The first aim is to identify the factors that influence the outcome (deprescription or continuation of preventive cardiovascular medication) of the deprescribing consultation in which patient and GP discuss deprescribing. The second aim is to identify predictors of successful stopping preventive cardiovascular medication.

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PART 1

Current practice



