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SUMMARY

Cardiovascular disease (CVD) contributes highly to mortality and is the leading cause of years of life lost globally. In many countries, recommendations to reduce the prevalence of CVD are integrated in guidelines. However, although the goal of these guidelines is the same, there is no consensus about the optimal preventive care. In search for further optimisation, medical knowledge progresses, resulting in regular revisions of guidelines in this area. The latest revision of the Dutch guideline was in 2012. It was unclear what this new guideline would imply for daily practice. This thesis' research questions relate to the implications the revision of the guideline had in daily practice. To best address these research questions, a combination of quantitative and qualitative research, the so-called mixed methods approach, is used in this thesis.

1. OVERVIEW OF THIS THESIS' FINDINGS

1.1. Part 1
The findings in Chapter 2 show that the revision of the Dutch CVRM guideline had considerable impact on patient care. The revision has led to shifts in risk categories (high, medium, and low risk) in 20% of the patients using preventive cardiovascular medication (antihypertensive and/or lipid-lowering drugs). Furthermore, 12% of the patients shift in drug recommendation, notably: with unchanged initial risk factor values. In the Netherlands, following our estimates, approximately 60% of the patients using cardiovascular medication to prevent a first cardiovascular event, strictly speaking, have no indication for using this medication according to the current Dutch CVRM guideline.

1.2. Part 2
The ECSTATIC study that is described in Chapter 3 shows that, compared to usual care, mean systolic blood pressure (SBP) in patients who did an attempt to have their medication deprescribed (the intervention) is 6 mmHg higher after two years of follow-up. The total cholesterol and low-density lipoprotein (LDL) cholesterol levels are both on average 0.2 mmol/L higher compared to the usual care group. These differences in SBP and LDL-cholesterol level between intervention group and usual care group are already present after three months of follow-up.

Compared to the patients in the usual care group using antihypertensive drugs at baseline, SBP is on average 13 mmHg higher in the patients in the intervention group who had still stopped antihypertensive drugs after two years. The LDL-cholesterol level...
of the patients who had stopped lipid-lowering drugs after two years of follow-up, was on average 1.5 mmol/L higher compared to the LDL-cholesterol level of the patients in the usual care group using lipid-lowering drugs at baseline. After an attempt to deprescribe preventive cardiovascular medication is made, the risk of having hypertension (SBP ≥140 mmHg) after two years of follow-up is approximately 20% to 60% higher compared to the usual care group, and the risk of having hypercholesterolemia (LDL-cholesterol level ≥2.5 mmol/L) is approximately 5% to 15% higher.

Predicted CVD risk increased by 2.0 versus in the intervention group and 1.9 percentage points in the usual care group; the difference of 0.1 (95% CI -0.3 to 0.6) fell within the pre-specified non-inferiority margin. Thus the ECSTATIC study reveals that an attempt to deprescribe preventive cardiovascular medication in general practice with predicted low-risk is safe in the short term (two years).

The most frequently reported adverse effects of deprescribing and reasons to restart medication are: hypertension, headache, nervousness/stress, and palpitations. There is no indication of serious adverse effects of deprescribing in the short term.

Furthermore, the ECSTATIC study shows that after implementation of a structured deprescribing strategy in general practice, 65% of the low-risk patients attempt to have their medication deprescribed, and that 27% of the initial intervention group is still without medication after two years.

A structured deprescribing strategy in low-risk patients in general practice is 70% to 80% likely to be cost-effective for a willingness-to-pay for one Quality Adjusted Life Year (QALY) between €20,000 and €50,000. However, implementation of a structured deprescribing strategy is not recommended, because it makes no difference in total healthcare costs, nor in quality of life of the patients. Furthermore, the effectiveness of the deprescribing strategy is fairly low (27% persistent quitters).

1.3. Part 3
Chapter 4 shows that low-risk patients, who discuss deprescribing of preventive cardiovascular medication with their GP during a deprescribing consultation fear the consequences of deprescribing. Therefore, they appreciate the availability of follow-up care and the possibility to restart medication. Chapter 4 and 5 show that patients are generally positive towards deprescribing. They rely on the information and expertise of their GP to help determine whether deprescribing is justified. Individual patients balance the risks and benefits of deprescribing differently and have different preferences with regard to an attempt to deprescribe. One of the reasons for GPs to advise deprescribing is the low-risk of the patients when recalculated following the current guideline. In addition, the GPs base their view concerning deprescribing on the presence of additional
risk factors such as a positive family history of CVD or an unhealthy lifestyle, and on the earlier advice of the specialist to continue/start medication.

Chapter 6 shows that the four strongest baseline predictors for successfully stopping preventive cardiovascular medication in low-risk patients in general practice are: 1) having a SBP $\leq 140$ mmHg; 2) using preventive cardiovascular medication $\leq 10$ years; 3) using either an antihypertensive or a lipid-lowering drug; and 4) using $\leq 1$ class of antihypertensive drugs. When all four predictors are positive, the probability that a patient has still stopped the preventive cardiovascular medication after two years is approximately 50%.

**2. CONCLUSION**

In conclusion, this thesis shows that an attempt to deprescribe preventive cardiovascular medication in 40 to 70 year old low-risk patients under surveillance of the GP is safe in the short term. The deprescribing consultation should be patient-centered in order to optimally judge overtreatment.

Decision-making could be improved if more personalised risk scores were available, that assess an individual’s CVD risk and benefit of treatment. Opportunities for future development of these personalised risk scores lie in the use of routinely registered patient data.

Overall, this thesis’ findings provide both practical tools for GPs to judge overtreatment in low-risk patients, as well as valuable information for policy makers revising the CVRM guideline.