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Revised guidelines for cardiovascular risk management — time to stop medication?

A practice-based intervention study

Abstract

Background
According to the new Dutch guideline for cardiovascular risk management, patients with a low risk of cardiovascular mortality may have insufficient benefit to warrant medication. Therefore, numerous patients per general practice may be treated unnecessarily.

Aim
To explore the feasibility and consequences of a re-evaluation programme for patients without target organ damage who were treated for hypertension and/or hypercholesterolaemia.

Design and setting
Practice-based intervention study in six general practices.

Method
Patients treated for hypertension and/or hypercholesterolaemia without target organ damage ($n = 833$) were invited to re-evaluate their cardiovascular risk and were advised whether or not to stop medication. Patients who discontinued medication were followed for 6 months. To determine indicators for successful stopping, logistic regression analyses were performed, and differences between practices were analysed.

Results
About two-thirds of the patients were re-evaluated and 61% of them had a low calculated risk, especially younger patients, females, and non-smokers. Of these, 42% were advised to stop medication, especially younger patients and non-smokers. Of those who discontinued medication, 40% had restarted within 6 months. After 6 months, 80 of the 833 patients (9.6%) had not restarted medication. There were no important side effects related to stopping medication.

Conclusion
Over 50% of patients without target organ damage treated for hypertension and/or hypercholesterolaemia may have insufficient benefit to warrant medication. Younger patients, females, and non-smokers in particular are more likely to have an insufficient indication for medication. GPs' and nurse practitioners' views seem to play a role in advising to stop or to restart medication.

Keywords
general practice; guidelines; hypercholesterolaemia; hypertension; primary prevention; primary care.

INTRODUCTION

The importance of cardiovascular risk management in general practice is increasing.[1,2] However, although many patients without target organ damage will benefit from treatment of hypertension and/or hypercholesterolaemia, the therapy is costly and side effects are common.[3–5] To improve the cost–benefit ratio, several consecutive (inter)national guidelines have been developed. Previously, the Netherlands had separate guidelines for hypertension and hypercholesterolaemia until, in 2006, the interdisciplinary guideline *Cardiovascular Risk Management* was launched,[6] which marked a change from thinking in terms of individual risk factors (disease management) into thinking in terms of absolute risk (risk management). The recommendations in this guideline are based on the integrated SCORE function, which includes age, sex, smoking behaviour, systolic blood pressure, and high-density lipoprotein (HDL)-cholesterol to total cholesterol ratio.[7] In cases of a calculated 10-year risk of cardiovascular mortality of 10% or more, treatment to decrease systolic blood pressure to 140 mmHg or lower, and low-density lipoprotein (LDL) cholesterol to 2.5 mmol/l or lower is advised. Patients with a lower risk may have insufficient benefit to warrant medication. Consequently, numerous patients per practice may be unnecessarily treated based on the earlier (and now obsolete) Dutch guidelines. Negative consequences of this overprescribing include the waste of resources (for example, money and manpower), risk of adverse side effects, and unnecessary medical usage.

When implementing the new Dutch guideline in the authors' general practices, the question arose as to how many patients receiving treatment for their 'presumed' cardiovascular risk had in fact now 'lost' their indication for medication based on the new guideline and, if so, were they prepared to stop medication. Although withdrawal of medication from patients with well-controlled blood pressure is reported to be successful,[8–10] these latter studies concerned withdrawal of medication in normotensive patients.

To the authors' knowledge, there are no studies with a broader scope with regard to integrated cardiovascular risk management. Therefore, this study explored the feasibility and consequences of a re-evaluation programme for patients without target organ damage who were treated for hypertension and/or hypercholesterolaemia in general practices.

METHOD

Practices and patients

In six collaborating general practices with 10 GPs, in Katwijk (an urbanised rural town in the Netherlands), serving a total of 17 200 patients (2500–3000 per practice), patients were selected who had no known target organ damage but were receiving medication for hypertension and/or

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How this fits in

According to the new Dutch guideline for cardiovascular risk management, patients with a low risk of cardiovascular mortality may have insufficient benefit to warrant medication. In this study, the feasibility and consequences of a re-evaluation programme for patients without target organ damage treated for hypertension and/or hypercholesterolaemia in general practice was explored. The results suggest that stopping medication in patients with a low risk for cardiovascular mortality is safe. GPs' and nurse practitioners' views seem to play a role in advising to stop or to restart medication.

hypercholesterolaemia. In the Netherlands, all patients are registered at a general practice, which also keeps the electronic patient record with information on diagnoses and medication.

From the electronic patient records, the study selected all patients aged 25–75 years who were prescribed drugs in the past 12 months with the following cardiovascular-related Anatomical Therapeutic Chemical (ATC) codes: C02 (antihypertensives), C03 (diuretics), C07 (beta-blocking agents), C08 (calcium-channel blockers), C09 (agents acting on the renin–angiotensin system), and C10 (lipid-modifying agents).[11] All patients who were coded as being diagnosed with cardiovascular disease were excluded, that is, codes K74, K75, K76, K89, K90, K91, K92, and T90, according to the International Classification of Primary Care, version 1 (ICPC-1).[12] The selected patients were then manually screened and excluded in the case of non-coded cardiovascular disease, or when taking drugs for indications other than hypertension or hypercholesterolaemia (for example, for migraine). Patients on the final list were invited by mail to re-evaluate their risk of cardiovascular mortality and were asked for written informed consent to participate in the present study.

Re-evaluation

In the period January 2008 to November 2009 (23 months), patients were invited for a re-evaluation by one of the nurse practitioners at the general practice. At intake the nurse practitioners registered comorbidity (asthma/chronic obstructive pulmonary disease [COPD], digestive tract, urogenital tract, psychosocial, and/or musculoskeletal problems), number of oral drugs taken (0–2/>2), number of oral cardiovascular drugs taken (0–2/>2), prevalence of cardiovascular disease in first-degree relatives (no/yes), and smoking behaviour (no/yes).

The nurse practitioners then calculated the patient's risk of cardiovascular mortality in the next 10 years, according to the new Dutch guideline. For patients treated for hypertension or hypercholesterolaemia, the medical history was searched for the pretreatment levels of either blood pressure or cholesterol. If unknown, a systolic blood pressure of 180 mmHg was assumed, and, in the case of medical treatment for hypercholesterolaemia, a HDL-cholesterol to cholesterol ratio of 8.0 was assumed. These levels were chosen because this strategy would minimise the number of underestimated levels (as a sort of worst-case scenario). For patients aged between 66 and 75 years, the calculated risk for patients aged 65 years was used, which is the highest ranked age reported in the guideline.

The new guideline advises medication in cases of a high calculated risk: a 10-year risk of cardiovascular mortality of 10% or more or, in the case of an additional risk factor (for example, obesity or family history), of 5% or more. In cases of a lower risk, patients were advised to visit their GP to discuss continuation of medication. If patients decided to stop medication, the GP handed them a personalised medication-reduction schedule which, in complicated cases (such as polypharmacy), had been discussed with a pharmacist (for example, Box 1). Then, based on previous reports of long-term diuretic medication,[13] and a relapse of high blood pressure in the case of withdrawal,[8–10,14] an individual follow-up took place, which involved measuring blood pressure, serum lipid levels, and possible adverse events (for example, oedema, headache, high blood pressure, high cholesterol, feeling unwell, other problems). In cases of stopping diuretics, follow-up took place after 1, 2, 4, and 12 weeks, for stopping other antihypertensive medication after 4 and 12 weeks, and after stopping only statins after 12 weeks.

For patients who decided to stop medication, it was checked whether they restarted cardiovascular drugs within 6 months and, for those who did, the most important reason(s) for doing so were registered. Whatever the decision, all patients were offered a follow-up.

Registration and analysis

The outcome measures were: (1) attendance for re-evaluation, (2) calculated cardiovascular risk, (3) advice to stop

Box 1. Example of a medication-reduction scheme

Patient A with a calculated 3% risk of cardiovascular mortality

Medication: hydrochlorthiazide 1 daily dose 25 mg, metoprolol 1 daily dose 50 mg

Reduction scheme:

- Week 1: hydroclorthiazide 1 daily dose 25 mg and metoprolol 1 daily dose 25 mg
- Week 2: hydroclorthiazide 1 daily dose 25 mg and metoprolol 1 daily dose 12.5 mg
- Week 3: follow-up control; hydroclorthiazide 1 daily dose 25 mg and metoprolol stop
- Week 4: hydroclorthiazide stop
- Weeks 5, 7, 9, and 16: follow-up control

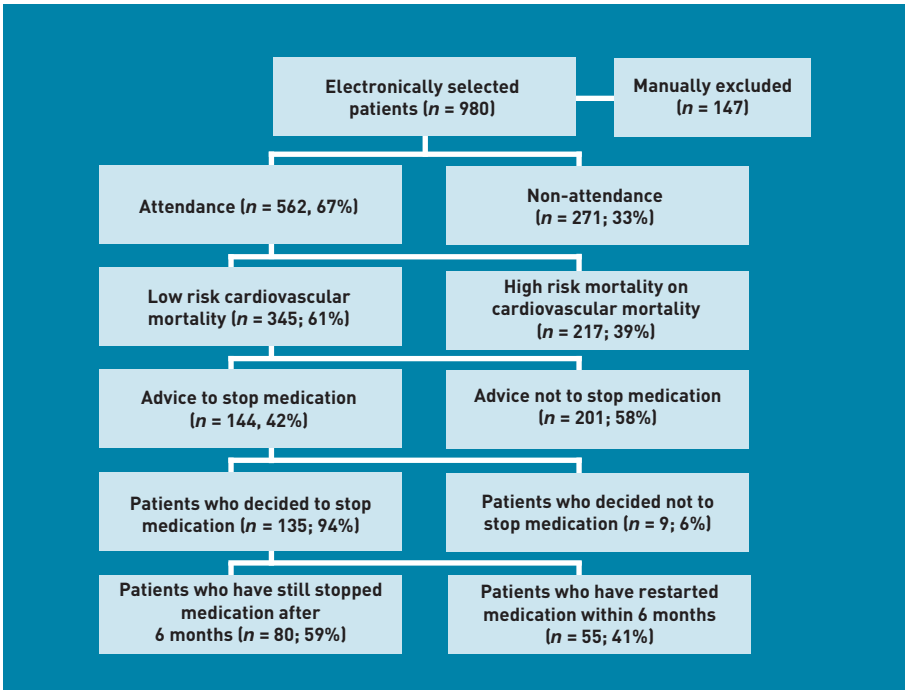

Figure 1. Flow chart of the study patients.

medication, (4) patients' decision to stop medication, and (5) patients' compliance with the discontinuation at 6 months.

To determine indicators for successful stopping of medication, first, univariate analyses were performed; Student's *t*-test in the case of a normal distribution and the Wilcoxon test in other cases. In the multivariate backward logistic regression analyses, variables with $P<0.20$ in the univariate analysis were included (P entry 0.05, P removal 0.10). To assess the prognostic value of determinants, a prognostic model was built by backward stepwise logistic regression, and the area under the receiver operating characteristic curve (AUC) was calculated. In addition, differences between practices were analysed by one-way analysis of variance and the Bonferroni post hoc test. Data analysis was performed with the Statistical Package for Social Sciences for Windows (SPPS 17.0).

Table 1. Data on included patients, attendance, low calculated cardiovascular risk, and advice to stop medication by practice

Practice	Included patients	Attendance, *n* (% of patients)	Low calculated risk *n* (% of attendance)	Advice to stop medication, *n* (% of low risk)
1	176	140 (79.5)	62 (44.3)	12 (19.4)
2	103	73 (70.9)	38 (52.1)	20 (52.6)
3	191	87 (45.5)	61 (70.1)	49 (80.3)
4	158	114 (72.2)	79 (69.3)	34 (43.0)
5	145	103 (71.0)	65 (63.1)	16 (24.6)
6	60	45 (75.0)	40 (88.9)	13 (32.5)
Total	833	562 (67.5)	345 (61.4)	144 (41.7)

RESULTS

Attendance for re-evaluation

After computerised selection of 980 patients, 147 met the exclusion criteria. Of the remaining 833 invited patients, 562 (67%) were re-evaluated in a consultation (Figure 1). There were no differences between the re-evaluated and not re-evaluated patients regarding sex and age, although there were fewer smokers in the re-evaluated group (20.5% versus 33.3%, respectively). Attendance was similar in five of the six practices (that is, 71–80% attendance). One practice had a 46% attendance, but also had no differences regarding sex and age (Table 1).

Calculated cardiovascular risk

Over 60% of the re-evaluated patients had a low 10-year risk of cardiovascular mortality (Table 2). Being female, being younger, not smoking, taking two or fewer different oral drugs, and a lack of a family history of cardiovascular disease were independent predictors for having a low calculated risk of cardiovascular mortality (Table 3). The AUC of this model is 0.87. There were large differences between the practices in the calculated low risk (range 44–89%).

Advice to stop medication

About 40% of the patients with a low risk of cardiovascular mortality were advised to stop cardiovascular medication. Non-smokers and younger patients were more often advised to stop medication. The AUC of this model is 0.62. There were large differences between practices in the percentage of patients advised to stop medication (range 19–80%).

Patients' decision to stop medication

Most patients who were advised to stop medication decided to stop (135 of 144; 94%). Of those with a low calculated risk, nearly 40% decided to stop (135 of 345). Of all initially selected patients, 16% stopped medication (135 of 833).

Of the patients who initially discontinued their medication, 55 (41%) restarted their medication within 6 months (most of them within 3 months). The reasons for restarting medication were headache (n = 12), ankle oedema (n = 2), not feeling well (n = 9), and high blood pressure and/or high cholesterol (n = 32). However, of the latter 32 patients with high blood pressure and/or high cholesterol who restarted medication, in 21 patients the raised blood pressure and/or cholesterol levels did not result in a risk of cardiovascular mortality that was sufficiently high enough to advise (the restart of)

Table 2. Characteristics of the patients with a high risk and a low risk

	Female, *n* (%)	Age in years, mean (SD)	Smokers, *n* (%)	Comorbidity[a], *n* (%)	>2 Oral drugs, *n* (%)	>2 Oral cardiovascular drugs, *n* (%)	Cardiovascular disease in family, *n* (%)
High risk (*n* = 217)	105 (48.4)	64.5 (7.3)	55 (25.5)	113 (32.8)	142 (65.4)	32 (14.7)	123 (56.7)
Low risk (*n* = 345)	214 (62.0)	54.5 (8.5)	53 (15.4)	84 (38.7)	196 (56.8)	25 (7.2)	139 (40.3)
Advice to continue medication (*n* = 201)	122 (60.7)	55.4 (9.0)	38 (18.9)	74 (36.8)	112 (55.7)	14 (7.0)	81 (40.3)
Advice to stop medication (*n* = 144)	92 (63.9)	53.2 (7.7)	15 (10.4)	39 (27.1)	84 (58.3)	11 (7.6)	58 (40.3)
Still stopped after 6 months (*n* = 80)	50 (62.5)	51.8 (7.0)	6 (7.5)	23 (28.8)	21 (26.3)	1 (1.3)	33 (41.3)
Restarted within 6 months (*n* = 55)	36 (65.5)	53.9 (7.9)	8 (14.5)	13 (23.6)	16 (29.1)	7 (12.7)	23 (41.8)
Not stopped (*n* = 9)	6 (66.7)	58.7 (7.6)	1 (11.1)	3 (33.3)	4 (44.4)	3 (33.3)	2 (22.2)

SD = standard deviation. [a]Asthma/chronic obstructive pulmonary disease (COPD), digestive, urogenital, psychosomatic, and/or musculoskeletal problems.

medication according to the new guideline.

Those who used more than two oral drugs were more likely to restart medication (Spearman's rho –0.24; $P = 0.005$). No other characteristics were associated with restarting medication. After 6 months, 80 patients (9.6%) of the total 833 patients had still discontinued their medication; these were mainly younger patients, females, and non-smokers.

DISCUSSION

Summary

According to the revised guideline, more than half (61%) of the patients without target organ damage who were treated for hypertension and/or hypercholesterolaemia may have had insufficient benefit to warrant their medication. Overall, younger patients, females, and non-smokers were more likely to stop medication. Of those who initially discontinued their medication, 40% had restarted within 6 months; however, their 'restart status' often lacked an indication related to high cardiovascular risk according to the new guideline. After 6 months, 80 out of 833 (9.6%) patients selected after applying exclusion criteria had still discontinued their medication.

Strengths and limitations

To the authors' knowledge, this is the first study to explore the feasibility and consequences of a re-evaluation programme for patients without target organ damage treated for hypertension and/or hypercholesterolaemia in general practice. The patients in the participating practices were comparable to the general Dutch population regarding the percentage of patients treated for hypertension and/or hypercholesterolaemia and the male to female ratio of these patients.[15–17] Therefore, this study probably gives a representative impression of the feasibility and consequences of such a programme in Dutch general practice and, perhaps, in other countries with a comparable healthcare system.

The follow-up period was only 6 months, but because most patients who restarted medication did so within 3 months, it can be assumed that this 6-month period is sufficient to provide a reliable insight.

There were differences between the participating practices regarding attendance, calculated risk, and advice to stop medication (Table 1). This might be caused, in part, by individual GPs and nurse practitioners. For example, a GP and/or nurse practitioner who is not totally convinced about the advantage of stopping medication may influence attendance and subsequent advice to stop medication. The differences between the practices regarding the calculated risk may be due to the threshold for prescribing medication in the past. Patients from practices with a lower tendency to prescribe medication in the past are more likely to have a higher cardiovascular risk at re-evaluation than patients from practices with a higher tendency in the past to prescribe.

Apart from the possible impact of the GP/nurse practitioner, the patient's smoking behaviour may also play a role in the advice to stop or continue medication. This might be explained by the belief that smokers, notwithstanding a low calculated

Table 3. Final models for determinants of low cardiovascular risk and subsequent advice to stop medication: multivariate logistic regression analysis; adjusted odds ratio (95% confidence interval)

	Low cardiovascular risk (*n* = 562)	Advice to stop medication (*n* = 345)
Female sex	4.4 (2.7 to 7.3)	–[a]
Age (continuous variable)	0.8 (0.8 to 0.8)	1.0 (0.9 to 1.0)
Non-smokers	4.0 (2.2 to 7.2)	2.5 (1.3 to 5.0)
More than two different oral drugs	0.6 (0.4 to 1.0)	–[a]
Negative family history of cardiovascular risk	4.3 (2.7 to 7.1)	–[a]

[a]Not in final model.

risk, are, nevertheless, still at risk.

However, neither the influence of the GP/nurse practitioner nor individual smoking behaviour can sufficiently explain the high percentage of patients (58%) who were advised not to stop their medication in the case of a low calculated risk. Undoubtedly, other unexplored factors have played a role.

After the electronic selection, manual screening led to the exclusion of an additional 147 patients (15%). The large differences between practices show that encoding medical problems according to the ICPC codes had not been sufficiently implemented in each practice.

Finally, by using the calculated risk for patients aged 65 years for patients aged 66–75 years, the study may have underestimated patients' calculated risk. However, this possible underestimation may (at least) partially be compensated by having assumed high pretreatment levels of blood pressure and/or cholesterol, since most of the missing data had to be imputed in this older age group.

Comparison with existing literature

The study finding that it is feasible to stop medication in hypertensive patients is in line with other studies.[9,10] In contrast to the findings of Walma *et al*,[13] only a few of the patients in the present study restarted medication because of oedema; most restarted because of raised blood pressure.

In this study, about 40% of those who initially stopped medication restarted it within 6 months. This is similar to the findings of Espeland *et al*, but lower than the 55% restarting patients reported by Aylett *et al*.[9] Patients in the present study who used more than two cardiovascular drugs before stopping medication were more likely to restart medication within 6 months, which is in line with the review study of Nelson *et al*.[14] However, these three latter studies concerned withdrawal from antihypertensive medication in normotensive patients,[9,13,14] whereas the present study re-evaluated the need for medication in both normotensive and (presumed) hypertensive patients.

Although Kok *et al* calculated that implementation of the new Dutch guideline for cardiovascular risk management would lead to a considerable increase in the number of individuals requiring treatment,[4] it is noteworthy that they did not include in their calculation a possible re-evaluation of patients with cardiovascular therapy. If they had done so, the result of their calculation would have been far more cost-effective.

Implications for practice and research

The present study shows that 10% of patients treated for hypertension and/or hypercholesterolaemia have still discontinued medication after 6 months; this is after having undergone re-evaluation, being shown to have a low risk for cardiovascular mortality, and being advised and prepared to stop medication. In the group of patients who initially stopped their medication, no important adverse effects (for example, heart failure or cardiovascular events) were seen during follow-up; therefore, it can be assumed that stopping medication in this group is safe. Of course, it is not known what the morbidity and mortality will be in the discontinuing versus the continuing group in the next 10 years. However, as the new guidelines are based on extensive clinical evidence, it can be assumed that stopping superfluous medication in patients with a low risk of cardiovascular mortality will not, of itself, increase this mortality rate. Based on these results, the authors think that a re-evaluation of the indication for antihypertensive and/or cholesterol-lowering therapy based on the revised cardiovascular guideline is useful. To improve efficiency, this re-evaluation programme could, for example, be initially focused only on non-smoking patients who are younger than 60 years. This could lead to 22% of the invited patients (62 of 278 patients) eventually stopping their medication. Further restriction to non-smoking females aged ≤60 years leads to a proportion of 25% (39 of 156 females). However, in this latter case, 18 of the 833 patients, who otherwise would have been invited to stop their medication, would be 'missed'.

In addition, the views of the GPs, nurse practitioners, and patients seem to play a role in attendance and advising whether or not to stop medication, and restarting medication after withdrawal. Therefore, the authors recommend further exploration of these views on discontinuing preventive cardiovascular medication, to enable better information to be given to patients and to overcome differences in the views of GPs and nurse practitioners.

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Ethics committee

Medical Ethics Committee of the Leiden University Medical Center.

Provenance

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Competing interests

The authors have declared no competing interests.

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