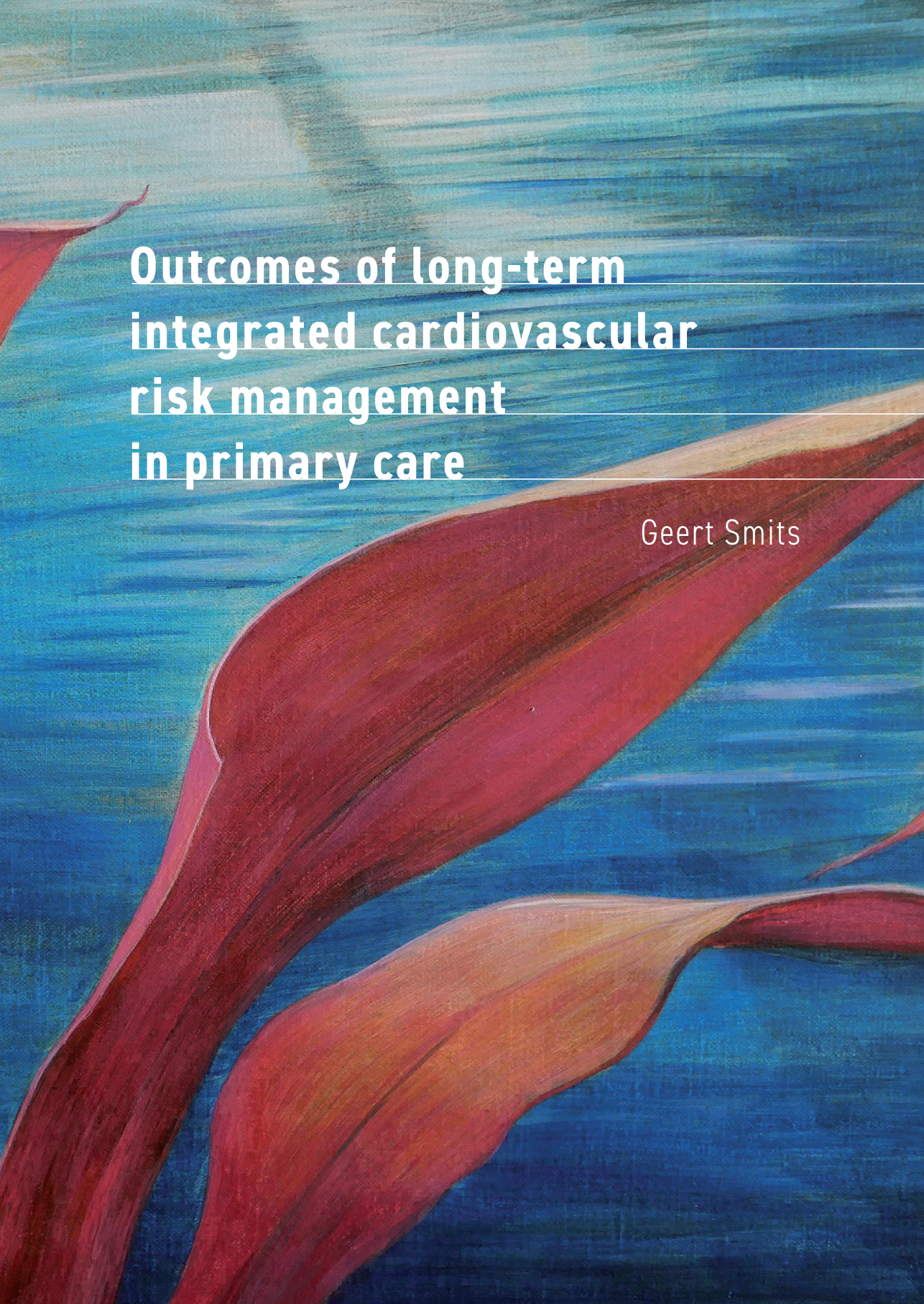


Outcomes of long-term integrated cardiovascular risk management in primary care

Geert Smits

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integrated cardiovascular risk management
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Colofon

Outcomes of long-term integrated cardiovascular risk management in primary care
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Outcomes of long-term integrated cardiovascular risk management in primary care

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Uitkomsten van langdurig, geïntegreerd cardiovasculair risicomanagement in de eerste lijn

Proefschrift

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Contents

Chapter 1	General introduction	**7**
Chapter 2	Stepwise implementation of a cardiovascular risk management program in primary care (BMC Prim Care. 2022)	**19**
Chapter 3	Patient characteristics and reasons for discontinuation in a cardio vascular risk management program in The Netherlands (BMC Prim Care. 2024)	**37**
Chapter 4	Cardiovascular risk reduction with integrated care: results of 8 years follow-up (BMC Prim Care. 2023)	**53**
Chapter 5	Sex differences and trends in managing cardiovascular risk factors in primary care (BJGP Open. 2024)	**71**
Chapter 6	Practice visitations in primary care to improve performance of cardiovascular risk management (BJGP Open. 2024)	**91**
Chapter 7	Improving practice performance of systolic blood pressure in general practice with targeted intervention and compulsory support (Huisarts Wet 2017)	**109**
Chapter 8	Does long-term, nurse-led, integrated CVRM care reduce CVD incidence in primary care? (under review)	**119**
Chapter 9	General discussion	**139**
Chapter 10	Summary in English and in Dutch	**153**
	Dankwoord	**164**
	Curriculum vitae	**167**



1

General Introduction

Governmental ambitions on Chronic Disease Prevention

The epidemic of cardiovascular diseases

Cardiovascular risk factors

Cardiovascular risk management

The gap between research and daily practice

Cardiovascular risk management (CVRM) and primary care

Cardiovascular risk management and primary care groups

Use of real world data

Aim and outline of this thesis

Governmental ambitions on Chronic Disease Prevention

In the first decade of this century it became clear that, between 2005 and 2025, the number of people with one or more chronic conditions would rise sharply due to aging, unhealthy lifestyle behavior better treatment options and hence increased survival. Chronic conditions lead to increased health care demands by the patient and are an important cause of reduced labor participation and incapacity for work [1-5]. In 2008, the Dutch government expressed 4 ambitions:

- slow down the increase in the number of people with a chronic disease,
- postpone the age of a first manifestation,
- prevent or postpone complications and
- improve the quality of life for people with a chronic condition.

Cardiovascular disease is considered as one of the most important chronic conditions. A promising concept was a programmatic approach (the terms "integrated approach" or "disease management program" are synonymous, in this thesis we will use the term "integrated care"), which is patient-centered and focuses on early recognition, prevention and self-management. Important elements of this programmatic approach are:

1 Introduction and implementation of national and international evidence-based guidelines. A guideline describes the minimum requirements for good care for a certain condition
2 More attention for indicated and care-related prevention through lifestyle improvements
3 Investigate how self-management can be optimally deployed
4 Improvement of multidisciplinary collaboration between (primary) health care providers [6]

The epidemic of cardiovascular diseases

According to the 2017 Global Burden of Disease report, cardiovascular diseases (CVD) are responsible for more than 17 million deaths worldwide [3]. CVD is associated with high healthcare costs, many premature deaths and loss of quality of life. In 2015, incidence and prevalence of CVD in Europe were 11.3 million and 85 million respectively, with an annual increase in absolute CVD cases and hospital discharges over the past 25 years. Between 2005 and 2013, prevalence of diabetes mellitus (DM) in Europe increased with 28% [4]. DM is a major cause of CVD and kidney failure. Chronic kidney disease may be even more common than DM, is an independent risk

factor for CVD and a predictor for hospitalization, cognitive dysfunction and poor quality of life [5]. In 2017, one in four deaths accounted for CVD in the Netherlands, ranging second after cancer with 30%. While the death rate in The Netherlands for CVD is gradually decreasing between 1980 and 2017, the number of hospital admissions for CVD is increasing, due to invasive treatment [6].

Cardiovascular risk factors

The Framingham Heart Study, initiated in 1948, was the first initiative that identified major cardiovascular risk factors such as increasing age, male sex, smoking, elevated total cholesterol, high density lipoprotein (HDL) cholesterol and elevated systolic blood pressure [7]. In the following years predisposing risk factors were added, amongst them family history of premature coronary heart disease, obesity, unhealthy diet, physical inactivity and ethnic and socio-economic factors [8]. Most of these risk factors were modifiable, which offered an excellent opportunity to reduce the risk of developing a cardiovascular disease (CVD). With a targeted approach to assess and treat modifiable risk factors aiming on high risk individuals it was possible to reduce or postpone the occurrence of these diseases. Nowadays, there is overwhelming evidence that treatment of modifiable risk factors lead to a reduction of cardiovascular morbidity and mortality [9–17]. It was estimated that with eliminating these factors it is possible to prevent or postpone 90% of myocardial infarction and stroke worldwide [18,19].

Cardiovascular risk management

The gap between research and daily practice

In the last 30 years, evidence based national and international guidelines on cardiovascular risk management have been published, who make recommendations on identification, treatment and follow up of high risk patients for a (recurrent) cardiovascular disease [20,21]. Although multifactorial interventions on cardiovascular risk factors show improvements in blood pressure, cholesterol, body mass index, waist circumference and physical activity and reduction of vascular morbidity and mortality [22–25], surveys repeatedly show that adherence to guidelines is insufficient [26–28]. In the most recent EUROASPIRE V survey (2020), conducted in primary care in 16 European countries among high risk patients without a previous cardiovascular disease, it was found that nearly 20% was smoker, nearly 45% was obese (body mass index ≥ 30 kg/m^2) and in patients treated for high blood pressure or high cholesterol less than 50% reached the recommended target for systolic blood pressure (< 140/90 mm) Hg and LDL-cholesterol (< 2,6 mmol/l) [28].

Cardiovascular risk management (CVRM) and primary care

According to the European Society of Cardiology (ESC) 'the primary care physician is the key person to provide CVD prevention in a systematic approach and prioritizing persons at high risk, with a structured and intensive intervention' [21]. The vast majority of patients in the Netherlands are registered in a general practice. Due to an often life-long relationship, the general practitioner (GP) has a relation of trust with the patient and his relatives and is aware of the social context in which problems arise. GPs themselves consider general practice as the most appropriate setting for prevention and think that identification of elevated CVD risk, treatment thereof, and follow up of these patients is worthwhile [29].

With a national CVRM guideline advising on patient identification, measurements, treatment and follow up, the care standard CVRM 2009, focusing on the organization of CVRM care distinguished 4 core elements for good risk management [30]:

- Support with the patients self-management by drawing up an individual care plan and setting up treatment goals
- Decision support based on evidence based guidelines
- Clinical information systems for collecting patient data which can be used for evaluation and feedback
- A central care giver who supports the patient perform the individual care plan.

In the highly protocolized prevention programs, a central care giver role was delegated to a practice nurse (PN), as research had shown that PNs in primary care provide high quality and equivalent care to physicians/GPs [31-33]. The PN is a registered nurse, with an additional 1 year training in protocolized CVRM. The PN has her own consultation hours and is responsible for a regular follow up. Based on shared decision making the PN supports patients with life style changes and when necessary refers to a smoking cessation program, a dietician or other primary health care providers. Moreover, the PN supports patients with medication intake and adjustments in close collaboration with the GP.

Cardiovascular risk management and primary care groups

In the last 2 decades, many care groups have been set up to organize chronic care programs in primary care. A care group is an organization with a legal personality in which health providers work together. The care group is responsible for the coordination and provision of contracted care in a particular region. The term 'care group' refers to the principal contactor of the bundled payment contract, not to the team of health care professionals that provide the actual health care [34]. GPs are the most important players in the care groups. With the care group responsible for the organization of chronic care, it is possible for GPs and other primary health care workers to deliver high quality, guideline based chronic care. Care groups negotiate with health insurers about integrated financing (bundled payment) for which all care for

a chronic patient is provided. Between 2005 and 2008 10 care groups experimented with bundled payment contracts and integrated care for diabetes mellitus. Evaluation in 2009 of 3 years integrated diabetes care recommended

- a stepwise introduction for other chronic conditions with a care standard as starting point,
- negotiating and financing a bundled payment contract and
- agreements about measuring quality based on performance indicators [35].

Most involved in integrated CVRM care were the GP (59,5%), the practice nurse (43,9%), practice assistant (41,8%) and dietician (21,4%) while the physiotherapist, the pharmacist, the specialist for internal medicine and the cardiologist were less than 5% involved. To improve quality within care groups, instruments most commonly used were mirror information and visitation of practices [36].

National benchmark data on quality indicators have been developed for 3 chronic care programs (Diabetes mellitus, CVRM and Asthma/COPD) and have been reported annually since 2010 by LOK (Landelijk Overleg Ketenzorg, since 2013 InEen). The number of care groups delivering benchmark data from 3 chronic care programs between 2010 and 2021 are given in table 1.

Table 1. **Number of care groups (CG)**

Year	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
CG (N)	120	140	140	138	138	131	130	130	142	142	*	*
CG (N) delivering data for												
Diabetes	49	66	70	92	113	105	114	110	109	113	100	98
COPD		34	41	67	102	95	107	103	105	106	95	96
CVRM: secondary prevention			27	40	62	68	87	87	92	97	86	90
CVRM: primary prevention				23	40	50	69	78	86	91	81	89

* Numbers not registered

In 2021, 98 care groups delivered data for benchmarking on 1 or more care programs, representing 82% of the Dutch population [37]. Annual benchmark reports show that the measured quality of delivered care based on registration and outcome indicators has increased in recent years, however with considerable variation between participating care groups. In 2019, InEen formulated proposals to reduce care group variation on registration and outcomes [38].

Use of real world data

Real world data play an increasing role in monitoring and improving health care

processes, adherence to guidelines and standards and reduction of health care costs. Maddox et al describe 3 important real world data sources for the delivery of (cardiovascular) care: electronic health records (EHR), clinical registries (CR) and administrative claim data [39]. Both EHRs and CRs are prone to missings and errors, but if collected in a structured manner they are useful for improving quality of health [40,41]. Administrative claim data can be used for linking health care costs to certain procedures for example optimizing treatment for HF and readmission rates [42] or improved survival after cardiac revalidation [43].

Primary care in the Netherlands has a longstanding tradition of recording patient data electronically. Although part of the registration is plain text, diagnoses are coded according to the International Coding of Primary Care (ICPC) and medication is coded according to the Anatomical Chemotherapeutical Classification Code (ATC). With the introduction and implementation of chronic care programs, care groups started with structured patient data collection in a multidisciplinary information system for integrated care.

Primary care group PoZoB started with nurse-led, integrated CVRM care on April 1st 2010. Eligible patients were invited by the PN for a risk assessment, physical examination, determining treatment goals and regular follow up. The care group collected anamnestic, biometric, laboratory and medication data in a multidisciplinary information system (Care2U). Until 2013, the care group experienced difficulties to link 8 different EHRs to Care2U and the collected data were insufficient, but between 2013 and 2020 it was possible to monitor registration and outcomes of cardiovascular risk factors accurately.

Until now, data on the effectiveness of integrated CVRM care in a primary care setting is lacking. The PoZoB data allow for evaluation of long-term participation in an integrated CVRM care program. Evaluation of this topic, focusing on the effect of the program on risk factors and outcomes, is important to gain insight into the way in which multidisciplinary guidance and treatment of patients on high risk for a (new) cardiovascular event should be carried out in daily practice.

Aim and outline of this thesis

The aims of this dissertation are **1** to describe how the primary care group PoZoB organized and implemented long-term, nurse-led, integrated CVRM between 2010 and 2020, in general practices in and around Eindhoven, The Netherlands and **2** to investigate to what extent integrated CVRM care is effective in reducing cardiovascular risk factor levels and **3** to investigate whether integrated CVRM care leads to a reduction of cardiovascular disease incidence.

In **chapter 2** we describe the rationale and design of the CVRM care program with which primary care group PoZoB started on April 1 2010
In **chapter 3** we evaluate reasons for discontinuing the CVRM care program and compare patient characteristics of participants who discontinue with patients who continue with the CVRM care program between 2010 and 2018
In **chapter 4** we describe 3 intermediate outcomes of participation in the CVRM care program (systolic blood pressure, LDL-cholesterol and smoking status) between 2011 and 2018
In **chapter 5** we analyze sex differences of seven cardiovascular risk factors (systolic blood pressure (SBP), low density lipoprotein (LDL)-cholesterol, estimated glomerular filtration rate (eGFR), smoking status, body mass index (BMI), responsible alcohol intake and the degree of exercise according to the Dutch norm for healthy exercise) between 2013 and 2019
In **chapter 6** we describe the effect of practice visitations between 2016 and 2019 on registration and outcomes to reduce inter practice variation
In **chapter 7** we evaluate the effect of practice visitations on the outcome "SBP ≤ 140 mm Hg in patients < 80 years" in 11 general practices that perform below the minimal norm
In **chapter 8** we compare cardiovascular disease incidence of patients that participate in a long-term, nurse-led CVRM care program (PoZoB) with patients receiving CVRM care from their GP and sometimes from a PN that participate in the Julius Huisartsen Netwerk (JGPN)
In **chapter 9** we give an overview of the main findings and methodological issues are discussed

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2

Stepwise implementation of a cardiovascular risk management care program in Primary Care

Smits G, Hollander M, van Doorn S, Bots ML
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Abstract

Background: Primary care plays a pivotal role in sustainable cardiovascular risk management (CVRM) but little is known about the organizational process of implementing the guidelines. The aim of the study was to describe the approach taken by a primary care group to implement the CVRM guideline.

Methods: Stepwise introduction and implementation of a programmatic CVRM care program was organized and facilitated by the care group between April 2010 and January 2013 in 137 affiliated general practices with 188 general practitioners (GPs), in the vicinity of Eindhoven in The Netherlands. Care group support comprised sufficient staff, support with data extraction based on ICPC and ATC codes and with identification of eligible patients by scrutinizing patient health records and adequate coding of disease conditions.

Results: Patient selection based on availability of structured information on ICPC codes and risk factor levels from the electronic health records, led to 38,675 eligible patients in 2013. December 2019, the CVRM program was still running in 151 practices with 51,416 patients receiving programmatic CVRM care. Linking problems between 8 different electronic health record systems and the multidisciplinary information system for integrated care delayed adequate data collection until the beginning of 2013.

Conclusion: Commitment of affiliated GPs, a structured approach with adequate coding of diagnoses and risk factors, central data registration and additional funding for sufficient staff support are important conditions for the introduction and implementation of successful and sustainable programmatic CVRM care. This approach constitutes the basis for long-term follow up and annual evaluation.

Key-words: Primary care, General Practice, Cardiovascular disease, Programmatic care, Practice Nurse, Implementation

Introduction

Cardiovascular diseases (CVD) are the most important cause of morbidity and mortality in low, middle and high income countries [1,2]. The most important modifiable risk factors for CVD are smoking, unhealthy lifestyle (alcohol consumption, unhealthy diet, physical inactivity), overweight, elevated blood

pressure, unfavorable lipid levels and diabetes mellitus. These are considered to be responsible for 80-90% of preventable CVD [3]. National and international guidelines have been published to recommend approaches for prevention [4,5,6]. According to the Prevention Guideline of the European Society of Cardiology, "the general practitioner (GP) has a unique role in identifying individuals at risk for CVD and assessing their eligibility for intervention based on their risk profile" [7].

In The Netherlands many GPs are joint together in local or regional 'care groups'. A care group is an organization with a legal entity in which health care providers work together. The care group is responsible for the coordination and provision of contracted care in a particular region [8]. Care groups negotiate with regional health insurers about a bundled payment contract/integral funding. By joining a care group, practices benefit from a negotiated renumeration, support with implementation and regular education for health care providers. Care groups also organize chronic care programs for several conditions, such as diabetes mellitus type 2 (DM2), asthma/COPD (A/C) and cardiovascular risk management (CVRM). These chronic care programs are performed by a registered nurse with an additional training, in close collaboration with a GP. The Primary Care group PoZoB (Praktijk ondersteuning Zuid-oost Brabant) originated from an initiative of 6 smaller GP collectives, to which many other GPs voluntarily joined. PoZoB started with the implementation of chronic care programs for DM2 and A/C in 2005 and 2008 respectively, followed by CVRM in 2010. The content of the CVRM care program was based on the 2006 CVRM guidelines of the Dutch Society of General Practice [4]. The guideline provided the GP with recommendations on who to screen but made no recommendations on how to organize screening. Furthermore, the effect of strict application of the guideline in terms of cardiovascular risk control and prevention of vascular events in general practice had not been evaluated. This provided the 'research gap' at the start of the study. To the best of our knowledge, we are among the first describing the introduction and stepwise implementation of a carefully designed cardiovascular risk management program offered by a primary care group.

Methods

Study population

At the start of the CVRM implementation project in 2010, the care group comprised 137 GP practices (188 GPs) with 402,623 registered patients living in the southeastern part of the province of Brabant, and the western part of the province of Limburg in The Netherlands.

Conditions for starting

Before starting the implementation process, the PoZoB primary care group contacted every individual practice to identify suitability for participation in the CVRM care program, defined as

- participation in running chronic care programs for DM2 and A/C, and
- having sufficient hours deployed for the practice nurse (PN) and the GP.

The number of hours needed was estimated by the care group based on the number of participating patients, the number of annual consultations and the consultation time. If these conditions were met, the implementation process could start. Implementation start was linked to quarterly renumeration, therefore practices started every 3 months. The implementation start of 137 practices (188 GPs) quarterly is given in table 1.

Table 1. **Practices and GPs starting implementation programmatic CVRM care**

Year	2010			2011				2012			
Quarter	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Practices (n)	26	0	16	15	26	24	20	4	2	2	2
GPs (n)	41	0	19	16	35	29	32	7	3	4	2

Study design

We designed the study as a non-experimental retrospective cohort study embedded in routine clinical practice.

Implementation steps that were taken

The stepwise implementation comprised 4 steps: **1** Data extraction; **2** Inclusion/exclusion of eligible patients; **3** Consultation; **4** Follow up.

1 Data extraction.

Data extraction occurred from the patient electronic health record (EHR) to identify an increased risk for cardiovascular disease or with a history of cardiovascular disease. Extraction of data was carried out by a certified organization for multidisciplinary data management and scientific research ("Meetpunt Kwaliteit", since 2015 INZO = Instituut voor ZorgOptimalisatie). Potential eligibility for the program was based on medical diagnosis, and/or prescribed medication in patients older than 18 years and/or on labels that practices already used for identifying patients. Medical diagnosis was linked to the International Classification of Primary Care (ICPC) code and prescribed medication was linked to the Anatomical Therapeutical Chemical (ATC) classification. The ICPC and ATC codes used for identification are listed in Supplementary table 1.

2 Inclusion/exclusion of eligible patients.

The PN plays an essential role in step 2, 3 and 4 of the implementation process. For in- and exclusion, the EHR was scrutinized by the PN if diagnoses or risk factors were set correct, based on discharge letters from the specialist. Practices were given one year to complete the EHR investigation for correct ICPC codes and labeling, invite patients and start with CVRM care. A mandatory group course was offered to the GP and PN to standardize registration of patients. During this year, all practices were visited two or three times by specialized care group nurses to monitor progress and to discuss unclear diagnoses. If necessary, staff nurses were reachable by phone to discuss in- or exclusion in the CVRM care program.
Criteria for inclusion and exclusion in the CVRM care program were:

1 Patients with CVD or kidney disease:
- documented ischemic or atherosclerotic heart disease (myocardial infarction and angina pectoris), heart failure, atrial fibrillation, aneurysm of the abdominal aorta, peripheral arterial disease, transient ischemic attack, ischemic or hemorrhagic stroke, chronic kidney disease and
- primarily treated in primary care and
- aged 18 years or above.

2 Patients without a history of CVD or kidney disease but at high risk of CVD:
- a 10 year cardiovascular mortality risk > 5%, based on the SCORE table from the 2006 CVRM guidelines of the Dutch Society of General Practice [4] or
- use of blood pressure lowering or lipid lowering drugs in men aged ≥ 55 years and women aged ≥ 60 years or
- Systolic blood pressure > 180 mm Hg and/or total cholesterol > 8 mmol/l ever measured, independent of the 10 year mortality risk. Furthermore, these patients needed to be primarily treated in primary care and aged 18 years or above.

Exclusion criteria for both groups were:
- primarily treated by a specialist in a hospital or at an outpatient clinic or
- diabetes mellitus (as they received cardiovascular risk management in a diabetes care program).

Criteria are based on the CVRM guidelines of the Dutch Society of General Practice [4].

Those eligible were flagged in the EHR using the Care2U system. Care2U is a multidisciplinary information system for integrated care and was introduced in 2010. Care2U data registered by the PN ended up automatically in the EHR. All patients were labeled in Care2U and in the EHR as follows:
- V1: Patients at high risk for CVD, treatment and follow up by the GP/PN
- V2: Patients at high risk for CVD, treatment and follow up by a specialist in hospital or out-patient clinic

- V3: Patients at high risk for CVD, refusing care by a GP/PN
- Z1: Patients with CVD, treatment and follow up by the GP/PN
- Z2: Patients with CVD, treatment and follow up by a specialist in hospital or out-patient clinic
- Z3: Patients with CVD, refusing care by a specialist

Ultimately, only patients who had their treatment and follow up in primary care (V1 and Z1) were included in the CVRM care program.

3 Consultation

Once a patient was eligible for CVRM care he/she received an invitation letter from the general practice to make an appointment with the PN. If the patient did not respond within 2 weeks, the practice assistant called the patient. During the first consultation the patient was asked whether he/she was willing to participate in the CVRM care program. Time for the intake was estimated 45 minutes and was often split in 2 visits to the practice. The intake comprised an interview, check of in- and exclusion criteria, a physical examination and referral for blood testing to the local laboratory to complete the cardiovascular risk profile. The main items from the interview the PN conducted with the patient are summarized in table 2.

Table 2. **Summary of the aspects addressed during PNs interview**

• Physical, psychological and social well-being, stress related problems, sexual problems
• Cardiovascular (familial) history: 1st degree family member (< 60 years) with previous CVD
• Cardiovascular complaints: - Chest pain - Shortness of breath - Palpitations - Headache - Blurred vision - Fatigueless - Swollen ankles - Leg pain while walking
• Daily food intake: - Salt intake less than 6 grams a day - 200 grams of vegetables a day and 2 pieces of fruit - Eat fatty fish twice a week - Reduce saturated fat intake - Alcohol intake
• Smoking
• Exercise 30 minutes a day, 5 days a week
• Laboratory results
• Cardiovascular medication use - Adherence (based on patients estimate how often medication was forgotten every week) - Possible side effects and interactions - New prescription(s)

The protocolized physical examination, based on the CVRM guidelines of the Dutch Society of General Practice, assessed blood pressure, height and weight and body mass index (BMI kg/m²), heart rate and waist circumference. Blood and urine samples were taken for fasting glucose, lipids (total cholesterol, HDL, LDL and triglycerides) and kidney function (serum creatinine, estimated glomerular filtration rate (eGFR) and proteinuria). Blood tests performed less than 3 months ago could also be used. Blood sampling was performed at a local hospital laboratory or at a local diagnostic health center. Based on test results, for patients without a history of a cardiovascular disease and without preventive cardiovascular medication, a 10 year cardiovascular risk was estimated using the Systematic Coronary Risk Evaluation (SCORE) table from the 2006 CVRM guidelines of the Dutch Society of General Practice[4]. For patients younger than 55 (men) or 60 (women) years of age the SCORE had to be calculated based on blood pressure or cholesterol levels before starting medication. If the SCORE was ≤ 5%, the patient was not eligible for the CVRM care program.

4 Treatment and follow-up

After determining the cardiovascular risk profile, the PN made an individual care plan with the patient and supported self-management by informing about CVD or risk factors and motivating the patient to take the lead in coping with it in the best possible way. The PN discussed the individual care plan with the GP, who had final medical responsibility. The PN was responsible for preparing and discussing the individual care plan with the patient, comprising non-pharmacological and pharmacological treatment. Although treatment goals were set in shared decision with the patient, in most cases targets values were used according to the 2006 CVRM guidelines of the Dutch Society of General Practice[4], which are listed in Supplementary table 2.

If necessary, the PN referred the patient to a smoking cessation program, a physiotherapist or a dietician. If lifestyle advise resulted in insufficient effects on the risk factors level, blood pressure or lipid lowering medication could be initiated after consultation with the GP. When a cardiovascular event occurred or a patient failed to meet target values for blood pressure or lipids after maximum drug therapy, the GP referred to or consulted a specialist according to the criteria outlined in table 3.

Table 3. **Referral recommendations**

Criteria for consultation of a nephrologist:
• Patients < 65 years with a eGFR 45-60 ml/min/1.73 m²
• Rapid deterioration of the renal function (> 5 ml/min/1.73 m²/year)
• Patients > 65 years with a eGFR 30-45 ml/min/1.73 m²
• Increase of albuminuria despite adequate pharmacological treatment
Criteria for referral to a specialist:
• A new cardiovascular event
• Failure to meet target values despite adequate medication
• Familial dyslipidemia
• Premature, familial or undefined vascular disease
• Suspicion of secondary hypertension.
• Hypertension emerged in a short time and at young age (< 35 years)
• Suspected malignant hypertension (diastolic blood pressure > 120 mm Hg or clinical manifestations appropriate to cerebral complications like reduced consciousness, delirium, confusion, sudden impairment of vision or epileptic phenomena)
• Macro-albuminuria (Albumin-Creatinine Rate > 30 mg/mmol) and/or eGFR (< 30 ml/min/1.73 m²)
• Patients with suspected underlying kidney disease, familial kidney disease or specific sediment abnormalities

Regular follow up was agreed with the patient, depending on presence of comorbidity, complexity, achievement of treatment goals and advice according to the CVRM guideline. Patients were seen at least once a year by the GP to discuss laboratory results and seen 1-3 times a year by the PN to discuss lifestyle improvement and setting of new treatment goals if needed or wanted. In order to involve practices as much as possible in the development of the CVRM care program, the care group organized annual feedback meetings to discuss results and regular education for GPs and PNs on cardiovascular-related subjects.

Results

Data collection and registration

In 2010 patient data (anamnestic, biometric, laboratory) were collected in Care2U. Data registered in Care2U automatically ended up in the patients EHR and was accessible to the GP. Care2U automatically called patients for annual blood tests by linking the call to the date of birth. Due to registration problems in the EHR and to linking problems between 8 different EHR systems and Care2U, data collection was delayed and limited at the beginning. In the first quarter of 2013 these problems were finally solved. From April 2013, Care2U data were monitored monthly and every practice was able to view their data (process and outcome) any time.

Patients participating in the integrated CVRM care program

On April 1st 2010, 30 practices (41 GPs) with 87,458 registered patients started with the selection process which led to the identification of 11,891 patients suitable for integrated CVRM care (13.6 % of the registered patients). Because 400 patients (0,5%) eligible for primary prevention, decided not to take part in the program and for 3037 patients (3,5%) cardiovascular care was delivered in hospital or outpatient clinic, 8,454 patients (9.7%) participated in the CVRM care program: 5,988 high risk patients (6.8%) and 2466 CVD patients (2.8%). Due to quarterly renumeration, practices could start implementation every 3 months. In January 2013, 137 practices and 38,675 patients had started with integrated CVRM care. Another 8 practices started in 2013, 2014 and 2015. Between 2016 and 2019 6 new practices affiliated to the care group. The number of practices and GPs, eligible patients and baseline characteristics of participating patients between 2010 and 2019 are listed in table 4.

Table 4. **Number of practices/GPs, eligibility and baseline characteristics of participating patients**

Year	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
Practices (n)*	42	122	137	140	143	145	148	149	151	151
GPs (n)*	60	172	188	191	194	196	199	200	202	202
Registered pat*	87,458	378,099	402,623	406,119	416,433	422,296	401,077	405,956	422,452	436,009
Eligible pat*	11,896	50,937	54,990	61,709	63,846	65,692	64,877	65,166	67,194	68,989
(%)	13.6	13.5	13.7	15.2	15.3	15.6	16.2	16.0	15.9	15.8
Particip pat **	8,454	34,630	38,675	39,504	42,554	45,139	48,222	46,400	48,397	51,416
(%)	9.7	9.2	9.6	9.7	10.2	10.7	12.0	11.4	11.5	11.8
Age (mean)**	±	67.2	67.8	68.1	68.5	68.9	69.5	69.5	69.8	70.1
Male (%)**	±	47.1	47.4	46.9	47.2	47.3	47.9	48.2	48.7	48.9
Second prev (%)**	29.2	28.6	33.3	35.3	37.0	38.2	40.6	43.9	44.3	45.2
≥ 70 Years (%)**	±	42.6	43.6	44.7	46.2	47.6	50.5	51.5	52.8	54.3

* Numbers from accountability reports (2010-2015) and quarterly reports (2016-2019)

** Numbers from Care2U data (2010-2019)

± Incomplete data

Second prev: Patients eligible for CVRM care with an established CVD

Facilitating factors and barriers for implementation

Facilitating factors for implementation were:

- sufficient time given to PNs to provide patients with correct ICPC coding,
- mandatory education for PNs and GPs on scrutinizing the EHR and
- practice visitations by care group staff members every 3 months to discuss progress.

Because all affiliated practices had given commitment, there were basically no serious barriers for implementation. Practicability in daily practice is mainly determined by sufficient time and care group support.

Discussion

Summary

This paper describes the implementation of a CVRM care program in 137 practices within less than 3 years for 38,675 patients, a number that increased to 51,416 patients in 2019, comprising around 11% of patient GP population. Facilitating factors were interest and commitment of GPs, sufficient allocated time for tasks, education linked to regular feedback and monitoring and a program based on approved guidelines.

Comparison with existing literature

The gap between evidence and real world practice has been identified long ago [9]. Yet, the evidence based on the best design and the best implementation strategies for prevention of cardiovascular disease is still limited. Already in 2010, Grol and co-workers, showed that commitment for chronic care, a stepwise and structured approach, sufficient staff support and implementation with regular feedback, are important facilitators [10]. This has recently been confirmed again by Wandell and co-workers who showed that lack of time and lack of renumeration were amongst the most important barriers for selective prevention of cardiovascular diseases [11]. Organizational changes in patient care, in terms of enhancing performance of non-physicians (practice nurses), computer systems integrated in the electronic health care records networks of the GPs that allow for automated reminders and clinical decision support have been known to be effective in improving patient care with reduced costs and improve patient outcomes with multidisciplinary teams and integrated care services [12]. Standard registration, feedback loops with training followed by improvement strategies and education as part of a learning health care system has been advocated. Our approach developed and applied in 2010 by deploying PNs and negotiating an adequate reimbursement, addressed most of these issue and perhaps therefore, experienced little barriers. In addition to our approach, a recent review from the SPIN-EU group came up with an evidence based generic

"toolbox" for circumventing identified obstacles and harnessing facilitators in the design and implementation of cardiovascular prevention strategies. The development of the toolbox was based on data from five European countries, and may be of use in different communities, countries, and cultures[13].

Strengths and limitations

With all participating practices being affiliated to the care group, optimal reach, adoption and implementation of the CVRM program was assured. All practices in the Zuid-Oost Brabant region in The Netherlands were affiliated with the PoZoB care group. Practices covered rural, suburban and urban areas similar to the rest of The Netherlands, and can therefore be considered a representative sample of Dutch GPs.

The 2006 CVRM guidelines of the Dutch Society of General Practice have provided criteria to identify high risk patients[4]. When using structured files in the EHR as primary source for identification of eligible patients, the completeness and correctness relies on the ICPC and ATC coding of patients performed in general practice. The proportion of potentially eligible patients per practice based on ICPC and ATC codes varied between 14.8% and 30.3%, suggesting that inadequate coding may exist, potentially leading to a considerable number of high risk patients who unfortunately remain out of sight. This is in line with an evaluation in 2012 of ICPC coding in 311 Dutch practices showing that ICPC coding varied substantially between practices and between EHRs[14]. We emphasized that adequate coding of disease and medication is an important prerequisite for implementation of a CVRM program in general practice. Another consideration is that most patients (men ≥ 55 y, women ≥ 60 y) with prescribed medication for hypertension and hypercholesterolemia were automatically included in the CVRM care program, while we did not know whether de diagnosis hypertension and hypercholesterolemia was set correctly according to the National CVRM Guideline [4], which may have led to overrepresentation. Monitoring the CVRM care program by means of quarterly reports ensures that results can be followed closely and adjusted if necessary. This is in line with the principles of the "Learning Healthcare System" (LHS) in which daily care data from electronic health records are compared and discussed to create continuous learning and improved health care delivery[15].

Implications for research and/or practice

Using a Multidisciplinary Information System for data collection gives the opportunity for monitoring (i) the development of the CVRM care program and (ii) performance of individual practices based on process and outcome indicators over a long period of time. With annual collection of biometric and laboratory data it is possible to assess improvements in cardiovascular risk factors and reduction in cardiovascular events. In feedback meetings GPs and PNs were able to discuss further develop-

ment of the care program and in meetings between PNs and nurse staff, experiences were exchanged. As such, evaluation follows a qualitative approach according to the RE-AIM framework, which is based on 5 elements (Reach, Effectivity, Adoption, Implementation, Maintenance) for assessing the impact of innovation on individual and organizational level [16,17]. The CVRM care program provides a solid basis for scientific evaluation on registration and outcomes of CVRM care and its determinants to explore practice variation and identify modifiable factors for improvement. Real-world data, which are becoming increasingly important in providing evidence of treatment effectiveness in clinical practice, allow us to evaluate the effect of our program in terms of improved cardiovascular outcomes and reduced cardiovascular events, and against which costs.

Conclusion

In conclusion, commitment of affiliated GPs, a structured approach with adequate coding of diagnoses and risk factors, central data registration and additional funding for sufficient staff support are important conditions for the introduction and implementation of sustainable integrated CVRM care. This approach constitutes the basis for long-term follow up and annual evaluation.

Supplementary Table 1. **ICPC and ATC codes used to identify individuals potentially eligible for entering the CVRM care program**

Risk factors for cardiovascular disease (ICPC):
K85 high blood pressure
K86 high blood pressure without organ damage
K87 high blood pressure with organ damage
T82 obesity
T93 fat metabolic disorder
T93.1 high cholesterol
T93.2 other/combined fat metabolic disorder
P17 smoking
B85.1 of B85.4 impaired glucose tolerance
T90 diabetes mellitus
T90.1 diabetes mellitus, type 1
T90.2 diabetes mellitus type 2
T90.3 diabetes mellitus, non-specified
U99.01 kidney disease
U98.01 proteinuria
A29.1; A29.2; A29.3; A29.4 family history of cardiovascular disease
Prevalent Cardiovascular diseases (ICPC):
K74 angina pectoris
K75 acute myocardial infarction
K76 chronic ischemic heart disease
K91 atherosclerosis
K77 heart failure
K78 atrial fibrillation
K79.2 ventricular tachycardia
K83 non rheumatic valve disease
K84.02 cardiomyopathy
K89.1 transient ischemic attack
K90. stroke
K90.1 ischemic stroke
K90.2 hemorrhagic stroke
K92.1 peripheral arterial disease
K99.1 aneurysm aortae
ATC codes
Medication (ATC):
A10 anti diabetic medication
B01A Antithrombotic
B01AA Vit K antagonists
B01AC platelet aggregation inhibitors
C01 cardiac
C01AA digitalis glycosides
C01B anti-arrhythmic medication
C01DA nitrates
C02 antihypertensive medication
C03 diuretics
C04 vasodilatory medication
C07 beta-blockers
C08 calcium channel inhibitors
C09 RAAS inhibitors
C10 cholesterol lowering medication

Supplementary Table 2. **Guidelines for treatment of patients enrolled in the CVRM care program based on 2006 CVRM uidelines of the Dutch Society of General Practice**

Non pharmacological treatment:

- Referral to a smoking cessation program if indicated
- In case of overweight: aim for a BMI < 25 kg/m²
- Exercise: aim at moderate exercise at least 30 minutes a day, 5 days a week
- Maximum alcohol intake: 2 units a day for women, 3 units a day for men
- Nutrition:
  - less than 10 energy percent saturated fat and less than 1 energy percent transfat
  - preferably twice a week fatty fish
  - at least 200 grams of vegetables a day and 2 pieces of fruit
  - not more than 6 grams salt a day

Pharmacological treatment with blood pressure and/or cholesterol lowering medication:

- Patients without (a history of) cardiovascular disease
  - Patients with a 10 year mortality risk > 10 %: consider pharmacological treatment
  - Patients with a 10 year mortality risk of 5-10%: consider pharmacological treatment if one or more additional risk factors are present like familial burden of cardiovascular disease
  - Patients with a systolic blood pressure > 180 mmHg or a Total Cholesterol > 8 mmol/L are always treated regardless of the Risk SCORE
  - For smokers, quitting smoking is preferable to starting medication
- Patients with a (history of) CVD and a systolic blood pressure ≥ 140 mmHg are treated with antihypertensive medication
- Patients with a history of stroke or TIA: consider anti-hypertensive treatment even with systolic blood pressure < 140 mm Hg
- In patients with angina pectoris, heart failure or experienced myocardial infarction a beta blocker is indicated
- In all patients with experienced CVD acetylsalicylic acid is prescribed, unless there is indication for oral anticoagulant therapy (atrial fibrillation, valve replacement)
- In all patients with experienced CVD cholesterol lowering therapy is advised

Treatment targets according to the 2006 CVRM guidelines of the Dutch Society of General Practice

	Without CVD	With CVD
Systolic BP	< 140 mm Hg	< 140 mm Hg
Diastolic BP	< 90 mm Hg	< 90 mm Hg
Total Cholesterol	< 6.5 mmol/L	< 4.5 mmol/L
LDL Cholesterol	reduction ≥ 1 mmol/L	< 2.5 mmol/L
BMI	< 25 kg/m²	< 25 kg/m²
Waist circumference	Women: < 80 cm	< 80 cm
	Men: < 94 cm	< 94 cm
Fasting glucose	< 6 mmol/L	< 6 mmol/L
Potassium	3.5-5.0 mmol/L	3.5-5.0 mmol/L
Creatinine	Women: 60-100 umol/ L	60-100 umol/L
	Men: 75-110 umol/L	75-110 umol/L
Creatinine Clearance (eGFR)	≥ 60 ml/min/1.73m²	≥ 60 ml/min/1.73m²

Abbreviations PoZoB: Praktijkondersteuning Zuidoost Brabant; CVRM: cardiovascular risk management; GP: General Practitioner; ICPC: International Classification of primary Care; ATC-codes: Anatomical Therapeutic Chemical-codes; CVD: Cardiovascular diseases; DM: Diabetes mellitus; COPD: Chronic Obstructive Pulmonary Disease; PN: Practice Nurse; EHR: Electronic Health Record; CIS: Chain Information System; SCORE: Systematic Coronary Risk Evaluation: LHS: Learning Healthcare System; REAIM: Reach Effectivity Adoption Implementation Maintenance

Ethical approval Not applicable. All methods including the care groups protocol for data extraction, identification, examination and follow up were based on the 2006 CVRM guidelines of the Dutch Society of General Practice

Consent for publication Not applicable

Availability of data and materials No patient data have been used for this paper

Competing interests The authors declare that they have no competing interests

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3

Patient characteristics and reasons for discontinuation in a cardiovascular risk management program in The Netherlands

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Abstract

Background

Since 2010, an increasing number of patients have participated in a nurse-led integrated cardiovascular risk management program in The Netherlands. Because it is important to understand which patients discontinue and why, when evaluating the effectiveness of the care program, the aim was to identify the reasons for discontinuation.

Methods

Electronic health records of 3,997 patients enrolled in a nurse-led, integrated cardiovascular risk management program that started on April 1st, 2010, were manually scrutinized for reasons for discontinuation between April 1st, 2010, and April 1st, 2018. In addition to death and moving to a diabetes care program, we describe 7 different reasons why patients discontinued the program and compared the patient characteristics of those who discontinued the program without specific reasons with those who remained in the care program for 8 years.

Results

Between April 1st, 2010, and April 1st, 2018, 1,190 participants (29.8%) discontinued the CVRM care program, of whom 271 participants died (6.8%) and 195 were transferred to a diabetes care program (4.9%). The remaining 724 patients (18.1%) participated 5 years before discontinuation. Of these, 67 (9.3%) had a previous cardiovascular event at the start of the program. In 355 patients, a specific reason for discontinuation was not found. At baseline, these patients less frequently had a history of CVD than those who continued the program for 8 years (1.7 vs 22.6%), were younger (62 vs 67 years), had less registered cardiovascular comorbidity (atrial fibrillation: 1.1 vs 7.2%; congestive heart failure 0.3 vs 1.2%; chronic kidney disease 0.0 vs 4.5%), were more often smokers (13.0% vs 4.3%) and took blood pressure- and lipid-lowering drugs twice as often.

Conclusions

In our study we observed that participants who discontinued the nurse-led, integrated CVRM care program between 2010 and 2018 without specific reason or on request were younger, without previous CVD, had less cardiovascular comorbidity and were better adjusted to medication. Exploring the patients' reasons for discontinuation can contribute to an individualized approach to prevent or reduce discontinuation.

Key words:
Primary health care, Cardiovascular risk management, Integrated care, Prevention

Introduction

Since 2010, cardiovascular risk management (CVRM) in The Netherlands has been increasingly organized by primary care groups [1]. In 2020, 1.2 million patients participated in an integrated CVRM care program organized by 86 primary care groups [2]. Care groups support general practices with integrated CVRM care, executed by a practice nurse (PN) who has her own consultation hours and guides eligible patients 1-4 times a year with lifestyle changes and medication adjustments in close collaboration with the general practitioner (GP). Prior consent of all participants was requested and obtained before the start of the program. To the best of our knowledge, it is unknown how often and why participants discontinue a long-term CVRM care program.

Most research on the topic has been performed in patients with a recent cardiovascular event participating in outpatient cardiac rehabilitation programs (CRP) in secondary care. Factors associated with discontinuing CRP were smoking, high body mass index (BMI), physical inactivity, cerebrovascular comorbidity, anxiety and depression and the patients' belief to handle their own problems [3–5], while among the positively associated factors for adherence were age > 65 years, psychological and medication counselling, assessment for patient satisfaction, relaxation therapy and diet classes [6]. Patients withdrawing prematurely from CRP had a twice as high risk for a subsequent cardiovascular event afterwards [7]. Moreover, patients who have a prolonged follow-up in primary care after in-hospital CRP adhere better to long-term treatment targets relating to lifestyle and medication than nonparticipants [8,9]. Unfortunately, we do not know whether these results are generalizable to long-term primary care programs, particularly the CVRM care program, in which many patients do not have cardiovascular disease. To the best of our knowledge, it is unknown how often and why participants discontinue a long-term CVRM care program. Understanding the reasons why patients discontinue can help providers design a program that better meets the wishes and needs of individual patients with consequently better compliance and ultimately a greater reduction in cardiovascular risk. Furthermore, information on discontinuation is helpful when assessing the effectiveness of such a program. To gain better insight into the discontinuation of a nurse-led integrated CVRM care program, the aims of the present study were 1) to determine how often participants discontinued and for what reasons and 2) to compare the patient characteristics of those who discontinued the program without a specified reason with those who continued the program for 8 years.

Methods

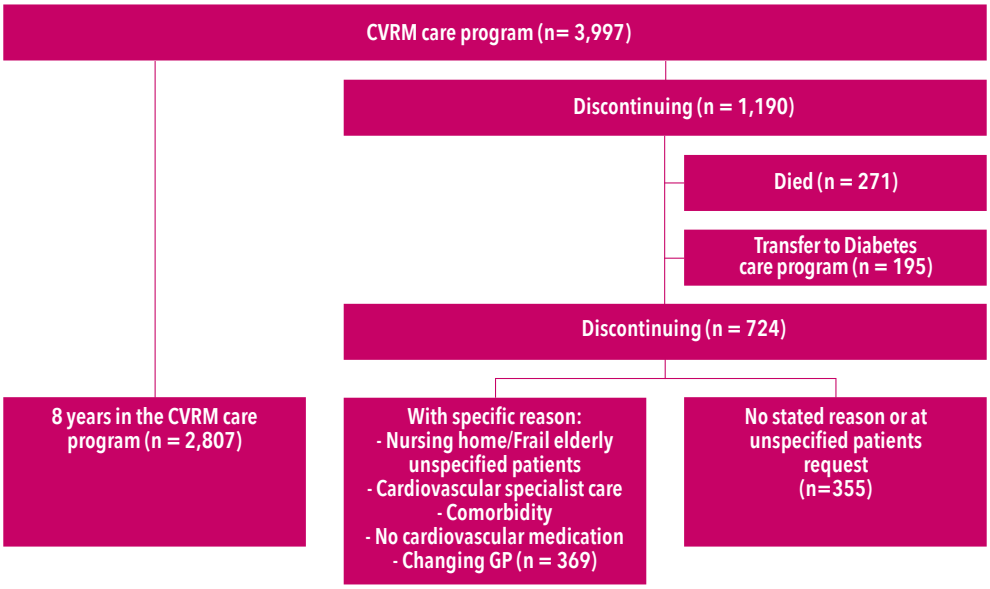
Setting

PoZoB is a primary care group in and around Eindhoven, southeast of The Netherlands, that supports affiliated GPs with the organization of 5 chronic care programs: diabetes type 2 (DM2), chronic obstructive pulmonary diseases (COPD), cardiovascular risk management (CVRM), psychiatric diseases and fragile elderly. The care group started with the implementation of a nurse-led integrated CVRM care program on April 1st, 2010, which has been described in detail elsewhere [10]. Practices affiliated with the care group are located in rural, semirural and urban settings comparable with other regions in The Netherlands and therefore can be considered representative. In 2018, the steering committee of PoZoB requested a thorough evaluation of adherence to the CVRM care program thereby defining our follow-up period to a maximum of 8 years.

Study design and study population

We performed a study using data from 13 practices (22 GPs, 46,642 registered patients) that had initiated an integrated CVRM care program on April 1st, 2010, with follow-up until April 1st, 2018. In total, 4,260 patients were eligible for the CVRM care program, of whom 263 declined participation, leaving 3,997 patients in this analysis (Figure 1). Eligibility for the integrated CVRM care program for both patients at high risk for cardiovascular disease (CVD) as well as for patients with a previous CVD was based on the 2006 CVRM guidelines of the Dutch Society of General Practice [11].

Figure 1. **Participants in the study**



Data collection

One author (GS) manually scrutinized 3,997 electronic health records (EHRs) of patients who enrolled in the nurse-led integrated CVRM care program on April 1st, 2010. We registered whether patients discontinued the program before April 1st, 2018, and for what reason. Furthermore, we collected all new diagnoses of acute myocardial infarction (AMI), transient ischemic attack (TIA), stroke, peripheral artery disease (PAD) with invasive or non-invasive treatment and abdominal aortic aneurysm (AAA) with invasive or non-invasive treatment that were recorded with the International Classification of Primary Care (ICPC) codes to distinguish between discontinuation in patients with and without an experienced cardiovascular event between April 1st 2010 and April 1st 2018. To only include patients with established PAD or AAA, patients with suspected mild PAD or AAA with specialist follow-up but without any treatment were excluded. Routine baseline patient care data were registered by the PN in the multidisciplinary registration system (Care2U). These comprised data from history taking, physical examination, laboratory results, and medication prescriptions based on the Anatomical Therapeutic Chemical (ATC) codes.

Reasons for discontinuing the CVRM care program

A priori we registered 9 reasons for discontinuation:

- death;
- diagnosed with diabetes mellitus and transition to a diabetes care program;
- admission to a nursing home or frail elderly program;
- returning to cardiovascular specialist care;
- returning to specialist care in connection to non-cardiovascular comorbidities;
- high-risk patients not on cardiovascular medication;
- changing GPs;
- without stated reason;
- at unspecified patient request.

"Nursing home", "returning to cardiovascular specialist care", "no cardiovascular medication", "changing GPs" and "comorbidity" were considered discontinuation with a specific reason, while "without stated reason" and "unspecified patient request" were considered discontinuation without a reason. An overview is given in table 1.

Table 1. **Reasons for discontinuing the CVRM care program**

Reasons for discontinuing (n, %)	Discontinuing in total population (n = 3,997)*	Discontinuing in patients with previous CVD (n = 855)	Discontinuing in patients on high risk for CVD (n = 3,142)
Died (%)	271 (6.8)	105 (2.6)	166 (4.2)
Diabetes Care Program (%)	195 (4.9)	51 (1.3)	144 (3.6)
Frail elderly program/Nursing home (%)	123 (3.2)	45 (1.2)	78 (2.0)
Cardiovascular specialist care (%)	64 (1.6)	3 (0.4)	61 (1.5)
No cardiovascular medication (%)	81 (2.0)	0 (0.0)	81 (2.0)
Comorbidity (%)	23 (0.6)	1 (0.03)	22 (0.6)
Changing GP (%)	78 (2.1)	12 (0.4)	66 (1.7)
Without stated reason (%)	158 (4.0)	0 (0.0)	158 (4.0)
Unspecified patients request (%)	197 (4.9)	6 (0.02)	191 (4.8)
Total (%)	**1,190 (29.8)**	**223 (5.6)**	**967 (24.2)**

* All percentage values in table 1 refer to the total population (n=3,997)

Ethical considerations

The use of patient data in this study was conducted following privacy legislation in the Netherlands. All patients participating in the integrated CVRM care program have been informed of the possibility that their anonymized data may be used for evaluation purposes. Data drawn from the patient EHR contained only age and sex, making it impossible for investigators to identify individual patients.

Analysis

For patient characteristics, categorical variables were reported as numbers and percentages. Continuous variables were reported as the means with standard deviation (SD). Baseline variables of patients who discontinued the program with and without a specific reason were compared with patients who participated during the full 8 years. No formal statistical testing was performed, as the interest was mainly descriptive and not focused on causality where confounding should be addressed by adjustment. Data were analysed using SPSS (version 22, IBM corp).

Results

On April 1st, 2010, 3,997 patients participated in the care program, comprising 855 patients (21.4%) with a previous CVD and 3,142 patients (78.6%) with a high risk for suffering a CVD in the future. The mean age of the patients was 67.5 years (SD 10.5),

and 47% were men. Between April 1st, 2010, and April 1st, 2018, 1,190 patients discontinued the CVRM care program, of whom 271 patients died and 195 patients continued in the diabetes care program. This left 724 patients discontinuing the CVRM care program with or without a specific reason, of which 355 patients discontinued with "no reason stated" or "at unspecified request". These 355 patients participated 4.4 years in the integrated CVRM care program. The remaining 369 patients discontinued treatment for a number of specific reasons, which are listed in Table 1. Of the 355 patients who discontinued treatment without reason, 349 (98.3%) were classified as having a high risk for CVD, and 6 had a previous CVD (1.7%) (table 2). When we compared the patient characteristics of those who discontinued treatment without a stated reason and at patient request (n = 355) with those who were 8 years in the care program (n = 2,807), the following results became apparent. Patients who discontinued treatment were 4.6 years younger at baseline than those who participated for 8 years. Mean systolic blood pressure (SBP), LDL cholesterol and BMI were comparable at baseline: 141.3 mm Hg vs 141.4 mm Hg, 3.41 mmol/l vs 3.35 mmol/l and 27.0 kg/m² vs 27.9 kg/m², respectively. Compared to patients who participated for 8 years, those patients who discontinued the program without reason were more often smokers (13.0% vs 4.3%) and more often were prescribed blood pressure lowering (BPL) medication (63.7% vs 25.5%) and lipid modifying (LM) medication (26.2% vs 11.7%). Furthermore, there were fewer registered comorbidities: atrial fibrillation (AF): 1.1% vs 7.2%, congestive heart failure (CHF): 0.3% vs 1.2% and chronic kidney disease (CKD): 0.0% vs 4.5% in those who discontinued and completed treatment, respectively (table 2).

Table 2. **Patient characteristics at baseline (April 1st, 2010)**

	8 year CVRM care (n = 2,807)	Discontinuing CVRM care (n = 724)	
		With specific reason (n=369)*	Without reason (n=355)**
Age (SD)	66.8 (9.7)	71.6 (10.0)	62.2 (11.8)
Years in CVRM care program (SD)	8.0 (0.0)	5.3 (2.0)	4.4 (1.7)
Previous CVD (%)	634 (22.6)	62 (16.9)	6 (1.7)
High risk for CVD (%)	2,173 (77.4)	307 (83.1)	349 (98.3)
Men (%)	1311 (46.7)	153 (41.5)	176 (49.6)
Mean LDL-cholesterol (SD)	3,35 (0.9)	3,40 (1.0)	3,41 (1.0)
Mean SBP (SD)	141.5 (17.1)	142.6 (18.4)	141.3 (16.5)
Mean BMI (SD)	27.9 (4.8)	28.3 (6.9)	27.0 (4.7)
Smoking Status (%)			
Yes	4.3	4.2	13.0
No	39.7	35.8	36.0
Before	8.6	6.9	11.8
Not registered	51.1	49.2	39.4
Cardiovascular comorbidity registered (%) ***			
AF	7.2	5.3	1.1
CHF	1.2	1.1	0.3
CKD	4.5	5.0	0.0
Cardiovascular medication registered (%) ****			
BPL-medication	25.5	39.7	63.7
LM-medication	11.7	12.7	26.2

* With reason: Nursing home, Return to cardiovascular specialist, No cardiovascular medication, Comorbidity, Changing GP

** Without reason: No stated reason or unspecified patient request

*** Comorbidity: AF: atrial fibrillation; CHF: congestive heart failure; CKD: chronic kidney disease

**** Cardiovascular medication: BPL: blood pressure lowering; LM: lipid modifying

Discussion

In this study, we evaluated the discontinuation of patients in a nurse-led, integrated CVRM care program and the reasons and patient characteristics associated with discontinuation. Patients who discontinued the care program without stated reason or at unspecified patient request seemed generally younger, nearly all without a previous cardiovascular disease, had less registered cardiovascular comorbidity, were more often smokers and took twice as much blood pressure lowering and lipid

modifying medication at baseline compared to participants who stayed 8 years in the program.

Comparison with literature

Although 1.2 million patients participated in a nurse-led integrated CVRM program in The Netherlands in 2020, to the best of our knowledge, no studies have been published on the frequency and reasons for discontinuation after being enrolled in a long-term CVRM care program [2]. Badenbroek et al evaluated reasons why patients did not participate in a health check and, if they did, why they did not visit their GP despite the estimated increased risk. More than half of the non-responders thought they did not have a cardiovascular disease, and a quarter had forgotten to make an appointment or reported having no time [12]. A personal approach, more information on cardiovascular diseases, their risks and consequences and the value of health checks were among the most important reasons to reconsider nonparticipation [13]. Much research on nonparticipation and discontinuation comes from studies in participants of longer term outpatient cardiac rehabilitation programs (CRP) using a multifactorial approach, targeting unhealthy lifestyle behaviour and medication adherence to reduce the risk of a recurrent CVD [14]. While lack of interest or the notion that the program is not beneficial were often mentioned reasons for nonparticipation [5,15,16], discontinuation was often associated with older age [5,14], female biological sex, [17–19], comorbidity [20], unemployment [19], lower education, a sedentary lifestyle, being divorced or single [21] and smoking [22]. A longitudinal study by Rao and colleagues, however, reported lower adherence to CRP in patients younger than 55 years [23]. Adherence to a CRP, which usually takes a limited number of sessions within 3 months, is, however, difficult to compare with a lifelong program in primary care with guidance once or twice a year. In our study, patients who discontinued treatment without a stated reason or at unspecified request participated in the program for an average of 4.4 years. It is possible that patients might have found their own way to implement lifestyle improvements in daily life activities [5,24]. It could also be very well that the 355 patients who discontinued without stated reason or at request perceived continuation as not beneficial and inconvenient with working hours after a number of years because 230 of them (65%) were 65 years or younger, although being employed is known as a reason for better adherence [15,19]. A German study on participants in a regional disease management program in primary care for patients with diabetes observed that those who were younger and employed were more at risk for dropping out [25]. Furthermore, nearly all patients who discontinued treatment without reason or at request were without cardiovascular disease (98.3%). They were, in fact, asymptomatic, which might well be a reason for discontinuing CVRM care because the necessity to continue is perceived as less urgent. This notion is supported by the study of Gucciardi et al., where asymptomatic pa-

tients or patients with few symptoms tended to drop out more often than symptomatic diabetic patients [26]. If death and transfer to the diabetes care program are not taken into account, 724 participants (18%) discontinue with the CVRM care program within 8 years, making it an annual discontinue rate of 2.25%. The aforementioned German study reported a 5.5% drop out within less than 3.5 years [25]. A meta-analysis with 41 randomized controlled trials on diabetes management interventions with a follow-up time between 1.5 and 48 months reported a drop-out rate ranging between 1.1% and 39.8% [27]. The results of this meta-analysis, however, comprised data from clinical trials and might not be comparable with data from real-world studies such as ours.

Potential implications for routine care

Based on the observations in our study, it could be considered to offer less frequent follow-up to younger participants without a previous CVD, those well-adjusted to medication and on target for systolic blood pressure and LDL cholesterol and smoking to increase their motivation to continue with integrated CVRM care. Alternatively, cardiovascular risk factor information could still be collected from those dropping out during regular consultation hours with the GP when the patient, for another non-vascular reason, comes to visit the GP, particularly since in The Netherlands, patients generally visit their GP once every 3-5 years [28]. Alternative data collection may continue with automated calls for blood tests and involving patients in self-management activities such as home blood pressure measurements and weight measurements, thus minimizing direct involvement of the practice. An additional advantage may be that a differentiated approach to participants leads to less work pressure in primary care as a result of the annual increasing number of participants in the CVRM care program. A potential role for the pharmacy may be explored, since a substantial proportion of those who discontinue used lipid- or blood pressure-lowering medication. Finally, it is important to explore the patient's motivation for discontinuing the CVRM care program. If we know the patient's personal values and beliefs about the necessity of participation, we will be able to motivate them more effectively [29].

Implications for future research

Loss of follow-up may bias the findings when studying the long-term effect on achieved risk factor level, medication prescription and/or cardiovascular disease incidence. Our findings point towards a potential for bias when studying controlled risk factor levels after 8 years or over. As a considerable percentage of those lost to follow-up had controlled risk factor levels, the remainder of the participants will have a lower percentage of controlled levels, attenuating the potential effect of a programmatic approach.

Strengths and limitations

To our knowledge, this is the first study that examined discontinuation from a nurse-led, integrated cardiovascular risk management program in primary care in The Netherlands. We were able to carefully scrutinize possible reasons for discontinuation in a large sample of Dutch patients receiving programmatic CVRM care. Second, this patient sample was largely unselected, covered both urban, suburban and rural areas in The Netherlands and therefore in itself was representative of the Dutch population.

It is important to evaluate discontinuation because i) long-term participation is an indicator for the success of the program and ii) if we understand why participants discontinue, we may be able to better tailor the program to the patient's individual preferences.

A limitation is that we could not further specify the reasons "without stated reason" and "at unspecified request". This would have given us better insight into the patient's motivation for discontinuation, but it calls for registration of that information at the source. Unfortunately, no further information was available on the patient's self-management skills or successful lifestyle improvements before discontinuing the care program, and we did not have information about the patient's private situation, such as education level or marital status. In addition, we did not have information on depression and anxiety, as it is known that these comorbidities lead to discontinuation and reduced motivation to change lifestyle behaviour [30]. Lastly, the large and representative sample notwithstanding, the descriptive nature of this study warrants caution when interpreting differences in patient characteristics between patients who continue the program and those who discontinue.

Conclusion

In our study we observed that participants who discontinued the nurse-led, integrated CVRM care program between 2010 and 2018 without specific reason or on request were younger, without previous CVD, had less cardiovascular comorbidity and were better adjusted to medication. Exploring the patient's reasons for discontinuation can contribute to an individualized approach to prevent or reduce discontinuation.

Abbreviations CVRM: Cardiovascular risk management; DM2: Diabetes type 2; COPD: Chronic obstructive pulmonary disease; PN: Practice nurse; GP: General practitioner; CRP: Cardiac rehabilitation program; BMI: Body mass index; PoZoB: Praktijkondersteuning Zuidoost Brabant; CVD: Cardiovascular disease; AMI: Acute myocardial infarction; TIA: Transient ischaemic attack; PAD: Peripheral artery

disease; AAA: Aortic abdominal aneurysm; EHR: Electronic health record; ATC: Anatomical therapeutic chemical; SD: Standard deviation; BPL: Blood pressure lowering; LM: Lipid modification; AF: Atrial fibrillation; CHF: Congestive heart failure; CKD: Chronic kidney disease

Ethical approval All methods including the care groups protocol for data extraction, identification, examination and follow up were based on the 2012 CVRM guidelines of the Dutch Society of General Practice and approved by the Julius Centre for Health Sciences and Primary Care, University Medical Centre Utrecht, The Netherlands. Before starting with integrated CVRM care informed consent was given by patients to use anonymized data for evaluation and scientific research.

Consent for publication Not applicable

Availability of data and materials Anonymized patient data derived from the multidisciplinary information system (Care2U) can be send by mail on request: g.smits@pozob.nl

Competing interests The authors declare that they have no competing interests.

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Cardiovascular risk reduction with integrated care: results of 8 years follow up

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Abstract

Background

Care groups organize integrated cardiovascular risk management programs in primary care for high risk patients. Results of long term cardiovascular risk management are scarce. The aim was to describe changes in low density lipoprotein cholesterol, systolic blood pressure and smoking between 2011 and 2018 in patients participating in an integrated program for cardiovascular risk management organized by a care group in The Netherlands.

Aim

To explore whether long-term participation in an integrated cardiovascular risk management program could lead to the improvement of 3 important risk factors for cardiovascular disease.

Methods

A protocol was developed for delegated practice nurse activities. A multidisciplinary data registry was used for uniform registration. The care group organized annual education for general practitioners and practice nurses on cardiovascular topics and regular meetings for practice nurses only to discuss complex patient cases and implementation issues. From 2015 onwards, the care group started with practice visitations to discuss performance and support practices with organizing integrated care.

Results

In patients eligible for primary prevention as well as for secondary prevention similar trends were observed: lipid modifying and blood pressure lowering medication increased, mean low density lipoprotein cholesterol and mean systolic blood pressure decreased, patients on target for low density lipoprotein cholesterol and systolic blood pressure increased and the proportion of non-smokers with both low density lipoprotein cholesterol and systolic blood pressure on target increased. Improved registration between 2011 and 2013 was partly responsible for the sharp increase of patients on target for low density lipoprotein cholesterol and systolic blood pressure.

Conclusion

In patients participating in an integrated cardiovascular risk management program, we saw annual improvements in 3 important cardiovascular risk factors between 2011 and 2018.

Keywords
primary health care, cardiovascular risk management, integrated care, practice nurse

Introduction

Cardiovascular disease (CVD) accounts for 45% of deaths and 64 million disability adjusted life years (DALY) in Europe [1], with reduced quality of life in patients after a myocardial infarction and stroke [2,3]. The occurrence of CVD can be largely attributed to modifiable risk factors such as elevated blood pressure, unfavorable lipids, obesity, smoking, physical inactivity, unhealthy diet and alcohol intake of which it has been suggested that adjustment to normal levels could prevent 80-90% of all myocardial infarctions and ischemic strokes [4,5]. Addressing these risk factors with a multifactorial and multidisciplinary approach is recommended by national and international guidelines [6,7]. With a long tradition in programmatic prevention and a longstanding relationship with patients and their families, general practitioners (GPs) play a key-role in a multidisciplinary approach for the prevention of CVD. Both patients and GPs endorse the usefulness of prevention in primary care [8]. The National Guideline for cardiovascular risk management (CVRM) indicates how to identify patients with an increased risk of CVD and advised on cardiovascular risk reduction with lifestyle improvements and drug therapy [6]. Moreover, the guideline provides advice on task delegation, such as to the practice nurse (PN), a registered nurse with an additional 1 year training. Having their own consultation hours, PNs perform protocolized programmatic CVRM care, focusing on life style and treatment of blood pressure and cholesterol. Involvement of trained nurses has shown to be equivalent to physician care regarding health outcomes for patients, process of care, referrals to specialists and costs [9]. Additionally, compared with GPs, nurse-delivered CVRM in primary care led to better outcome measures on systolic blood pressure, total cholesterol and LDL-cholesterol after 1 year [10].

Surveys carried out in several European countries showed poor implementation of international CVRM guidelines in primary care and disappointing rates of cardiovascular risk factor control [11,12]. A comprehensive approach is generally needed to overcome many barriers for following guidelines and treatment targets [13]. Successful introduction and implementation of a guideline depends highly on a rigorous preparation and evaluation [14]. Between 2005 and 2010 in The Netherlands, many GPs organized themselves in primary care groups who became responsible for the organization and provision of high-quality, guideline based CVRM care [15]. Care groups negotiate with regional health insurance organizations about structural renumeration for the organization of integrated CVRM care. Practices benefit

from negotiated renumeration, care group support with implementation and regular education for GPs and PNs, implicating that all practices are affiliated to the care group. The care group receives a negotiated renumeration from health insurance companies for every participating patient in the care program. In 2020, 86 care groups offered CVRM care to 15.5 million registered patients in The Netherlands. In the Eindhoven region, southeast of The Netherlands, 3 care groups (Praktijk ondersteuning Zuid oost Brabant: PoZoB, Stichting Gezondheidscentra Eindhoven: SGE and De Ondernemende Huisarts: DOH) with around 300 affiliated GPs offer integrated CVRM care. PoZoB implemented integrated CVRM care in 137 practices (188 GPs) between April 1st 2010 and January 1st 2013. Since long term results of its effect on cardiovascular risk factors are scarce, we describe the changes in LDL-cholesterol, systolic blood pressure (SBP) and smoking status of patients enrolled in a CVRM care program between 2011 and 2018.

Methods

Design

The CVRM implementation program was designed as a dynamic observational cohort study, with a run in period (2010-2015) for optimizing data collection and protocol development, aiming at improvements in registration and outcomes identical for all participating practices. From 2015 to 2018 the care group focused on visitation of individual practices to discuss practice organization and outcomes of integrated care.

Study population

The study was performed in the region Eindhoven, southeastern part of The Netherlands, in 145 general practices affiliated to the primary care group PoZoB. The care group covers rural, suburban and urban practices similar to other parts of The Netherlands and therefore can be considered as representative. Between 2010 and 2013, 137 practices (406,119 registered patients) followed a stepwise implementation for integrated care and another 8 practices started implementation between 2013 and 2015. Eligibility for participation in integrated CVRM care was based on in- and exclusion criteria given in table 1. Details of the stepwise implementation have been described elsewhere [16].

Table 1. **Criteria for participation in the CVRM program***

Inclusion criteria for patients eligible for primary prevention • A 10 year cardiovascular mortality risk > 5%, based on the SCORE table from the 2006 CVRM guidelines of the Dutch Society of General Practice (6). • Prescription of blood pressure lowering or lipid modifying drugs in men aged ≥ 55 years and women aged ≥ 60 years. • Systolic blood pressure > 180 mm Hg and/or total cholesterol > 8 mmol/l ever measured, independent of the 10 year mortality risk. • The patient is primarily treated in primary care and aged 18 years or above.
Inclusion criteria for patients eligible for secondary prevention: • Documented previous ischemic or atherosclerotic heart disease (myocardial infarction and angina pectoris), heart failure, atrial fibrillation, aneurysm of the abdominal aorta, peripheral arterial disease, transient ischemic attack, ischemic or hemorrhagic stroke, chronic kidney disease. • The patient is primarily treated in primary care and aged 18 years or above.
Exclusion criteria for both groups were: • Primarily treated for cardiovascular disease risk by a specialist in a hospital or at an outpatient clinic. • Diabetes mellitus (patients receive cardiovascular risk management in a diabetes care program). • Patients younger than 18 years.

* CVRM program: cardiovascular risk management program

Interventions between 2010 and 2018

Registration

A multidisciplinary registry for integrated care (Care2U), set up from April 1st 2010 onwards, collected data mainly from PNs, but other primary health care workers like dieticians and physiotherapists could add data as well. Data in Care2U automatically ended up in the GPs Electronic Health Record (EHR) and were visible for individual practices in real time. Laboratory test results ended up automatically in Care2U. Smoking status and all SBP measurements taken in one year were registered in Care2U, with the last measured SBP value visible in the data overview of every individual practice. Due to linking problems of Care2U with 8 different EHR systems, data from 2010 were incomplete but registration improved significantly in 2011 and 2012. In 2011, Care2U-data of 34,628 participating patients (mean age 67 years, 53% women, 29% with a previous CVD) was available, increasing to data of 48,397 patients (mean age 70 years, 51% women, 44% with a previous CVD) in 2018. Prevalence increased annually due to new affiliating practices after 2013, increased incidence of patients eligible for primary prevention and referrals from the specialist.

Integrated CVRM care

After assessment for eligibility, patients started with life style improvements and drug therapy. If necessary referral to another health care professional was made, such as a dietician, physiotherapist or a medical specialist. PNs used motivational interviewing in patients who wanted to quit smoking or referred to a "Stop Smoking"- program. Patients were monitored 1-4 times a year by the PN and once a year by the GP to evaluate cardiovascular risk factors. With the multidisciplinary information system all involved disciplines had access to the patient's data, facilitating communication between care givers and exchange of information.

Protocols

From the start of integrated CVRM care in 2010, a work protocol for the PN was available. The work protocol explains how to include patients in the CVRM care program and how to calculate the 10 year cardiovascular mortality risk based on the SCORE table [6]. In addition, the work protocol provides information about (i) a Minimal Intervention Strategy (MIS) for help with smoking cessation, (ii) how correct registration in Care2U should be done, (iii) when blood tests should be performed, (iiii) how to draw up an individual care plan and (iiiii) how to motivate patients to apply more self-management. Finally, the division of tasks between GP and PN is described. A protocol for correct blood pressure measurement was added in 2013.

Education

Annual education for GPs and PNs was organized by the care group and based on the most recent guidelines [6,17]. PNs received additional training in motivational interviewing and data processing. In separate meetings for PNs only, they discussed complex case studies and shared problems on practice organization. In feedback meetings GPs and PNs discussed Care2U benchmark data on registration and outcomes.

Practice visitations

The care group started with practice visitations in 2015, carried out by care group staff members to support practices with drawing up an annual practice plan and by formulating one or more areas in which a practice wanted to improve. From 2016 onwards, practice visitations were also used to discuss performance based on data from the quarterly reports.

Quarterly reports

The care group started with quarterly reports in 2016 that enabled practices to compare individual practice performance with care group performance. The care group established indicators for the prevalence, registration and outcomes of cardio-

vascular risk factors for participating practices. Standards were set for mean value, minimal norm and best practice, an often used method to compare individual performance with peer group performance [18]. Practices asking for support, having problems with organizing adequate CVRM care or performing below a minimal norm based on the care group standards were prioritized for visitation. In 2015 the care group started with visiting 52 practices and in 2016, 2017 and 2018 respectively, 98, 102 and 117 practices were visited at least once.

LDL-cholesterol toolkit

The LDL-cholesterol toolkit introduced in 2017, comprised two parts: a part for care givers to inform patients on the use and necessity of lipid lowering medication (e.g. statins) and "tips and tricks" in case of impaired patient adherence or side effects. The other part was written information for patients.

Data analysis

Data are presented as percentages and means with corresponding standard deviations, overall and in strata of primary and secondary prevention. Criteria for primary and secondary prevention are described in Table 1. All analyses were performed with IBM SPSS statistical software (version 22).

Results

Intervention studied

April 1st 2010 27 practices with 8,456 eligible patients, started with the implementation of integrated CVRM care. January 1st 2013, 137 practices with 38,675 eligible patients (mean age 67.8 years, 52.6% female, 43.6% ≥ 70 y, 33.4% with previous CVD) completed the implementation process with 149 practices and 48,397 participating patients (mean age 69.8 years, 53.1% female, 52.8% ≥ 70 years, 44.3% with previous CVD) participating in 2018. Because registration in Care2U was incomplete in 2010, annual results between 2011 and 2018 are shown. Baseline characteristics of participating patients eligible for primary and secondary prevention are given in table 2.

Table 2. **Characteristics of the study population (*)**

Year	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**
Registered patients in PoZoB care group (n)	378,099	402,623	406,119	416,433	422,296	401,077	407,661	416,648
Eligible for integrated CVRM care (n)	40,456	43,956	47,340	49,702	53,155	56,654	57,478	59,349
Participants (n)	34,628	38,675	39,503	42,551	45,138	48,222	46,400	48,397
Eligible but not participating	5,858	5,281	7,837	7,151	8,017	8,432	11,076	10,952
Participants eligible for primary prevention (%)	24,712 (71.4)	25,772 (66.6)	25,559 (64.7)	26,802 (63.0)	27,913 (61.8)	28,639 (59.4)	26,029 (56.1)	26,935 (55.7)
Age (y) (SD)	66.3 (10.0)	66.6 (9.9)	66.7 (9.7)	66.9 (9.7)	67.2 (9.8)	67.5 (10.1)	67.3 (10.1)	67.6 (10.1)
Male (%)	43.9	43.6	43.5	43.7	43.6	44.0	43.6	44.0
≥ 70 years (%)	36.9	37.8	37.8	38.9	40.2	42.4	42.6	43.8
Mean LDL in mmol/l (SD)	3.34 (0.93)	3.31 (1.1)	3.25 (0.92)	3.13 (0.93)	2.96 (0.92)	2.97 (0.92)	2.88 (0.89)	2.62 (0.81)
Mean SBP in mm Hg (SD)	140.8 (19.8)	139.5 (16.5)	138.3 (15.7)	137.7 (15.9)	137.2 (15.3)	136.8 (15.0)	136.7 (15.1)	136.4 (14.9)
Smoking (%)	4.0	8.5	12.3	11.6	11.4	11.3	10.8	10.4
Non-smoking/stopped smoking (%)	55.2	65.5	78.5	78.9	80.4	80.5	81.1	81.7
LL medication prescribed (%)	22.8	32.4	35.6	37.5	41.1	42.9	49.9	49.6
BPL medication prescribed (%)	47.1	61.1	61.0	59.0	60.8	61.1	67.4	69.7
LDL ≤ 2.5 mmol/l (%)	15.0	19.6	22.7	27.9	35.9	34.0	39.5	51.8
SBP ≤ 140 mm Hg (%)	35.1	49.1	59.9	60.0	61.8	62.8	63.4	64.0
Non-smoking/stopped smoking, LDL ≤ 2.5 mmol/l and SBP ≤ 140 mm Hg (%)	3.7	7.5	11.4	14.2	18.5	18.8	20.8	29.5
Participants eligible for secondary prevention (%)	9,916 (28.6)	12,903 (33.4)	13,944 (35.3)	15,749 (37.0)	17,225 (38.2)	19,583 (40.6)	20,371 (43.9)	21,462 (44.3)
Age (y) (SD)	69.7 (11.8)	70.3 (11.3)	70.8 (10.8)	71.3 (10.9)	71.6 (10.8)	72.5 (10.9)	72.3 (10.8)	72.6 (10.7)
Male (%)	50.1	55.0	52.9	53.0	53.2	53.4	54.0	54.7
≥ 70 years (%)	53.3	55.3	57.2	58.7	59.7	62.4	62.8	64.1
Mean LDL in mmol/l (SD)	2.81 (0.91)	2.81 (0.90)	2.79 (0.90)	2.71 (0.90)	2.56 (0.89)	2.58 (0.88)	2.58 (0.87)	2.33 (0.82)
Mean SBP in mm Hg (SD)	138.1 (18.0)	137.1 (17.8)	136.5 (17.4)	135.9 (16.7)	136.1 (17.0)	135.6 (16.7)	135.2 (16.6)	135.0 (16.5)
Smoking (%)	4.2	9.8	14.4	13.5	13.4	12.8	12.2	12.2
Non-smoking/stopped smoking (%)	43.7	57.0	74.4	74.7	76.6	77.1	77.1	78.5
LL medication prescribed (%)	38.6	49.6	53.8	51.7	58.4	60.4	60.5	61.3
BPL medication prescribed (%)	49.6	58.8	62.8	60.8	65.8	66.9	66.7	68.6
LDL ≤ 2.5 mmol/l (%)	27.7	35.6	42.2	46.6	54.4	49.6	54.3	65.8
SBP ≤ 140 mm Hg (%)	32.9	48.3	62.6	61.8	62.2	63.2	63.4	64.5
Non-smoking/stopped smoking, LDL ≤ 2.5 mmol/l and SBP ≤ 140 mm Hg (%)	6.5	13.7	21.7	24.0	28.1	26.3	29.0	36.5

Abbreviations: SD: Standard Deviation; LL medication: Lipid Lowering medication; BPL medication: Blood Pressure Lowering medication; SBP: Systolic Blood Pressure; LDL: LDL-cholesterol

(*) Reported proportions include all participating patients

Registration

Registration in Care2U of LDL-cholesterol, SBP and smoking status improved significantly in 2011 and 2012 and remained stable in the subsequent years with missing data for LDL-cholesterol, SBP and smoking status of less than 10%. Registration data are given in table 3.

Table 3. **Registration of LDL-cholesterol*, SBP ** and smoking status between 2011 and 2018**

Year	2011	2012	2013	2014	2015	2016	2017	2018
LDL-cholesterol *(%)	72.7	86.3	96.4	97.1	97.6	92.4	97.8	98.0
SBP** (%)	58.9	79.0	93.8	91.7	92.8	92.4	91.6	91.9
Smoking status (%)	55.9	71.6	90.1	89.7	91.1	91.0	91.8	91.6

LDL-cholesterol* : Low Density Lipoprotein-cholesterol. SBP**: Systolic Blood Pressure

Risk factor trends in patients eligible for primary prevention

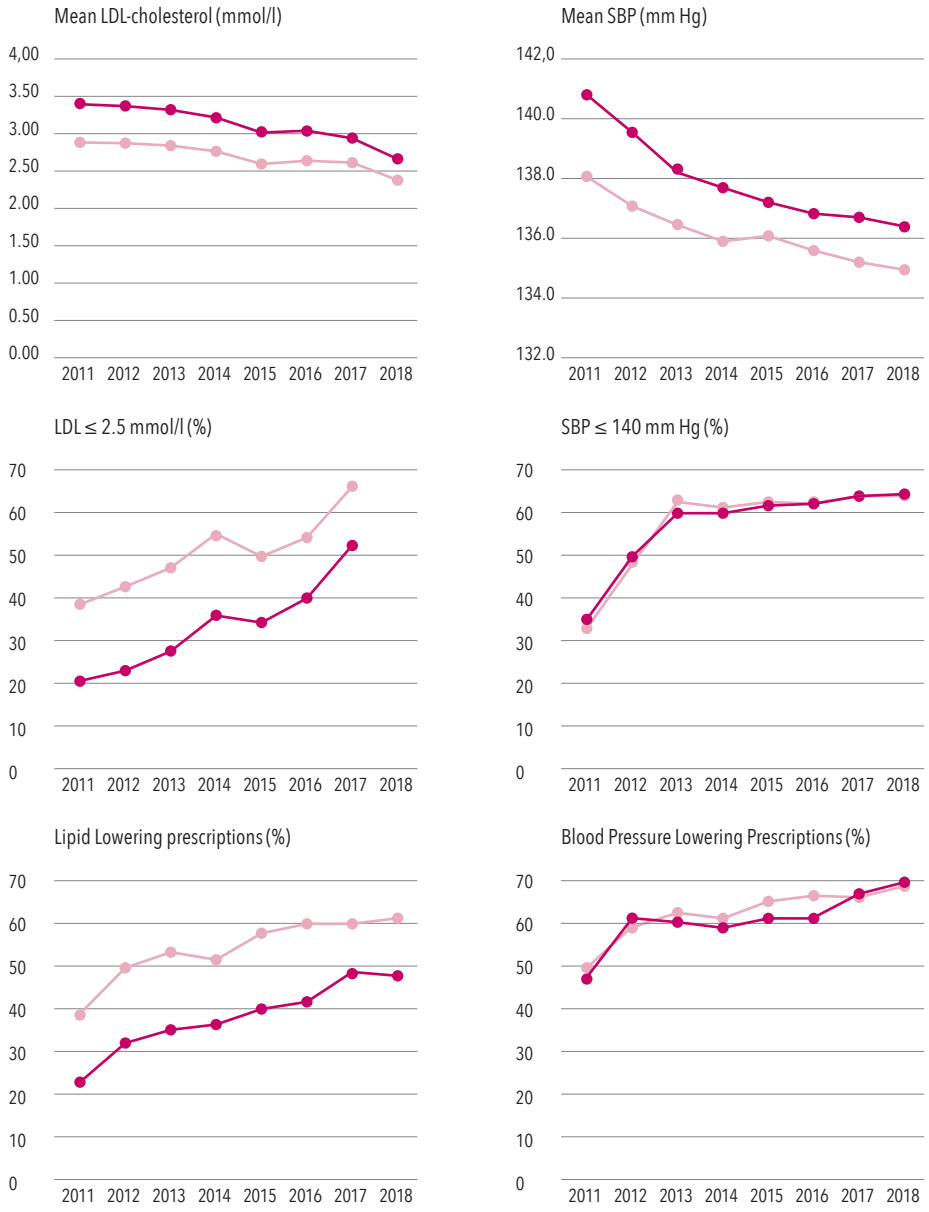
Cholesterol lowering prescriptions increased from 22.8% (2011) to 49.6% (2018). Blood pressure lowering prescriptions increased from 47.1% to 69.7%. Mean LDL-cholesterol decreased from 3.34 mmol/l to 2.62 mmol/l. Mean SBP decreased from 140.8 mmHg to 136.4 mmHg. The proportion of patients on target for LDL-cholesterol increased from 15.0% to 51.8%. The proportion of patients on target for SBP increased from 35.1% to 64.0%. The proportion of smoking patients decreased from 12.3% to 10.4% between 2013 and 2018. The proportion of non-smoking patients with LDL-cholesterol and SBP on target increased from 3.7% to 29.5%. A lower proportion of cholesterol lowering prescriptions in the primary prevention group resulted in higher mean LDL-cholesterol levels and a lower proportion of patients on target throughout all the years. On the other hand, despite similar proportions on target for SBP and blood pressure lowering prescriptions in both the primary and the secondary prevention group, mean SBP levels were slightly higher in the primary prevention group. A possible explanation is that PNs accept slightly elevated SBP values (140-150 mm Hg) more easily in patients without previous CVD.

Risk factor trends for patients eligible for secondary prevention

Cholesterol lowering prescriptions increased from 38.6% to 61.3%. Blood pressure lowering prescriptions increased from 49.6% to 68.6%. Mean LDL-cholesterol decreased from 2.81 mmol/l to 2.33 mmol/l. Mean SBP decreased from 138.1 mm Hg to 135.0 mm Hg. The proportion of patients on target for LDL-cholesterol increased from 27.7% to 65.8%. The proportion of patients on target for SBP increased from 32.9% to 64.5%. The proportion of smoking patients decreased from 14.4% to 12.2% between 2013 and 2018. The proportion of non-smoking patients with LDL-cholesterol and SBP on target increased from 6.5% to 36.5%. Figure 1 shows the course of mean LDL-cholesterol and

mean SBP, the proportion of patients on target for LDL-cholesterol and SBP and the proportion of lipid lowering and blood pressure lowering prescriptions.

Figure 1. **Mean LDL-cholesterol (mmol/l) and SBP (mm Hg), LDL-cholesterol and SBP on target (%) and Lipid Lowering and Blood Pressure Lowering prescriptions (%) between 2011 and 2018**



line: Primary prevention; line: Secondary prevention

SBP: Systolic Blood Pressure; LDL: Low Density Lipoprotein

Discussion

Summary

The study showed that with offering comprehensive support, consisting of protocolized involvement of PNs, a multidisciplinary registration system, regular education and feedback, practice visitations, quarterly benchmark reports and a LDL-cholesterol toolkit, a considerable improvement in 3 important cardiovascular risk factors in patients on high risk for or with previous CVD was observed.

Strengths and limitations

There is a number of strengths related to this study. First, the multidisciplinary information system (Care2U) allowed us to include a large study population with information from routine clinical practice. Second, all participating practices followed the same protocol for stepwise implementation and follow-up [16]. Third, data collection did not interfere with day-by-day practice, resulting in real life monitoring of a large number of patients at high risk of CVD in primary care. Fourth, data were collected over a period of 8 years which allowed us to visualize a clear development of both registration and outcomes.

There are also some limitations. First, because all affiliated practices started with programmatic CVRM care, this study contains no reference group. A causal relationship between care group support and outcomes therefore cannot be demonstrated. Long-term research, comparing integrated CVRM with care as usual would therefore be desirable. Second, some data on LDL-cholesterol, SBP and smoking status between 2010-2018 were missing, especially between 2010 and 2013. It remains uncertain whether this was solely due to technical problems, lack of time for the PN or not delivered care. However, the number of missing between 2013 and 2018 was generally well below 10%, and its impact on the results may be small [19]. Still, data registration could improve if PNs were given sufficient time to fulfill the administrative tasks. Third, although 24% of the patients has a non-Western European background, due to Dutch legislation it was not possible to compare the results within ethnic groups.

Comparison with existing literature

To our knowledge, this is amongst the first studies that evaluates comprehensive care group support and long-term outcomes of integrated CVRM care in The Netherlands. Comparison with other studies is difficult because the study design is often a randomized controlled trial (RCT) with a limited follow up period. Outcomes from RCTs comparing structured care delivered by PNs with care as usual show varying results. In two Dutch studies, PNs achieved equal or better results for the management of asthma, COPD, diabetes and cardiovascular risk factors after 1 year, com-

pared to GP care [10,20]. A nurse-led, multifaceted risk assessment and management program (RAMP) in hypertension patients reduced mean SBP and LDL-cholesterol and increased the proportion of patients on target for SBP and LDL-cholesterol as well as medication prescriptions after 1 year if compared to care delivered by GPs. Baseline SBP was 148.7 mm Hg, leaving a lot of room for improvement [21]. Another RCT, conducted in rural China, compared the delivery of a comprehensive intervention by family doctors (standardized medication, advice on both life style changes and medication adherence) with care as usual for hypertensive patients with or without diabetes. Increased prescribing rates of antihypertensive and lipid lowering medication were seen in the intervention group as well as significant reductions in smoking rates and salt intake but no differences in SBP and LDL-cholesterol after 1 year [22]. A recent meta-analysis by Stephen et al showed significant improvements in nurse-led hypertension management in primary care after 6 months [23]. Van Bussel and co-workers, assessing a nurse-delivered multicomponent cardiovascular prevention program in general practice for patients between 70 and 78 years without cardiovascular disease found no differences in cardiovascular risk profile after a mean follow up period of 6 years, although the intervention reduced SBP and the proportion of smokers in the first 2 years of the study [24]. Marchal et al assessed the effect of integrated CVRM care delivered by PNs compared to usual care offered by the GP in a randomized setting. They found no differences in SBP and LDL-cholesterol between the intervention and care as usual group after 1 year [25]. Yet, with mean baseline values for SBP and LDL-cholesterol of 136.7 mmHg and 2.8 mmol/l respectively, it seems difficult to improve within such a short period. It is known that implementation of a chronic care program and monitoring improvements is a lengthy process requiring regular adjustment [26]. With increasing awareness for CVRM and PNs participating in almost all general practices in The Netherlands, integrated CVRM care has become care as usual, thus reducing the contrast between study groups and partial explaining the lack of effectiveness in performed RCTs. This potential limitation could pave the way for long-term longitudinal cohort studies in the near future. Our study showed that in patients participating in integrated CVRM care between 2011 and 2018, we saw a substantial decrease in mean SBP, mean LDL-cholesterol and non-smoking participants, an increase in blood pressure lowering and lipid modifying prescriptions and an increase in patients on target for SBP and LDL-cholesterol. Finally, the proportion of non-smoking patients with SBP and LDL-cholesterol on target increased between 2011 and 2018 from 3.7% to 29.5% in patients eligible for primary prevention and from 6.5% to 36.5% in patients eligible for secondary prevention. Bager et al, described 8-year trends in blood pressure control, blood lipid control and smoking habits in hypertensive patients without CVD or diabetes, using a Swedish primary care register. They observed similar but smaller improvements in patients on target for systolic blood pressure and smok-

ing, but very little improvements in patients on target for LDL cholesterol, leading to only 10% of all patients with 3 risk factors in control [27]. It is very possible that participation in an integrated CVRM care program led by a PN in our study contributed to better outcomes. Taking into account that with every mmol LDL reduction a reduction of 25% in major adverse cardiovascular events (MACE) can be achieved, a 10 % reduction in MACE with every 5 mm Hg SBP reduction and a 32% reduction in MACE with smoking cessation [28,29,30], this implicates that for this large number of care group participants a considerable cardiovascular risk reduction is achieved. These findings indicate that with affiliation to a care group, adequate monitoring, subsequent treatment and long term follow up it is possible to realize clinical relevant improvements, resulting in a substantial risk reduction for CVD.

Implications for research

In The Netherlands, care groups represent more than 15 million registered patients, which is 88% of the population. In 2020, with aggregated data from 86 primary care groups on integrated CVRM care it is possible to compare registration and outcomes to further improve results [31].

Abbreviations PoZoB: Praktijkondersteuning Zuidoost Brabant; SGE: Stichting Gezondheidscentra Eindhoven; DOH: De Ondernemende Huisarts; CVRM: Cardiovascular risk management; GP: General Practitioner; CVD: Cardiovascular diseases; PN: Practice Nurse; EHR: Electronic Health Record; RCT: Randomized Controlled Trial

Ethical considerations All methods including the care groups protocol for data extraction, identification, examination and follow up were based on the 2006 CVRM guidelines of the Dutch Society of General Practice and approved by the Julius Centre for Health Sciences and Primary Care, University Medical Centre Utrecht, The Netherlands. Informed consent was given by patients participating in the CVRM care program to use anonymized data for evaluation and scientific research. Due to legislation in The Netherlands, general practitioners are not allowed to register the ethnicity of their patients in the EHR.

Consent for publication Not applicable

Availability of data and materials Anonymized patient data derived from the multidisciplinary information system (Care2U) can be send by mail on request: g.smits@gmail.com

Competing interests The authors declare that they have no competing interests.

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5

Sex differences and trends in managing cardiovascular risk factors in primary care: a cohort study

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Abstract

Background

Most treatment targets in the Guidelines for cardiovascular risk management in The Netherlands make no distinction between women and men.

Aim

To explore sex differences in achieving treatment targets of cardiovascular risk factors in patients that participated in a nurse-led, integrated CVRM care program in primary care between 2013 and 2019.

Methods

For each year, we assessed outcomes of three biological risk factors (systolic blood pressure, low density lipoprotein-cholesterol and estimated glomerular filtration rate) and four lifestyle factors (smoking, physical activity, alcohol intake and body mass index). Points (1=on target; 0=not on target) were assigned, for each participant scores for biological risk factors, lifestyle factors and an overall score were constructed. Using the annual results, we applied, multivariable regression models to study trends (per year) over time and differences in trends between women and men.

Results

From 2013 to 2019 the number of participants increased from 24,889 to 38,067, mean age increased from 67.3 to 71.5 years, with around 52% women each year. The mean number of the seven modifiable risk factors on target increased significantly from 4.6 to 4.9 in women, and from 4.7 to 5.0 in men, with no statistical difference between women and men. The existing differences between women and men in 2013 in the number of lifestyle factors on target or the number of biological risk factors on target did not materially change over time.

Conclusion

Integrated cardiovascular management care leads to improvements in cardiovascular risk factors on target, equally well in women than in men. The differences in being on target between women and men that existed in 2013 were still present in 2019.

Key words

primary health care, cardiovascular risk management, sex differences, prevention, long-term trends

How this fits in

Guidelines for cardiovascular risk management make no distinction in treatment

targets between women and men, except for responsible alcohol intake. Between 2013 and 2019, improvements in being on target for seven modifiable risk factors was similar for women as for men who participated in a nurse-led, integrated cardiovascular risk management program. The existing difference between women and men in 2013 on target for biological risk factors (systolic blood pressure, low density lipoprotein-cholesterol, estimated glomerular filtration rate) did not change over time, whereas the difference for being on target regarding lifestyle risk factors (alcohol, non-smoking, healthy exercise, body mass index) showed a more favorable trend.

Introduction

Cardiovascular disease (CVD), in particular ischemic heart disease (IHD) and stroke, is a leading cause of morbidity and mortality worldwide with a large societal impact in terms of life years lost and reduced quality of life [1]. Treatment of underlying, modifiable risk factors such as unhealthy diet, insufficient physical inactivity, tobacco use, being overweight, obesity, harmful use of alcohol, raised blood pressure, raised blood glucose, unfavorable blood lipids, and impaired renal function can reduce the risk of myocardial infarction and stroke [2,3]. Large-scale treatment of these modifiable risk factors in individuals can help reduce the risk at population level.

In the Netherlands, nearly all residents are registered with a general practitioner (GP), who has a long-term relationship with their patients and is well aware of the medical history. The GP therefore is the key healthcare provider to initiate, coordinate, and provide long-term follow-up for CVD prevention [4]. Since 2010, GPs are increasingly organized within primary care groups that offer nurse-led, integrated cardiovascular risk management (CVRM), based on national and international guidelines, to patients eligible for participation in the CVRM care program. In 2022, around 85% of all Dutch GPs were affiliated to a primary care group offering nurse-led, integrated CVRM care to 1.2 million patients, around 400,000 with and 800,000 without an established CVD. The CVRM care program is carried out by a practice nurse (PN) supervised by the GP. The PN guides and supports eligible patients with adjustment of medication, adherence and lifestyle improvements. Although the CVRM guidelines do not distinguish between women and men regarding risk factor management and treatment targets, several cross-sectional studies pointed towards differences in assessment of risk factor information [5] and achieving treatment targets between women and men [6–9].

Long term longitudinal studies on this topic are lacking, despite that increased awareness on sex differences in long term CVRM care may further improve cardio-

vascular health in the population.

We set out to explore trends in being on target for three biological risk factors (systolic blood pressure (SBP), low density lipoprotein (LDL)-cholesterol and estimated glomerular filtration ratio (eGFR)) and four lifestyle factors (smoking status, daily degree of (self-reported) exercise, overweight and (self-reported) daily alcohol intake) in women and men with and without an established CVD receiving nurse-led, integrated CVRM in Dutch primary care between 2013 and 2019.

Methods

Setting

The study was performed in the region Eindhoven, southeast of The Netherlands. The PoZoB primary care group comprised 137 affiliated general practices in 2013 with 415,000 registered patients, covering rural, suburban and urban practices and can be considered as representative for the situation in The Netherlands. Identification of patients eligible for the CVRM care program occurred stepwise between 2010 and 2013 and was described in detail previously [10,11].

Study population

Patients eligible for the integrated CVRM care program visited the PN 1-4 times a year. Conditions for eligibility were based on the 2012 CVRM Guidelines of the National College of General Practitioners [12]. These conditions were similar for all new patients that entered the CVRM care program until 2019. The in- and exclusion criteria for the eligibility of integrated CVRM care are described in Box 1. A distinction was made between patients with an without an established CVD. At least once a year a history was taken by the PN regarding medication adherence and lifestyle adjustments, followed by a protocolized physical examination to assess blood pressure, pulse frequency, height and weight to calculate body mass index (BMI). Furthermore, blood and urine tests were taken for measurement of fasting glucose, serum lipids, renal function (expressed as eGFR and albuminuria). Data was collected in the care group multidisciplinary information system (Care2U), a separate database for the chronic care programs. Data in Care2U were automatically transferred to the patient's electronic health record (EHR).

Box 1. **Inclusion/exclusion criteria for participation in the CVRM care program**

Inclusion criteria for very high risk patients:

- Patients with a documented atherosclerotic CVD, including angina pectoris, myocardial infarction, chronic ischemic heart disease, coronary sclerosis, transient ischemic attack (TIA), cerebral infarction, intermittent claudication or aneurysm of the abdominal aorta and
- The patient is primarily managed by the general practitioner (GP) and
- Aged 18 years or older

Inclusion criteria for high risk patients:

- No previous CVD and
- Use of antihypertensive or lipid lowering drugs or
- A 10-year CVD morbidity and mortality risk > 10%, based on the Dutch guideline for CVRM (4) or
- A SBP > 180 mm Hg and/or a TC/Hdl-ratio > 8, regardless of the 10-year CVD risk and
- The patient is primarily managed by the GP and
- Aged 18 years or older

Exclusion criteria for all patients:

- Diabetes Mellitus (DM), as these patients receive CVRM in a DM program
- Patient receives CVRM care in the hospital or outpatient clinic from a medical specialist

Risk factor targets

Risk factor targets were derived from the National Guideline for CVRM 2012 [4]:

- biological risk factors: SBP ≤ 140 mm Hg, LDL-cholesterol ≤ 2,5 mmol/l, eGFR ≥ 60 ml/min/1,73m²,
- lifestyle related risk factors: body mass index (BMI) ≤ 25 kg/m², sufficient physical exercise (according to the Dutch norm for healthy exercise: 5 days a week at least 30 minutes moderate exercise/day), non-smoking, and the number of alcoholic units per day (≤ 1 for women, ≤ 2 for men). Points were assigned for risk factor control, where a risk factor on target was 1 point, not on target was 0 points. Thus, three and four points for biological and lifestyle risk factors respectively, could make up to a total score of seven points.

Statistical analyses

First, the dataset comprised seven cross-sectional datasets (2013-2019). Each year was restricted to those individuals that had information on all seven targets, and so the analyses are considered a complete case analysis. General characteristics of the studied population are presented as means and standard deviation (SD) for continuous variables and as percentages for categorical variables for each year. Second, annual mean number of the risk factors on target are presented graphically by year

with corresponding 99% confidence limits, for women and men, and in strata of previous cardiovascular history. Next, multivariable linear regression models were applied to obtain the slope (change per year) in the number of factors lifestyle on target, risk factors on target and all 7 modifiable factors on target. Slopes were presented with 99% confidence intervals. Results were presented for women and men separately, and additionally in strata of individuals with and without a previous cardiovascular history. Finally, annual sex specific graphs are presented in a supplement to show the percentage of for each risk factor being on target in the population. Statistical analyses were performed with SPSS statistical software version 27.

Results

General characteristics as annual cross-sectional datasets of the eligible population for the period 2013 up to 2019 are presented in table 1 (women) and in table 2 (men). In women, we saw an increase of patients on target for LDL-cholesterol (2013: 28%, 2019: 49%), SBP (2013: 66%, 2019: 70%) and eGFR (2013: 79%, 2019: 84%), BMI (2013: 34%, 2019: 35%), responsible alcohol consumption (2013: 87%, 2019: 89%), and non-smoking (2013: 87%, 2019: 88%) and a decrease in sufficient physical activity (2013: 80%, 2019: 75%).

In men we saw an increase of patients on target for LDL-cholesterol (2013: 36%, 2019: 58%), SBP (2013: 67%, 2019: 72%), eGFR (2013: 87%, 2019: 88%), BMI (2013: 26%, 2019: 28%), responsible alcohol consumption (2013: 87%, 2019: 90%), non-smoking (2013: 83%, 2019: 87%) and a decrease in sufficient physical activity (2013: 83%, 2019: 80%).

Table 1. **General characteristics of the studied PoZoB population for WOMEN (n= 118,409), presented by calender year**

Year	2013	2014	2015	2016	2017	2018	2019
Number of women	13,269	15,234	17,126	17,215	17,457	18,688	19,420
Age in years (mean, SD)	69.4 (10)	69.9 (10)	70.3 (10)	70.5 (10)	70.8 (10)	71.2 (10)	71.5 (10)
% Enrolled for secondary prevention	30	32	33	35	38	38	39
% LDL ≤ 2.5 mmol/l	28.1	34.1	42.9	42.2	44.3	57.2	48.7
% SBP ≤ 140 mmHg	66.2	66.6	67.5	68.8	69.7	70.0	70.2
% eGFR ≥ 60 mL/min/1.73 m²	79.4	83.7	87.1	84.1	82.9	83.7	84.1
% BMI ≤ 25 kg/m²	33.8	33.8	34.3	34.3	34.1	34.3	34.7
% currently non smoking	86.5	86.7	86.9	86.8	87.3	87.5	87.9
% sufficiently physical active	80.2	76.9	75.9	75.0	75.2	75.1	75.0
% on guideline based alcohol consumption	86.8	86.8	87.1	87.7	87.8	88.1	88.7
% on blood pressure lowering medication	65.3	63.3	64.7	63.6	68.7	70.4	74.5
% on lipid modifying medication	42.1	43.3	47.4	47.9	53.0	53.1	55.2
number of lifestyle factors on target (max 4) (mean, SD)	2.9 (0.2)	2.8 (0.2)	2.8 (0.2)	2.8 (0.2)	2.8 (0.2)	2.9 (0.2)	2.9 (0.2)
number of biological risk factors on target (max 3) (mean, SD)	1.7 (0.3)	1.8 (0.3)	2.0 (0.3)	2.0 (0.3)	2.0 (0.3)	2.0 (0.3)	2.0 (0.3)
number of all modifiable factors on target (max 7) (mean, SD)	4.6 (0.7)	4.7 (0.7)	4.8 (0.7)	4.8 (0.7)	4.8 (0.7)	5.0 (0.7)	4.9 (0.7)

Table 2. **General characteristics of the studied PoZoB population for MEN (n= 107,879), presented by calender year**

Year	2013	2014	2015	2016	2017	2018	2019
Number of women	11,620	13,342	15,175	15,423	16,123	17,549	18,647
Age in years (mean, SD)	67.0 (9.5)	67.6 (9.7)	67.9 (9.8)	68.3 (9.9)	68.6 (10)	69.1 (10)	69.4 (10)
% Enrolled for secondary prevention	40	41	43	45	48	50	50
% LDL ≤ 2.5 mmol/l	35.9	41.6	49.5	49.3	52.9	66.1	57.7
% SBP ≤ 140 mmHg	67.2	68.5	68.8	70.3	71.9	72.5	71.7
% eGFR ≥ 60 mL/min/1.73 m²	87.2	89.5	91.5	88.5	87.5	88.3	88.3
% BMI ≤ 25 kg/m²	26.2	26.5	26.6	26.8	26.9	27.4	27.5
% currently non smoking	83.3	84.3	85.0	85.3	86.0	86.5	87.2
% sufficiently physical active	83.2	80.4	79.6	78.9	78.9	79.4	79.6
% on guideline based alcohol consumption	87.1	87.4	87.7	88.2	88.9	89.3	90.1
% on blood pressure lowering medication	62.6	60.9	62.8	62.2	67.8	69.0	73.2
% on lipid modifying medication	48.0	48.7	53.0	54.8	61.2	61.1	63.9
number of lifestyle factors on target (max 4) (mean, SD)	2.8 (0.8)	2.8 (0.8)	2.8 (0.8)	2.8 (0.8)	2.8 (0.8)	2.8 (0.8)	2.8 (0.8)
number of biological risk factors on target (max 3) (mean, SD)	1.9 (0.8)	2.0 (0.7)	2.1 (0.7)	2.1 (0.8)	2.1 (0.8)	2.3 (0.7)	2.2 (0.8)
number of all modifiable factors on target (max 7) (mean, SD)	4.7 (1.1)	4.8 (1.1)	4.9 (1.1)	4.9 (1.1)	4.9 (1.1)	5.1 (1.1)	5.0 (1.1)

If we look at the changes over time (table 3) in the total population, we see that the number of seven modifiable factors being on target increased with 0.054 per year [99% CI 0.050-0.058] in women and with 0.055 per year [99% CI 0.051-0.060] in men. Similar relations were found for the number of biological risk factors on target. Only for lifestyle factors, improvement was more pronounced in men than in women, without reaching statistical significance. In individuals with and without an established CVD, we see similar results in terms of direction and magnitude.

Table 3. **The relation between calendar year and number of modifiable risk factors on target, for men and women overall and in patients with and without an established CVD. ****

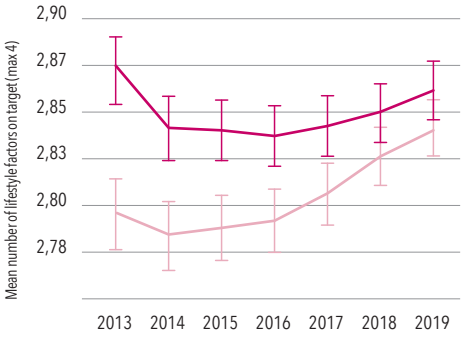
	Men		Women	
	Estimated slope (per year)*	99% Confidence limit	Estimated slope (per year)*	99% Confidence limit
Lifestyle score	0.006	0.003; 0.009	0.0	030; -0.030
Biological risk factor score	0.049	0.046; 0.052	0.054	0.051; 0.057
All 7 factor score	0.055	0.051; 0.060	0.054	0.050; 0.058
Patients with an established CVD				
Lifestyle score	0.006	0.001; 0.011	0.020	-0.040; 0.070
Biological risk factor score	0.044	0.040; 0.049	0.045	0.040; 0.050
All 7 factor score	0.050	0.044; 0.057	0.047	0.039; 0.054
Patients without an established CVD				
Lifestyle score	0.006	0.002; 0.010	-0.010	-0.040; 0.030
Biological risk factor score	0.054	0.050; 0.058	0.059	0.056; 0.063
All 7 factor score	0.060	0.054; 0.066	0.059	0.054; 0.064

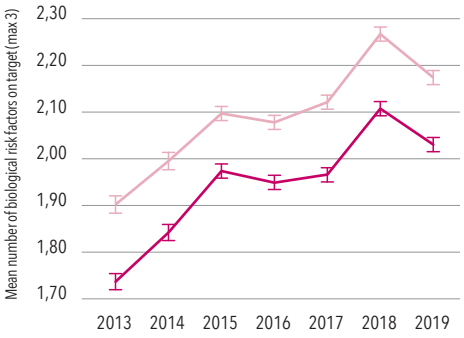
* Estimates reflect the change in the outcome (number of factors on target) per calendar year increase. The relation was assessed using multivariable linear regression models adjusted for age and CVD history, when appropriate. We provide 99% confidence limits (corresponding to a p value of 0.01). So when the 0 is not in the confidence limits, the statistical significance p value < 0.01.

** when the 99% confidence intervals of the estimated slopes of those for women with those for men do not overlap, is an conservative approach to indicate statistical significance with a p value < 0.01.

In figures 1-3, the mean number on target for lifestyle riskfactors, biological riskfactors and the total number of riskfactors are given for the entire population, for the population without an established CVD and for the population with an established CVD, respectively.

Figure 1. **Mean number of factors on target with 99% confidence limits between women and men over time for** the entire population **(unadjusted results). From top to bottom: lifestyle risk factors (n=4), biological risk factors (n=3) , all factors (n=7).**
The ▬ line reflects women, the ▬ line men.





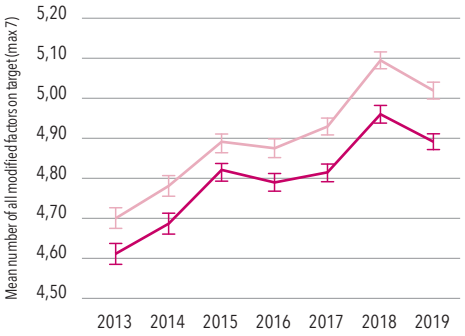


Figure 2. **Mean number of factors on target with 99% confidence limits between women and men over time for the population** without an established cardiovascular disease **(unadjusted results). From top to bottom: lifestyle risk factors (n=4), biological risk factors (n=3) , all factors (n=7). The ▬ line reflects women, the ▬ line men.**

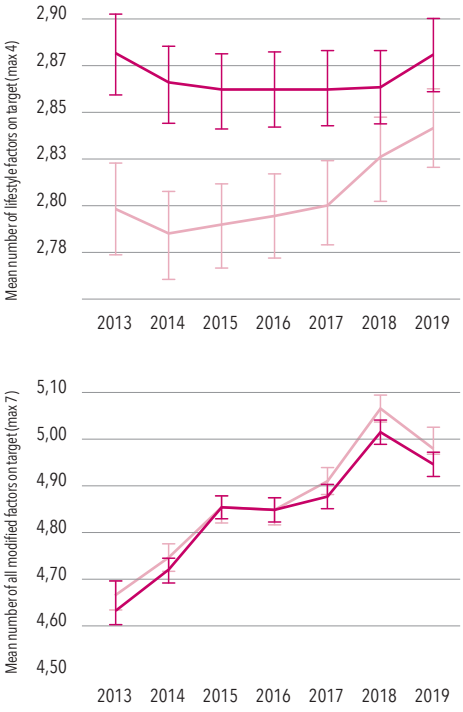
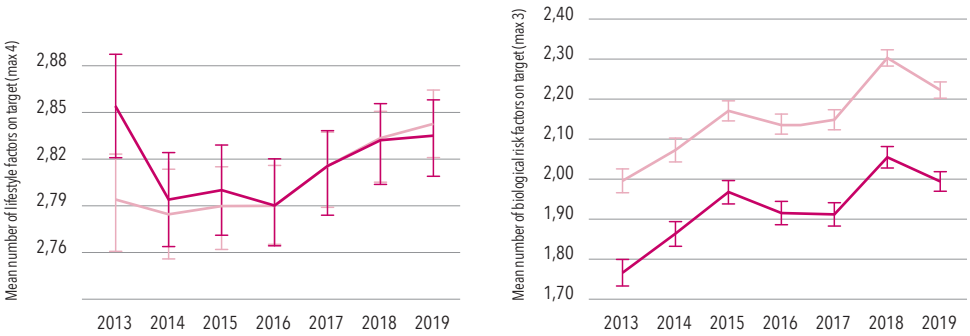
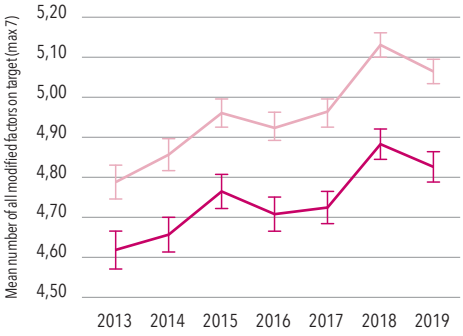


Figure 3. **Mean number of factors on target with 99% confidence limits between women and men over time for the population** with an established cardiovascular disease **(unadjusted results). From top to bottom: lifestyle risk factors (n=4), biological risk factors (n=3), all factors (n=7). The ▬ line reflects women, the ▬ line men.**





In the supplementary files information on sex differences and trends by year in percentage of the population on target is presented for each of the risk factors separately (S1-S7) and for the percentage of patients on BPL and LM medication (S8 and S9). Regarding individual risk factors, the mean levels of achieved targets and trends over time did not differ between women and men for BMI, LDL-cholesterol, SBP and eGFR. However, for the risk factor "non-smoking", the gap between women and in men became smaller, because the improvements observed were stronger in men than in women. The gap widened for the risk factors "physical activity" and "responsible alcohol consumption", because of slightly stronger improvements in men (S1-S7). Furthermore, the gap between women and men on BPL medication slightly seems to narrow (S8), but the gap between women and men on LM medication is growing (S9).

Discussion

Summary

In this study we evaluated sex differences and trends in the management of cardiovascular risk factors of patients that participated in a nurse-led, integrated CVRM care program between 2013 and 2019. Women with an established CVD did worse than men in both biological and lifestyle risk factors, women without an established CVD did worse than men in biological, but better in lifestyle risk factors. In most risk factors, differences between men and women were small except for BMI. Sex differences observed at the start of the study remained present until 2019, with hardly any changes in the magnitude of the differences.

Comparison with existing literature

To our knowledge, The Netherlands is the only country that offers wide-spread, continuous, long-term, nurse-led integrated CVRM care to high risk patients

with and without an established CVD. Health survey data from the UK and the US on cardiovascular risk factors show decreasing trends in patients with hypertension, hypercholesterolemia and smoking, with women better than men in control for hypertension and non-smoking, but worse than men for hypercholesterolemia [13,14]. Both studies showed a decrease of patients with their BMI on target, affecting more women than men, while in our study the BMI remained unchanged overtime with women more often on target for BMI than men. In our study, we found that women were more likely to be non-smokers, but the gap between women and men was narrowing. It is known that women have more problems achieving long-term tobacco abstinence, however reasons for this are unclear [15]. Regarding physical activity we found conflicting results. The decrease in sufficient physical activity in our study was confirmed in a study of Kotseva et al who saw no increase in physical activity in coronary patients between 1999 and 2013 [16], while a minimal increase in the prevalence rate of physical activity between 2007 and 2018 was observed in the US [17].

Although in our study improvements were seen for both sexes between 2013 and 2019 in six out of seven risk factors, management in 2019 was still suboptimal with 49%, 70% and 84% of the women on target for LDL-cholesterol, SBP and eGFR, respectively and 56%, 72% and 88% of the men on target, respectively. Control of SBP was a little lower in women compared to men (70% vs 72%), although women were slightly more often prescribed BPL medication than men (75% vs 73%). LM medication was more often prescribed to men (2013: 42% vs 48%) over time and the gap seems to have only increased in subsequent years (2019: 55% vs 64%). Sex differences in prescribing LM medication may be explained by the fact that women were 2 years older than men (2013: 69.4 y vs 67.0 y in 2013 and 71.5 y vs 69.4 y in 2019), which might have translated in more comorbidity, more comedication and more reluctance to increase LM medication, both by the patient as well as the PN or the GP [18]. Furthermore, it is known that women are more worried of safety and side effects of statins and are more willing to try natural remedies such as diet and exercise to lower their LDL-cholesterol [10,20]. Many studies on sex differences in primary care with a cross-sectional design reported that women less likely had their LDL-cholesterol on target [5,21–24] and more likely had their SBP on target [5,22–24].

Strengths and limitations

A major strength is that we able to visualize a long-term trend in reaching CVRM targets in a large cohort of patients that participate in an integrated CVRM care program. Second, eligibility for the nurse-led CVRM care program was based on criteria from the national CVRM guideline [12] which increases the external validity (i.e., generalizability). Third, with three biological and four lifestyle risk factors it was possible to present a fairly complete picture of CVRM in high-risk patients with

and without a previous CVD. Fourth, the percentage of missing data for the seven risk factors was only 10% annually, due to data collection by trained PNs in the care group's multidisciplinary information system (Care2U). There is also a number of limitations. First, we have no information on care givers and patients' arguments for not starting or increasing medication or lifestyle adjustments. Second, some lifestyle risk factors (alcohol intake, physical activity) were self-reported and differences on reporting of these risk factors may exist. Third, we did not have data on dietary habits, another important lifestyle risk factor.

Implications for research and practice

To reduce sex differences in biological risk factor control, primary health care givers need to explore reasons for not prescribing or increasing medication, especially in women. An individual care plan, in which the lifestyle adjustments chosen by the patient are registered, may contribute to improved exercise, changing dietary habits and weight loss.

Conclusion
Pharmacological treatment and control in women should receive more attention to improve outcomes of biological risk factors.

Notes

Ethical approval The pseudonymized data used were only accessible in the secured research environment of the PoZoB primary care group. No formal assessment by the medical ethics committee of the Utrecht University Medical Centre was necessary because of the retrospective nature of research using non-traceable information.

Data availability Data for this article were provided by the PoZoB primary care group and JGPN. Data will be shared on request to the corresponding author with permission of the care groups' board and with permission of the JGPNs board.

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Competing interests The authors have declared no competing interests.

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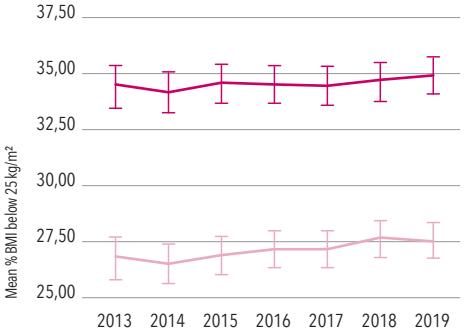
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Figure S1. **Patients with BMI ≤ 25 kg/m² (%) over time, by sex**



BMI: body mass index

Figure S2. **Non-smoking patients (%) over time, by sex**

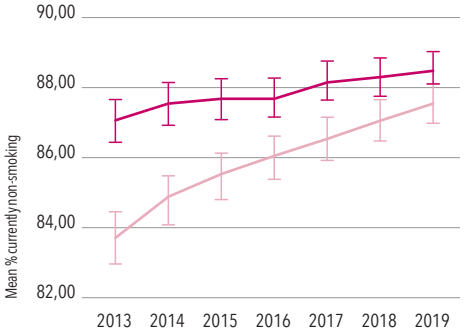


Figure S3. **Patients on sufficient daily Physical Activity (%) over time, by sex**

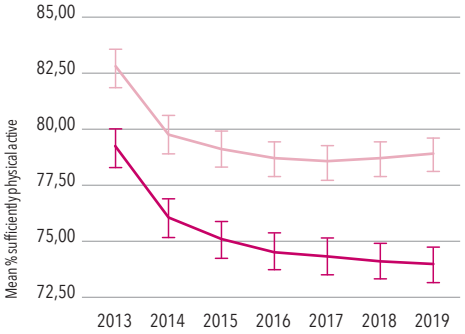


Figure S4. **Patients on responsible daily alcohol intake (%) over time, by sex**

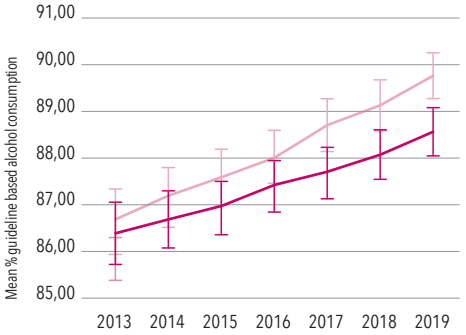
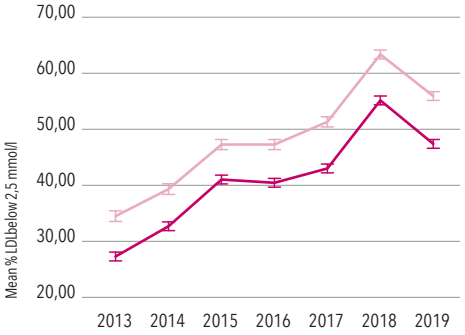
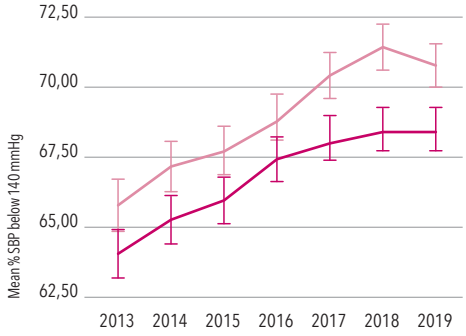


Figure S5. **Patients with LDL-cholesterol ≤ 2.5 mmol/l (%) over time, by sex**



LDL-cholesterol: low density lipoprotein cholesterol

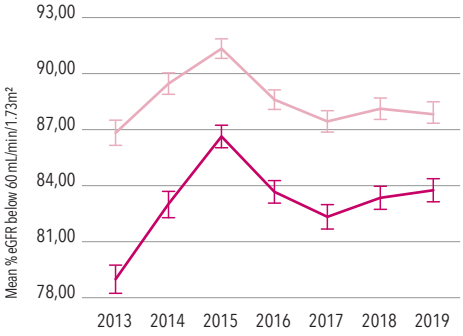
Figure S6. **Patients with SBP ≤ 140 mm Hg (%) over time, by sex**



SBP: systolic blood pressure

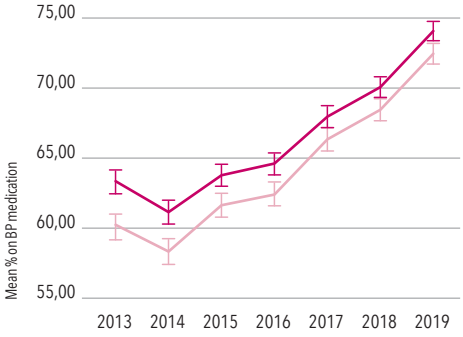
The ▬ line reflects women, the ▬ line men.

Figure S7. **Patients with eGFR ≥ 60ml/min/1.73m² (%) over time, by sex**



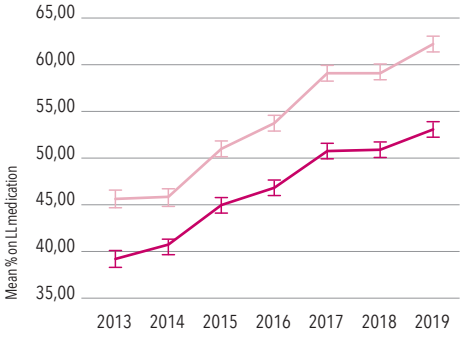
eGFR: estimated glomerular filtration ratio

Figure S8. **Patients taking BPL medication (%) over time, by sex.**



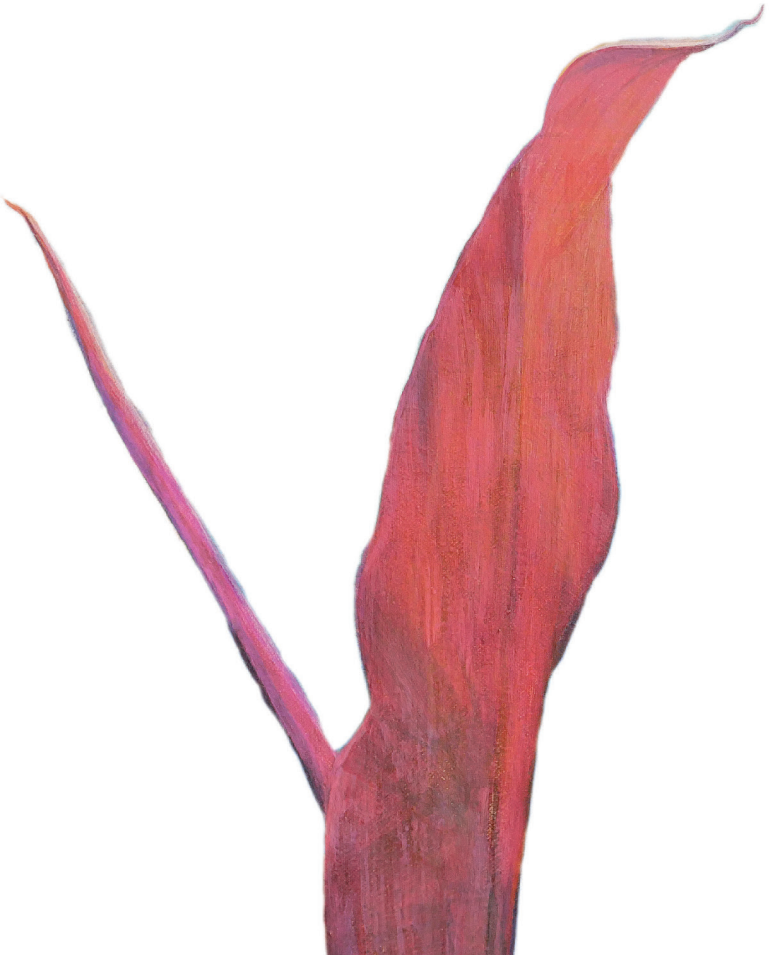
BPL medication: Blood pressure lowering medication

Figure S9. **Patients taking LM medication (%) over time, by sex.**



LM medication: Lipid modifying medication

The ▬ line reflects women, the ▬ line men.



6

Practice visitations in primary care to improve performance of cardiovascular risk management

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Abstract

Background

Despite programmatic protocolized care and structured support, considerable variation is observed in completeness of registration and achieving targets of cardiovascular risk management between individual general practitioners in The Netherlands.

Aim

To determine whether completeness of registration and achieved targets of cardiovascular risk factors improves with practice visitation.

Design and setting

Observational study utilizing the care group database (2016-2019) comparing changes in registration and achieved targets in non-visited practices and visited practices.

Methods

We compared completeness scores of registration and scores of targets achieved before visitation and 1 year after visitation. Data were analyzed on patient level and on general practitioners level. Separate analyses were performed among general practitioners who were ranked in the lower 25% of score distributions.

Results

We observed no clinically relevant improvements in completeness of registration and targets achieved in 2017, 2018 and 2019 that could be attributed to visitations in the previous year, both on individual patient level as on aggregated level per general practice.

In practices ranked in the lower 25% of the distribution, improvements over time were clinically relevant and larger than the overall changes. Yet, these findings were irrespective of the number of practice visitations.

Conclusion

Practice visitations in our setting did not seem to lead to improvements in practice performance, nor in completeness of registration of risk factors or in reaching predefined target goals for cardiovascular risk factors.

Keywords

practice visitations, cardiovascular risk management, primary care, prevention

How this fits in

Although comprehensive care group support was identical for all affiliated general practices from the start with integrated CVRM care in 2010, considerable variation in performance between practices regarding completeness of registration and reaching predefined targets was observed after a few years. To reduce inter practice variation the care group started with individual practice visitations in 2016 to support practices with the organization of integrated CVRM care. Low and moderate performing practices were visited 2 or 3 times a year, while average and good performing practices were not visited or were visited once a year. Completeness of registration and reaching targets did not seem to improve, regardless the number of visitations.

Introduction

Since the introduction of national and international guidelines cardiovascular risk management (CVRM) is increasingly organized and implemented by primary care groups in The Netherlands [1,2]. Primary care groups are responsible for the provision of a high-quality, evidence-based CVRM care program for affiliated practices. The implementation of the CVRM care program was delegated to a practice nurse (PN) supervised by the general practitioner (GP). The PN guided eligible patients with medication adjustments and supported with stop-smoking, changing unhealthy food habits and increasing exercise. The care group supported practices with protocols, small group interactive education, audit and feedback (A&F), outreach visits and reminders, as it is known that a comprehensive approach is most beneficial to improve implementation [3]. A&F is a widely used component in clinical programs, but it's effect is shown to be modest [4–8]. To what extend A&F is of value to programmatic CVRM is not yet known. Therefore, the aim of the present study was to investigate whether A&F delivered during practice visitations lead to improvements in completeness of registration and reaching predefined targets among participating practices in the CVRM care program between 2016 and 2019.

Methods

Study design and study population

We carried out a dynamic cohort study using data that were routinely collected from 128 practices affiliated to the PoZoB primary care group in 2016. The care group implemented a nurse-led, integrated CVRM care program between 2010 and 2013. The practices were located in and around Eindhoven, in the southeast of The Nether-

lands. They were a mixture of rural, semi-rural and urban practices and can be considered representative for the Dutch situation.

Data collection

In 2016 data was collected from 48,258 patients eligible for integrated CVRM care. Conditions for eligibility for the CVRM care program were based on the National CVRM guideline 2012 and have been described in detail elsewhere [9,10]. Patient data was collected in the care group's multidisciplinary registration system (Care2U). For the present analyses we excluded practices that changed hands between 2016 and 2019, because starting GPs often have other priorities than organizing disease management programs. We therefore used data from 128 practices (40,525 eligible patients) where the same GP was employed between 2016 and 2019.

Care group support and benchmark indicators

Between 2010 and 2015 the care group supported with work protocols, peer group meetings for the PN and education for GPs and PNs on cardiovascular related topics. From 2016 onwards, the care group started publishing quarterly benchmark reports in which individual practices could compare their performance with overall care group performance. Indicators used for defining performance were i) registration of: systolic blood pressure (SBP), LDL-cholesterol, estimated glomerular filtration rate (eGFR), body mass index (BMI), range of exercise (based on the Dutch norm for healthy physical exercise), alcohol intake and smoking status and ii) outcomes: the proportion of patients on target for SBP (≤ 140 mm Hg), LDL-cholesterol (≤ 2.5 mmol/l), BMI (≤ 25 kg/m^2), the proportion of non-smokers, the proportion on blood pressure lowering treatment and the proportion on lipid modifying treatment. For every indicator the care group mean and standard deviation was calculated which was used as benchmark for individual practices. Mean plus 1 standard deviation was defined as "best practice" and mean minus 2 standard deviations as "minimal norm". Standards were discussed in staff meetings and confirmed in the care group Advisory Board of General Practitioners. With these standards set, every individual practice was given an impression about their performance with the overall care group as comparator.

Practice visitations

In 2016 the care group started with practice visitations to discuss performance based on the benchmark data and offer support to improve the organization of CVRM. Important goals of the visitations were building a relationship of trust and emphasize the partnership between practice and care group. In case of low performance, the care group supported with the analysis of possible causes, made prac-

tices primarily responsible and co-owner of the solution and provided temporary guidance. Visitations were performed by a university trained staff member with an additional education in management and organization. Practices having difficulties with organizing and implementing the CVRM care program (discontinuity of staff, insufficient hours for the PN, no regular consultations between GP and PN) and practices with a number of indicators below the minimal norm were initially prioritized for visitation. Practices could also request a visitation. The visitations usually lasted 1-1.5 hours and in almost all cases were carried out by one staff member. In exceptional cases the visit was carried out by 2 persons if a specific problem needed to be explained. Practice members attending the visits were the GP, the PN and in some cases the manager of a health center. Based on a standard 8 item questionnaire shown in Box 1, practice organization and performance was discussed with the GP and the PN. An example of items discussed during a practice visitation is given in Supplementary Box 1.

Box 1. **Items discussed with the practice during visitation**

- Is the practice using a result-orientated approach (focus on how to interpret information from the quarterly reports and improving to at least the minimum standard?
- Is the practice applying or, if necessary, deviating from guidelines?
- Is there regular and structured consultation between GP and PN and is there agreement on the follow up policy so the PN feels supported by the GP?
- Is there adequate mail processing and registration in the multidisciplinary information system?
- Does the PN have sufficient hours in relation to the workload?
- Is there discontinuity due to illness of the GP or the PN?
- Are there major differences in practice population?
- Are there linking problems with a laboratory, electronic registration system or multidisciplinary registration system?

Data analyses

We started with the registration of SBP, LDL-cholesterol, eGFR, BMI, alcohol intake, (self-reported) range of exercise and smoking status in 2016 on an individual patient level. An item registered = 1, not registered = 0, adding up to an individual patient score between 0 and 7. This was followed by the same procedure for reaching the predefined targets: SBP ≤ 140 mm Hg, LDL-cholesterol ≤ 2.5 mmol/l, BMI ≤ 25 kg/m², not smoking, use of blood pressure lowering medication and the use of lipid modifying medication, adding up to an individual patient score between 0 and 6. Next, the mean number of scored items per individual patient in practices with no visit (V0), with one visit (V1) and with more than one visit (V2/3) in 2016 were compared with the scores observed in those patients in 2017 (the next year). As the

study was designed as a dynamic cohort study, patients may leave the study and new eligible patients may enter the study. We compared only those patients that were in the study for both time periods. A similar procedure was applied for the 2017-2018 and 2018-2019 comparisons. Descriptive analyses were run and presented for overall and in strata of visitation frequency (mean with standard deviations), crude difference in completeness and reaching targets (mean and standard error). In order to evaluate whether the observed differences were confounded, multivariable linear regression models were run in which age, sex, care program (eligible for secondary prevention or eligible for primary prevention) and general practitioner were taken into account as potential confounders. As sensitivity analyses we repeated the analyses with aggregated scores on general practitioner level, where now visitations involved the practice rather than individual patients.

Patient involvement

Since the study was aiming at data derived from the multidisciplinary information system for integrated care, patients were not actively involved.

Ethical considerations

Data used for the analysis were pseudonymised when extracted from the multidisciplinary information system. Before uploading to the secure network the data was encrypted, implicating that individual patient data were not identifiable during analyses.

Results

The number of patients potentially reached through these visits is presented in table 1. General cardiovascular characteristics of the population is presented in table 2.

Table 1. **Characteristics of the study population: practices, visitation, and number of patients potentially reached by the visitations**

Outcome		2016	2017	2018
Practices participating in the study		128	128	128
Number of visitations per practice:				
	No visitation	38	37	27
	1 visitation	87	71	79
	2 visitations	3	16	20
	3 visitations	0	4	2
Patients potentially affected through the visitation (N):				
	No visitation	11,492	11,814	8,543
	One visitation	26,678	20,999	23,508
	Two or more visitations	1,277	5,642	7,083
Total patients involved		39,447	38,275	39,134

Table 2. **Mean characteristics of the studied population, by year**

	2016		2017		2018	
	(N=39,447)		(N=38,275)		(N=39,134)	
Age (Mean, SD)	69	10	69	10	70	11
Women (%)	52		52		52	
High risk patients without CVD (%)	59		56		55	
Smoking (%)	13		12		12	
Sufficient PA (%)	76		76		76	
BPL-medication (%)	63		66		68	
LM-medication (%)	49		55		54	
eGFR ≥ 60 ml/min/1.73m² (%)	79.8		78.6		79.7	
	Mean	SD	Mean	SD	Mean	SD
Alc (drinks/day)	0.84	1.2	0.82	1.1	0.83	1.1
BMI (kg/m²)	27.3	4.3	27.4	4.6	27.3	4.5
SBP (mmHg)	136	15.7	136	15.5	135	15.5
LDL (mmol/l)	2.8	0.91	2.7	0.89	2.4	0.82

N: number of participants with the characteristic; PA: Physical Activity, based on the Dutch norm for healthy movement; BPL: blood pressure lowering medication; LM: Lipid modifying medication; eGFR: estimated Glomerular Filtration Rate

Alc: Alcohol; SBP: Systolic Blood Pressure; LDL: Low Density Lipoprotein cholesterol; BMI: Body Mass Index

Completeness of registration

The mean score on completeness of registration using the individual patient data was 6.28 (standard deviation 1.35) in 2016, 6.15 (1.65) in 2017 and 6.37 (1.33) in 2018 (table 3). Results using individual patient data showed no clinically relevant improvements in completeness of registration overall. There is a tendency that improvements are larger in practices with 2 or more visitations as compared to those with no or 1 visitation. Yet, the improvement in total score remains small in magnitude, despite reaching statistical significance also when confounding factors were taken into account (table 3, last column). The mean scores using data aggregated on GP level were 6.00 (0.69) in 2016, 6.20 (0.83) in 2017 and 6.38 (0.26) in 2018 (supplementary table 1). Results using the data aggregated on GP level, followed the same pattern: no clinical relevant improvements overall and in practices with no visitations and 1 visitation and small improvements in practices with 2 or more visitations in 2016 and 2017. Visitations in 2018 did not change completeness of registration overall, nor across strata of visitation on GP level in 2019 and analysis did not show different results in either direction, magnitude or clinical relevance (Supplementary Table 1).

Table 3. **Completeness of registration of CVRM information using individual patient records**

	Mean completeness year 1	Mean completeness score (SD) year 2	Mean difference between score (SE) (year 2 - year 1)	Multivariable # difference (99% CI)
2016-2017				
Overall	6.28 (1.35)	6.28 (1.39)	0.003 (0.010)	NA
0 visitations	6.33 (1.32)	6.28 (1.37)	-0.045 (0.018)	ref value
1 visitation	6.27 (1.35)	6.28 (1.39)	0.009 (0.011)	0.077 [0.021; 0.133]
2 or more visitations	5.93 (1.55)	6.27 (1.41)	0.338 (0.058)	0.355 [0.208; 0.503]
2017-2018				
Overall	6.12 (1.71)	6.37 (1.33)	0.250 (0.011)	NA
0 visitations	6.20 (1.53)	6.41 (1.29)	0.202 (0.018)	ref value
1 visitation	6.30(1.34)	6.36 (1.34)	0.054 (0.013)	-0.089 [-0.14; -0.032]
2 or more visitations	5.21 (2.68)	6.31 (1.39)	1.104 (0.041)	-0.152 [-0.239; -0.065]
2018-2019				
Overall	6.37 (1.33)	6.34 (1.35)	-0.032 (0.009)	NA
0 visitations	6.38 (1.32)	6.26 (1.43)	-0.120 (0.020)	ref value
1 visitation	6.35 (1.35)	6.34 (1.35)	-0.012 (0.012)	0.106 [0.044; 0.167]
2 or more visitations	6.42 (1.27)	6.43 (1.25)	0.011 (0.021)	0.121 [0.041; 0.201]

adjusted for year specific age, sex, care program and general practitioner using a multivariable linear regression model with the difference in score as dependent variable.

SD= standard deviation; SE = standard error; CI= confidence interval

Reaching predefined targets

The mean score on reaching the targets using the individual patient data was 3.21 (SD 1.30) in 2016, 3.28 (1.37) in 2017 and 3.51 (1.28) in 2018 (table 4). Results based on individual patients showed no clinically relevant improvements in reaching targets overall nor in practices with no visitation and 1 visitation and small improvements in practices with 2 or more visitations in 2016 and 2017. Visitations in 2018 did not show improvements in reaching targets overall in 2019, nor in strata across visitation. Adjustment for potential confounding factors did not affect the findings (table 4, last column).

The mean score on reaching targets using data aggregated on GP level was 3.08 (0.57) in 2016, 3.36 (0.64) in 2017 and 3.56 (0.46) in 2018. Results using the data aggregated on GP level showed no clinically relevant improvements overall and in practices with no visitation and 1 visitation and small improvements in practices with 2 or more visitations in 2016 and 2017. Visitation in 2018 did not show improvements in reaching targets overall in 2019, nor across strata of visitation and analysis did not show different results in either direction, magnitude or clinical relevance (Supplementary Table 2).

Table 4. **Reaching predefined targets using individual patient records**

	Mean number on target (SD) year 1	Mean number con target (SD) (SD) year 2	Mean difference between score (SE)	Multivariable # difference (99% CI)
2016-2017				
Overall	3.21 (1.30)	3.36 (1.28)	0.144 (0.009)	NA
0 visitations	3.22 (1.31)	3.31 (1.28)	0.089 (0.017)	Ref value
1 visitation	3.22 (1.29)	3.37 (1.28)	0.147 (0.011)	0.067 [0.16; 0.12]
2 or more visitations	3.02 (1.34)	3.59 (1.23)	0.573 (0.050)	0.450 [0.32; 0.59]
2017-2018				
Overall	3.28 (1.37)	3.51 (1.27)	0.230 (0.010)	NA
0 visitations	3.32 (1.32)	3.53 (1.26)	0.215 (0.017)	Ref value
1 visitation	3.41 (1.25)	3.50 (1.28)	0.090 (0.012)	-0.091 [-0.144; -0.038]
2 or more visitations	2.72 (1.72)	3.53 (1.25)	0.805 (0.030)	0.017 [-0.063; 0.097]
2018-2019				
Overall	3.51 (1.28)	3.48 (1.26)	-0.0308 (-0.009)	NA
0 visitations	3.52 (1.29)	3.46 (1.26)	-0.0552 (0.012)	Ref value
1 visitation	3.52 (1.27)	3.48 (1.26)	-0.0416 (0.012)	0.060 [-0.052; 0.065]
2 or more visitations	3.46 (1.28)	3.50 (1.24)	0.0344 (0.022)	0.132 [0.056; 0.208]

adjusted for year specific age, sex, care program, and general practitioner using a multivariable linear regression model with the difference in score as dependent variable.

@ targets are assessed for only those that have at least one measurement that determine the target score.

Results among those GPs ranking lowest 25% of the distribution

From a clinical perspective, the approach tends to be that modest performing GPs are visited more than once a year. Our findings show that among these groups statistically significant improvements in completeness of registration and reaching the target occurs and its magnitude is more pronounced than that found in the whole population (Supplementary Table 3 for the 2017-2018 period). Yet, these improvements were equally visible, regardless the number of visitations. Although the magnitude of the change seemed more pronounced in the group visited twice or more, the differences between visitation groups were not statistically significant.

Discussion

Summary

In our observational study performed in primary care, we evaluated the value of practice visitations to integrated CVRM in primary care. We observed no improvement in practices that were visited 2 or more times compared to practices with no visitation or 1 visitation. However, in those practices performing according to the lowest 25% on registration and predefined targets, improvements were seen irrespective of the number of visitations. Ideally, one would like to investigate the possible association between improvement in registration and achieved outcomes and a reduction of cardiovascular events. Yet, the care program and the care group's multidisciplinary registration were not a priori developed and designed for complete registration of clinical event outcomes.

Strengths and limitations

This study has a number of strengths. First, the large number of participants leads to a high representativeness. Second, because data collection and visitations did not interfere with daily practice routine, this further adds to the generalisability. Third, we included only practices where the GP was employed during the study period, minimizing bias due to changes in practice organization and care giver. The study has a number of limitations. First, it was a non-randomized, observational study leading to a substantial risk of confounding bias in the estimates of the effect of visitation. Yet, we did adjust for expected confounding factors in our analysis. Second, technical problems or lack of time may have contributed to the fact that targets might not have been registered but were still achieved, leading to an underestimation of the effect. Third, we realize that, as a consequence of the care group's decision to use binary cut points, reductions in SBP for example, remain unnoticed if the cut-off is not met, leading to underestimation of improvements in some patients. Fourth, prescriptions of BPL and LM medication were used as performance

indicator, without knowing whether medication was indicated which could have led to some overestimation. Fifth, PoZoB supported affiliated practices for several years in various ways which have been described in detail, resulting in annual improvements of performance [9]. This might have contributed to the lack of effect on performance of additional practice visitations.

Comparison with the literature

The results of our study are in contrast with a systematic review in 2012 that concluded that A&F overall leads to positive but highly variable effects [5]. A&F showed positive effects in some studies on hypertension management and prescription rate [11–14], while in other studies on adherence to guidelines and decrease in first ever strokes it did not [15,16]. Comparison of these studies with our study is, however, difficult because of the heterogenous designs, interventions tested and the difference in primary outcome. There is a number of reasons that possibly contribute to the lack of results in our study. First, overall mean registration rate was already high in 2016 [17], making it difficult for practices to realize further improvements. Second, absenteeism due to illness of primary care staff and lack of replacement can ensure that regular follow up is lagging behind, resulting in poorer registration [18]. Third, due to privacy restrictions, it was not possible to take caregivers characteristics such as age, sex and number of years working as a GP into account. Finally, GPs and PNs may have clinical considerations for not reaching targets such as older age combined with side effects of medication, polypharmacy, the patient's reluctance to intensify therapy and near-target indicators [19].

Implications for future research and clinical practice

Research showed that feedback was more effective if performance was low, if given face to face by a colleague, on more than one occasion and with well-defined goals [6,20]. The current study showed that feedback given during annual visitations was not of additional value regarding improvements in clinical performance. Practice visitations however, could be used i) to explore whether the general practice is motivated to improve ii) to explore what a practice needs to improve and iii) to emphasize the non-punitive character of A&F in order to maintain a trustful relationship. Future research could focus on the reasons why GPs and PNs deviate from current guideline targets. Furthermore, individual patient targets registered as such in the care group's multidisciplinary registration system, should be taken into account when evaluating practice performance. Finally, given the fact that practice visitations are a time consuming and therefore costly operation, care groups may consider other possibilities to support health care providers, such as interventions aimed at improving patient self-management skills, taking the patients preferences into account and consider the patient as a partner as this patient-centred approach is

aiming less on performance but more on a better health related quality of life and more satisfied health care providers [21,22].

Conclusion

Practice visitations in our setting did not seem to lead to improvements in practice performance, nor in completeness of registration of risk factors or in reaching predefined target goals for cardiovascular risk factors.

Notes

Ethical approval The pseudonymized data used were only accessible in the secured research environment of the PoZoB primary care group. No formal assessment by the medical ethics committee of the Utrecht University Medical Centre was necessary because of the retrospective nature of research using non-traceable information.

Data availability Data for this article were provided by the PoZoB primary care group. Data will be shared on request to the corresponding author with the care groups' board permission.

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Table S1. **Completeness of registration using aggregated information per general practice**

	Mean completeness score (SD) year 1	Mean completeness score (SD) year 2	Mean difference between score (SE)
2016-2017			
Overall	6.00 (0.69)	6.20 (0.80)	0.20 (0.08)
0 visitations	6.03 (0.67)	6.22 (0.87)	0.18 (0.14)
1 visitation	6.00 (0.67)	6.18 (0.78)	0.18 (0.09)
2 or more visitations	5.40 (1.24)	6.30 (0.25)	0.89 (0.62)
2017-2018			
Overall	6.20 (0.83)	6.37 (0.28)	0.18 (0.07)
0 visitations	6.30 (0.35)	6.44 (0.52)	0.14 (0.06)
1 visitation	6.33 (0.31)	6.33 (0.27)	0.001 (0.05)
2 or more visitations	5.64 (1.76)	6.39 (0.33)	0.75 (0.33)
2018-2019			
Overall	6.38 (0.26)	6.36 (0.28)	-0.02 (0.03)
0 visitations	6.39 (0.23)	6.34 (0.35)	-0.05 (0.07)
1 visitation	6.34 (0.27)	6.35 (0.26)	0.005 (0.04)
2 or more visitations	6.49 (0.22)	6.42 (0.24)	-0.07 (0.06)

Table S2. **Reaching targets using aggregated information per general practice**

	Mean target score (SD) year 1	Mean target score (SD) year 2	Mean difference between score (SE)
2016-2017			
Overall	3.08 (0.57)	3.36 (0.62)	0.28 (0.06)
0 visitations	3.04 (0.63)	3.33 (0.67)	0.28 (0.12)
1 visitation	3.10 (0.54)	3.36 (0.60)	0.26 (0.06)
2 or more visitations	2.86 (0.41)	3.69 (0.21)	0.83 (0.30)
2017-2018			
Overall	3.36 (0.64)	3.56 (0.41)	0.21 (0.06)
0 visitations	3.40 (0.52)	3.61 (.44)	0.21 (0.09)
1 visitation	3.43 (0.50)	3.53 (.44)	0.09 (0.06)
2 or more visitations	3.05 (1.02)	3.59 (0.9)	0.55 (0.19)
2018-2019			
Overall	3.56 (0.46)	3.48 (0.39)	-0.08 (0.05)
0 visitations	3.59 (0.45)	3.48 (0.30)	-0.11 (0.10)
1 visitation	3.56 (0.42)	3.50 (0.40)	-0.06 (0.05)
2 or more visitations	3.54 (0.59)	3.42 (0.46)	-0.12 (0.15)

SD= standard deviation; SE=standard error

Table S3. **Completeness score and target score in the lowest 25% practices**

Means (SD) in completeness score and target score and differences in scores between 2017-2018, in strata of visitation among those GP practices that were in the lowest 25% of the completeness score or target score, whenever applicable.

	Mean score (SD) year 2017	Mean score (SD) year 2018	Mean difference between scores (SE)
Completeness score			
0 visitations	5.84 (0.22)	6.47 (0.24)	0.62 (0.08)
1 visitation	5.85 (0.33)	6.40 (0.22)	0.55 (0.10)
2 or more visitations	4.50 (2.31)	6.44 (0.39)	1.94 (0.67)
Target score			
0 visitations	2.58 (0.36)	3.64 (0.59)	1.05 (0.16)
1 visitation	2.61 (0.46)	3.45 (0.49)	0.83 (0.16)
2 or more visitations	1.93 (1.17)	3.63 (0.20)	1.70 (0.38)

Box S1. **Example of a visitation**

This general practice was visited twice in 2017, the first visit was March 2017, the second visit was September 2017
Attending the meetings: GP, PN and the care group's staff member
Number of registered patients: XXXX
The practice is participating in 4 chronic care programs and 2 other projects

Items that were discussed:

Problems regarding practice organization:

- An improvement process is underway with regard to the practice organization (dissociation)
- The number of working hours for the PN was sufficient in March as well as in September
- Collaboration between GP and PN is good
- The practice assistant has no specific tasks within the CVRM care program
- The GP has organized a team-meeting to make working agreements regarding collaboration within care program

Problems regarding registration in the multidisciplinary registration system (Care2U):

- Extra attention is necessary, especially for the registration of process indicators of the CVRM care program
- The PN uses the practice overviews in Care2U to keep an eye on missing data

Problems regarding the CVRM care program:

- March 2017: Extra attention is necessary for registration and outcome indicators for patients with and without an established cardiovascular disease (CVD).
- September 2017: Registration has improved, extra attention for the outcome "systolic blood pressure on target (≤ 140 mm Hg)" is still necessary.
- A start has been made with the implementation of the patient's individual care plan
- Performance of the outcome "LDL-cholesterol on target (< 2.6 mmol/l)" is lower than the care groups benchmark, but not below the minimal norm: there is a lot of resistance among patients taking statins



7

Improving practice performance of systolic blood pressure in general practice with targeted intervention and compulsory support.

This is an adapted and translated version of: Willems N, Romeijnders A, Smits G. Verminderen van praktijkvariatie in de eerste lijn.
Huisarts Wet 2017;60(11): 580-3.

Abstract

Background

Despite guidelines and comprehensive support by a primary care group, a large variability was observed between general practices in the percentage of patients with a systolic blood pressure ≤ 140 mm Hg, participating in a nurse-led, integrated cardiovascular risk management program in The Netherlands.

Aim

Describing the care group's approach to reduce inter practice variation by supporting practices that performed below a minimal norm for the percentage of patients with a systolic blood pressure ≤ 140 mm Hg.

Method

The care group developed a benchmark, comprising a standard, a best practice norm and a minimal norm, to monitor performance. By establishing such a benchmark, practices performing below the minimal norm could be identified, including the percentage of patients with a systolic blood pressure ≤ 140 mm Hg. Based on an 8-item questionnaire, practice organization was analysed and practices performing below the minimal norm were asked to draw up an improvement plan.

Results

The minimal norm for the percentage of patients with a systolic blood pressure ≤ 140 mm Hg in 2016 was 51%. On January 1st 2016, 11 practices performed below the minimal norm. These practices were visited in 2016 and with care group support, 8 practices had improved to above the minimal norm on January 1st 2017.
Conclusion With comprehensive problem analysis and targeted support, 8 out of 11 low-performing practices improved on the percentage of patients < 80 years with their SBP ≤ 140 mm Hg.

Highlights:

- Although primary care group PoZoB scores well on quality indicators in the national benchmark, inter practice variation (IPV) is large
- Best practices improve every year with the quality cycle in the care program and with education
- For practices performing below the lowest level ("minimal norm") it is difficult to improve without support from the care group
- Intensive and compulsory support can help to improve practices that perform below the minimal norm

Introduction

The primary care group PoZoB is a cooperative association with 190 affiliated general practitioners (GPs) that focuses on improving the quality of chronic healthcare. In 2005, 2008 and 2010 PoZoB implemented 3 chronic care programs: Diabetes type 2 (DM2), Asthma/COPD (A/C) and Cardiovascular Risk Management (CVRM). Implementation of the nurse-led, integrated CVRM care program started April 1st 2010 in 30 general practices and January 1st 2013 137 practices had implemented the program. The aim of the CVRM care program was to reduce cardiovascular risk by improving unhealthy lifestyle and treatment of high blood pressure and high cholesterol. Although the CVRM guidelines recommend well-defined systolic blood pressure (SBP) goals [1,2], between 2013 and 2016 a large variation between individual practices was observed in the percentage of patients on target for SBP (≤ 140 mm Hg).

In the present paper we describe the PoZoB approach to support 11 practices that performed below a predefined minimal norm for SBP on target (≤ 140 mm Hg) and thereby reduce inter practice variation.

Methods

Setting

PoZoB is a primary care group that supports 156 general practices in the Eindhoven region, southeast of The Netherlands. The care group comprises general practices in a rural, semirural and urban setting and therefore can be considered as representative for the Dutch situation.

Benchmark definition

After the implementation of a nurse-led, integrated CVRM care program between 2010 and 2013 [3], initially the care group focussed on improving registration of cardiovascular risk factor and recommended guideline targets with comprehensive support, identical for all affiliated practices. Routine care data regarding registration and outcomes on the performance of patients participating in the integrated CVRM care program were collected in the care group's multidisciplinary information system (Care2U) and all-time visible, allowing practices to work on improvements themselves. Performance improved annually, however with a large inter practice variation. In 2016, the initial quality objective shifted towards quantitative objectives to reduce inter practice variation and improve those practices that performed below a predefined benchmark. To visualize and evaluate practice performance, PoZoB developed benchmarks for the CVRM care program based

on the prevailing (inter)national guidelines. These benchmarks were developed by the National College of General Practitioners [4]. The norm for a benchmark was determined by the mean value of all affiliated practices for one indicator based on the Care2U-data that were available on January 1st 2016. In the current paper we focussed on the "percentage of patients < 80 years on high risk for CVD with a systolic blood pressure ≤ 140 mm Hg" on January 1st 2016. The lowest border ("minimal norm") of the benchmark was defined as the mean value minus 2 standard deviations of the distribution. The upper level of the benchmark, i.e. "best practice", was defined as mean value plus 1 standard deviation. This was done for 23 items for CVRM. In consensus meetings these benchmark cut points were discussed between care group staff nurses and physicians and confirmed in the care group's Advisory Board of General Practitioners. After final consensus, the cut points were adopted and fixed for 2 years to allow practices to reflex on improvements. From January 2016 onwards, every practice received a quarterly report in which each individual practice performance was shown and could be compared with the overall PoZoB performance.

Implication of low benchmark for a practice

For practices with 7 or more benchmarks below a minimal norm, PoZoB developed a structured intervention based on a 8 item questionnaire and offered support in which practices were obliged to participate. The quarterly reports made low benchmarks visible and gave the care group the opportunity to intervene in the short term. Practices were visited by a PoZoB staff member who analysed practice organization and practice performance together with the GP and the PN in which various sources of probable causes of low performance were discussed. The 8 items of the comprehensive analysis are listed in table 1. Based on these discussions, the situation in the practice was analysed, taking all possible factors into account. Depending on the nature, severity and duration of the lower performance, it was agreed whether the practice will independently tackle the problems or receive (compulsory) support from the care group. In practices with 7 or more indicators below the lowest benchmark the improvement plan was drawn up together with the care group and closely monitored for 3-6 months. If the result on improvement was insufficient, guidance was intensified until results improved. PoZoB required that these practices make an active effort to reach the minimum benchmark as soon as possible. If this was not successful in a reasonable period or the practice did not want to cooperate, the affiliation with the practice could be terminated.

Results

In 2016, 156 general practices were affiliated to the PoZoB care group, with 45,139 pa-

tients participating in the integrated CVRM care program. Mean age was 68.9 years (SD 10.4), with 52.7% female participants and 61.8% high risk patients without previous CVD. Based on the Care2U-data for SBP on January 1st 2016, the benchmark for "SBP ≤ 140 mm Hg in patients below 80 years" was set on 68.4%, with the highest level ("best practice") at > 77.3% and the lowest level ("minimal norm") < 50.8%.

The intervention in patients with a high risk for cardiovascular disease

Figure 1 shows the practice variation between 156 practices on SBP in patients < 80 years on January 1st 2016. Practice variation ranged from 39.1% and 84.9% with 21 practices considered "best practice" and 11 practices performing below the lowest level. Figure 2 shows the changes in proportion of patients on target for SBP in those 11 practices on January 1st 2016 (before the intervention) and on January 1st 2017 (after the intervention). Within one year after the start of the intervention 8 practices improved towards the lowest 2015 benchmark. In 2017, 4 new practices scored below the lowest level for SBP. The number of best practices on SBP increased from 21 to 47 between January 2016 and July 2017 (without any intervention).

Figure 1. **Percentage of patients < 80 years on high risk for CVD with a SBP ≤ 140 mm Hg on January 1st 2016. Every vertical grey line represents 1 general practice.**

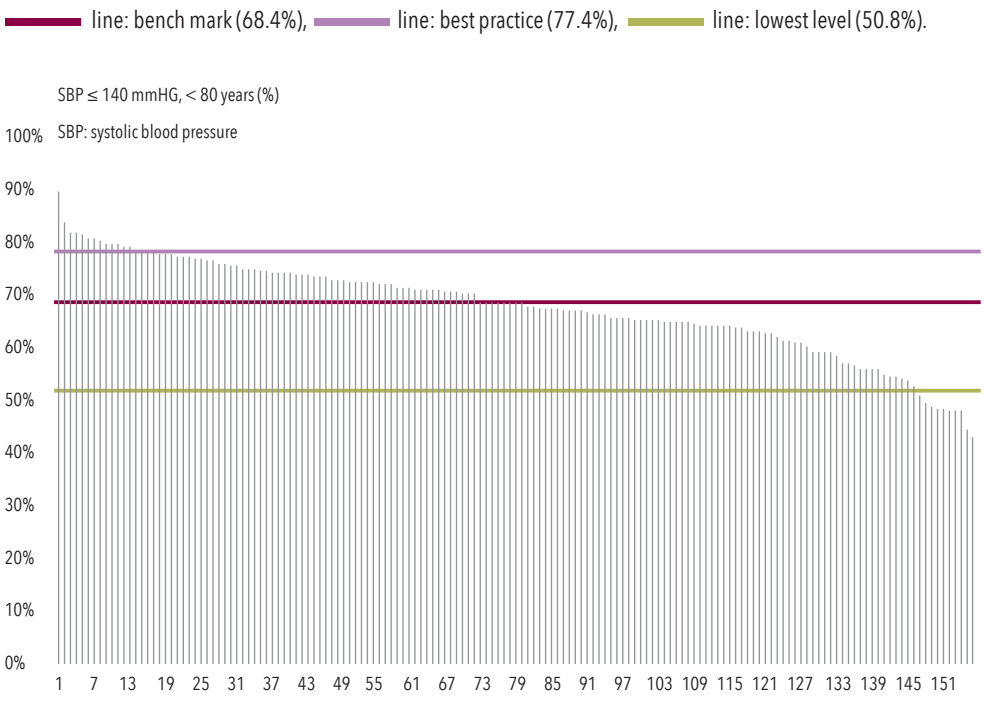


Figure 1. **Percentage of patients < 80 years with SBP on target in 11 practices on 1-1-2016 (bars) and on 1-1-2017 (bars)**



line: bench mark (68.4%), line: best practice (77.3%), line: lowest level (50.8%).

SBP: systolic blood pressure

Discussion

Summary

Within 1 year, after analysing organisation and offering targeted support, 8 out of 11 low performing practices improved on the percentage of patients < 80 years with a SBP ≤ 140 mm Hg to above the minimal norm. Support focussed on practice organization, promotion of expertise and commitment to the objectives of the care group.

Causes of low performance

According to the visiting staff member, causes of low performance were often multifactorial, due to long-term absence of the GP or the PN because of illness, a recent take-over or a previously poorly organized practice. They also reported that most GPs and PNs were motivated to improve their performance, based on the information from the quarterly reports, minimum standards and tailor-made support. The intervention had increasing support amongst affiliated practices [5]. Many best prac-

tices improved every year without additional support from the care group. Support from the care group however, remained necessary, because on January 1st 2017 4 other practices scored below the minimum standard for SBP in patients < 80 years.

Not all GPs showed enthusiasm. Sometimes there was resistance, too little attention and time for the care program, financial rather than substantive aspects appeared more important. It helped that financing went through the care group and care group management could demand results on behalf of all the affiliated GPs. For GPs who did not make sufficient efforts, participation in the care group could come up for discussion.

The PoZoB GPs have showed their solidarity to support GPs who wanted to improve their performance. In case of long-term illness of practice-staff, a recent take-over or a poorly organized practice, support of a solidary and professional organization was of great importance. GPs needed to become familiar with result-oriented thinking, to work with minimal standards and to evaluate associated results. However, every GP agreed that inter practice variation in SBP between 40-90% in patients at risk for cardiovascular disease was not acceptable.

Strengths and limitations

The current paper describes the efforts the PoZoB care group made to improve practice performance. Strength and limitations therefore are not related to the study, but to the care group approach to support low-performing practices. With a predefined benchmark and predefined levels for "best practice" and "low-performance", it was possible to identify low-performing practices. The data used to determine performance were collected in Care2U, which did not interfere with daily practice. With the 8-item questionnaire practice organization was discussed, problems became visible and targeted support could be offered in the short term.

A limitation is that we evaluated only 1 outcome of a very limited number of practices, which tells us nothing about overall improvements. Second, this evaluation lacks a control group, implying that there was no evidence that the improvements observed were the result of our intervention.

Comparison with literature

Until now, little is known about reducing practice variation in primary care for patients participating in a chronic care program. Wensing found that many strategies were not or at most a little bit effective [6]. Improvement processes needed continuous attention, were time consuming and sustainable results were difficult to achieve. Educational interventions had modest effects if directed to physicians on hypertension control [7]. Furthermore, comprehensive support was most beneficial and feedback was most effective if performance was low [8,9].

Implications for research and daily clinical practice

A number of initiatives were taken by the care group to support practices with improving their performance: i) practices were asked to drew up an annual practice plan to record where the practice wanted to work on in the coming year. With these goals set, practices could focus on certain parts of the care process (for example "registration"), which could be easily evaluated during visitation after 1 year, ii) performance in the best practices was analysed to find successful strategies or profiles that could be implemented in practices that performed on a lower level and iii) age, comorbidity and co-medication of participants in the CVRM care program should be taken into account when discussing practice performance because these conditions could be an important consideration for both caregivers and patients for not starting or not adjusting medication [10].

Conclusion

With comprehensive problem analysis and targeted support, in 8 out of 11 low-performing practices improved the percentage of patients < 80 years with their SBP ≤ 140 mm Hg .

Table 1. **8-item questionnaire to analyse practice organisation**

1	a result-orientated approach (focus on how to interpret information from the quarterly reports and improving to at least the minimum standard.
2	applying or, if necessary, deviating from guidelines
3	regular, structured consultation between GP and PN and following up agreements so the PN feels supported by the GP
4	adequate mail processing and registration in the multidisciplinary information system
5	sufficient hours for the PN to do the work
6	discontinuity of GP or PN
7	differences in practice population
8	linking problems with a laboratory, electronic registration system or multidisciplinary registration system

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8

Does long-term, nurse-led, integrated CVRM care reduce CVD incidence in primary care?

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Abstract

Background

The impact of long-term, nurse-led, integrated cardiovascular risk management in primary care on cardiovascular disease incidence has not been previously investigated.

Methods

We compared cardiovascular disease incidence between 2013 and 2019 in 16,723 high-risk patients without established cardiovascular disease or diabetes receiving integrated cardiovascular risk management and extensive care group support (PoZoB) with 34,072 similar patients receiving a mixture of usual care and integrated care without any support (JGPN). In both patient groups, we estimated the incidence of acute myocardial infarction, transient ischemic attack, stroke, peripheral artery disease and abdominal aortic aneurysm.

Results

The incidence (per 1,000 person-years) of a first event for patients aged 45 to 84 years in PoZoB was 17.5 (95% CI 16.2-18.9) for men and 13.6 (12.6-14.7) for women. The corresponding JGPN results were 22.2 (21.1-23.3) for men and 15.8 (15.0-16.7) for women. The event-specific incidence rates (PoZoB versus JGPN) for acute myocardial infarction were 3.7 vs 6.1 (men) and 2.0 vs 2.4 (women); those for transient ischemic attack were 4.5 vs 5.3 (men) and 4.6 vs 4.5 (women); those for stroke were 5.0 vs 6.1 (men) and 3.8 vs 5.3 (women); those for peripheral artery disease were 2.6 vs 3.0 (men) and 2.0 vs 2.0 (women); and those for abdominal aortic aneurysm were 2.3 vs 1.9 (men) and 1.0 vs 0.8 (women).

Conclusion

The results are compatible with a lower incidence of cardiovascular disease in women and men exposed to long-term integrated cardiovascular risk management. The magnitude of the relation could not be assessed due to unsolvable incomparability between the cohorts due to the nature of routine data collection in primary care.

Keywords

primary health care, prevention, cardiovascular risk management, disease incidence, observational design

Introduction

Cardiovascular diseases are the leading causes of death worldwide and are caused mainly by modifiable risk factors and unhealthy lifestyles, such as hypertension, hypercholesterolemia, diabetes, obesity, lack of exercise, smoking and unhealthy food habits [1]. International guidelines on cardiovascular risk management (CVRM) recommend a multidisciplinary approach for all patients at high risk of developing cardiovascular disease. Most of these programs are orchestrated in primary care in close collaboration with medical specialists and allied professionals [2]. In The Netherlands, a nurse-led, integrated CVRM care program has been increasingly organized by primary care groups since 20103 based on the CVRM Guidelines of the National Society of General Practitioners [4,5]. Important components of such programs include identifying eligible patients, performing cardiovascular risk assessments, and subsequently managing cardiovascular risk factors [6]. Follow-up, guidance and support with lifestyle changes and medication adjustments are delegated to a practice nurse (PN), a registered nurse with additional training in protocolized CVRM.

Studies on the effectiveness of nurse-led, integrated CVRM care programs in general practice are scarce, and the results are heterogeneous. Some studies have shown improvements in CVD risk factors such as blood pressure, LDL-cholesterol and some lifestyle changes [7-11], while others have not [12]. Follow-up in these studies was often limited to 6-12 months, with varying designs, interventions and target populations. It therefore remains unknown whether the implementation of long-term, nurse-led, integrated CVRM care could lead to a reduction in cardiovascular events; therefore, an evaluation of the effectiveness of the CVRM care program in primary care is desirable. The aim of this study was to compare the incidences of cardiovascular disease (acute myocardial infarction [AMI], transient ischaemic attack [TIA], stroke, peripheral artery disease [PAD] and abdominal aortic aneurysm [AAA]) between 2013 and 2019 in high-risk patients without established CVD or diabetes mellitus who participated in a nurse-led, integrated CVRM care program (PoZoB) with similar high-risk patients who participated in the Julius General Practice Network (JGPN) and who received a mixture of CVRM care, which varied between usual care and integrated care.

Methods

Setting

The patients who received integrated care were registered in 137 general practices (188 GPs, 405,000 registered patients) affiliated with the PoZoB primary care group located in and around Eindhoven, southeastern part of The Netherlands. The JGPN

comprised 72 general practices (372,000 registered patients) from the city of Utrecht and its vicinity in the centre of The Netherlands.

Design

We used data collected in routine clinical primary care practice in two longitudinal cohort studies. The PoZoB cohort comprised 16,723 patients at high risk for CVD without established CVD or diabetes mellitus receiving nurse-led, integrated CVRM care. PoZoB data regarding the CVRM care program were collected in a separate multidisciplinary information system (Care2U) and used for regular evaluation and feedback to affiliated practices. The JGPN cohort comprised 34,072 high-risk patients without established CVD or diabetes mellitus receiving a mixture of care as usual or integrated CVRM care. The database that was used by the JGPN contained pseudonymized routine healthcare data extracted from structured and unstructured fields within the electronic health records (EHRs) of all patients [13]. Medical information on disease conditions was registered within the general practice EHR according to the ICPC codes. In addition, information on performed measurements (such as height, weight, blood pressure), laboratory information (lipids, renal function, glucose) and prescribed medication was registered. The last extraction of the data was performed between December 2017 and August 2019. Practices affiliated with the PoZoB care group and the JGPN are located in rural, suburban and urban surroundings, which makes them representative for the situation in The Netherlands.

PoZoB approach regarding CVRM care

The PoZoB primary care group started with stepwise implementation of a nurse-led, integrated CVRM care program on April 1st, 2010, a process that has been described in detail elsewhere [6]. In 2013, all 137 affiliated practices implemented the CVRM care program. The care group supported practices with protocols, toolkits and regular education on CVRM-related topics, teleconsultation, inter vision for PNs to discuss complex case studies and annual consultation and feedback (C&F) meetings for GPs and PNs [14]. In 2016, the care group started with practice visitations to discuss practice organization and offer support to low-performing practices.

JGPN approach regarding CVRM care

There was no structured CVRM care program for JGPN patients, which meant that in some practices, care as usual was delivered by the GP, and in some practices, integrated CVRM care was delivered by a PN, initiated by the general practice itself. Moreover, systematic screening of eligible patients, consultation and feedback meetings and practice visits to evaluate and improve CVRM care were lacking in the JGPN.

Patient populations

The PoZoB cohort comprised patients who were eligible for integrated CVRM care, based on the Dutch Guidelines for CVRM [5]. The eligibility criteria are presented in Table 1. For this project, we selected PoZoB patients who were defined as "without an established cardiovascular disease and without diabetes mellitus", i.e. a primary prevention cohort.

The JGPN cohort for this project was constructed using information from the start of the JGPN in 2000 to the end of 2018. We constructed a cohort of patients registered on Jan 1st 2013, at the JGPN. An established cardiovascular disease was defined as an ICPC code before January 1st, 2013, indicating a CVA (K90), a TIA (K89), CHF (K77), other ischaemic cardiac conditions (K76), AMI (K75), angina (K74), atrial fibrillation (K78), evidence of PAD (K91, K92), or renal failure (U99.01). All patients who received an ICPC for AMI, TIA, stroke, PAD or AAA after January 1st, 2013, were defined as having experienced incident events.

Table 1. **Inclusion and exclusion criteria for integrated CVRM care** [4]

Inclusion criteria for very high risk patients:
• Patients with a documented atherosclerotic CVD, including angina pectoris, myocardial infarction, chronic ischemic heart disease, coronary sclerosis, transient ischemic attack (TIA), cerebral infarction, intermittent claudication or aneurysm of the abdominal aorta and
• The patient is primarily managed by the general practitioner (GP) and
• Aged 18 years or older
Inclusion criteria for high risk patients:
• No established CVD and
• Use of antihypertensive or lipid lowering drugs or
• A 10-year CVD morbidity and mortality risk > 10%, based on the Dutch guideline for CVRM (4) or
• A SBP > 180 mm Hg and/or a TC/HdI-ratio > 8, regardless the 10-year CVD risk and
• The patient is primarily managed bij the GP and
• Aged 18 years or older

Next, based on the available routine clinical information in the database, a selection of patients who met the inclusion and exclusion criteria from the PoZoB cohort were selected (table 1). This selection was based on the following steps. First, all individuals with an established cardiovascular disease or diabetes mellitus before January 1st, 2013, were excluded, leaving all individuals without an established cardiovascular disease and free from diabetes mellitus. Next, men aged 55 years and women aged 60 years or older who were prescribed either lipid lowering or blood

pressure lowering agents were selected. Next, those with a systolic blood pressure of 160 mmHg or above or a total cholesterol level of 8.0 mml/l or above were selected. Finally, of the remaining individuals, those with a SCORE risk estimate of 5% or above were selected. As complete information on the SCORE risk was limited in the JGPN for all participants, those aged 66 years or older were considered to be at high risk. This procedure led to an overall JGPN cohort of 34,072 individuals.

Outcome

The primary outcome of the study was the composite of 5 atherosclerotic diseases that occurred between Jan 1st, 2013, and Jan 1st, 2019, as registered with an ICPC code in the multidisciplinary registration system: AMI (ICPC: K75), TIA (ICPC: K89), stroke (ICPC: K90), PAD (K92.01) and AAA (ICPC: K99.01).

Analyses

For each patient, follow-up in years was estimated, with the start date determined as January 1st, 2013, coinciding with the start of the integrated care project in the PoZoB cohort, and the end date determined as the end of the study (December 31st, 2018), death, loss to follow-up, whatever came first. For the JGPN cohort, follow-up time was estimated as the time from baseline (January 1st, 2013) up to the time the event was registered, the time a patient was no longer registered at the GP practice or the end of follow-up (last extraction date), whichever date came first. Incidence rates were presented per 1,000 person-years of follow-up and stratified by biological sex and age categories, i.e., < 45 years, 45-54 years, 55-64 years, 65-74 years, 75-84 years and ≥ 85 years. For the main comparisons, we restricted our analysis to those age groups that had limits at both ends, e.g., 45-84 years, but not for estimates in age groups with undefined limits (<45 years and ≥ 85 years) because the age distribution in the latter groups may considerably differ across studies.

We additionally used direct standardization to compare the cohorts. This means that, using the age- and biological sex-specific JGPN incidence rates as a reference, we estimated that the expected absolute number of events that should have occurred had the same incidence rates for PoZoB as for JGPN. We next calculated the ratio observed/expected as a measure of effect.

Ethical considerations

The use of patient data will be conducted following privacy legislation in The Netherlands. GPs affiliated with the PoZoB care group and GPs participating in the JGPN inform their patients who their anonymized data can be used for evaluation or research purposes and offer the possibility to opt-out. The anonymized data set included only age and sex, thus making it impossible for investigators to identify individual patients [13].

Results

The general characteristics of those aged 45-84 years from both the PoZoB and JGPN cohorts are presented in Table 2. At baseline, the PoZoB participants were younger than the JGPN participants. Information on risk factor measurements was less available in the JGPN database than in the PoZoB database. Based on the data, PoZoB participants had lower total cholesterol levels and systolic and diastolic blood pressure levels, and more patients were prescribed blood pressure- and lipid-lowering medication (Table 2).

Table 2. **General characteristics of the cohorts at baseline (2013)**

	PoZoB		PoZoB		JGPN		JGPN	
	Women	N (%)	Men	N (%)	Women	N (%)	Men	N (%)
Participants (Total)		9,495		7,228		18,987		15,085
Participants (45-85 years)		9,257 (100)		7,063 (100)		16,707 (100)		13,542 (100)
Age Mean (SD), age.	67.2 (8.8)	9,257 (100)	64.1 (9.0)	7,063 (100)	68.5 (8.5)	16,707 (100)	66.3 (8.8)	13,542 (100)
BMI Mean (SD), kg/m²	27.8 (4.7)	7,531 (81.4)	27.7 (3.6)	5,587 (79.0)	27.7 (5.1)	3,411 (20.4)	27.5 (4.1)	2,811 (20.8)
TC Mean (SD), mmol/l	5.4 (1.0)	8,276 (89.4)	5.0 (1.0)	6,172 (87.4)	5.9 (1.1)	5,790 (34.7)	5.4 (1.1)	4,351 (32.1)
HDL Mean (SD), mmol/l	1.5 (0.4)	8,274 (89.4)	1.2 (0.3)	6,171 (87.4)	1.5 (0.4)	5,755 (34.4)	1.3 (0.3)	4,325 (31.9)
LDL Mean (SD), mmol/l	3.2 (0.9)	8,739 (94.4)	3.1 (0.9)	6,526 (92.4)	3.6 (1.0)	5,476 (32.8)	3.4 (0.9)	4,234 (31.3)
Trigl Mean (SD), mmol/l	1.5 (0.7)	8,262 (89.3)	1.6 (0.9)	6,159 (87.2)	1.6 (1.0)	5,538 (33.1)	1.8 (1.3)	4,323 (31.9)
SBP Mean (SD), mmHg	137.9 (15.7)	8,490 (91.7)	138.0 (14.7)	6,260 (88.6)	145.0 (20.7)	6,847 (41.0)	146.0 (19.9)	4,785 (35.3)
DBP Mean (SD), mmHg	79.4 (9.0)	8,460 (91.4)	81.0 (9.2)	6,230 (88.2)	83.0 (11.0)	6,818 (40.8)	85.0 (11.3)	4,774 (35.3)
F Gluc mean (SD), mmol/	5.4 (0.6)	8,183 (88.4)	5.5 (0.8)	6,075 (86.0)				
Alc mean (SD)	0.6 (1.0)	7,825 (84.5)	1.2 (1.4)	5,784 (81.9)	1.4 (1.0)	1,123 (6.7)	2.0 (1.6)	1,392 (10.3)
eGFR >=60 ml/min/1.73 m² (%)	73.7	6,822	78.9	5,574				
BPL: yes (%)	62.7	5,800	57.5	4,153	39.3		37.5	
LL: yes (%)	37.6	3,482	37.4	2,643	14.7		16.4	
Smoking Status								
Not registered (%)	12.6	1,156	16.4	1,162				
No smoking (%)	52.0	4,814	34.6	2,441				
Smoking before (%)	25.0	2,313	37.6	2,654				
Smoking yes (%)	10.5	968	11.5	812	7.4		8.2	

BMI=body mass index; TC = total cholesterol; HDL: High density lipoprotein; LDL Low density lipoprotein; Trigl: triglycerides; SBP: systolic blood pressure; DBP: diastolic blood pressure; F Gluc: fasting glucose; eGFR: estimated glomerular filtration rate; BPL: blood pressure lowering; LM: lipid modifying

During follow-up, 1,300 first events (639 in men, 661 in women) occurred in patients aged 45-85 years in the PoZoB cohort, and 2,947 events (1,580 in men, 1,367 in women) occurred in the JGPN cohort. The incidence (per 1,000 person-years) of a first event for patients aged 45 to 84 years in PoZoB was 17.5 (95% CI 16.2-18.9) for men and 13.6 (12.6-14.7) for women. The corresponding JGPN results were 22.2 (21.1-23.3) for men and 15.8 (15.0-16.7) for women.

Tables 3 and 4 provide information on the number of individual events, years of follow-up and incidence rates. The event-specific incidence rates (PoZoB versus JGPN) for AMI were 3.7 vs 6.1 (men) and 2.0 vs 2.4 (women); those for TIA were 4.5 vs 5.3 (men) and 4.6 vs 4.5 (women); those for stroke were 5.0 vs 6.1 (men) and 3.8 vs 5.3 (women); those for PAD were 2.6 vs 3.0 (men) and 2.0 vs 2.0 (women); and those for AAA were 2.3 vs 1.9 (men) and 1.0 vs 0.8 (women).

Table 3. **Events 2013-2019 for AMI, TIA, CVA, PAD and AAA of the PoZoB cohort**

ICPC	Age (years)	# events PoZoB	Person years of follow-up PoZoB	Incidence/ 1000 person years	95% low	95% high	# events PoZoB	Person years of follow-up PoZoB	Incidence/ 1000 person years	95% low	95% high
		Men	Men	Men			Women	Women	Women		
K75	< 45	1	665	1,5	0,2	10,7	1	607	1,6	0,2	11,7
	45-54	5	3,961	1,3	0,5	3,0	4	3700	1,1	0,4	2,9
	55-64	44	16,345	2,7	2,	3,6	22	14,547	1,5	1,0	2,3
	65-74	6	12,951	4,9	3,8	6,2	37	21,438	1,7	1,3	2,4
	75-84	24	3,679	6,5	4,4	9,7	32	8,901	3,6	2,5	5,1
	>=85	0	176	0,0	0,0	0,0	1	536	1,9	0,3	13,2
	Total 45-84	136	36,936	3,7	3,1	4,4	95	48,586	2,0	1,6	2,4
K89	< 45	2	660	3,0	0,8	12,1	0	611	0,0	0,0	0,0
	45-54	5	3,958	1,3	0,5	3,0	9	3,697	2,4	1,3	4,7
	55-64	50	16,365	3,1	2,3	4,0	34	14,546	2,3	1,7	3,3
	65-74	73	12,595	5,8	4,6	7,3	102	21,299	4,8	3,9	5,8
	75-84	36	3,658	9,8	7,1	13,6	77	8,766	8,8	7,0	11,0
	>=85	5	164	30,5	2,7	73,2	7	517	13,5	6,5	28,4
	Total 45-84	164	36,576	4,5	3,8	5,2	222	48,308	4,6	4,0	5,2
K90	< 45	0	665	0,0	0,0	0,0	0	610	0,0	0,0	0,0
	45-54	11	3,955	2,8	1,5	5,0	11	3,709	3,0	1,6	5,4
	55-64	52	16,378	3,2	2,4	4,2	52	14,574	3,6	2,7	4,7
	65-74	84	12,941	6,5	5,2	8,0	84	21,381	3,9	3,2	4,9
	75-84	38	3,680	10,3	7,5	14,2	38	8,834	4,3	3,1	5,9
	>=8	4	170	23,5	8,8	62,7	4	525	7,6	2,9	20,3
	Total 45-84	185	36,954	5,0	4,3	5,8	185	48,498	3,8	3,3	4,4
K92.01	< 45	0	665	0,0	0,0	0,0	0	609	0,0	0,0	0,0
	45-54	7	3,952	1,8	0,8	3,7	7	3,710	1,9	0,9	4,0
	55-64	37	16,366	2,3	1,6	3,1	37	14,524	2,5	1,8	3,5
	65-74	41	13,024	3,1	2,3	4,3	41	21,396	1,9	1,4	2,6
	75-84	12	3,722	3,2	1,8	5,7	12	8,896	1,3	0,8	2,4
	>=85	1	172	5,8	0,8	41,3	1	534	1,9	0,3	13,3
	Total 45-84	97	37,064	2,6	2,1	3,2	97	48,526	2,0	1,6	2,4
K99.01	< 45	0	665	0,0	0,0	0,0	0	611	0,0	0,0	0,0
	45-54	2	3,960	0,5	0,1	2,0	0	3,716	0,0	0,0	0,0
	55-64	25	16,424	1,5	1,0	2,3	11	14,603	0,8	0,4	1,4
	65-74	41	13,027	3,1	2,3	4,3	28	21,492	1,3	0,9	1,9
	75-84	17	3,724	4,6	2,8	7,3	9	8,956	1,0	0,5	1,9
	>=85	0	176	0,0	0,0	0,0	0	539	0,0	0,0	0,0
	Total 45-84	85	37,135	2,3	1,9	2,8	48	48,767	1,0	0,7	1,3

All person years of follow-up is based on the subtraction of date first event and the baseline date. That is why it differs across groups.

Table 4. **Events 2013-2019 for AMI, TIA, CVA, PAD and AAA of the JGPN cohort**

ICPC	Age (years)	# events JGPN	Person years of follow-up PoZoB	Incidence/ 1000 person years	95% low	95% high	# events JGPN	Person years of follow-up PoZoB	Incidence/ 1000 person years	95% low	95% high
		Men	Men	Men			Women	Women	Women		
K75	< 45	13	4,454	2.9	1.7	5.0	3	3,983	0.8	0.2	2.3
	45-54	28	7,718	3.6	2.5	5.3	10	7,457	1.3	0.7	2.5
	55-64	157	20,039	7.8	6.7	9.2	35	16,967	2.1	1.5	2.9
	65-74	163	30,904	5.3	4.5	6.1	83	43,555	1.9	1.5	2.4
	75-84	80	11,841	6.8	5.4	8.4	83	20,775	4.0	3.2	5.0
	>=85	12	2,688	4.5	2.5	7.9	24	5,899	4.1	2.7	6.1
	Total 45-84	428	70,502	6.1	5.5	6.7	211	88,754	2.4	2.1	2.7
K89	< 45	3	4,487	0.7	0.2	2.1	15	3,937	3.8	2.3	6.3
	45-54	28	7,755	3.6	2.5	5.2	24	7,402	3.2	2.2	4.8
	55-64	75	20,227	3.7	3.0	4.6	56	16,981	3.3	2.5	4.3
	65-74	176	30,836	5.7	4.9	6.6	145	43,356	3.3	2.8	3.9
	75-84	98	11,805	8.3	6.8	10.1	136	20,659	6.6	5.6	7.8
	>=85	29	2,654	10.9	7.6	15.7	44	5,853	7.5	5.6	10.1
	Total 45-84	377	70,623	5.3	4.8	5.9	361	80,996	4.5	4.0	4.9
K90	< 45	13	4,461	2.9	1.7	5.0	9	3,979	2.3	1.2	4.3
	45-54	29	7,772	3.7	2.6	5.4	11	7,455	1.5	0.8	2.7
	55-64	85	20,318	4.2	3.4	5.2	68	16,945	4.0	3.2	5.1
	65-74	180	30,991	5.8	5.0	6.7	194	43,349	4.5	3.9	5.2
	75-84	136	11,783	11.5	9.8	13.7	194	20,671	9.4	8.2	10.8
	>=85	26	2,683	9.7	6.6	14.2	78	5,836	13.4	10.7	16.7
	Total 45-84	430	70,864	6.1	5.5	6.7	467	88,420	5.3	4.8	5.8
K92.01	< 45	0	4,496	0.0	0.0	0.0	2	3,987	0.5	0.1	2.0
	45-54	17	7,792	2.2	1.4	3.5	12	7,434	1.6	0.9	2.8
	55-64	68	20,345	3.3	2.6	4.2	40	16,948	2.4	1.7	3.2
	65-74	90	31,075	2.9	2.4	3.6	76	43,562	1.7	1.4	2.2
	75-84	36	11,966	3.0	2.2	4.2	54	20,837	2.6	2.0	3.4
	>=85	8	2,694	3.0	1.5	5.9	8	5,933	1.3	0.7	2.7
	Total 45-84	211	71,178	3.0	2.6	3.4	182	88,781	2.0	1.8	2.4
K99.01	< 45	0	4,496	0.0	0.0	0.0	1	3,992	0.3	0.0	1.8
	45-54	8	7,816	1.0	0.5	2.0	1	7,475	0.1	0.0	0.9
	55-64	31	20,454	1.5	1.1	2.2	13	17,041	0.8	0.4	1.3
	65-74	95	31,105	3.1	2.5	3.7	41	43,668	0.9	0.7	1.3
	75-84	50	11,938	4.2	3.2	5.5	18	20,935	0.9	0.5	1.4
	>=85	9	2,702	3.3	1.7	6.4	7	5,944	1.2	0.6	2.5
	Total 45-84	134	71,313	1.9	1.6	2.2	73	89,119	0.8	0.7	1.0

All person years of follow-up is based on the subtraction of date first event and the baseline date. That is why it differs across groups.

Table 5 provides information on the calculation of the absolute number of cardiovascular events observed for which the JGPN incidence rates were applicable to the PoZoB population during the entire study period. Overall, a lower number of events in the PoZoB was observed (observed/expected ratio < 1.0) for AMI, TIA, stroke and PAD in men and for AMI, CVA, and PAD in women. However, the effects seem to differ by age.

Table 5. **Applying the JGPN incidence rates to the PoZoB cohort to estimate the number of events prevented**

ICPC	Age (years)	# events observed in PoZoB	Person years of follow-up in PoZoB	Incidence/ 1000 PY in JGPN	# events expected based on JGPN data	Ratio of observed/ expected # events	# events observed in PoZoB	Person years of follow-up in PoZoB	Incidence/ 1000 PY person in JGPN	# events expected based on JGPN data	Ratio of observed/ expected # events
		Men					Women				
K75	< 45	1	665	2.9	2 0	52	1	607	0.8	0	2.19
	45-54	5	3,961	3.6	14	0.35	4	3,700	1.3	5	0.81
	55-64	44	16,345	7.8	128	0.34	22	14,547	2.1	30	0.73
	65-74	63	12,951	5.3	68	0.92	37	21,438	1.9	41	0.91
	75-84	24	3,679	6.8	25	0.97	32	8,901	4.0	36	0.90
	>=85	0	176	4.5	1	0.00	1	536	4.1	2	0.46
	Total 45-84	136	36,936	6.1	224	0.61	95	48,586	2.4	116	0.82
K89 <	45	2	660	0.7	0	4.53	0	611	3.8	2	0.00
	45-54	5	3,958	3.6	14	0.35	9	3,697	3.2	12	0.75
	55-64	50	16,365	3.7	61	0.82	34	14,546	3.3	48	0.71
	65-74	73	12,595	5.7	72	1.02	102	21,299	3.3	71	1.43
	75-84	36	3,658	8.3	30	1.19	77	8,766	6.6	58	1.33
	>=85	5	164	10.9	2	2.79	7	517	7.5	4	1.80
	Total 45-84	164	36,576	5.3	195	0.84	222	48,308	4.5	215	1.03
K90	< 45	0	665	2.9	2	0.00	0	610	2.3	1	0.00
	45-54	11	3,955	3.7	15	0.75	11	3,709	1.5	5	2.01
	55-64	52	16,378	4.2	69	0.76	52	14,574	4.0	58	0.89
	65-74	84	12,941	5.8	75	1.12	84	21,381	4.5	96	0.88
	75-84	38	3,680	11.5	42	0.89	38	8,834	9.4	83	0.46
	>=85	4	170	9.7	2	2.43	4	525	13.4	7	0.57
	Total 45-84	185	36,954	6.1	224	0.83	185	48,498	5.3	256	0.72
K92.01	< 45	0	665	0.0	0	NA*	0	609	0.5	0	0.00
	45-54	7	3,952	2.2	9	0.81	7	3,710	1.6	6	1.17
	55-64	37	16,366	3.3	55	0.68	37	14,524	2.4	34	1.08
	65-74	41	13,024	2.9	38	1.09	41	21,396	1.7	37	1.10
	75-84	12	3,722	3.0	11	1.07	12	8,896	2.6	23	0.52
	>=85	1	172	3.0	1	1.96	1	534	1.3	1	1.39
	Total 45-84	97	37,064	3.0	110	0.88	97	48,526	2.0	99	0.98
K99.01	< 45	0	665	0.0	0	NA*	0	611	0.3	0	0.00
	45-54	2	3,960	1.0	4	0.49	0	3,716	0.1	0	0.00
	55-64	25	16,424	1.5	25	1.00	11	14,603	0.8	11	0.99
	65-74	41	13,027	3.1	40	1.03	28	21,492	0.9	20	1.39
	75-84	17	3,724	4.2	16	1.09	9	8,956	0.9	8	1.17
	>=85	0	176	3.3	1	0.00	0	539	1.2	1	0.00
	Total 45-84	85	37,135	1.9	70	1.22	48	48,767	0.8	40	1.20

All person years of follow-up is based on the subtraction of date first event and the baseline date. That is why it differs across groups.

*NA: Not Available

Discussion

In this study, among patients at high risk for a cardiovascular event but without an established cardiovascular disease or without diabetes mellitus, we observed a lower incidence of cardiovascular events in women with AMI and stroke and in men with AMI, TIA, stroke and PAD who participated in a long-term, nurse-led integrated CVRM care program between 2013 and 2019 than in women and men who received care initiated by a GP without care group support.

While our results may suggest a possible beneficial effect of long-term, nurse-led integrated CVRM care in the PoZoB cohort, there are a number of methodological aspects of the study to consider. First, in an ideal world, a randomized controlled trial would have been the most appropriate design to assess the effect of our intervention. This is because randomization generally takes care of a comparable prognosis (i.e., the risk of an event) between the intervention arms at baseline. Despite our efforts, in our study, several measured risk factors were not well balanced between the treatment arms (better levels in the PoZoB participants). Because the JGPN is based on routinely collected information, the availability of measured risk factors was much more limited, which severely hampers multivariable regression analyses to adjust for imbalances at baseline. Furthermore, in addition to differences in known patient characteristics, imbalances in not measured differences that might also affect cardiovascular risk further hamper a valid comparison. However, as age and biological sex are very important risk factors and are related to many measured and unmeasured risk factors, we presented our results in small age and sex strata (tables 3 and 4) and provided estimates of the observed/expected ratio based on age-specific strata (table 5). Second, the PoZoB participants on one side and the JGPN participants on the other side were selected differently. PoZoB participants were rigorously assessed for inclusion in the integrated CVRM care program based on conditions from the Dutch Guidelines for CVRM [4], including information on the primary treating responsible health professional. Patients could decline to participate in the CVRM care program (between 2013 and 2019, the annual non-participation rate was 15-20%), leading to a healthier sample (lower risk). Selection from the JGPN was based on extraction from real-world data in the electronic health care records and thus on the availability of the information listed in Table 1. Non participation was not an issue. Third, treatment and follow-up in JGPN patients at high risk for CVD were left to the GPs' judgement (i.e., routine clinical care). Sometimes the national CVRM guidelines were followed, but sometimes they were not. This may have led to a more heterogeneous selection of JGPN patients in this study compared to the PoZoB population. Whether this affects the event incidence is not known. Finally, participation in the integrated CVRM care program meant that a predetermined data set was registered annually in a standardized matter by the PoZoB primary care group. Registration of the JGPN data was

based solely on routine practice data without agreements about minimal registration. This not only may have caused missing information on important risk factors such as LDL-cholesterol or smoking status, but the registration of outcomes may also be different between cohorts. Research has shown that the quality of registration in multidisciplinary registries for chronic diseases is more accurate than the quality of registration in the patient's EHR [15]. This may have further increased the differences in outcomes between PoZoB and JGPN.

Therefore, to allow for a definite result on the efficacy of a long-term CVRM care program, a prospective, randomized controlled design would have been necessary [16]. Unfortunately, at present, this is not feasible: in 2022, the vast majority of general practices in the Netherlands were affiliated with a primary care group that organized nurse-led, integrated CVRM care [17]. Practices that have organized CVRM care without the support of a primary care group are unknown. The upcoming emulation target trial approach seems to be a promising way to study the effect of an intervention based on observational data. However, this demands careful preparation, and it seems that the GP databases are not yet fit for purpose [18].

To our knowledge, this is the first study to compare the incidence of cardiovascular events in patients receiving long-term, nurse-led integrated CVRM care with that in patients receiving CVRM care offered by GPs.

Until now, international studies in primary care that evaluated nurse-led clinics focused on improving cardiovascular risk factors and showed varying results after 1-2 years of follow-up. The positive effects were not sustained [19–24]; therefore, long-term guidance and support were suggested, as well as early participation and multiple annual visits [25,26]. None of the studies evaluated the relationship between long-term, nurse-led integrated CVRM care and the occurrence of (new) cardiovascular events.

Two cluster randomized controlled trials (RCTs) carried out in primary care in The Netherlands that compared nurse-led CVRM care with usual care showed no benefits favouring the intervention. One RCT conducted by van Bussel et al included patients aged 70-80 years and showed some improvements in cardiovascular risk factors after 1 year but no reduction in cardiovascular morbidity or mortality after 6 years [11]. The second RCT, conducted by Marchall et al, revealed no differences in systolic blood pressure, LDL cholesterol or smoking status after 1 year [12]. Differences in disease incidence, however, were not evaluated. The authors suggested that the reasons for the lack of effectiveness were as follows:

- the intervention may have been too short, as it is known that it takes time to reorganize practice organization and to master a new working method with different quality requirements [27];
- the possible lack of intensity of the intervention; and
- the observation that usual care was already at a high level.

However, a randomized study conducted by van den Dries et al. in older primary care patients with atrial fibrillation (AF) showed a significant reduction in mortality after 2 years in patients who received comprehensive care every 3 months compared to patients who received care as usual [28].

Implications for future research

As nearly all GP practices in The Netherlands use EHRs for data registration, this may offer the possibility of conducting emulation target trials in the future, given that the data are "fit for this purpose". Guidelines are available if a target trial is considered as well as an evaluation tool to assess the risk of bias [29]. Regardless of the research design used to evaluate the effectiveness of integrated CVRM care, the question seems justified as to whether such a study is still necessary and feasible. Given the effect of integrated CVRM on blood pressure and lipid levels, further research should focus on improving CVRM by addressing themes such as adherence to blood pressure and lipid lowering medication, personalized CVRM care and optimizing the efficiency of the organization of the CVRM care program.

Conclusion

The results are compatible with a lower incidence of cardiovascular disease in women and men exposed to long-term integrated cardiovascular risk management. The magnitude of the relation could not be assessed due to unsolvable incomparability between the cohorts due to the nature of routine data collection in primary care.

Abbreviations PoZoB: Praktijk ondersteuning Zuidoost Brabant; JGPN: Julius General Practitioner Network; CVRM: Cardiovascular risk management; ICPC: International Classification of Primary Care; GP: General Practitioner; CVD: Cardiovascular diseases; PN: Practice Nurse; EHR: Electronic Health Record; RCT: Randomized Controlled Trial; AMI: acute myocardial infarction; TIA: transient ischemic attack; PAD: peripheral artery disease; AAA: abdominal aortic aneurysm.

Ethical approval All methods including the care groups protocol for data extraction, identification, examination and follow up were based on the 2012 CVRM Guidelines of the Dutch Society of General Practice and approved by the Julius Centre for Health Sciences and Primary Care, University Medical Centre Utrecht, The Netherlands. Before starting with integrated CVRM care informed consent was given by

patients to use anonymized data for evaluation and scientific research.

Consent for publication Not applicable

Availability of data and materials Anonymized patient data derived from the multidisciplinary information system (Care2U) can be send by mail on request to g.smits@pozob.nl after approval by the care group's Board of General Practitioners.

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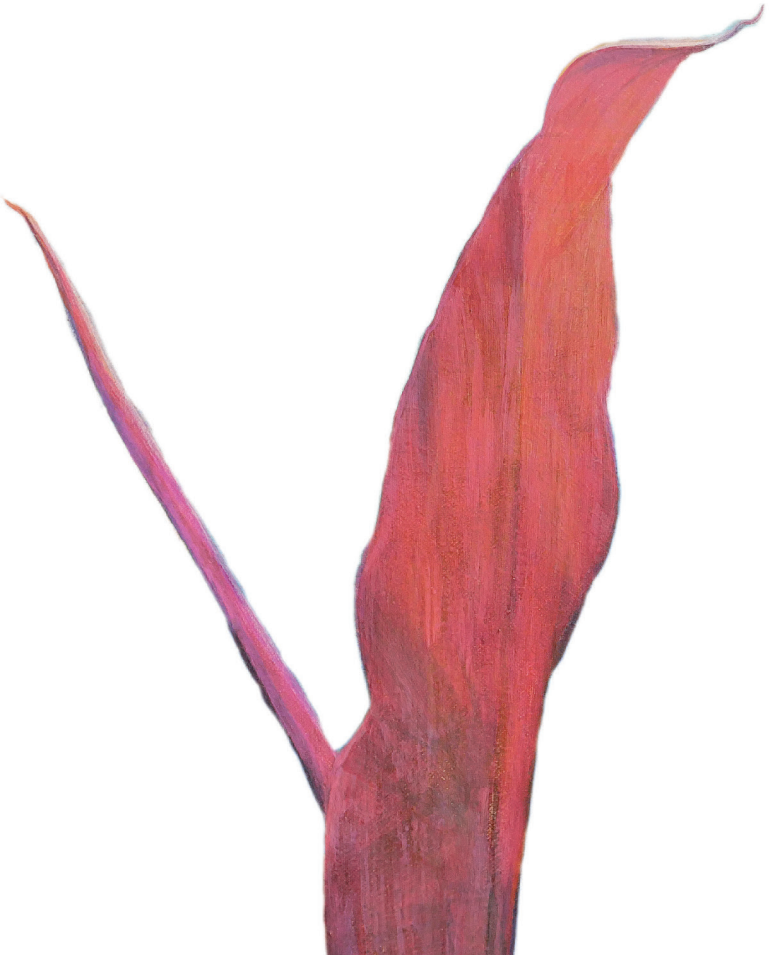
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9

General Discussion

Introduction

Due to an aging population, unhealthy lifestyle, early detection and better treatment options, the number of patients with one or more chronic conditions in general and cardiovascular diseases in particular will rise sharply until 2040 [1]. In The Netherlands, with nearly every citizen registered in a general practice, general practitioners (GPs) often have a long-term and continuous relationship with their patients and thus a complete overview of the patient's physical and mental well-being. Therefore, primary care seems the most appropriate place to organize care for patients with chronic conditions. About 20 years ago, primary care groups were founded and started with the organization and implementation of chronic care programs for diabetes type 2 (DM2), asthma and chronic obstructive pulmonary diseases (A/C) and cardiovascular risk management (CVRM). The CVRM care program started in 2010, and until 2023 many care groups implemented the program, covering 14 million (82%) inhabitants of The Netherlands. On January 1st 2023, nationwide, 470,000 patients with an established CVD and 790,000 high risk patients without established CVD participated in the CVRM care program [2]. Primary care group PoZoB (Praktijk ondersteuning Zuid-oost Brabant) started with integrated CVRM care on April 1st 2010 and implemented the program in 137 general practices between 2010 and 2013. The participation rate of general practices in the PoZoB region was very high. Based on data from one regional health insurer (VGZ), only 5 out of 214 practices (2%) were not affiliated to one of the 3 primary care groups, indicating that the CVRM care program was widely implemented.

Despite the comprehensive support from primary care groups, it is not clear whether the current strategy is optimal, effective, and whether improvements for integrated CVRM care are needed, and for which patients. At the start of the CVRM care program, no formal conditions were imposed, neither on the organization nor on the outcomes of CVRM care, except that existing CVRM guidelines had to be followed as much as possible.

The aims of this dissertation were:

- to describe how the primary care group PoZoB organized and implemented long-term, nurse-led, integrated CVRM care between 2010 and 2020 in general practices in and around Eindhoven, The Netherlands and
- to assess to what extent integrated CVRM care is effective in improving cardiovascular risk factor levels and
- to what extent it leads to a reduction of cardiovascular disease incidence.

This final chapter starts with summarizing the main results of the studies described in this thesis. Next, we discuss the necessity and feasibility to investigate a causal relation between integrated CVRM care and a reduction of cardiovascular events in The Netherlands. We then describe aspects of a learning health care system (LHS)

that can be used as a model to improve the evaluation and ultimately the quality of integrated CVRM care in the future. This chapter ends with recommendations for further research and final conclusions.

Main results

In **chapter 2** we describe the four steps (data extraction; in- and exclusion of eligible patients; consultation and follow-up) the PoZoB primary care group took to implement a nurse-led, integrated CVRM care program in 137 general practices and the support offered to practices: protocols, annual consultation and feedback (C&F) meetings, regular inter vision for practice nurses (PNs), and education for GPs and PNs.

Among the 4,000 patients eligible for integrated CVRM care in 2010, the majority participated between 2010 and 2018. A relatively small group (9%) discontinued the program without a specific reason or on request after an average participation of 4 years. These patients were 4.5 years younger compared to participants who remained in the program, almost all (98%) were without a previous CVD, had less cardiovascular comorbidity and were more often prescribed cardiovascular medication (**chapter 3**).

In patients that participated between 2010 and 2018 we observed an annual decrease in mean systolic blood pressure (SBP) and mean low density lipoprotein (LDL)-cholesterol, a decrease in the number of smokers and an increase in proportion of patients with these three risk factors on target compared to the baseline values in 2010 (**chapter 4**).

We evaluated differences in reaching predefined target level between women and men for 3 biological risk factors (systolic blood pressure, LDL-cholesterol and eGFR) and 4 lifestyle risk factors (smoking, body mass index, physical activity and alcohol intake). Biological and lifestyle risk factors in women with an established CVD were less often on target compared to men with an established CVD. For women without an established CVD compared to men without an established CVD, lifestyle factors were more often on target, while biological risk factors were less often on target (**chapter 5**). Differences between women and men, present at the start in 2013, persisted during 7 years of follow up.

In **chapter 6** we describe that annual practice visitations in 2016, 2017 and 2018 did not improve overall performance of the GP on registration and performance on outcomes (being on target) in the following year. The 25% lowest performing practices in 2017 improved to the level of all other practices, but this occurred independently of the number of visitations.

When focused on blood pressure only, visitations in 2016 in GP practices that per-

formed under the minimal target (< 51% of participants) for "systolic blood pressure ≤ 140 mm Hg in patients younger than 80 years" led to improvements in 8 out of 11 practices in 2017 (**chapter 7**).

We compared high-risk PoZoB participants free from an established CVD who received long-term, nurse-led, integrated CVRM care and extensive care group support with high-risk patients in the Julius General Practice Network (JGPN) in the Utrecht region who received a diversity of care as usual and integrated care without care group support on the occurrence of cardiovascular disease between 2013 and 2019. Compared to JGPN we observed lower incidences in PoZoB-men for myocardial infarction, transient ischemic attack, stroke and peripheral artery disease and in PoZoB-women for myocardial infarction and stroke. Due to differences in baseline characteristics and a non-randomized design of the study, conclusions on the possible effectiveness of long-term, nurse-led integrated CVRM care should be drawn with caution (**chapter 8**).

Based on the findings of our studies we conclude that the answer to the question whether integrated CVRM care leads to a reduction of cardiovascular events is still not given. In the next paragraph we address the topic whether it is feasible and necessary to investigate a causal relation between integrated CVRM care and a reduction of cardiovascular events.

Is it feasible and necessary to investigate a causal relation between integrated CVRM care and a reduction of cardiovascular events in The Netherlands?

After implementation of the CVRM care program in the PoZoB region, we observed annual improvements on SBP, LDL cholesterol and non-smoking (**chapter 4**). Theoretically, beneficial changes in cardiovascular risk factors such as SBP, LDL cholesterol and smoking will lead to a reduction of cardiovascular events [4–7]. The CVRM care program was primarily designed to improve preventive cardiovascular care and not for research purposes. This hampers the interpretation whether improvements in risk factors are due to the care program or due to natural history of the population. To assess a causal relation between long-term, nurse-led, integrated CVRM care and a reduction in cardiovascular events a randomized study design is the best option. Randomized controlled trials performed in The Netherlands, comparing integrated CVRM care with care as usual, showed no positive effects on risk factors after 1 year [8] or CVD incidence after 6 years follow-up [9]. Contamination may be underlying these findings, meaning that regardless of whether integrated care or non-integrated CVRM care is offered, GPs follow the same guideline targets for SBP and LDL cholesterol. This most likely leads to smaller differences in risk factor levels between the groups, as was seen in the trial of Marchal et al [8]. Small differences in risk factors, and a relatively short follow-up together with overall good quality

of care in the care as usual group due to following the long-standing guidelines for CVRM in The Netherlands make a null result happen. That makes the conduct of a prospective randomized controlled care not feasible, because a very large sample size is needed with very long follow-up (for the events to occur).

An alternative to demonstrate a causal relation is to improve observational data collected in such a manner that it can be used to design a target trial. For that, meeting a number of well-defined conditions is needed [10]. Until now, data collected in the care groups multidisciplinary information system does not meet these conditions.

To obtain insight regarding pulmonary and metabolic co-morbidity we need to integrate data from the current chronic care programs (astma/COPD, diabetes type 2 and CVRM) as it is known that registration in a multidisciplinary information system is better than registration in the patient's EHR [11]. Data from the integrated multidisciplinary information system must then be linked to data from the patient's EHR. This second aspect is important because the EHR contains information that is needed to address the research question: the intervention being carried out, measurements that are collected and possible confounders. Furthermore, EHR data provide information on events and importantly on loss to follow-up such as transfer to a nursing home, moving to another general practice, not willing to participate and death. Such a target trial must be properly set up in advance, at the start of the project.

Given the complexity of conducting a target trial due to the extensive registration, it is also worth considering whether an investigation into the causal relation is really necessary, given the widespread implementation of integrated CVRM care in The Netherlands [12] and the existing indirect evidence that risk factor reduction is associated with a reduction in cardiovascular events [4–7].

In summary a target trial seems doable, yet challenging due to the complexity of the study design and the extensive registration. Thus, if we want to continue with long-term, nurse-led, integrated CVRM, we need to integrate the care group data for in-dept analyses to improve registration and outcomes of integrated CVRM care. If we organize the PoZoB primary care group towards a learning health care system (LHS), the execution of a target trial, necessary to reliably determine the effectiveness of integrated CVRM care, will be simplified.

The learning health care system

An LHS is defined as "a health care organization with a culture of health system improvement were rapid analyses of internal data are integrated in existing evidence to produce relevant knowledge that is put into practice". It was first described by the institute of Medicine (IOM) in 2007 [13] and can be characterized by five domains:

Science and informatics, Patient-clinician partnership, Incentives, Continuous learning culture and Organizational structure and governance [14]. We describe these domains as a framework for further development of the CVRM care program in daily practice.

Science and informatics

According to Nash et al, the implementation of an LHS in primary care as a way to improve quality of care is still in its infancy. In 2021, they performed a systematic scoping review that resulted in 21 LHSs all appearing in an early stage of development, with only one LHS running uniquely in primary care [15]. Amongst the many obstacles described were the fragmented information across different points of service and the presence of various EHRs that made it difficult to link uniform data across many practices [16,17]. In The Netherlands however, CVRM is one of three chronic disease management programs that were organized by primary care groups for which a multidisciplinary information system was used to collect predefined datasets developed by the Royal Society of General Practitioners [18,19]. The PoZoB care group made the data real-time available for individual practices and gave GPs and PNs the opportunity to (re)act on registration and performance. From 2016 onwards, data on registration and outcomes of integrated CVRM care have been used to compare practice performance with care group performance (**chapter 6**). In the future, the PoZoB care group could focus on involving practices in quality improvement initiatives and the use of "best-practice" performance [20,21].

The first important step to expand and standardize information however, is the integration of data from 3 chronic care programs and linking them to the patient's EHR data.

Patient-clinician partnership (PCP)

Patient-clinician partnership is considered to be one of the most important elements of the LHS [22]. It is possible to define patient-clinician partnership on two different levels. First, in relation to the individual care plan set up with the PN. This could for example mean:

- make patients responsible for their individual care plan, including their willingness to start or increase medication, agreements on biological treatment targets and lifestyle targets;
- ask patients about their preferences on how consultation should take place (physical or online) and their willingness to participate in group lifestyle programs;
- by giving patients access to their individual patient data and
- by providing patients a possibility to comment online on aspects of the integrated care program.

Second, to engage patients in a focus group or advisory board to give feedback on their experiences with the CVRM care program, to advice on availability and accessibility of health care services [14,23].
Although the PoZoB care group supported and encouraged PNs in drawing up an individual care plan (ICP) together with the patient in which treatment goals were recorded and evaluated, the correct use of an ICP has never been evaluated. It is therefore unknown whether its use has led to better treatment adherence. Currently, there is no Patients Advisory Board to advise GPs and PNs on the delivery of chronic care.

Incentives

Two important incentives can be distinguished:

- Incentives to improve registration and quality of care. By participating in the PoZoB care group individual practices agreed to the objectives: delivering quality of care according to evidence-based guidelines, at the lowest possible costs, in primary care if possible and in hospital if necessary. Agreements made between the care groups Board and individual practices were implemented after permission of the members. The incentive is based on the intrinsic motivation of participating practices to improve their performance after given consent for this approach.
- Financial incentives to reward care that is provided. The care group negotiated annually with health insurers on additional renumeration for care provided to participants in a chronic care program. This mainly rewarded volume of care instead of quality of care. Although the renumeration is fixed in recent years, volume is still the most important driver for a financial incentive, despite the missing values regarding registration and outcomes of cardiovascular risk factors that were made visible in the multidisciplinary information system. One may wonder, if lacking registration implicates that care is not delivered or simply not registered. It may be preferred if the primary care group rewards registration (a minimal, fixed registration per patient to ensure that integrated care has been offered by either the PN or the GP) instead of volume (number of patients participating in the care program). Alternatively, the care group could reward a practice at most if registration meets a certain percentage of participants in a chronic care program.

Continuous learning culture

Since the start of the integrated CVRM care program in 2010, the care group has offered various forms of education to both GPs and PNs described in **chapter 2**. Since 2016, regional collaboration with four surrounding hospitals has led to regional transmural agreements (RTAs) and additional education on specific cardi-

ovascular topics (atrial fibrillation, heart failure, acute coronary syndrome, aortic valve disease, stroke and transient ischemic attack). Until recently, the PoZoB care group used a single disease approach for three common conditions. An increasingly older group of participants dealing with multi-morbid conditions is facing complex medication and lifestyle regimens, for whom a standard consultation is insufficient, ineffective and time-consuming for patients as well as for health care providers [24]. This is currently recognized by authorities, who recommend suggestions for the integration of chronic care programs and a patient-centered approach [25]. Potential benefits of this patient-centered approach however, were inconclusive: while improvements in mental health were seen, evidence for improved patient-reported outcomes, medication adherence, patient-related health behavior and provider-related behavior was uncertain. Furthermore, the review indicated that targeting specific problems for patients with co-morbid conditions may be more effective [26]. A scoping review on elements of patient-centered care reported that educational tools for patients such as self-care with pharmacotherapy or empowerment strategies to promote a positive attitude, knowledge and skills to enhance health and, on the other hand, appropriate training for health care providers such as feedback by trainers were associated with positive health outcomes [27].

Research on integrating chronic care programs where patient and caregiver satisfaction has been taken into account is currently underway [28]. A first pilot in the north-western part of The Netherlands showed that involving local stakeholders, sufficient time and renumeration were necessary for a successful transformation to a patient-centered approach, leading to a better understanding of the patient's wishes and priorities and subsequently to better patient and caregiver satisfaction [29].

Within the PoZoB care group, PNs have been included in the transformation from a protocolized, single disease-approach to a personalized care-approach ("Het andere gesprek"), in which the patient's wishes and possibilities are explicitly taken into account and ownership of the problem and solution-oriented action are placed with the patient. Solutions in goal-setting and action plans often focus on lifestyle improvements of a single disease [30], therefore this new approach requires sufficient training, because PNs have difficulty letting go of their old way of working [31]. Challenges may be to make this approach mandatory for all PNs and introduce the patient-oriented consultation to GPs.

Organizational structure and governance

The PoZoB primary care group is a cooperative association, initially founded to implement chronic care programs in affiliated general practices. The care group has set itself the goal of contributing in scientific research and to participate in initiatives to improve cardiovascular care together with surrounding hospitals. In the

first years, a number of PhD students worked within the organization, in close collaboration with Tilburg University. Since 2016, the care group started a collaboration with a consortium of 4 regional hospitals ("Nederlands Hart Netwerk; NHN"), whereby regional transmural agreements (RTAs) on 4 important cardiac topics have been made. An RTA CVRM is currently being compiled in which agreements between specialists, GPs, PNs and physician assistants (PAs) are recorded.
In summary, to optimize the evaluation of integrated CVRM care in the future and to meet the conditions for a target trial, it is important that we increase the research potential of available routine data. In addition, we need to support PNs in the transformation from a single disease-approach to a patient centered-approach and finally, we need to take the patient's preferences into account, which most likely will improve both patient and care giver satisfaction.

Final conclusions and recommendations for future research

The outcomes of this thesis showed that progress has been made with the implementation of long-term, nurse-led, integrated CVRM care. This approach has been successfully adopted in the Eindhoven region. We showed improvements in biological risk factors and lifestyle risk factors being on target in patients that participate in the CVRM care program.

The most important, yet still unanswered research question is, whether we can demonstrate a possible reduction in cardiovascular disease incidence due to integrated CVRM care. To demonstrate effectiveness, a target trial will be necessary. This should be done, starting with an inventory following the target trial criteria [10]. Second, to optimize the target population for integrated CVRM care, both time restricted and age restricted eligibility could be evaluated. Third, studies into cost-effectiveness should be performed.

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10

Summary in English and in Dutch

Summary in English

Cardiovascular diseases (CVD) are the leading cause of death in Europa as well as in the rest of the world. In addition, CVD are responsible for a reduced quality of life for the individual patient and for enormous costs for society as a whole. To reduce the burden of CVD it is important to treat cardiovascular risk factors, including high blood pressure, high cholesterol, smoking, physical inactivity, unhealthy food habits and obesitas.

In The Netherlands, primary care has been charged with preventive tasks for many years. Since 2005, the prevention of a number of chronic conditions has been added: diabetes mellitus type 2, astma/chronic obstructive pulmonary diseases (COPD) and cardiovascular risk management (CVRM). The organization of these chronic care programs is in the hands of primary care groups, to which local or regional general practices are affiliated. The care programs are organized according "chronic care model (CCM)" principles, the use of evidence-based guidelines, a care design focused on patients with one or more chronic diseases and a team of care givers who work together to provide the best possible care and to support the patient with managing the chronic condition him-/herself. The central care-giver is a practice nurse (PN), a nurse with additional training in protocolized care, supervised by the general practitioner (GP).

The CVRM care program comprises:

- detection of possible patients based on National Guidelines for CVRM,
- identifying risk factors by means of anamnesis, physical examination and laboratory testing to determine eligibility,
- drawing up a treatment plan and iiii) ensure regular follow-up.

In 2010 seven care groups, including the PoZoB primary care group, started with the CVRM care program and in 2023 1.3 million patients throughout The Netherlands participated in the program, 500,000 with and 800,000 without an established cardiovascular disease. Until now, it is not clear wether participation in the program leads to a reduction in occurring cardiovascular events. The few studies that have been conducted in The Netherlands, have not been able to provide a clear answer tot his question.

This theses describes:

- the implementation of the CVRM care program in the PoZoB between 2010 and 2013,
- the steps taken to improve the CVRM care program and
- a comparison between PoZoB patients participating in a long-term, nurse-led, integrated CVRM care program with extensive care group support and Julius GP Network-patients receiving CVRM care from their GP and sometimes from a PN without further support.

Chapter 2 describes the working method the PoZoB care group used to implement nurse-led, integrated CVRM care in affiliated practices. The work method comprised four steps:

- identification of potentially eligible patients based on ICPC and ATC codes from the patients electronic health record (EHR),
- inclusion/exclusion for participation in the CVRM care program,
- inviting patients for a consultation to determine cardiovascular risk factors based on anamnesis, physical examination and laboratory testing and then drawing up a treatment plan together with the patient and
- make arrangements for regular follow-up to evaluate agreed treatment goals.

Of 3,997 patients that started on April 1st 2010 with nurse-led, integrated CVRM care, 2,807 patients still participated after 8 years and 1190 patients (29.8%) had discontinued the program before April 1st 2018. 355 patients (8,9%) discontinued without a specific reason or on request after participating around four years. Compared to patients who participated in the program for the entire 8 years, patients who discontinued without a reason or on request were younger (62 years vs 67 years), were nearly all without an established CVD (1.7% vs 22.6%), had less often atrial fibrillation (1.1% vs 7.2%), congestive heart failure (0.3% vs 1.2%) and chronic kidney disease (0.0% vs 4.5%) and finally, were taking twice as often blood pressure lowering and cholesterol lowering medication (**chapter 3**).

In **chapter 4** we show the results of long-term, nurse-led, integrated CVRM care. Three cardiovascular riskfactors (systolic blood pressure (SBP), low density lipoprotein (LDL)-cholesterol, non-smoking) improved annually between 2011 and 2018 in participants with and without an established CVD. Moreover, the number of participants on target for SBP (≤ 140 mm Hg) and LdL-cholesterol (< 2.6 mmol/l) increased, as well as the number of participants with a combination of 3 risk factors on target.

In **chapter 5** we evaluated sex differences and trends in the management of 3 biological riskfactors (SBP, LDL-cholesterol and eGFR) and 4 lifestyle risk factors (body mass index: BMI, non-smoking, responsible alcohol intake and sufficient daily exercise according to the Dutch Norm of Healthy Exercise). The (usually) small differences, present between men and women in 2013, were still present in 2019. The mean number of lifestyle riskfactors on target was slightly better in women compared to men, overall and in patients without an established CVD. The mean number of biological risk factors on target was better in men overall, in men without an established CVD and in men with an established CVD.

Overall, in both men and women, the percentages of 5 out of 7 riskfactors on target improved between 2013 and 2019: SBP, LdL-cholesterol, eGFR, non-smoking and responsible alcohol intake, the BMI remained unchainged and the number of

participants reporting sufficient exercise decreased. We observed the largest difference between men and women on target for LDL-cholesterol and for eGFR, where men were more often on target than women. Finally, cholesterol lowering medication was clearly more often prescribed to men than to women.

Based on data from the multidisciplinary information system (Care2U), the care group started with comparing individual (practice) performance (registration and outcomes) with care group performance in 2016. Standards were set for "best practice", "average performance" and "low performance" for a number of registration and outcome indicators. With 3-monthly rapports, individual practices could compare their performance with care group performance and work on improvements. Practices were visited by a staff member at least once a year to evaluate practice performance and offer support, if necessary. In **chapter 6**, we evaluated whether these practice visitations in 2016, 2017 and 2018 led to improvements in registration and outcomes in 2017, 2018 and 2019, respectively. Neither individual patient data nor aggregated data on practice level showed clinically relevant improvements in both completeness of registration and in reaching predefined targets. Yet, we found the largest improvements in practices with 2 or more visitations.

We further evaluated the 25% lowest performing practices in 2017 to see whether the number of visitations influenced completeness of registration and outcomes and we observed statistically significant improvements in completeness of registration and in reaching predefined targets in 2018. Although the largest improvements were seen in the group visited twice or more, differences between visitation groups were not statistically significant.

In **chapter 7** we describe the results of practice visitations in 2016 in 11 practices that performed below a minimal standard for one outcome indicator: "systolic blood pressure ≤ 140 mm Hg in patients < 80 years". With comprehensive problem analysis and targeted support, 8 out of 11 practices improved above the minimal standard. The original paper was published in 2017 in "Huisarts en Wetenschap".

The paper in **chapter 8** was given the enigmatic title: Does long-term, nurse-led, integrated CVRM care reduce CVD incidence in primary care? In fact, this was one of our main objectives for this thesis. We compared the disease incidence of 5 cardiovascular diseases from 2013 to 2019 between PoZoB-participants without an established CVD that received long-term, nurse-led, integrated CVRM care plus extensive care group support and Julius General Practitioner Network (JGPN)-participants without an established CVD that received CVRM care from their GP and sometimes from a PN without further support. The disease incidence per 1,000 patient years (PoZoB vs JGPN) was 17.5 vs 22.2 for men and 13.6 vs 15.8 for women. The disease incidence was lower in PoZoB-men compared to JGPN-men for acute

myocardial infarction (AMI), transient ischemic attack (TIA), cerebral vascular incident (CVA) and peripheral artery disease (PAD) and higher for abdominal aortic aneurysm (AAA). The disease incidence was lower in PoZoB-women for AMI and CVA, equal for PAD and higher for TIA and AAA. Conclusions regarding the reliability of these outcomes should be drawn with great caution due to the observational design and the risk of bias.

In **chapter 9** the main results are summarized. Next, we make proposals to improve data collection with the aim of carrying out a target trial and finally, we used 5 principles of the learning health system (LHS) to discuss improvements of CVRM care and we make proposals to increase the effectivity of the CVRM care program.

Wetenschappelijke samenvatting in het Nederlands

Hart- en vaatziekten (HVZ) zijn zowel in Europa als wereldwijd de belangrijkste doodsoorzaak. Daarnaast zijn HVZ verantwoordelijk voor een verminderde kwaliteit van leven voor de patiënt en enorme kosten voor de samenleving in zijn geheel. Hart- en vaatziekten (HVZ) worden vooral veroorzaakt door een ongezonde leefstijl, met hoge bloeddruk, hoog cholesterol, roken, onvoldoende beweging en ongezonde voeding als belangrijkste risicofactoren. Er is overweldigend bewijs dat het terugdringen van deze risicofactoren het risico op (nieuwe) HVZ vermindert.

Preventie, of het voorkomen van HVZ is van het grootste belang. Zo'n 15 jaar geleden is in Nederland een start gemaakt met een geïntegreerde aanpak van risicofactoren voor HVZ, waarbij d.m.v. multidisciplinaire interventies getracht wordt de kans op een eerste of een nieuw cardiovasculair event (CVE) te verminderen. Dit zogenaamde geïntegreerde cardiovasculair risico management (CVRM) wordt aangeboden in de eerste lijn en is gebaseerd op principes van het chronische zorgmodel, te weten:

- een gecoördineerde samenwerking tussen verschillende zorgverleners die als doel hebben de zelfredzaamheid van de patiënt te verbeteren,
- een centraal aanspreekpunt (de praktijkondersteuner huisartsen: POH),
- het aanbieden van "evidence-based" zorg volgens de meest recente inzichten,
- gebruik makend van klinische informatie systemen voor data verzameling en evaluatie doeleinden,
- een patiënt die gemotiveerd is en gestimuleerd wordt om zijn chronische aandoening zoveel mogelijk zelf te managen en regie te houden over zijn/haar behandeldoelen.

De organisatie van het CVRM zorgprogramma is in handen van zogenaamde zorggroepen, waarbinnen lokale of regionale zorgaanbieders (voornamelijk huisartsen) zijn verenigd. Het CVRM zorgprogramma omvat het opsporen van patiënten die in aanmerking komen voor deelname aan het programma en de behandeling en het opvolgen van aanwezige risicofactoren, zoals hoge bloeddruk en cholesterol, roken, overgewicht, onvoldoende lichaamsbeweging, ongezonde voeding en psychische stress. De begeleiding wordt gedaan door de POH, daarbij gesuperviseerd door de huisarts.

In 2010 zijn de eerste 7 zorggroepen gestart met de uitrol van het zorgprogramma CVRM, onder wie de zorggroep PoZoB (Praktijkondersteuning Zuid-oost Brabant) en medio 2023 nemen in Nederland 1,3 miljoen patiënten deel aan het CVRM zorgprogramma, 500.000 met een doorgemaakte HVZ en 800.000 met een hoog risico op het krijgen van een HVZ. Tot op heden is niet duidelijk of het CVRM zorgprogramma effectief is, d.w.z. dat niet duidelijk is of (langdurige) deelname aan het programma ook daadwerkelijk leidt tot een vermindering van het optreden van

(nieuwe) HVZ. De schaarse gerandomiseerde onderzoeken die zijn uitgevoerd hebben die vraag niet eenduidig kunnen beantwoorden. Het indirecte bewijs wat tot nu toe voorhanden is, gaat uit van langlopende cohort studies die beperkte zeggingskracht hebben.

Dit proefschrift beschrijft

- hoe de zorggroep PoZoB tussen 2010 en 2013 het CVRM zorgprogramma in 137 huisartspraktijken geïmplementeerd heeft
- welke stappen zijn gezet in de jaren nadien om de kwaliteit van de geleverde zorg te verbeteren en
- een vergelijking tussen PoZoB-deelnemers zonder doorgemaakte HVZ die tussen 2013 en 2019 deelnamen aan het CVRM zorgprogramma met patiënten uit het Julius Huisartsen Netwerk (JHN) zonder HVZ die in dezelfde periode CVRM zorg ontvingen van de huisarts en soms van een POH.

In **Hoofdstuk 2** beschrijven we de stappen die de zorggroep heeft gezet om het CVRM zorgprogramma in de aangesloten praktijken te implementeren. Deze stappen waren:

- identificatie van patiënten aan de hand van ICPC en ATC codering in het huisartsinformatie systeem (HIS),
- bepaling van inclusie of exclusie voor deelname aan het CVRM zorgprogramma. Patiënten die al een hartvaatziekte hadden doorgemaakt kwamen automatisch in aanmerking voor deelname. Bij patiënten zonder hartvaatziekte werd d.m.v. anamnese, lichamelijk onderzoek en laboratoriumonderzoek het 10 jaar hart-vaat risico bepaald door de POH. Nadat de patiënt toestemming had gegeven voor deelname werd
- hij/zij uitgenodigd voor het opstellen van een behandelplan, waarbij aandacht werd geschonken aan medicamenteus behandelbare risicofactoren en verbetering van ongezonde leefstijlfactoren. Tot slot werd de patiënt
- uitgenodigd voor regelmatige controles om het afgesproken behandelplan te evalueren en behandeldoelen aan te passen.

We concludeerden dat betrokkenheid van gemotiveerde huisartsen, een gestructureerde aanpak met adequate codering van diagnosen en risicofactoren, centrale dataregistratie en voldoende ondersteuning door de zorggroep belangrijke voorwaarden zijn voor een succesvolle implementatie van het CVRM zorgprogramma.

In **hoofdstuk 3** beschrijven we dat van de 3997 deelnemers die op 1 april 2010 gestart waren met het CVRM zorgprogramma, na 8 jaar 1190 deelnemers (29,8%) voortijdig waren gestopt. Van deze 1190 deelnemers waren er 355 (8,9%) gestopt zonder duidelijke reden of op eigen verzoek, na gemiddeld 4 jaar deelname. In vergelijking

met de deelnemers die de volle 8 jaar aan het CVRM zorgprogramma deelnamen, waren deze 355 vroegtijdige stoppers jonger (62 vs 67 jaar), hadden bijna nooit een eerdere hartvaatziekte gehad (1,7% vs 22,6%), hadden minder vaak cardiovasculaire co-morbiditeit (boezemfibrilleren: 1,1% vs 7,2%; hartfalen: 0,3% vs 1,2%; chronische nierschade: 0,0% vs 4,5%) en gebruikten twee keer zo vaak bloeddrukverlagende en cholesterolverlagende medicatie. Het exploreren van mogelijke redenen om te stoppen en het aanbieden van een individuele follow-up kan eraan bijdragen dat patiënten toch blijven deelnemen aan het CVRM zorgprogramma.

In **Hoofdstuk 4** laten we zien dat bij patiënten die tussen 2011 en 2018 deelnamen aan het CVRM zorgprogramma 3 belangrijke risicofactoren verbeterden. Terwijl het aantal deelnemers in die periode toenam van 34.628 in 2011 naar 48.397 in 2018, gingen de gemiddelde systolische bloeddruk (SBP), het gemiddelde LDL-cholesterolgehalte en het percentage rokers jaarlijks omlaag bij zowel deelnemers met als zonder een doorgemaakte HVZ. Ook het percentage deelnemers met en zonder doorgemaakte HVZ met een SBP ≤ 140 mm Hg en een LDL-cholesterol ≤ 2,5 mmol/l ging jaarlijks omhoog, alsmede het percentage deelnemers met een combinatie van de 3 risicofactoren goed ingesteld. Tot slot stegen ook de percentages deelnemers met bloeddrukverlagende en cholesterol verlagende medicatie jaarlijks. Bij langdurige deelname aan het CVRM zorgprogramma is het mogelijk om jaarlijkse verbeteringen te realiseren in systolische bloeddruk, LDL-cholesterol en rookgedrag, leidend tot een aanzienlijke vermindering van de kans op het krijgen van een (nieuwe) hartvaatziekte.

In **hoofdstuk 5** onderzochten we man-vrouw verschillen in de behandeling van 3 medicamenteus beïnvloedbare risicofactoren (bloeddruk, cholesterol en nierfunctie) en 4 leefstijl factoren (body mass index (BMI), roken, verantwoord alcohol gebruik en beweging) in de periode 2013-2019. Vijf van de 7 risicofactoren (SBP ≤ 140 mm Hg, LdL ≤ 2,5 mmol/l, eGFR ≥ 60 ml/min/1,73 m2, verantwoord alcoholgebruik, roken), verbeterden in de bovengenoemde periode. De gemiddelde BMI veranderde tussen 2013 en 2019 niet en het percentage deelnemers dat aangaf voldoende te bewegen (volgens de Nederlandse Norm Gezond Bewegen) nam in dezelfde periode af. De meestal kleine man-vrouw verschillen die bij aanvang in 2013 aanwezig waren bleven tot 2019 onveranderd aanwezig. Het verschil tussen de percentages niet rokende vrouwen en mannen werd tussen 2013 en 2019 kleiner.

Voor de gehele populatie geldt dat in de periode 2013-2019 het gemiddeld aantal leefstijlfactoren op streefwaarde bij mannen iets lager is dan bij vrouwen, terwijl het gemiddeld aantal medicamenteuze risicofactoren op streefwaarde duidelijk hoger is bij mannen dan bij vrouwen. Dit geldt zowel voor deelnemers zonder doorge-

maakte hartvaatziekte als voor deelnemers met een doorgemaakte hartvaatziekte. De meeste risicofactoren verbeteren tussen 2013 en 2019 bij zowel mannen als vrouwen (SBD, LDL-cholesterol, eGFR, verantwoord alcoholgebruik en roken), de gemiddelde BMI veranderde niet bij zowel mannen als vrouwen en het percentage deelnemers wat aangaf voldoende te bewegen nam af bij zowel mannen als vrouwen. De grootste man-vrouw verschillen waren zichtbaar bij de risicofactoren "LDL ≤ 2,5 mmol/l" en "eGFR ≥ 60 ml/min/1,73 m2", waar mannen duidelijk vaker de streefwaarde haalden dan vrouwen. De resultaten van deze studie laten zien dat de man-vrouw verschillen die in 2013 werden gezien aanwezig bleven tijdens de gehele studie periode. De verschillen in behandeling van leefstijlfactoren waren meestal klein. De verschillen in behandeling van medicamenteuze factoren waren meer uitgesproken, m.n. de behandeling van het LDL-cholesterol en de eGFR, die bij vrouwen duidelijk minder vaak op streefwaarde waren. Tenslotte zagen we dat vrouwen minder vaak cholesterolverlagende medicatie kregen voorgeschreven dan mannen.

In **hoofdstuk 6** hebben we gekeken of praktijkvisitaties tussen 2016 en 2019 leidden tot verbetering van de registraties en de uitkomsten van diverse risicofactoren met als doel om de variatie tussen praktijken te verminderen. Voor deze visitaties werd gebruik gemaakt van 3-maandelijkse rapportages, waarin de registraties en uitkomsten van individuele praktijken werden vergeleken met het gemiddelde van registraties en uitkomsten van de gehele zorggroep. Op basis van deze zorggroep gemiddelden werden normen vastgesteld voor "best practice" en "onder de norm". Deze normeringen werden tijdens visitaties gebruikt om met de praktijk in gesprek te gaan. Aan de hand van een 8-delige vragenlijst werd nagegaan hoe praktijken hun registraties en uitkomsten zouden kunnen verbeteren. De cijfers laten zien dat praktijkvisitaties in 2016, 2017 en 2018 niet leidden tot significante verbeteringen wat betreft registratie en uitkomsten in het daaropvolgende jaar. Als we kijken naar de 25% minst presterende praktijken in 2017, dan zien we dat deze praktijken significant verbeteren in 2018, zowel wat de registratie aangaat alsook de uitkomsten, maar dat dit niet afhankelijk is van het aantal keren dat de praktijk bezocht is. De conclusie was dat praktijkvisitaties in de huidige opzet niet leidden tot verbetering van zowel registratie als uitkomsten van zorg.

Hoofdstuk 7 is een vertaling van een eerder gepubliceerde paper in Huisarts en Wetenschap in 2017. Het beschrijft de relatie tussen praktijkvisitaties en het verbeteren van een specifieke uitkomstindicator, te weten "systolische bloeddruk ≤ 140 mm Hg bij deelnemers jonger dan 80 jaar". Na een of meerdere praktijkbezoeken waarbij de werkwijze in de praktijk werd geëvalueerd verbeterde in 8 van de 11 praktijken bovengenoemde indicator tot boven de minimale norm.

In **hoofstuk 8** wordt de incidentie van 5 cardiovasculaire aandoeningen (acuut myocard infarct: AMI, transient ischemic attack: TIA, cerebro vasculair accident: CVA, perifeer arterieel vaatlijden: PAV en aneurysma van de buikaorta: AAA), opgetreden tussen 2013 en 2019, vergeleken tussen deelnemers aan een integraal CVRM zorgprogramma (PoZoB) en patiënten opgenomen in het Julius Huisartsen Netwerk (JHN) die CVRM zorg van de huisarts ontvingen en soms door een POH, zonder verdere ondersteuning. Na een follow-up van 7 jaar bleek de incidentie per 1000 persoonsjaren PoZoB vs JHN 17,5 vs 22,2 voor mannen en 13,6 vs 15,8 voor vrouwen. Bij mannen werd een lagere incidentie gevonden bij PoZoB-deelnemers voor AMI, TIA, CVA en PAV, en een hogere incidentie voor AAA. Bij vrouwen werd een lagere incidentie gevonden bij PoZoB deelnemers voor AMI en CVA, een vergelijkbare incidentie voor PAV en een hogere incidentie voor TIA en AAA. De conclusie van de studie is dat, ondanks de hoopvolle uitkomsten in het voordeel van integrale CVRM zorg, de betrouwbaarheid van de gevonden resultaten (zeer) beperkt is. De paper doet een aantal voorstellen hoe de observationele data verbeterd kunnen worden zodat ze gebruikt kunnen worden voor een zogenaamde “target trial” omdat een gerandomiseerde onderzoeksopzet om diverse redenen in de Nederlandse situatie niet mogelijk is.

Het proefschrift wordt afgesloten met **hoofdstuk 9** waarin de belangrijkste resultaten worden samengevat. Er zijn tussen 2010 en 2020 vele verbeteringen gerealiseerd, maar een definitief antwoord of integrale CVRM zorg leidt tot een afname van de incidentie van hartvaatziekten is nog steeds niet gegeven. Aan de hand van een vijftal onderdelen van een “lerend zorg systeem” worden voorstellen gedaan welke stappen de zorggroep kan nemen om de zorg verder te verbeteren. Dit betreft o.a. het integreren van de bestaande chronische zorgprogramma’s en een meer holistische benadering van de patiënt en zijn ziekte, waarbij de patiënt nog nadrukkelijker dan nu het geval is de regie krijgt over het zorgproces. De kans is groot dat hierdoor zowel de patiënt tevredenheid als de zorgverleners tevredenheid zullen toenemen. Data integratie en samenwerking met een academisch centrum bieden de mogelijkheid om de effectiviteit van integrale CVRM zorg in de toekomst beter te evalueren.

Dankwoord

Op 25 september 2024 om 17.00 uur, na het voltooien van de samenvatting, staat het proefschrift in grote lijnen op papier. Het treurige is dat ik niet meer precies weet wanneer ik eraan begonnen ben. Dat komt waarschijnlijk ook omdat ik een buitenpromovendus ben en niet aan een regulier promotietraject deelnam. Het was een eenzaam maar fascinerend project waar ik veel van heb geleerd en waar ik veel plezier aan heb gehad. Achteraf heb ik spijt dat ik er niet eerder mee begonnen ben, maar gedane zaken nemen nu eenmaal geen keer. Hoe het ook zei, het promotietraject was voor mij een verrijking, een kadootje!

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De Beoordelingscommissie: Prof. dr. Pim Assendelft, Prof. dr. Geert-Jan Geersing,

Prof. dr. Fabrice Martens, Prof. dr. Frank Visseren en Prof. dr. Oscar Franco wil ik bedanken voor het lezen en beoordelen van het manuscript.

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Tot slot, als je zoals ik met promotieonderzoek begint op een leeftijd dat de kinderen al uit huis zijn, hebben ze er geen last van. Toch zei Eefje regelmatig, als ze uit Eindhoven terug naar huis kwam: "Zit papa weer achter de cijfertjes?". Ik beloof plechtig dat dit niet meer gebeurt. Saskia, je hebt wel eens gezegd dat je me "looser" zou vinden als ik de promotie niet afmaakte. Welnu, ik ben klaar, nu is het jouw beurt. Pim, we gaan nog allerlei leuke dingen doen in Frankrijk, ik heb er zin in. Kinderen, ik ben trots op jullie.

Monique van Vlodrop, het boekje is prachtig geworden. De deur in Grandchamp staat voor jullie open!

Sandra, als (bijna) laatste genoemd, maar eigenlijk moet je bovenaan staan. Je hebt me geen strobreed in de weg gelegd. We hebben al oneindig veel fantastische avonturen beleefd en dat blijven we wat mij betreft doen. Je bent de zon in mijn leven.

Tot slot, mijn ouders, ze zijn al vele jaren geleden overleden. Wat zouden ze trots zijn geweest.

Roermond, 26 september 2024

Curriculum vitae

Geert werd geboren op 24 juli 1956 te Arcen, gemeente Arcen en Velden. Na het Atheneum in Venlo ging hij fysiotherapie studeren in Deventer van 1978 tot 1983. In 1983 startte hij de studie Geneeskunde aan de (toen nog) Rijksuniversiteit Limburg, tegenwoordig Maastricht University. Van 1989 tot 1991 werkte hij als arts-assistent cardiologie in het Maasland ziekenhuis te Sittard en het Universiteitsziekenhuis te Antwerpen, België.

Van 1992 tot 1994 volgde hij de huisartsopleiding in Maastricht en in 1994 startte hij als huisarts in een duo-praktijk in Posterholt, Limburg, waar hij tot 2002 werkte. In 2002 en 2003 werkte hij als huisarts in West-Australië. Na terugkomst in Nederland begon hij als solist in Weert waar hij werkte tot 2020. In 2009 en 2010 organiseerde hij samen met de Hagro-manager Pauline Roelands programmatische CVRM zorg voor de huisartsen in Weert. De meeste praktijken in Weert zochten in 2010 vervolgens aansluiting bij de zorggroep PoZoB te Veldhoven voor de chronische zorgprogramma's. In 2011 startte hij als stafarts CVRM bij PoZoB voor 4 uur per week om programmatische CVRM zorg verder te ontwikkelen en te verbeteren. In 2013 en 2014 volgde hij de opleiding tot kaderhuisarts Hartvaatziekten, georganiseerd door Maastricht University. In 2020 begon hij met het promotietraject en tot op heden werkt hij parttime als stafarts CVRM bij PoZoB.

Geert is getrouwd met Sandra Driessen en heeft vier kinderen: Nina, Pim, Saskia en Eefje.

