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A randomized controlled trial in Norwegian pharmacies on effects of risk alert and advice in people with elevated cardiovascular risk

Karianne Svendsen[a,*], Vibeke H. Telle-Hansen[b], Lisa T. Mørch-Reiersen[c], Kjersti W. Garstad[c], Kari Thyholt[b], Linda Granlund[b], Hege Berg Henriksen[a], Jon Michael Gran[d], David R. Jacobs Jr[e], Kjetil Retterstøl[a,f]

[a] Department of Nutrition, Institute of Basic Medical Sciences, University of Oslo, P.O. Box 1046 Blindern, 0317 Oslo, Norway
[b] Mills AS, P.O. Box 4644 Sofienberg, 0506 Oslo, Norway
[c] Boots Norge AS, Maridalsveien 300, 0872 Oslo, Norway
[d] Oslo Centre for Biostatistics and Epidemiology, Oslo University Hospital and University of Oslo, Norway
[e] Divison of Epidemiology & Community Health, School of Public Health, University of Minnesota, 1300 S. 2nd Street, Minneapolis 55455, MN, United States
[f] The Lipid Clinic, Oslo University Hospital Rikshospitalet, P.O. Box 4950, Nydalen, 0424 Oslo, Norway

A B S T R A C T

We investigated if alerting subjects to elevated total cholesterol (TC), hemoglobin A1c (HbA1c) and blood pressure (BP) (cardiovascular disease (CVD) risk factors that are usually asymptomatic), and if providing advice would result in reduced risk. We conducted a multicenter (50 community pharmacies) parallel three-arm 8-week randomized controlled trial (RCT) with a 52-week follow-up visit. During six days of screening, TC, HDL- and LDL-cholesterol, triglycerides, HbA1c, BP and body mass index (BMI) were assessed in 1318 individuals. Of these, 582 with a measured and predefined elevated ad hoc CVD risk score were randomized to either Alert/advice (n = 198) (immediately alerted of their screening result and received healthy lifestyle-advice), Advice-only (n = 185) (received only advice) or Control (n = 199) (not alert, no advice). Changes in risk score and self-reported health-related behaviors (diet, alcohol, physical activity) were assessed in pharmacies after 8 weeks (N = 543; 93%). Although the primary analysis showed no significant difference between groups, the Control group had the largest reduction in risk score of 14%. The total (uncontrolled) sample (N = 543) reduced the risk score by 3.2% beyond estimated regression towards the mean and improved their health-related behaviors. Among the 65% (n = 377) who returned 52 weeks after baseline, 14% reported started using CVD preventive medication after the screening. The study demonstrated that while assessing risk factors and behaviors in pharmacies proved efficient and possibly led to a small risk decrease, alerting people to their screening result did not seem to be more effective than a self-directed approach. ClinicalTrials.gov identifier: NCT02223793.

1. Introduction

Important risk factors for cardiovascular diseases (CVD) are high LDL-cholesterol (LDL-C), blood pressure, body mass index (BMI) and blood glucose and/or type 2 diabetes (T2D) (Kaplan et al., 2017). All of these risk factors are modifiable through health-related behavior changes in diet, physical activity and by smoking cessation (World Health Organization, 2010; Global Burden of Disease Mortality Causes of Death Collaborators, 2016). Even small changes in dietary factors affecting the CVD risk factors are associated with clinically meaningful reductions in CVD events (World Health Organization, 2010; Law et al., 1994). High levels of LDL-C, blood glucose and blood pressure are however usually asymptomatic, which can be exemplified by the estimation that over 50% of individuals with T2D are undiagnosed (Whiting et al., 2011). Without knowing one's risk factor levels, targeted decisions on how to lower risk are not likely (Mooney and Franks, 2011).

Randomized controlled trials (RCT) have demonstrated that intensive diet and lifestyle interventions can reduce risk of T2D and CVD, both in primary- (Hoskin et al., 2014; Hjermann et al., 1981; Estruch et al., 2018) and secondary prevention (Pi-Sunyer et al., 2007). A common feature of such intervention studies is structured counseling by dietitians and physicians, usually in health care clinics, (Estruch et al., 2018) research clinics or in hospitals (Sialvera et al., 2017). However, specialized clinics suffer from high costs and limited capacity. Alternatively, intervention strategies involving community health workers and pharmacists hold considerable promise for improving public health (Jeet et al., 2017). We have previously demonstrated the potential of

* Corresponding author at: P.O. Box 1046 Blindern, 0317 Oslo, Norway.
E-mail addresses: karianne.svendsen@medisin.uio.no (K. Svendsen), vtelle@oslomet.no (V.H. Telle-Hansen), lisa.therese.morch-reiersen@sykehusapotekene.no (L.T. Mørch-Reiersen), kwgarstad@gmail.com (K.W. Garstad), kari@foseninnovasjon.no (K. Thyholt), Linda.Granlund@helsedir.no (L. Granlund), h.b.henriksen@medisin.uio.no (H.B. Henriksen), j.m.gran@medisin.uio.no (J.M. Gran), jacob004@umn.edu (D.R. Jacobs Jr), kjetil.retterstol@medisin.uio.no (K. Retterstøl).

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Acronyms

ASCVD	Atherosclerotic cardiovascular disease
BMI	Body mass index
CVD	Cardiovascular disease
FFQ	Food frequency questionnaire
HbA1c	Hemoglobin A1c
LDL-C	Low density lipoprotein-cholesterol
LR	Linear regression
RCT	Randomized controlled trial
RTM	Regression towards the mean
TC	Total cholesterol
T2D	Type 2 diabetes
VISA (-study)	Vascular lifestyle-Intervention and Screening in pharmacies

pharmacies as a source to identify individuals who are unaware of their high total cholesterol (TC) concentration (Svendsen et al., 2018a). Conversely, we do not know the effects of alerting individuals to their elevated CVD risk factors. The concept is, however, not new. Waldron et al. (2011) stated that people's awareness of their own risk could encourage them to take actions that reduce that risk, especially if risk was high. Our overall aim was to study if alerting subjects to their elevated symptom-free CVD risk factors and providing simple advice would lead to changes in CVD risk score, risk factors and health-related behaviors (composite foods, physical activity, smoking and alcohol) when performed in community pharmacies. The a priori primary hypothesis was that CVD risk factor alert and/or health-related behavior would lead to changes in CVD risk score over an 8 weeks period compared with a control group that received neither alert nor advice.

2. Methods

2.1. Study design

This study was a parallel three-group 8-week RCT implemented within the Vascular lifestyle-Intervention and Screening in pharmacies (VISA) study (Svendsen et al., 2018a). Pharmacy staff screened volunteers for eligibility during September 8–13, 2014, in 50 community pharmacies (Boots Norge AS) countrywide in Norway. The protocol included biochemical and anthropometric measures and questionnaires that resulted in calculation of an ad hoc CVD risk score (CVD risk score) that also was used to assign participants to groups. Changes in the CVD risk score, risk factors and health-related behaviors were measured and compared after 8 weeks (end of intervention) and after 52 weeks (follow-up). All participants provided verbal and written informed consent. The study received ethical approval from the Norwegian Regional Ethical Committee Health South–East (reference number 2013/1660) and was conducted in accordance with The Helsinki Declaration. National Institutes of Health, ClinicalTrials.gov identifier: NCT02223793. Reporting of this paper is aligned with CONSORT standards (CONSORT, 2010).

2.2. Biochemical and anthropometric measures

The protocol included biochemical and anthropometric screening of lipids (TC, HDL-C, LDL-C, triglycerides), hemoglobin A1c (HbA1c), blood pressure, height, and weight performed by pharmacy staff (pharmacists, technicians or nurses) in a private room within each pharmacy. The initial step was finger-prick measurements of lipids and HbA1c, both by using the measurement device Alere Afinion™AS100. The device calculated LDL-C using Friedewald's formula. At triglycerides > 4.52 mmol/L, LDL-C was not calculated, and at triglycerides > 7.34 mmol/L, HDL-C could not be measured. After waiting for about 5 min, two consecutive measurements of blood pressure were performed seated by A&D Medical blood pressure Monitor™ Model UA-767Plus30. The average of the two measurements was recorded. Standing height was measured using a wall mounted height board with erect posture and feet against the baseboard. Participants were weighed on a digital scale without shoes and in light clothing (National Health and Nutrition Examination Survey, 2004). To ensure that the protocol was similar in all pharmacies, standardized operating procedures were prepared for each study visit. At baseline, a common procedure was prepared for each of the groups. Pharmacy staff completed practical training and an online e-learning course prior to each study visit.

2.3. Eligibility criteria screening

Volunteers could only attend the screening if they fulfilled the following inclusion criteria: Age ≥ 18 years, not pregnant/lactating and not taking lipid lowering-, blood pressure lowering-, or anti-diabetic-medication. Furthermore, no history of CVDs, T2D or type 1 diabetes mellitus was allowed. Participants also had to understand Norwegian.

2.4. Randomization (baseline)

Screening-results were recorded in an electronic program created by programmers in LINK medical Research AS Oslo, Norway (not otherwise involved in the study). The program calculated a predefined CVD risk score that was used to assign participants to the RCT. The CVD risk score was a summarization of scores ranging from zero (favorable measures) to four (very unfavorable measures), assigned for each of TC,

Table 1
Individual scores for each risk factor used to calculate ad hoc risk score.

	Score			
	0	1	2	4
Systolic and diastolic blood pressure[a]	< 131 sys and/or < 86 DIA mm Hg	SYS BP ≥ 131 and/or DIA ≥ 86 mm Hg	SYS BP ≥ 140 and/or DIA ≥ 90 mm Hg	SYS BP ≥ 160 and/or DIA ≥ 100 mm Hg
Total cholesterol	< 5 mmol/L	≥5.00 mmol/L	≥6.00 mmol/L	≥7.00 mmol/L
HDL-cholesterol[b]	> 1.0 mmol/L	< 1.0 mmol/L		
HbA1c	< 5.6%	≥5.6%	≥5.8%	≥6.4%
Body mass index	< 30 kg/m^2	> 30 kg/m^2		
Age	> 50 years	< 50 years	≤40 years	

HDL, high density lipoprotein. HbA1c, hemoglobin A1c. BMI, Body mass index.
[a] Mean of two measurements was recorded. Only the highest value of Systolic and diastolic blood pressure was included in risk score calculation.
[b] If HDL was not calculated (triglycerides were > 7.34 mmol/L), score 0 was assigned HDL.