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

Karianne Svendsen, Vibeke H. Telle-Hansen, Lisa T. Mørch-Reiersen, Kjersti W. Garstad, Kari Thyholt, Linda Granlund, Hege Berg Henriksen, Jon Michael Gran, David R. Jacobs Jr, Kjetil Retterstøl

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 (Pl-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...
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, LDL-C, HbA1c, body mass index and age. 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).

### Table 1

| Score | 0 | 1 | 2 | 4 |
|-------|---|---|---|---|
| Systolic and diastolic blood pressure* | < 121 sys and/or < 86 DIA mm Hg | SYS BP ≥ 121 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 | > 1.0 mmol/L | < 1.0 mmol/L | | |
| HbA1c | < 5.6% | ≥ 5.6% | ≥ 5.8% | ≥ 6.4% |
| Body mass index | < 30 kg/m² | ≥ 30 kg/m² | | |
| Age | > 50 years | < 50 years | | ≤ 40 years |

* Mean of two measurements was recorded. Only the highest value of Systolic and diastolic blood pressure was included in risk score calculation.

* If HDL was not calculated (triglycerides were > 7.34 mmol/L), score 0 was assigned HDL.
HDL-C, HbA1c, blood pressure, BMI and age following the convention of Table 1. Age was included because presence of elevated CVD risk factors is more alarming in younger age (Kaplan et al., 2017). A CVD risk score of ≥ 4 served as inclusion criteria because it indicated moderately elevated risk of CVD (World Health Organization, 2010). The exceptions were if HbA1c ≥ 7.0%, TC ≥ 12.00 mmol/L, systolic blood pressure ≥ 170 mm Hg and/or diastolic blood pressure ≥ 100 mm Hg; these participants were given advice and excluded from further study participation. Participants were randomized using block size 9, stratified by sex and pharmacy to: Alert/advice, Advice-only or Control, in the ratio 1:1:1.

2.4.1. Alert/advice intervention group
Participants in the Alert/advice group received advice on health-related behaviors to reduce CVD risk verbally and in the form of an intervention brochure. To insure that participants understood their numeric risk factors (Rothman et al., 2008), participants were alerted to their CVD risk factors using a “know your risk factors-card” developed by the VISA-study investigators. Here, level of each risk factor was categorized into predefined color-zones according to general recommendations (Piepoli et al., 2016); green (favorable), yellow (slightly unfavorable) and orange (unfavorable) and red (clearly unfavorable). Pharmacy staff was requested to give advice on risk factors corresponding to ≥ yellow color-zone.

2.4.2. Advice-only intervention group
At baseline, the Advice-only group received the intervention brochure, of which pharmacy staff addressed advice on health-related behaviors, but no risk alert. They were told their result would be available at the 8-week visit.

2.4.3. Control group
The Control group received neither risk alert nor intervention brochure at baseline, but was told that their result would be available at the 8-week visit.

2.5. 8-Week visit (end of intervention)

The 8-week visit included an in-pharmacy screening for the CVD risk factors and alerting all participants to their screening result (same as Alert/Advice at baseline) and possible changes from baseline. Those in the Control group also received the intervention brochure. Participants were informed that they would be invited back for a follow-up visit, 52 weeks after baseline.

2.6. 52-Week follow-up visit

Prior to the 52-week follow-up visit, participants who had completed the RCT were given an appointment at the same place, weekday and time as at the 8-week visit if possible. The procedure for the 52-week follow-up visit was similar to the 8-week visit.

2.7. Questionnaires

The protocol included three questionnaires: screening questionnaire, food frequency questionnaire (VISA-FFQ) and a follow-up questionnaire.

2.7.1. Screening questionnaire
Prior to the screening, participants filled out a screening questionnaire (developed by the VISA-study investigators) which had been pretested and described previously (Svendsen et al., 2018a). Data obtained from the questionnaire included age, sex, highest attained educational level, smoking status and prevalence of CVD in first-degree relatives.

2.7.2. VISA-FFQ

Participants self-reported their health-related behaviors through the validated 62-item VISA-FFQ, at all visits (Svendsen et al., 2018b). The FFQ covers habitual dietary intake (grams per day) of foods eaten the last 1–2 months, including both frequency and amount of food item. For the purpose of this paper, foods were combined into composite food groups. For example, SFA dairy consisted of whole/high fat milk, milk products and cheese. VISA-FFQ also assesses number of cigarettes/day and length of moderate intensity- and vigorous intensity-physical activity (Henriksen et al., 2018).

2.7.3. Follow up-questionnaire

At the 52-week follow-up visit, a four-page follow-up questionnaire developed by the VISA-study investigators was completed by participants. The questionnaire was intended to tell how participants perceived the screening result and to study one-year effects of the RCT. For the purpose of this paper, we used data from the question (translated): “To the best of your recollection, did you experience during the examination last year that TC, HbA1c and/or blood pressure were higher than expected, lower than expected, as expected or do not know/do not remember”. Moreover, we used self-reported information on physician control for measures of TC, HbA1c/blood glucose and blood pressure and medication initiation during the previous year.

2.8. Outcomes

The primary outcome was change in CVD risk score from baseline to the 8-week visit between intervention and control groups. Secondary outcomes were change in CVD risk factors and health-related behaviors between baseline, 8- and 52-week visits both between- and within groups. Other secondary outcomes included observing the uncontrolled trends for the total sample in CVD risk score from baseline to the 8-week visit, to describe how the screening result was perceived at baseline, and to assess the frequency of physician control and medication use reported at the 52-week visit.

2.9. Statistics

Continuous variables were presented with mean and standard deviation (SD) and with mean difference and 95 percentage confidence intervals (95% CI) when approximately normally distributed. Median and quartiles (Q) were given for non-normally distributed data, whereas categorical variables were described by frequencies (n/N) and percentages. Statistical description and analyses of data were performed using SAS software version 9.4 for Windows if not otherwise specified. Significance level was set to 5% (two-sided).

The primary outcome, change in CVD risk score between groups, was assessed using linear regression (LR) of which 2 degrees of freedom F-test was the primary analysis for the 8-week visit. Only complete cases were included. We ran unadjusted and analyses adjusted for age and sex, and included pharmacy as random effect in a linear mixed model. As a secondary approach, we used multiple imputations to test the sensitivity for missing observations (the 39 participants who did not return at the 8-week visit) (IDRE Statistical Consulting Group, 2016). Findings were very similar to complete case analysis and are therefore not presented. Secondary outcomes (change in CVD risk factors) were analyzed using unadjusted and age and sex adjusted LR between baseline and 8-week visit and between 8- and 52-week visits adjusted for baseline. Secondary outcomes (health-related behaviors) were analyzed by Wilcoxon Signed rank test for repeated measures within groups and Kruskal Wallis test of differences between groups.

Other secondary outcomes were analyzed for the total (uncontrolled) sample. Due to the study’s high cut-off inclusion criteria and repeated measurements, effects of regression towards the mean (RTM) was estimated and accounted for in the total change in CVD risk score (Hannan et al., 1994). We calculated RTM using the fixed cut-point.
censoring (CVD risk score ≥ 4 points), following the method proposed by Hannan et al. (1994). Confidence intervals were calculated based on 10,000 bootstrap samples using the statistical software R.

2.9.1. Power calculation

Sample size was estimated assuming a 10% 8-week reduction in CVD risk score in the Alert/advice group compared with the Control group following the convention of Laake et al. (2007). With significance level 5% (two-sided) and power 80%, the estimated sample size needed in each group was ~200. We assumed ≤ 10% drop out rate in each group, and were aiming to recruit 220 participants in each group.

2.10. Study participants

Out of 1805 that were available for screening for eligibility, 73% (n = 1318) consented and measured the CVD risk factors. Of them, one participant withdrew consent, 656 (49.8%) were excluded due to CVD risk score ≤ 4, and 79 (6.0%) were excluded due to systolic blood pressure ≥ 170 mm Hg (n = 35) and/or diastolic blood pressure ≥ 100 mm Hg (n = 57), HbA1c ≥ 7.0% (N = 5), TC ≥ 12.0 mmol/L (n = 1) (Fig. 1).

In total 582 (44.2%) satisfied the inclusion criteria for the RCT and were randomized as follows; 198 in Alert/advice group, 185 in Advice-only group and 199 in the Control group. After 8 weeks, 543 (93.3%) participants from 48 pharmacies completed the RCT by returning to pharmacies to the 8-week visit (Fig. 1). Fifty-two weeks after baseline, 377 (65%) participated in the 52-week follow-up visit.

3. Results

3.1. Baseline characteristics

We included 582 individuals of whom 28% (n = 165) were men and 72% (n = 417) were women with mean age 56.5 years ± 14.6. There were no significant differences between groups in any baseline characteristics (Table 2).

3.2. Primary outcome

In primary unadjusted analysis, we found that the 8-week RCT was not significantly related to changes in CVD risk score reduction between groups (F-value = 2.78, p = 0.06). Adjustment for age and sex did not substantially alter the unadjusted results. In secondary unadjusted analysis we observed that the Control group reduced CVD risk score by 14.1% (− 0.76 (95% CI: − 1.02 to − 0.50)) compared to 6.7% reduction in the Alert/advice group (primary intervention) (− 0.36 (95% CI: − 0.62 to − 0.09)), p = 0.03. Findings for the less intense intervention group (Alert-only) were close to those for the Control group, with 13.7% risk score reduction (− 0.71 (95% CI: − 0.99 to − 0.44)) (versus control p = 0.8, versus Alert/advice p = 0.06) (Table 3). This pattern of findings persisted even when the 48 level pharmacy variable was added as a random effect.

3.3. Secondary outcomes

We observed significant but small 8-week reductions within one or more groups for TC, LDL-C, HbA1c, systolic- and diastolic blood pressure, but no significant differences between groups (Table 3). These

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**Fig. 1. CONSORT (2010) flow chart of participants in a pharmacy-based randomized controlled trial.**
Mean change in cardiovascular risk factors after an 8-week randomized controlled trial in pharmacies in 2014 (n = 543).

- Reduced their intake of foods high in sugar (soda, sweets etc.) (p = 0.01).
- Within-group changes were accompanied by changes in health-related index.
- Baseline characteristics of the study sample participating in a randomized controlled trial (Table 2).

### Table 2

| Demographics | Alert/Advice (N = 198) | Advice-only (N = 185) | Control (N = 199) |
|--------------|------------------------|-----------------------|------------------|
| % (n/N) | % (n/N) | % (n/N) |
| Men | 28.8 (57/198) | 24.3 (45/185) | 31.7 (63/199) |
| ≤ 13 years of schooling | 54.7 (104/190) | 52.0 (91/175) | 57.7 (109/189) |
| Smokers* | 14.2 (28/197) | 18.7 (34/182) | 20.3 (40/197) |
| CVD in first-degree relatives | 31.0 (61/197) | 25.3 (46/182) | 28.3 (56/198) |
| Risk factors and age | | | |
| Mean ± SD | Mean ± SD | Mean ± SD |
| Age, years | 55.7 ± 14.4 | 57.4 ± 14.6 | 56.5 ± 15.0 |
| HbA1c% | 5.6 ± 0.3 | 5.6 ± 0.3 | 5.6 ± 0.3 |
| Total cholesterol, mmol/L | 6.7 ± 1.1 | 6.6 ± 1.2 | 6.5 ± 1.1 |
| LDL-cholesterol, mmol/L | 4.0 ± 1.0 | 3.9 ± 1.1 | 3.9 ± 0.9 |
| HDL-cholesterol, mmol/L | 1.7 ± 0.5 | 1.7 ± 0.5 | 1.7 ± 0.5 |
| Triglycerides, mmol/L | 2.1 ± 1.3 | 2.1 ± 1.2 | 2.1 ± 1.3 |
| BMI, kg/m² | 27.2 ± 5.2 | 26.8 ± 4.2 | 27.3 ± 4.6 |
| Systolic blood pressure, mmHg | 133.2 ± 18.2 | 131.7 ± 16.6 | 134.3 ± 15.7 |
| Diastolic blood pressure, mmHg | 81.9 ± 9.8 | 81.8 ± 9.6 | 82.1 ± 9.4 |

**CVD, cardiovascular disease. HbA1c, hemoglobin A1c (HbA1c). BMI, Body mass index.**

### 3.4. Other secondary outcomes

The total (uncontrolled) sample reduced 8-week CVD risk score by −11.5% (−0.61 (95% CI: −0.76 to −0.45)) from 5.3 ± 1.4 at baseline. After correction for expected RTM of −0.44 (95% CI: −0.38 to −0.50) using the calculation of Hannan et al. (1994), the remaining CVD risk score reduction was −3.2% (−0.17 (95% CI: −0.01 to −0.33)). Change in CVD risk score was highest correlated with change in TC calculated with Pearson correlation coefficient r = 0.6 (p < 0.01).

Of the 363 participants that completed the 52-week follow-up questionnaire, 50% (n = 188), 83% (n = 309) and 78% (n = 289) reported that measured TC, HbA1c and blood pressure at baseline, respectively were in accordance with their expectation. There was no significant trend between change in CVD risk score and categories of expectations towards the measured value. On private initiative 31.4% (n = 114), 14.3% (n = 52) and 39.1% (n = 142) had controlled their TC, HbA1c or blood pressure respectively after the 8-week visit. Only acetylsalicylic/other anticoagulants were allowed to be used at baseline. Fifty-two weeks after baseline, use of preventive medication had increased to 14.1% (n = 53). Statins and acetylsalicylic/other anticoagulants were both used by 4.5% (n = 18), anti-hypertensive medication was used by 3.2% (n = 12) and 2.3% used anti-diabetic medication (n = 5).

### 4. Discussion

The formal analysis of the RCT found no significant difference in the primary a priori outcome variable, namely CVD risk score change. Nevertheless, we observed reduced CVD risk score in all participants combined, beyond what would have been expected with RTM. Separate important outcomes of the pharmacy-based screening were identification of 79 subjects with either severe hypertension (blood pressure ≥ 170/100 mmHg), T2D (HbA1c > 7.0%) or severe hypercholesterolemia (TC > 12 mmol/L) who were referred to treatment, and that CVD risk lowering medication was initiated in 53 subjects.

In an attempt to reconcile the two interpretations of findings within the RCT, we performed a series of secondary analyses. These provided suggestive evidence of a finding opposite to the a priori hypothesis: That the Control group that received neither risk alert nor advice had the highest amount of risk reduction in the RCT after 8 weeks. The Control group’s change in CVD risk score was similar for those in the Alert-only group. Hence, the Alert/advice group appeared to have had the highest amount of risk reduction in the RCT after 8 weeks. The difference in CVD risk score between groups is consistent with self-reported non-significant greater increase in physical activity level for the Control and Advice.
only groups than in the Alert/advice group. However, it does not cor-
respond to dietary changes between groups; those appeared to be si-
milar across groups. Furthermore, overall considerable increase in
physical activity level and reductions in intake of SFA dairy and sugar
suggest compliance with the intervention material emphasizing more
exercise, eat healthy fats and less sugar. Hence, we keep the conclusion
that a completely self-directed effort is superior to risk alert followed by
advice, tentative, given that the formal analysis of the RCT did not find
a clear difference in response among the interventions and control.
Moreover, several others have observed that a brief intervention-
interation may not be sufficient to affect health behaviors (Hiliter et al.,
2011; Waldron et al., 2011).

We observed health enhancing behavior changes and favorable
changes in the CVD risk factors for the total sample after both 8 and
52 weeks. Consequently, we observed a reduced CVD risk score and
found that the reduction was beyond what would be expected due to
RTM. These findings of risk reduction after a pharmacy-based screening
is comparable to a systematic review of RCTs of pharmacists care
(Santschi et al., 2011). The initial screening for the RCT resulted in 6%
being referred to physician before randomization due to very high risk
factor levels. Fifty-two weeks after baseline, 14% were using CVD
preventive medicines. These results are likely to be beneficial of the
pharmacy-based screening, revealing possible underdiagnoses, as sup-
ported by a pharmacy screening study in Austria (Rohla et al., 2016).

5. Strengths and limitations

Strengths of the study include a loss to follow-up rate of only 7%
after 8 weeks with similar losses across randomized groups. At the 52-
week follow-up visit, ~35% were lost to follow-up, which affects the
representativeness of these results. However, we did not strive to get
participants who did not complete the RCT to attend the follow-up visit
due to restricted resources. Nevertheless, the sample was similar to the
baseline-sample. This study has several limitations. We did not use a
validated score as the primary outcome and inclusion criteria. Mostly
because relevant risk score calculators such as NORRISK (Selmer et al.,
2017) and the atherosclerotic CVD (ASCVD) algorithm (Goff et al.,
2014) could not be used in persons younger than 40 years. Bearing in
mind the nature of atherosclerosis with initiation early in life and a
slowly progression towards disease (Ference et al., 2017), we were
mind the nature of atherosclerosis with initiation early in life and a
slowly progression towards disease (Ference et al., 2017), we were
deal with an aging world population (World Health Organization, 2015), and to make health care convenient and accessible. Therefore, we endorse that pharmacy’s role as a health care provider holds promise for improving public health (Jeet et al., 2017). This may be particular advantageous in rural areas and areas with low population density, where physicians and centralized hospitals are less easily accessible for all (Midtun and Martinussen, 2005).

6. Conclusion

We performed a RCT to test whether alerting and advising participants to their risk status with a minimalistic intervention strategy could help to mitigate risk. We found that participants did not seem to make differential changes in relation to the level of advice or risk factor alerting that they received. There appears to have been a risk score response to the screening, given that the overall risk status of the screening participants in all groups was improved after both 8 and 52 weeks. Furthermore, participants listed several specific health-related behavior changes that they made. We also demonstrated with this study that pharmacies were efficient in finding, and referring high-risk individuals to proper treatment, and in recruiting and retaining participants with only 7% lost to follow-up after 8 weeks and 35% after 1 year.

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Authors’ contributions

LTMR, KGW, KS, VTH, KR, DRJ, KT and LG contributed to the conceptual design and implementation of the VISA-study. LTMR and KGW were responsible for management of pharmacy staff and their executing of the study. DRJ KS VTH JMG HBH and KR contributed to analyzing and interpretation of data. KS KR VTH DRJ had the responsibility for the final review of the study and input on revisions. All authors read and approved the final manuscript.

Declaration of conflicting interests

VTH, KT, LG were employees in Mills AS, and KGW and LTMR were employees in Boots Norge AS, at time of study initiation.

Conflicts of interest

KS, VTH and KR have received research grants from Mills AS. KS has also received grant from Visa hjertego’ (MILLS AS brand). DRJ is a consultant for California Walnut Commission. KR has received honoraria for meeting in advisory boards and lectures for Amgen, Chiesi, Sanofi, Mills DA, MSD (Norway) and for participation in meetings for Norwegian Directorate of Health and the Norwegian Medical Association.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.pmedr.2018.08.004.

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