Community pharmacies offer a potential high-yield and convenient arena for total cholesterol and CVD risk screening

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Abstract

Background: Moderately elevated blood total cholesterol (TC), blood glucose (BG) and blood pressure (BP) are rarely symptomatic and as such many individuals remain untreated. We studied the yield of an in-pharmacy screening for identifying undetected high TC and strategies to reach those with absence of prior measurement of TC, BG and BP.

Methods: A cross sectional TC screening study with complementary TC measurements and self-administered questionnaire was conducted for one week in each of 2012 and 2014 in 148 and 149 Boots[TM] Norge AS community pharmacies nationwide in Norway.

Results: Non-medicated adults (n=21090) with mean age 54.5±16.0 were included. The study population resembled the Norwegian population in regards to body mass index, educational level, smokers and physical inactivity level, but with an overrepresentation of middle-aged women. Of 20 743 with available data, 11% (n=2337) were unaware of their high TC ≥7.0 mmol/L, and an additional 8% were unaware of TC ≥6.2 mmol/L. >40% of the study sample had not measured TC or BG before. In order for future screenings to reach those that are less likely to have previously measured TC and BG, our results suggest that young, low-educated, overweight men and women should be targeted for TC measurement, whereas normal weigh men in all ages should be targeted for BG measurement.

Conclusions: In total 19% in an in-pharmacy screening were unaware of their elevated TC of ≥ 6.2 mmol/L. We also identified characteristics that could be used reach those who are less likely to have measured TC and BG.

Key words: Screening, community pharmacy, cholesterol-yield, cardiovascular disease, cholesterol

Introduction

Cardiovascular disease (CVD) is a major contributor to death worldwide (1), affected by the atherosclerotic process that has already started in childhood (2). Thus, for risk factors such as high blood total cholesterol (TC), blood glucose (BG) and blood pressure (BP), it is important both to reduce high levels and to maintain low values (2). However, moderately elevated levels of these risk factors are rarely symptomatic or give symptoms that tend to be easily ignored. Although early diagnosis of elevated levels can be accomplished through relatively inexpensive measurements of TC, BG and BP, many people remain untreated. The majority of individuals with familial hypercholesterolemia and over 50% of individuals with type 2 diabetes mellitus are undiagnosed (3, 4). Most premature CVDs are preventable by a healthy diet, and avoiding tobacco, alcohol abuse and insufficient physical activity in addition to adequate drug treatment (5). However, without knowing one's risk factor levels, targeted decisions to lower risk are not possible (6). The lower thresholds being recommended in current guidelines for medical treatment of elevated risk factors in an aging world population, imply that even more people will need treatment in the years to come (7, 8). Existing health care services may not easily have the capacity to deal with the increasing number of medical visits (9). Thus, the World Health Organization (WHO) calls for local, novel approaches to deliver health care services (10). Community pharmacies (pharmacies) have been suggested to play a role in CVD prevention, as they now perform some services which had earlier been reserved for physicians (11). This includes, among many others, measurements of TC and other lipids, BG and BP, in addition to providing lifestyle advice and counseling on smoking cessation (12).

Using TC concentrations and questionnaire information obtained in a TC screening study in pharmacies, our aim was to investigate yield in terms of detecting unknown high TC and

characteristics and prevalence of those whose TC, BG and BP had not previously been measured. We hypothesized that a pharmacy-based TC screening study would:

I) Attract individuals with characteristics similar to the general population.

II) Identify people whose TC, BG and BP have not been measured before and where a substantial number would get new and useful information on their TC level.

Methods

This cross sectional TC screening study is part of the "Vascular lifestyle-Intervention and Screening in pharmacies" (VISA) study. A complete and detailed description of the VISA study design is appended (Appendix 1). Briefly, the data analyzed in this paper arose from complimentary TC measurements and questionnaires offered six days in both 2012 and 2014 in Boots[TM] Norge AS community pharmacies. All pharmacies belonging to the Boots pharmacy chain (148 in 2012 and 149 in 2014) distributed across Norway, participated. The study was planned and conducted by the University of Oslo in collaboration with the for-profit organizations Boots, Mills AS, Grete Roede[TM], and a non-profit organization, the Norwegian Health Association. Participants became aware of the screening through national or locally means of advertisements. Health care providers in pharmacies (pharmacist, technicians or nurses) who had completed a training program consisting of a web-based educational module and practical training, executed the study.

The initial step in the TC screening study was to undergo point-of-care finger-prick TC measurements in a consultation room within each pharmacy. TC was measured using the Roche Diagnostics AS Accutrend Plus[TM] (available in all pharmacies) or the Alere AS Afinion™ AS100 (available in 50 pharmacies in 2014). Accutrend Plus captured TC concentrations of 3.88-7.76 mmol/L, and Afinion AS100 in the interval 2.59-12.95 mmol/L. All screenees were immediately provided with their TC value on completion of the assay

along with an interpretive brochure with diet and lifestyle advice for CVD prevention developed by the VISA-study investigators (13). For those with TC ≥ 7.76 mmol/L, a follow-up visit with a general practitioner (GP) was recommended.

Research study participation also depended on filling out an anonymous optically readable pre-coded questionnaire that was solicited when convenient during screening (translated versions of the questionnaire are appended). This screening questionnaire was developed by the VISA-study investigators, however, wording of the questions were borrowed from several validated questionnaires and from Statistics Norway (www.ssb.no). As approved by the Norwegian Regional Ethical Committee, consent for research participation was assumed by filling out the questionnaire. For statistical analyses, we used the following items: TC concentration, age, sex, educational attainment, height and weight (from which we computed body mass index (BMI) as kg/m^2), physical activity level, smoking status, prior measurement of TC, BG and BP, setting of previous TC measurement (pharmacy) and prior knowledge of TC level. Duration of the TC screening study was 15-20 minutes per participant (not counting waiting time).

Reporting of this paper follows the STROBE checklist for observational studies.

Study sample

Inclusion criteria were age ≥ 18 years, not being pregnant or lactating. In total 28 263 of screenees completed the questionnaire (18 624 in 2012 and 9639 in 2014). Only people who were not taking lipid-lowering medication were screened in 2014; consequently all those reported using lipid-lowering medication in 2012 were excluded from these analyses. Those with multiple unrealistically high/low/missing values or who had an unreadable questionnaire were also omitted, leading to a final inclusion of 21090 participants (Figure 1).

Data analysis

Descriptive statistics for the continuous variables were given as mean and standard deviation (SD), whereas categorical variables were expressed as frequencies and percentages. For comparison with the Norwegian population, the majority of data were obtained from Statistics Norway (the agency which has responsibility for official statistics in Norway). Due to lack of recent national data, TC concentration obtained from the most recent Tromsø-study (2015-2016) was used as reference for the Norwegian population. The Tromsø study is a longitudinal population study performed in the urban, northern part of Norway (14). We utilized two cut offs for high TC: TC concentrations of ≥ 7.0 mmol/L indicated a probable need for treatment, (15) whereas TC ≥ 6.2 mmol/L indicated that TC should be monitored because of the risk of developing higher TC (16). Missing values for smoking were assumed to indicate non-smoking, because the smoking question in the 2012 edition was constructed as if it should only be checked if smokers: "Do you smoke? About how many per day:" Similarly, missing values were taken to indicate "not measured" for previously measured TC, BG and BP.

Statistical analysis included chi-square test, independent sample t-test and logistic regression. For logistic regression, estimated probabilities (back transformed from their estimated logit) and odds ratios (OR) with corresponding 95% confidence intervals (95% CI) were presented.

The difference between age- and sex adjusted models and more fully adjusted models was minor, and the fully adjusted models (age, gender, BMI and education, smoking, physical inactivity and previous measures of the other two risk factors and TC categories for TC) were presented. All analyses were conducted using SAS version 9.4 for Windows. The significance level was set at ≤ 0.05.

Results

Population characteristics

Table 1 shows background characteristics. The majority (68.9%) was women, and mean age was 54.5 years (±16.0). Overweight/obesity defined as BMI ≥ 27 kg/m^2 (following the convention of Statistics Norway), was more prevalent in men (37.4%, n=2356) than women (26.0%, n=3529). The VISA study attracted older women but educational level (in particular percentage with high school as highest attained educational level), smoking, BMI ≥ 27 kg/m^2 and inactivity were similar to Statistics Norway's national data (Table 1).

Yield of screening

Total cholesterol

Prevalence of high TC defined as ≥7.0 mmol/L was observed in 0.9%, (n=18) of women and 1.4% (n=8) of men aged 18-29, as well as in 38.2% (n=779) and 30.1% (n=167) of women and men respectively, aged 60-69 years (Figure 2).

Table 2 presents the yield of the screening for unknown high TC. In total, 11.4% (n=2337) learned that their TC level was high (≥ 7.0 mmol/L), whereas an additional 1.6% (n=335) had a reinforced message, given that they already knew their TC was high. Characteristics of this group was similar to the total study sample, except for slightly older age (57-63 years) and a higher percentage of low-educated (16-22% with primary school).

With high TC defined as ≥ 6.2 mmol/L, 19.4% (N=3975) of the total sample were alerted of their high TC, whereas 7.3% (n=1501) already knew that their TC was ≥ 6 mmol/L. Witihin age groups, 0.24% (n=50) aged 18-29 years were made aware of an unknown elevated TC (≥ 6.2 mmol/L). The yield of detecting unknown high TC was however largest with 5.7% (n=1174) for 60-69 years old.

Likelihood of previous measurement

In total, 36.2% (n=7638) had measured TC, BG and BP previously, whereas 6.6% (n=1401) had not measured any of these before. Measuring one risk factor before was the strongest predictor of whether or not either of the others also had been measured. If TC had not been measured before, there was an observed 53% probability (OR 2.61 (95% CI: 2.43-2.80)) that BG had not been measured, and a 64% probability (OR 3.00 (95% CI: 2.65-3.39)) that BP had not been measured before. Being young, inactive, having low educational level, and being overweight/obese were all characteristics that were significantly associated with the odds of not having had TC measured before. Those whose measured TC ≤ 5.0 mmol/L (which was only known after the screening in the present study) had a two-fold increased odds of not having had TC measured before (OR 2.01 (95% CI: 1.80-2.32) compared to those who had measured TC ≥ 7.0 mmol/L. In contrast to TC and BP, age was not a strong predictor for the probability of previous BG measurement, but being male and normal weight were, as these characteristics were significantly associated with increased probability that BG had not previously been measured. The probability that BP had not previously been measured was overall low (8% for men and 6% for women) (supplementary Tables 3-5).

Discussion

We replicated what is well established, (17) and recently confirmed in the latest Tromsø Study (14), that women's TC level peaks later than for men. In Norway, the latest information on measured TC in multiple counties were reported more than ten years ago (5.6 mmol/L), and the present study reported that TC remained about same (5.5 mmol/L) (18). Compared to other longitudinal population health studies in Norway with similar age (but more equal gender) distribution, TC in the nationwide VISA study was also similar to the latest (2006-08) Nord-Trøndelag Health Study (rural county in Norway) with mean TC 5.4 mmol/L (19, 20) and the Tromsø Study (5.5 mmol/L) (14). Further, prevalence of high TC was highest in women and higher than other pharmacy screenings (21). Compared to health surveys in Sweden (1986-2009), we observed similar prevalence of TC $\geq$ 7.0 mmol/L for women over a similar age range and slightly lower prevalence for men (22). However, in contrast to the mentioned population health studies, the VISA-study population was non-medicated.

Results from the yield of screening (to whom useful and new knowledge of high TC was given) can be used to develop strategies to target those who would benefit the most from the screening. We found that 11% received new information, and an additional 2 % got repeated information about a TC level $\geq$ 7.0 mmol/L that should be treated (15). Their characteristics were similar to the general study population although slightly older and with a higher percentage of low educated. An additional 8% were informed about a previously unknown TC $\geq$ 6.2 mmol/L that should be monitored given the tendency for TC to increase with age, and the risks associated with long term exposure of high TC (2). Thus, the 0.3% young who were identified with a previously unknown TC of $\geq$ 6.2 mmol/L may be of special importance despite that the yield is low in absolute numbers. Attention to high risk in the young may also be of special importance in Norway given a reported recent increase in first myocardial infarction among people aged $\leq$ 45 years (23). Since only physicians can diagnose and

prescribe medication, yields of a pharmacy-based screening in a public health perspective also depend on ability to collaborate with physicians and other appropriate professionals.

We found that the likelihood that TC and BG were not previously measured were about twice as high as for BP. These findings are supported by a similar study in pharmacies in Austria (12). Future studies should explore possible barriers for why finger-prick measurements of TC and BG seems to be less frequent measures than BP. For TC, our results indicate that future screenings should target young men and women with low education and overweight, in order to reach those who are less likely to have measured TC previously and most importantly, those with unknown high TC. Whereas for BG, males in all ages that are normal weight should be targeted. Young males and immigrants are also less likely to visit their GP than their counterparts (24). At the same time, pharmacies and other retail-based clinics have longer opening hours and offer affordable drop-in appointments for health services (25), which are features that are seen to attract young and those with low education (26).

According to our data, measurement of one risk factor was associated with measuring other risk factors. These findings call for attention to the importance of initial screening for CVD risk factors. This should be highlighted in countries without governmental-initiated health surveys, in light of the recent observed unfavorable increase in TC levels in Finland (27) and in Sweden (28).

Strengths and limitations

First, we acknowledge that pharmacies are not research institutions. On the other hand, pharmacies seems highly accessible and successful in recruiting participants across geographical regions, age, sex and educational status. Like any other study based on voluntary enrollment of participants, screening in pharmacies may be subject to selection bias. However, although there was an overrepresentation of middle-age women, we showed that age, gender, and education biases may be similar to other conventional health studies (29, 30), and highly comparable to another pharmacy-based screening program in Austria (12). We also note that pharmacies have a broad product assortment in addition to prescription medicines, and that the customers are accordingly not limited to medicated patients with a diagnosis (25). The use of chain pharmacies (31) might be a strength of the study as it ensures consistency in training and monitoring of compliance to the protocol. Questionnaire limitations include that it was not validated and it was self-administered and only TC was objectively measured. There are several errors associated with self-reporting. However, self-report is quick and inexpensive and with few questions considered to be sensitive, this limitation may not be of great impact (32). We did find some peculiar findings that might indicate that the participants interpreted the question of previously measured TC incorrectly (for instance that subsequently measured low TC was associated with being less likely to have measured TC before). Another limitation was that we omitted all participants with an unreadable questionnaire and with unrealistic values of key variables. Also, different exclusion criteria in the two screening periods lead to later exclusion of potential participants. Exclusions were however performed to improve data quality and for comparison basis. Inconsistency in which time of the day and time of the year TC was measured, and the use of two different measurement devices with different precision levels may have affected the mean TC concentration. In total 7.9 % (n=1660) reported in 2014 that they had previously measured

their TC in pharmacies. Hence it is likely that these 1660 people are represented twice in the material, which could influence the analyses and interpretations of results.

Potential role of pharmacies

The present study demonstrates potential for pharmacies to complement the health care system by providing the important initial screening and advice for CVD risk factors (11). Although, the TC screening in this study was complementary, and results might therefore not be representative for the usual pay-service of TC measurement in pharmacies. Similar pharmacist-provided interventions are demonstrated to be successful in reducing risk of CVDs (33). This potential role of pharmacies should be recognized in countries were the health care system already is stressed with long waiting times, and where an aging population will further stress the expansion of current health care systems (8). Results from a study in Canada, with similar universal health care system as Norway, found that adding pharmacists to primary care also was a cost effective strategy for reducing CVD risk (34). Hence, expenses for marketing, staff and blood tests and the pharmacies' willingness to assess CVD risk factors must be considered and compared to potential yields of this and future in-pharmacy screenings. Future screenings in pharmacies should consider using the current results in developing strategies to reach those that could be expected to benefit the most from screening. In this regard, the screening questionnaire could be used to consider whether those who have already measured their CVD risk factors are reasonable to measure again.

Conclusion

We present a pharmacy-based screening for TC and previous assessment of CVD risk factors. The screening seems to be convenient in terms of attracting a large number of people across educational levels but with an overrepresentation of middle-aged women. The yield of identifying high TC that may need treatment in a non-medicated sample was substantial in absolute numbers, whereas 11%- 19% were unaware of their high TC levels of ≥7.0 and 6.2 mmol/L respectively. We found that prior measurement of TC and BG were less common than for BP. To increase the yield in terms of attracting those whose TC and BG are more likely not to have been measured before, our results suggest that young, overweight/obese males and females should be targeted for TC screening, and normal weight males in all ages for BG screening. It seems that point-of-care testing in pharmacies is convenient. Further studies are warranted to evaluate whether pharmacy-screening could be an asset to the health care system.

the study. Lastly, we are very grateful to Alere AS Norway for providing pharmacies with essential measurement devices at no cost.

Conflict of interests

MGB is, and LG was employed by Mills AS and KWG and LTMR were employees in Boots Norge AS at the time of the study initiation. Boots and Mills were involved in the design of the study but had no influence on the decision to submit the paper. KR, KS and VTH have received funding from Mills AS. KS has also received a grant from Vita hjertego' (MILLS AS brand). DRJ is a consultant for The California Walnut Commission. KR has received honorariums for meeting in advisory boards and lectures for Amgen, Chiesi, Sanofi, Mills AS, MSD (Norway) and for participation in meetings for Norwegian Directorate of Health and the Norwegian Medical Association.

Key points:

- Screening for CVD risk factors in Norwegian community pharmacies resulted in alerting 11-19% of total cholesterol concentrations that need attention

- An community pharmacy-based screening study was efficient and successful in recruiting > 20 000 that seemed representative for at least, but not limited to the middle-aged female Norwegian population

- Results from an in-pharmacy screening emphasize the importance of initial screening for CVD risk factors and to tailor future screening to target groups in order to reach those that would be most useful to screen

- Screening and identification of high risk of CVD in community pharmacies hold considerable promise for contributing to improve public health

Author's contributions

KS KWG LTMR MGB LG VHTH and KR were responsible for the conceptual design of the study. DRJ KS ITR VHTH and KR were responsible for analyzing and interpreting data. DRJ, KS, VHTH and KR had the major responsible for the review of the study and input on revisions. All authors read and approved the final manuscript.

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Table 1 Background characteristics of participants in the VISA study and the general Norwegian population.

	Norwegian population	Total, VISA N=21,090	Men, VISA N=6,516	Women, VISA N=14,285	p-value[1]
	Mean±SD %	Mean±SD % (n/N)	Mean±SD % (n/N)	Mean±SD % (n/N)	
Women, %	49.7[4]	68.9			
Age, years	39.4[5]	54.5±16.0	53.9±16.4	54.8±15.8	0.0004
TC, mmol/L	5.5[6]	5.5±1.1	5.4±1.0	5.7±1.1	<0.0001
BMI, kg/m	27.2[7]	25.4 ±4.0	26.3±3.6	25.0±4.1	<0.0001
Age ≤39 years, %	31.9[5*]	19.2 (3985/20706)	21.7 (1401/6445)	18.2 (2562/14066)	<0.0001
BMI≥27 kg/m, %	28.0[8]	29.6 (5953/20090)	37.4 (2356/6292)	26.0 (3529/13587)	<0.0001
Highest attained education level:					0.0333
Primary school, %	27.3[9]	15.6 (3149/20168)	15.5 (969/6252)	15.5 (2125/13671)	
High school, %	41.3[9]	41.3 (8325/20168)	40.0 (2499/6252)	41.8 (5720/13671)	
University/college 1-3 years, %	22.7[9]	25.0 (5034/20168)	26.2 (1639/6252)	24.5 (3351/13671)	

University college >3 years, %	8.7[9]	18.2 (3660/20168)	18.3 (1145/6252)	18.1 (2475/13671)	
Inactive[2], %	17[7]	17.5 (3629/20727)	20.7 (1331/6421)	16.0 (2248/14056)	<0.0001
Smokers[3], %	21[10]	19.8 (4186/21090)	17.2 (1118/6516)	20.9 (2996/14285)	<0.0001

N= of all available data for analysis for total, men and women.

VISA, Vascular lifestyle-Intervention and Screening in phArmacies; TC, Total cholesterol; BMI, Body Mass Index.

-TC was measured in pharmacy; all other data were self-reported.

- 289 people with missing gender are included in the total column.

[1] Independent sample t-test or Pearson chi-square for sex difference.

[2] Exercise, ≤1 time/week.

[3] Every day and occasional smoking.

[4-10] References (data available that were considered as representative to the Norwegian population in terms of data source and time were utilized): 4:(35), 5:(36) *16-39 years, 6:(14), 7:(19), 8:(37), 9:(38), 10:(39).

Table 2 Description of yield for various subgroups with available total cholesterol (TC) measurements.

Screened and with available TC values N= 20473								
TC previously measured							**TC not previously measured**	
n/N (%)	12095/20473 (59.1%)						8378/20473 (40.9%)	
	Recalled TC was high (≥7)		**Recalled TC was normal (<7)**		**Did not recall TC**			
n/N (%)	781/20473 (3.8%)		7941/20473 (38.8%)		3373/20473 (16.5%)			
	Measured TC ≥7	Measured TC <7	Measured TC≥7	Measured TC <7	Measured TC ≥7	Measured TC <7	Measured TC ≥7	Measured TC <7
n/N (%)	335/20473 (1.6%)	446/20473 (2.2%)	1142/20473 (5.6%)	6799/20473 (33.2%)	553/20473 (2.7%)	2820/20473 (13.8%)	642/20473 (3.1%)	7736/20473 (37.8%)
Comment on yield	**Useful** (better monitioring needed)	**Reassured**	**Useful**	Not useful	**Useful**	Not useful	**Useful**	Not useful

TC, total cholesterol, measured in mmol/L.

-Missing values are included in "TC not previously measured".

-For the purpose of yield, presentages are computed of the total available for analysis (n=20473).

Figure titles and legends:

Figure 1 Simplified flowchart of the study design and inclusion of participants in an

in-pharmacy screening for total cholesterol.

Figure 2 Illustrating mean total cholesterol (mmol/L) and prevalence (%) of total cholesterol

≥7 mmol/L according to gender and age groups (N=20473).

Supplementary files:

1. Appendix1_Complete description of the VISA study.pdf

2. Questionnaire 2012-pdf

3. Questionnaire 2014 –pdf