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Longitudinal cholesterol trends across socioeconomic groups in Norway: the influence of lipid-lowering drugs in the population-based Tromsø Study 1994–2016

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ABSTRACT

Objectives There is limited evidence regarding the impact of lipid-lowering drugs (LLDs) on the socioeconomic gradient in a longitudinal perspective. The study investigates the longitudinal socioeconomic gradient in total cholesterol levels and whether this is affected by the use of LLDs.

Design Population-based cohort study.

Setting Sample from adult inhabitants of Tromsø municipality, Norway, who participated in the Tromsø Study (1994–2016).

Participants 17 550 participants of the population-based Tromsø Study in 1994–1995 who were non-users of LLD, aged 25–78 years at baseline and who attended one or more of three subsequent surveys in 2001, 2007–2008 and 2015–2016 were included in the study.

Outcome measure Socioeconomic gradient in total cholesterol levels was compared among participants treated and not treated with LLDs during the observation period.

Results The total cholesterol levels across all educational groups increased from 1994–1995 to 2015–2016 among untreated women (+0.33 mmol/L to +0.48 mmol/L), except for those with primary education (−0.12 mmol/L). Total cholesterol levels decreased among untreated men (−0.40 mmol/L to −0.06 mmol/L, from lowest education to highest education), treated women (−1.88 mmol/L to −1.35 mmol/L) and men (−2.21 mmol/L to −1.84 mmol/L) across all educational groups. At baseline, we observed a significant inverse association between education and total cholesterol levels among non-users of LLDs. There was no clear educational gradient in total cholesterol levels among users of LLDs.

Conclusions Users of LLDs experienced a more substantial decrease in total cholesterol levels over time compared with non-users. The educational gradient in total cholesterol levels observed among non-users of LLD was not apparent among users.

STRENGTHS AND LIMITATIONS OF THE STUDY

⇒ The Tromsø Study is a population-based study with repeated measurements, allowing us to conduct a longitudinal study with four points of measurements over two decades.
⇒ The exact timing of use of lipid-lowering drugs (LLD) was unknown, which restricted us to investigate participants' LLD treatment at the time of their attendance.
⇒ Certain groups are underrepresented in the Tromsø Study, valuable information related to these groups may be missing.

INTRODUCTION

Cardiovascular disease (CVD) is a global health concern. As of 2017, CVD is responsible for 17.9 million annual deaths globally.[1] Despite the large reduction trend in CVD incidence and mortality rates over the previous decades,[2 3] it remains a leading cause of death worldwide.[4] A major reason for the decline in CVD mortality and incidence has been the development of prophylactic and therapeutic treatments, including lifestyle changes and drug therapy. This includes the decline in cigarette smoking, improved hypertension treatment and control, and the widespread use of lipid-lowering drugs (LLDs) to lower circulating cholesterol levels.[5] The 4S trial in 1994 provided an important breakthrough by demonstrating that the LLD simvastatin had a strong impact on CVD mortality.[6] After the publication of this trial, the use of different statin LLDs for secondary prevention increased considerably. However, there is insufficient evidence available regarding statin use for the primary prevention of CVD.[7] Despite this, statin use for the primary prevention of CVD has become standard for people at a high risk of CVD.[8]

Although there has been an overall decrease in cardiovascular-associated morbidity and

mortality in Western countries, individuals of lower socioeconomic backgrounds still face significantly higher risks of developing CVD compared with individuals from more privileged backgrounds.[9] A population-based Swedish study from 1984 to 2004 reported higher levels of total cholesterol among men with lower education levels than men with higher educational levels,[10] indicating a social gradient in total cholesterol levels. Moreover, Swedish authors also reported that LLD only contributed to reduce total cholesterol by 2% in their population in 2004.

Hyperlipidaemia arises from an interaction between genetic factors, environmental factors (including lifestyle) and socioeconomic influences.[11] Several epidemiological studies have reported that individuals with low socioeconomic status (SES) are more likely to adopt unhealthy behaviour, which leads to alterations in total cholesterol.[12 13] Consequently, individuals with lower education levels are likely to have an increased underlying risk for CVDs, highlighting the potential need for LLD treatment.[14] Previous studies from 2014 and 2017 based on the Tromsø Study have demonstrated a substantial decrease in secular mean total cholesterol levels over time in participants aged 25–96 years;[15] an educational trend in total cholesterol levels was observed among non-users of LLDs, but not among users of LLDs, at the cross-sectional level.[16] These previous studies have, however, not taken a longitudinal approach following the same individuals over time or including SES variables and thereby exploring differences in total cholesterol levels depending on LLD initiation. Moreover, research on longitudinal perspectives of SES on total cholesterol levels is lacking in the literature. In this study, education is used as proxy for SES. Using the population-based Tromsø Study, we investigated the longitudinal socioeconomic gradient in total cholesterol levels and whether this is affected by the use of LLDs.

MATERIALS AND METHODS

Study population

The Tromsø Study is an ongoing population-based study conducted by UiT The Arctic University of Norway in the municipality of Tromsø, Northern Norway. The Tromsø Study currently consists of seven surveys: Tromsø1 (1974), Tromsø2 (1979–1980), Tromsø3 (1986–1987), Tromsø4 (1994–1995), Tromsø5 (2001), Tromsø6 (2007–2008) and Tromsø7 (2015–2016). Total birth cohorts and random samples of women and men were invited to participate, and many participants completed several surveys.[17] Participants who attended in 1994–1995 (Tromsø4) and in at least one of the surveys conducted in 2001 (Tromsø5), 2007–2008 (Tromsø6) and 2015–2016 (Tromsø7) were included in this study (figure 1). We excluded participants from 1994–1995 (Tromsø4) who were users of LLDs (n=241), had missing information regarding their education (n=103) and were older than 80 years (n=5). In total, 17 550 participants aged 25–78 were included in the analyses.

Patient and public involvement

The Tromsø Study collaborated with the Tromsø municipality, the Troms County, health authorities, healthcare providers, participants and the general public. Some potential participants were involved as user representatives on a strategic level and in the planning of subprojects.[18] Furthermore, users, including healthcare providers and representatives from patient organisations, were involved in the detailed planning of subprojects and piloting of questionnaires. There was no patient or public involvement in this present study.

Measurements

The data used in this study were collected via self-reported questionnaires and physical examinations. Non-fasting venous blood samples were collected by trained personnel, while participants were sitting. Non-fasting serum total cholesterol (mmol/L) concentrations were analysed within 48 hours using CHOD-PAP enzymatic colorimetric methods and commercial kits (Boehringer-Mannheim, Germany (1994–1995)) and Roche Diagnostics (2001, 2007–2008, 2015–2016, Mannheim, Germany) at the Department of Laboratory Medicine, University Hospital of North Norway, Tromsø. Weight and height were measured by personal at examination site. Body mass index (BMI; kg/m^2) was calculated as weight (kg)

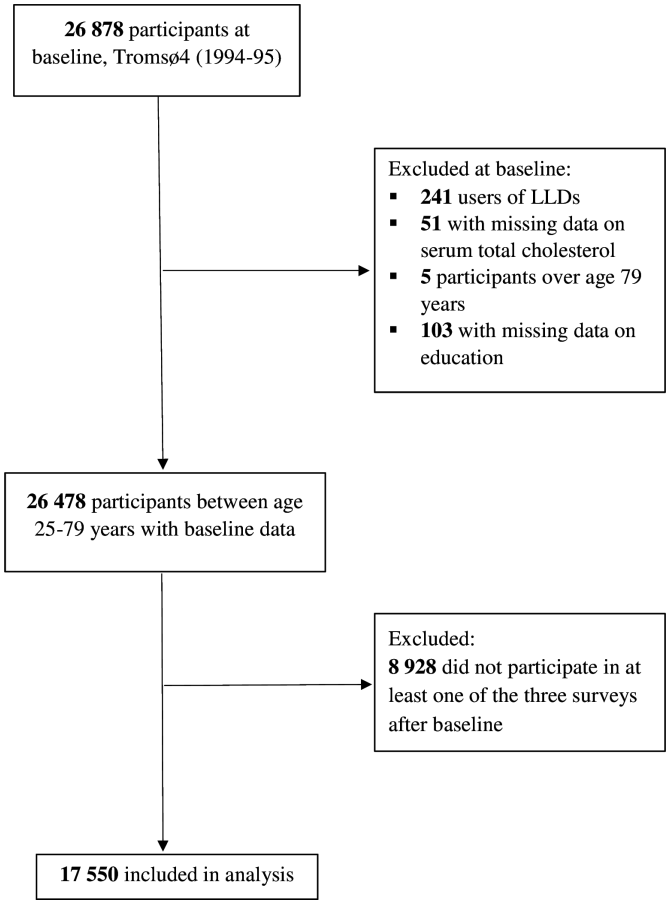


Figure 1 Flowchart of the participants. The Tromsø study 1994–2016. LLDs, lipid-lowering drug

divided by the square of height (m). Systolic and diastolic blood pressure were measured using the Dinamap Vital Signs Monitor 1846 (Critikon Inc., Tampa, FL, USA) in 1994–1995 and 2001 and the Dinamap ProCare 300 (GE Healthcare, Norway) in 2007–2008 and 2015–2016.

Educational level data was assessed through a self-reported questionnaire; four options were available for participants to tic of: (1) primary/secondary school, (2) upper secondary education, (3) college/university, less than 4 years and (4) college/university, 4 or more years. Whether participants currently use LLD was assessed by two methods of self-reporting. First, participants were asked to write a list of the medicine brand names they had used regularly during the preceding 4 weeks. Those who wrote a brand name with the Anatomical Therapeutic Chemical (ATC) code C10 were classed as user of LLD. Second, participants were asked if they were currently an LLD user (yes/no). The questionnaire information was checked by health personnel at the examination site. Information regarding participants' history of stroke and myocardial infarction (yes/no) and whether they were daily smokers (yes/no) was also assessed by self-reported questionnaires.

Statistics

All statistical analyses were sex-specific and conducted using Stata MP 17.0 (StataCorp LLC, College Station, TX). The descriptive study population characteristics and risk factors are presented as the mean and SD for the continuous variables or as a number and percentage for categorical variables.

Linear mixed models were used to estimate mean total cholesterol levels according to baseline education, time of survey and LLD use. The main models were adjusted for baseline age and included indicator variables for baseline education, time of survey, LLD use, and all two- and three-way cross-products between the indicator variables. A random intercept at the participant level was included to control for repeated observations within each subject. Using separate models, we tested for linear trends related to baseline education by modelling education as a continuous variable in the aforementioned models. We also used fitted models to estimate longitudinal change in total cholesterol levels from 1994–1995 (Tromsø4) to 2015–2016 (Tromsø7). Using separate models, we performed analyses for each of the baseline age groups: 25–49 years and 50–78 years. The age group cut-off was based on the distribution of age. We conducted a sensitivity analysis among the participants who attended all four surveys (ie, completely observed) to determine if the results were consistent with those from the main analysis.

RESULTS

In total, 17 550 participants aged 25–78 participated in 1994–1995 (Tromsø4) and in at least one of the Tromsø surveys in 2001 (Tromsø5), 2007–2008 (Tromsø6) and 2015–2016 (Tromsø7). Total cholesterol levels and systolic and diastolic blood pressure increased from 1994–1995 to 2001 and decreased until 2015–2016 in both women and men (table 1). The proportion of smokers in both sexes decreased in each survey from 1994 to 2016; yet, this decrease was greater in men. The proportion of participants with a history of CVD, BMI and LLD use increased in both sexes over time.

The prevalence of current LLD use increased over time across all educational groups but especially in the oldest age groups (table 2). A higher prevalence of LLD use was seen in men compared with women. LLD use was most prevalent in participants aged 60 and older regardless of sex, and its use increased over time in this age group.

In 1994–1995, a significant inverse association was observed between education and total cholesterol levels among all participants. At later time points, this association attenuated. In 2015–2016, no educational gradient was observed in either sexes or among users and non-users of LLDs (table 3 and figure 2). Among non-LLD users who were women, a small decrease in total cholesterol levels between 1994–1995 and 2015–2016 was observed. However, this was only seen among women with primary education (−0.12 mmol/L; 95% CI −0.17, −0.07) (table 3 and figure 2A), as total cholesterol levels increased over time among other educational groups. Among non-users of LLD who were men, total cholesterol levels decreased between 1994–1995 and 2015–2016 across all educational groups (table 3 and figure 2B). For participants who became LLD users, we observed a substantial decrease in total cholesterol levels between 2001 and 2015–2016 across all educational levels, ranging from −1.88 to −1.35 mmol/L in women and −2.21 to −1.84 mmol/L in men (table 3 and figure 2CD). Participants with the lowest educational levels demonstrated the highest decrease in total cholesterol levels.

Among women in age group 25–49 years who were non-users of LLD, we observed a mean increase in total cholesterol from 1994–1995 to 2015–2016, regardless of education level (online supplemental table 1). This was not observed among men in the same age group: their total cholesterol levels decreased over the years, except for men with college/university ≥4 years (online supplemental table 2). Women and men in age group 50–78 years demonstrated a mean decrease in total cholesterol levels across all educational groups. The decrease in total cholesterol levels over time was considerably larger among users of LLD than non-users, and larger among women and men in age group 50–78 years and in all educational groups.

Among non-users of LLD, a significant educational gradient was observed in women aged 25–49 years in 1994–1995, 2001 and 2007–2008 (online supplemental table 1) and in men during 1994–1995, 2007–2008 and 2015–2016 (online supplemental table 2). In women and men aged 50 years and older, an educational gradient was only observed in 1994–1995 and 2001. Among users of LLD, no educational gradient was observed in 2015–2016, except women in age group 25–49 years. The

Table 1 Crude descriptive characteristics by sex and survey. The Tromsø Study 1994–2016.

	Tromsø4 1994–1995	Tromsø5 2001	Tromsø6 2007–2008	Tromsø7 2015–2016
Women	9388 (53.5)	3880 (57.2)	5181 (54.0)	6351 (53.5)
Age, years				
25–29	1034 (11.0)	NA	NA	NA
30–39	2478 (26.4)	105 (2.7)	52 (1.0)	NA
40–49	2456 (26.1)	621 (16.0)	1271 (24.5)	678 (10.7)
50–59	1822 (19.4)	709 (18.3)	1059 (20.4)	2204 (34.7)
60–69	1196 (12.7)	1402 (36.1)	1907 (36.8)	2237 (35.2)
70–79	402 (4.3)	1043 (26.9)	892 (17.2)	1232 (19.4)
Total cholesterol, mmol/L	6.0 (1.3)	6.4 (1.2)	5.8 (1.1)	5.7 (1.0)
Systolic blood pressure, mmHg	131.7 (18.9)	140.5 (20.7)	138.0 (25.5)	132.4 (21.9)
Diastolic blood pressure, mmHg	77.4 (12.7)	83.3 (13.1)	76.3 (11.3)	74.2 (10.5)
History of cardiovascular diseases*	89 (1.0)	189 (5.1)	209 (4.2)	221 (3.6)
Lipid-lowering drugs, yes	NA	361 (9.3)	695 (13.4)	1076 (16.9)
Body mass index, kg/m2	24.6 (4.0)	26.5 (4.7)	26.6 (4.6)	27.0 (4.8)
Daily smoker, %	3318 (35.5)	1069 (27.8)	1091 (21.4)	963 (15.3)
Education				
Primary	3333 (35.6)	1962 (50.8)	1711 (35.4)	1876 (30.0)
Upper secondary	3385 (36.2)	1172 (30.4)	1736 (33.5)	1761 (28.2)
College/university <4 years	1332 (14.3)	386 (10.0)	719 (13.5)	1016 (16.3)
College/university ≥4 years	1304 (13.9)	339 (8.8)	948 (17.6)	1597 (25.5)
Men	8162 (46.5)	2897 (42.8)	4492 (46.0)	5517 (46.5)
Age, years				
25–29	839 (10.3)	NA	NA	NA
30–39	2023 (24.8)	53 (1.8)	19 (0.4)	NA
40–49	2303 (28.2)	463 (15.4)	1012 (22.5)	566 (10.3)
50–59	1654 (20.3)	347 (11.5)	924 (20.6)	1784 (32.3)
60–69	1025 (12.6)	1190 (39.5)	1751 (40.0)	2008 (36.4)
70–79	318 (3.9)	844 (29.1)	786 (17.5)	1159 (21.0)
Total cholesterol, mmol/L	5.5 (1.1)	6.1 (1.1)	5.5 (1.1)	5.3 (1.1)
Systolic blood pressure, mmHg	139.9 (16.2)	144.0 (19.0)	142.2 (21.2)	136.6 (18.7)
Diastolic blood pressure, mmHg	81.9 (12.1)	85.8 (13.0)	82.2 (10.8)	79.6 (10.1)
History of cardiovascular diseases*	228 (2.9)	365 (12.9)	450 (10.3)	539 (10.1)
Lipid-lowering drugs, yes	NA	414 (14.3)	805 (17.9)	1234 (23.4)
Body mass index, kg/m2	25.6 (3.2)	26.8 (3.5)	27.3 (3.7)	27.8 (3.9)
Daily smoker, %	2857 (35.1)	798 (27.7)	840 (18.2)	717 (13.1)
Education				
Primary	2382 (29.2)	1176 (40.8)	1180 (26.6)	1425 (26.3)
Upper secondary	3152 (38.7)	1039 (36.0)	1625 (36.6)	1770 (32.6)
College/university <4 years	1415 (17.4)	402 (13.9)	909 (20.5)	1135 (20.9)
College/university ≥4 years	1193 (14.7)	269 (9.3)	723 (16.3)	1093 (20.2)

Values are means with SD for continuous variables and number and percentage for categorical variables.
*Including stroke and myocardial infraction.

Table 2 Prevalence of current use of lipid lowering drug by sex, education, age and survey. The Tromsø Study 2001–2016.

	Tromsø5 2001	Tromsø6 2007–2008	Tromsø7 2015–2016
Women	361	695	1076
Education			
Primary	238 (12.4)	374 (21.9)	508 (27.1)
Upper secondary	73 (7.9)	203 (11.7)	287 (16.3)
College/university <4 years	9 (3.2)	50 (7.0)	108 (10.6)
College/university ≥4 years	23 (3.9)	56 (5.9)	149 (9.3)
Age, years			
30–39	0 (0)	0 (0)	NA
40–49	6 (1)	15 (1.2)	23 (3.4)
50–59	48 (6.8)	101 (9.5)	173 (7.8)
60–69	170 (12.1)	337 (17.7)	452 (20.2)
70–79	137 (13.1)	242 (27.1)	428 (34.0)
Men	414	805	1234
Education			
Primary	228 (17.8)	269 (22.8)	402 (28.2)
Upper secondary	106 (13.3)	288 (17.7)	390 (22.0)
College/university <4 years	28 (10.7)	141 (15.5)	221 (19.5)
College/university ≥4 years	32 (7.3)	94 (13.0)	189 (17.3)
Age, years			
30–39	0 (0)	0 (0)	NA
40–49	13 (2.8)	39 (3.8)	52 (9.2)
50–59	56 (16.1)	114 (12.3)	226 (12.9)
60–69	194 (16.3)	395 (22.6)	500 (24.9)
70–79	151 (17.9)	257 (32.74	456 (39.3)

Values are presented as number observations of lipid lowering drug user and percentage.

results from the sensitivity analysis (n=2710, analysis not shown) demonstrated similar trends in total cholesterol levels across all education groups and for both women and men across all age groups.

DISCUSSION

In this study, participants on LLD treatment experienced a substantial decrease in total cholesterol levels over time compared with those untreated, with a larger effect observed among men. An educational gradient in total cholesterol levels was observed among untreated participants but not among those treated.

The association between education and total cholesterol levels has been investigated previously.[13] However, the results have been inconsistent in the literature. While a Swedish study found an association between higher education and lower total cholesterol levels,[10] a UK study found no association between education and total cholesterol levels among men.[13] Similarly, an American study[19] found no association between educational level and total cholesterol levels. Several potential mechanisms thought to cause differences in mortality and morbidity related to SES have been studied. For instance, people with lower education levels are more likely to engage in harmful behaviours to their health, such as non-adherence to medication regime.[20] Individuals with higher education levels tend to exhibit greater health awareness, which could drive a more positive attitude towards cholesterol treatment.[14] Furthermore, previous studies have indicated that non-adherence to LLD treatment is more prevalent among individuals with lower SES,[21] while individuals with lower education levels are less likely to receive statin treatment.[22] Higher education levels are associated with health literacy,[23] which is important for medication adherence.[24] These factors can contribute to the widening of health inequalities in total cholesterol levels.

Our study highlighted differences among users and non-users of LLDs. An educational gradient was only observed among non-users, indicating that LLD treatment contributes to the longitudinal reduction of educational differences in total cholesterol levels. Eggen *et al*[16]

Table 3 Age adjusted mean cholesterol according to baseline education, survey and LLD use by sex. The Tromsø Study 1994–2016.

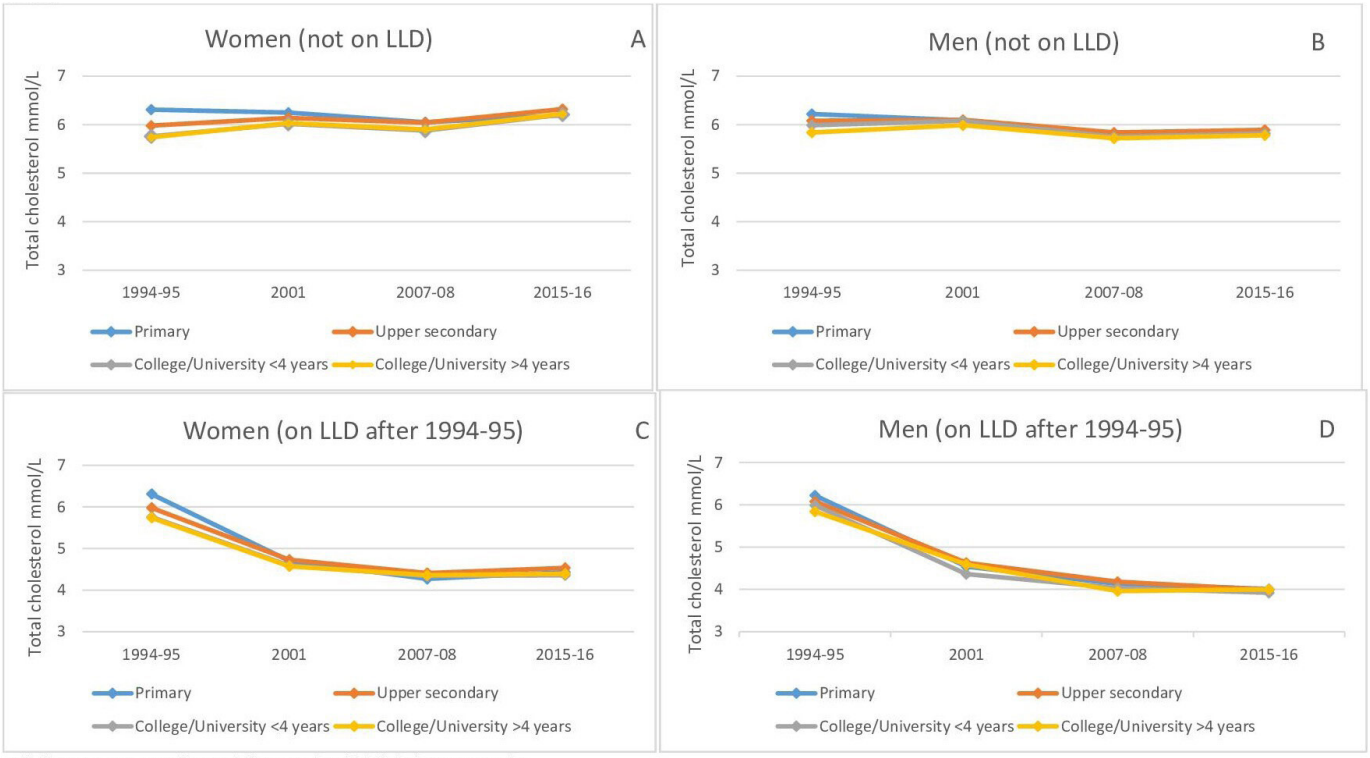
Education	Tromsø4 1994–1995	Tromsø5 2001	Tromsø6 2007–2008	Tromsø7 2015–2016	Change, Tromsø7 vs Tromsø4
Women					
Not on LLD in any survey					
Primary	6.31 (6.27, 6.35)	6.25 (6.20, 6.29)	6.05 (6.01, 6.10)	6.19 (6.14, 6.24)	−0.12 (−0.17,−0.07)
Upper secondary	5.98 (5.95, 6.02)	6.14 (6.09, 6.19)	6.04 (5.99, 6.08)	6.32 (6.27, 6.36)	0.33 (0.29, 0.37)
College/university <4 years	5.76 (5.70, 5.82)	6.02 (5.92, 6.11)	5.88 (5.80, 5.95)	6.21 (6.14, 6.27)	0.45 (0.39, 0.51)
College/university ≥4 years	5.74 (5.68, 5.80)	6.03 (5.93, 6.12)	5.90 (5.83, 5.98)	6.22 (6.16, 6.28)	0.48 (0.42, 0.54)
P-value*	<0.001	<0.001	<0.001	0.53	<0.001
		On LLD	**On LLD**	**On LLD**	
Primary		4.70 (4.59, 4.81)	4.27 (4.19, 4.36)	4.43 (4.35, 4.50)	−1.88 (−1.96, −1.81)
Upper secondary		4.37 (4.19, 4.55)	4.41 (4.30, 4.52)	4.53 (4.45, 4.62)	−1.45 (−1.53, −1.37)
College/university <4 years		4.59 (4.27, 4.92)	4.34 (4.13, 4.56)	4.36 (4.21, 4.50)	−1.40 (−1.55, −1.26)
College/university ≥4 years		4.57 (4.15, 4.99)	4.36 (4.13, 4.59)	4.39 (4.22, 4.55)	−1.35 (−1.51, −1.19)
P-value*		0.13	0.11	0.84	<0.001
Men					
Not on LLD in any survey					
Primary	6.22 (6.18, 6.26)	6.09 (6.03, 6.15)	5.79 (5.74, 5.85)	5.82 (5.76, 5.88)	−0.40 (−0.46, −0.35)
Upper secondary	6.08 (6.04, 6.12)	6.10 (6.04, 6.16)	5.84 (5.80, 5,89)	5.89 (5.84, 5.93)	−0.19 (−0.23, −0.15)
College/university <4 years	5.99 (5.93, 6.04)	6.08 (5.99, 6.17)	5.75 (5.68, 5.82)	5.82 (5.75, 5.88)	−0.17 (−0.23, −0.11)
College/university ≥4 years	5.84 (5.78, 5.90)	5.99 (5.88, 6.09)	5.72 (5.64, 5.79)	5.78 (5.71, 5.85)	−0.06 (−0.12, 0.00)
P-value*	<0.001	0.15	0.04	0.16	<0.001
		On LLD	**On LLD**	**On LLD**	
Primary		4.54 (4.43, 4.65)	4.13 (4.04, 4.22)	4.01 (3.92, 4.09)	−2.21 (−2.29, −2.14)
Upper secondary		4.63 (4.50, 4.77)	4.18 (4.09, 4.28)	3.99 (3.91, 4.06)	−2.09 (−2.16, −2.02)
College/university <4 years		4.36 (4.13, 4.58)	4.03 (3.89, 4.17)	3.92 (3.81, 4.03)	−2.07 (−2.17, −1.97)
College/university ≥4 years		4.59 (4.25, 4.94)	3.96 (3.79, 4.14)	4.00 (3.89, 4.13)	−1.84 (−1.96, −1.72)
P-value*		0.67	0.07	0.59	<0.001

Adjusted for age in 1994–1995 (Tromsø4).
*P value for linear trend by education.
LLD, lipid lowering drug.

and Flege *et al*[25] reported similar findings, indicating that LLDs contribute to reducing educational differences associated with total cholesterol levels. However, their results were on secular trends in total cholesterol levels. On the other hand, it is important to consider that the generous reimbursement policy in Norway may have played a role in reducing the social inequality observed in our study. In China, immediate reimbursement reduced the health inequality caused by SES.[26] Similarly, in a study in Italy, reimbursements contributed to increasing statin usage, while changes in reimbursement policies (ie, removal of co-payment) led to decreased statin use.[27]

In the present study, a decrease in total cholesterol levels was observed among users of LLD; yet, this decrease was larger among men. This finding aligns with another study, which observed a lesser decline in total cholesterol levels among women compared with men following statin treatment.[28] A larger reduction in cholesterol among men in general could possibly be explained by the fact that women have been shown to be less likely to be offered statin therapy and are more likely to decline statin therapy. However, even among statin users, women are more likely to discontinue statin therapy and more likely to discontinue due to side effects compared with men.[29]

We observed a general decrease in total cholesterol levels over time. A similar pattern has been observed regarding secular trends in total cholesterol levels,[30] although one longitudinal study reported an increase in total cholesterol levels.[31] Population-based studies of longitudinal trends in total cholesterol levels are scarce, particularly those that also assess the association of these levels with education and treatment with LLD. A decrease in total cholesterol levels without LLD treatment has



All figures were adjusted for age in 1994-95 (Tromsø4).

Figure 2 Observed estimated mean longitudinal cholesterol (mmol/L) in women and men over surveys and education among non-user of lipid-lowering drugs (LLD) (A and B) and user of lipid-lowering drugs from 2001 (Tromsø5) to 2015–2016 (Tromsø7) (C and D). The Tromsø Study 1994–2016.

previously been partially explained by dietary changes[32] or a reduction in smoking.[33] Hopstock *et al*[15] and Ferrières *et al*[34] found that individuals who used LLDs demonstrated larger decreases in total cholesterol levels than non-users; however, LLD use could only partly explain these changes.[15]

The Norwegian government's efforts to promote changes in smoking, physical activity and dietary behaviours over the past few decades may have played a role in this decline.[35] However, in the present study, we observed a substantial decrease in total cholesterol levels among users of LLD compared with non-users, indicating that LLD treatment contributes to reducing social inequality in cardiovascular health. There is a widening health gap between individuals with high and low SES in Norway and several other Western European countries,[36] particularly with respect to cardiovascular mortality and morbidity.[11] This highlights the necessity of finding optimal medical treatments. It is also important to acknowledge that the ability to engage in lifestyle changes is often associated with financial implications. Investing in good health requires exercise (eg, joining gyms and clubs), tobacco cessation (eg, paying for consulting) and a healthy diet (eg, buying fresh fruit and vegetables or lean meats).[37] LLDs in Norway are much cheaper due to the reimbursement policy which is available for all Norwegian citizens regardless of SES, therefore, their use could contribute to decreasing the educational gradient associated with total cholesterol levels in the Norwegian population and in countries with similar reimbursement policy.

This study has several strengths, including its population-based design and repeated measurements of total cholesterol levels and LLD use in the same individuals over a two-decade period. The self-reported education variable in the Tromsø Study has previously been validated.[38] However, this study has some limitations. The study lacks information about the exact time of LLD treatment, which restricted us to investigating participants' LLD treatment at the time of their attendance. There are some certain groups that are underrepresented in the Tromsø Study, including men, unmarried individuals, those with lower SES, residential renters and individuals born outside of Norway.[39] Therefore, valuable information related to these groups may be missing. Lastly, while it would not affect our results as we focused on trends over time, it is important to note that total cholesterol measurements in our study were non-fasting.

In conclusion, LLD users experienced a more substantial decrease in total cholesterol levels over time compared with non-users. The educational gradient in total cholesterol levels observed among LLD non-users was not apparent among users. Strategies aimed at making LLD more affordable and accessible for all social groups, such as reimbursement policies, may potentially reduce the social disparity associated with cholesterol management.

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Ethics approval The Tromsø Study involves human participants and was approved by the Regional Norwegian Data Protection Authority and the Regional Committee of Medical and Health Research Ethics in Norway (REC North). It was conducted according to the Declaration of Helsinki. This study was approved by the REC North (reference 60845) and the Norwegian Centre for Research Data (reference 809230). Participants gave informed written consent to participate in the Tromsø Study before taking part in 1994-2016 (Tromsø4-7).

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