

Determinants of inter-individual cholesterol level variation in an unbiased young male sample

Frank Jakobus Rübli^a, Maciej Henneberg^b, Dominik J. Schaer^c, Alexander Imbof^c, Boris Schleiffenbaum^d, Ulrich Woitek^e

^a Institute of Anatomy, University of Zurich, Zurich, Switzerland

^b Anatomical Sciences, University of Adelaide, Adelaide, Australia

^c Department of Internal Medicine, University Hospital Zurich, Zurich

^d Faculty of Medicine, University of Zurich, Zurich

^e Institute for Empirical Research in Economics, University of Zurich, Zurich

Summary

Question under study: affected by individual life style, the total cholesterol serum level is a major morbidity and mortality risk factor for atherosclerotic cardiovascular disease (CVD). We present total cholesterol values and their possible aetiological factors of young Swiss conscripts. Particularly, we study varying impact of these factors depending on different levels of individual cholesterol.

Methods: male conscripts (n = 19,272) of the 2005 census of the conscripts have been examined, reflecting ca. 59% of a total Swiss male birth cohort. Quantile regression allows us to analyse responses of arbitrary quantiles with respect to variables of interest.

Results: eleven percent of all conscripts show clinically important increased total cholesterol levels. There is a major association of high indi-

vidual cholesterol level with French regional language. The largest socio-economic subsample – agricultural and construction workers – show significantly higher individual cholesterol levels than employees in the industry sector and students, respectively.

Conclusions: we were able to find that culture, as indicated by the mother tongue, and socioeconomic status as indicated by profession/vocation, influence individual total cholesterol levels while climate as indicated by altitude does not have an influence on cholesterol levels. Such a broad screening programme offers a unique opportunity to target persons at high-risk for CVD morbidity and mortality already early in life.

Key words: atherosclerosis; blood; conscripts; quantile regression; risk factors; socio-economic; Swiss

Introduction

Individual life style, apart from genetic influences, affects the level of total serum cholesterol, a major morbidity and mortality risk factor for atherosclerotic cardiovascular disease (CVD) [1, 2]. Abnormal plasma lipid levels in particular are part of the so-called metabolic syndrome, a major public health problem in modern Western societies [3]. Particularly, it is known that the CVD death risk increases substantially for younger men with high serum cholesterol levels [2]. Yet, studies of the influence of the socio-economic status (SES) on serum cholesterol levels are largely lacking [4–6]. It is well known that socio-economic variables influence the nutritional status of a particular population [7]: the higher the real *per*

capita income, the greater the availability of food, both in terms of quantity and quality.

In Switzerland the conscription system of young male citizens provides a unique representative study sample of an economically prosperous and educationally egalitarian society with unrestricted access to a high-quality health care system. Because conscription is mandatory, the sample is unbiased and permits the study of cultural differences across the cantons, reflected, eg, by the existence of four different mother tongues within a 200 km radius. It has been shown that regional diversity significantly follows language boundaries, eg, with respect to number and times of meals per day or in terms of awareness of food-related problems [8].

We present total cholesterol values and their possible aetiological factors in young Swiss conscripts. Instead of traditional explorations of the percentage impact of a single factor on an individual's total cholesterol value, we focus on the vary-

ing impact of such a component depending on different levels of individual cholesterol. Other cardiovascular risk factors, such as body mass index values collected during recruitment, will be presented in another publication [9].

Material and methods

Male conscripts (n = 19,272; birth years 1984–1987) of the 2005 census of the draft Armed Forces were examined, reflecting ca. 59% of a total Swiss male birth cohort (Federal Statistical Office, FSO, www.statweb.admin.ch, Tbl. BEV016A). The newly introduced expanded recruitment concept of the Swiss Army, which is a draft army for male citizens, includes assessment of individual body dimensions (height, weight), sports performance indicators (distance covered during 12 min run) and voluntary laboratory tests (total cholesterol measured; Integra®, Roche). No cholesterol subfractions were determined and fasting status of individuals was not recorded. Average taxable income on the municipality level at the year of birth was used as a proxy of socio-economic status. To capture cultural influences, we used the main language in the individual's municipality, and considered the impact of altitude to control for climate. Full information is available for 15,304 conscripts. No specific ethical approval is required for anonymous Swiss governmental statistical data (Swiss data privacy act, SR 235.1; 19.6.1992).

All fully anonymous data were analysed with programs written in Matlab® (version 7.2.0.232 R2006a; The

MathWorks GmbH, Aachen, Germany; quantile regression code: <http://www.econ.uiuc.edu/~roger/research/rq/rq.html>). In the context of the present study, linear regression has the disadvantage that it explains the location of the cholesterol distribution only. Quantile regression allows us to analyse the impact of changes in variables of interest (eg, sports performance) on arbitrary quantiles of the cholesterol distribution [10] (see also further explanations in appendix). This is of particular interest when analysing data (eg, cholesterol) where the reaction of the tails of its distribution (extreme values) to aetiological factors (eg, sports performance) is important. We examined the quantiles of the cholesterol distribution on socio-economic status (= individual self-reported professions and vocations were grouped into main categories according to the *Berufsnomenklatur 2000* classification of the FSO), reflecting potential “peer-group” effects. Where possible, the data are in logs. This transformation allows interpreting the results as elastically, ie, as a percentage reaction of cholesterol levels to a one percent change in the explanatory variable, eg, BMI.

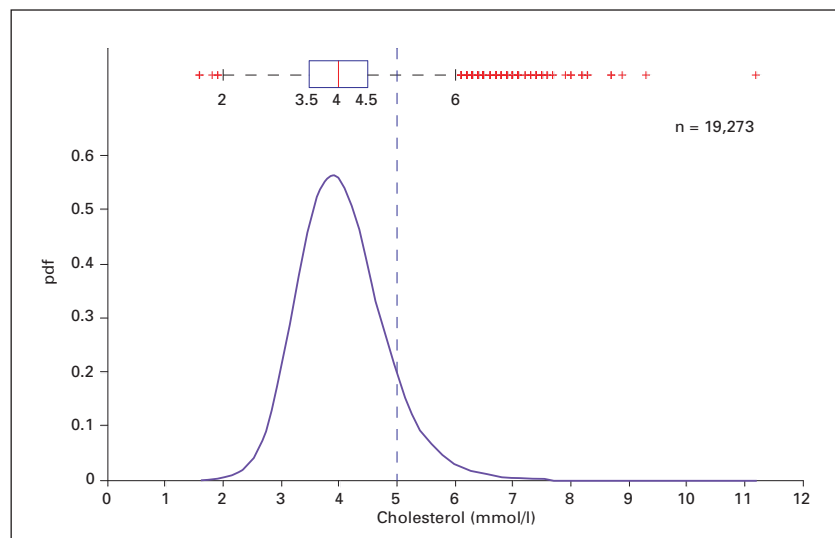
Results

Eleven percent of all conscripts had a total cholesterol level higher than the official European consensus guidelines (<5 mmol/l; [11]) (fig. 1). The solid curve displayed in figure 2 represents the percentage difference of cholesterol levels between certain age groups (18, 20, 21 years) and the reference age group (19 years) for the 5–95% quantile range. The dotted curves represent 95% confidence intervals. A significant impact of age – relative to the largest subsample of 19 year olds –

was found only for the age group of the 20 year olds with high total cholesterol (above 75th percentile), for all cholesterol levels at age 21, but not for the youngest age group. Whenever significant, the impact was relatively constant across quantiles. Figures 3–5 can be interpreted accordingly. A major association of high individual cholesterol level was French regional language (fig. 3). The largest socio-economic subsample – agricultural and construction sectors – showed significantly

Figure 1

Distribution of total cholesterol levels in young Swiss male conscripts. Sample averages: height: 178.1 cm, weight: 72.6 kg and body mass index: 22.86 kg/m².



higher individual cholesterol levels than employees in the industry sector and students, respectively, especially for the absolute lower values (fig. 4). Individual sports performance was negatively correlated with cholesterol level (significant

above the 35th percentile; fig. 5, see also the discussion in the appendix). This correlation was increasingly marked with higher absolute values of the latter. Body mass index and cholesterol were positively related, with a stronger correlation for

Factors influencing individual total cholesterol levels in Swiss male conscripts (solid line: estimated parameter, dotted lines: 95% bootstrap confidence interval; dashed horizontal line: zero response).

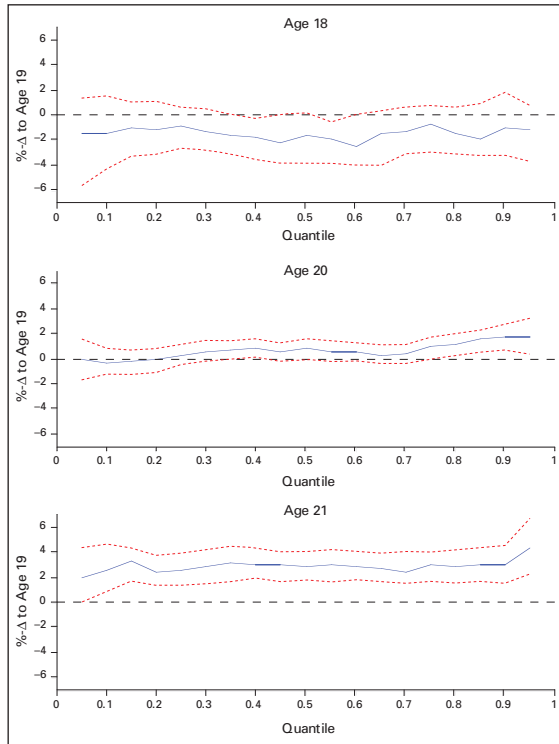


Figure 2

A significant impact of individual age can be found primarily for all cholesterol levels for the age group of the 21 year olds.

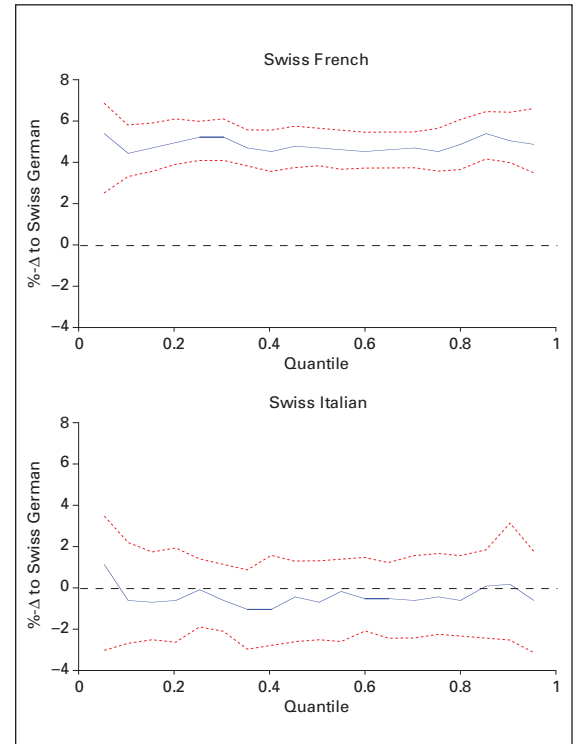


Figure 3

Conscripts with French language – unlike Italian – show significantly higher cholesterol values, for all quantiles, than their German-speaking counterparts (reference group).

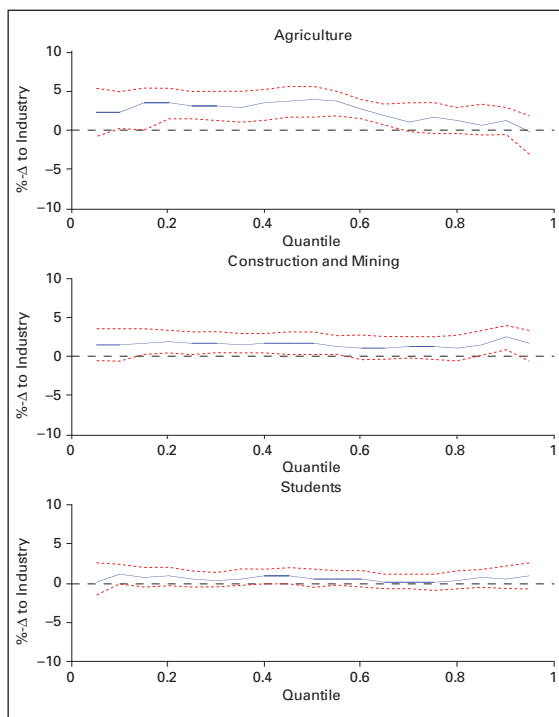
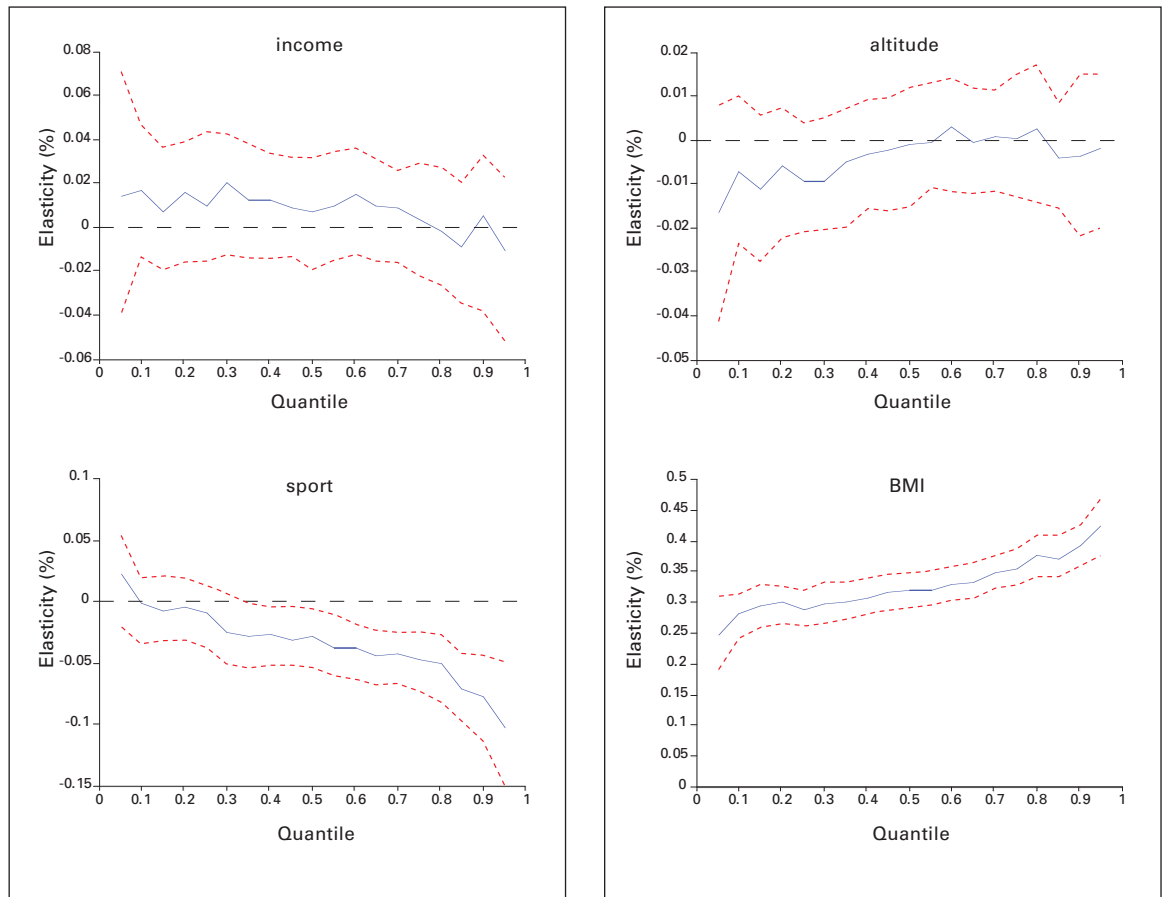


Figure 4

In comparison to the largest socio-economic subsample – industrial production (reference group) – employees in the agricultural and construction sectors show significantly higher values for most quantiles. Students show cholesterol values similar to the reference category.

Figure 5

The impact of income and altitude is not significant for all quantiles. Better sports performance reduces increasingly individual cholesterol the higher the latter is (significant only for individual values above the 35th percentile). BMI has a significantly positive influence on cholesterol for all quantiles.



higher cholesterol levels (fig. 5). The influence of climate – and thus altitude – on human body form is well known [12] since the work by Allen [13] and Bergmann [14]. Switzerland, in particular, with its wide range of habitats regionally varying from 280 metres above sea level up to 1430 me-

tres above sea level, is a model country for further exploring factors possibly influenced by altitude and thus climate. We found no significant impact of altitude on individual cholesterol; the same is true for municipality income (fig. 5).

Discussion

We were able to find and exclude various as yet unstudied factors influencing individual total cholesterol levels. Regional language has a high impact possibly reflecting ethno-cultural differences. A “peer-group”-like effect may be causative for the higher cholesterol values in certain professions. Our results originate from a representative sample of a highly developed, egalitarian society. The sample can be seen as representative for the following reasons: the size of the full sample (participants and non-participants) relative to a total male Swiss birth cohort is about 87%. A comparison of the height, weight and BMI distributions of participants and non-participants shows minimal differences only (fig. 6). In addition, we are not aware of a reason for non-participation which could cause a systematic bias. Generally, a higher percentage of non-participants was found in western cantons compared to their eastern counterparts, yet this should not constitute a bias since participants and non-participants of volun-

tary laboratory tests do not differ significantly in terms of individual height or weight and BMI.

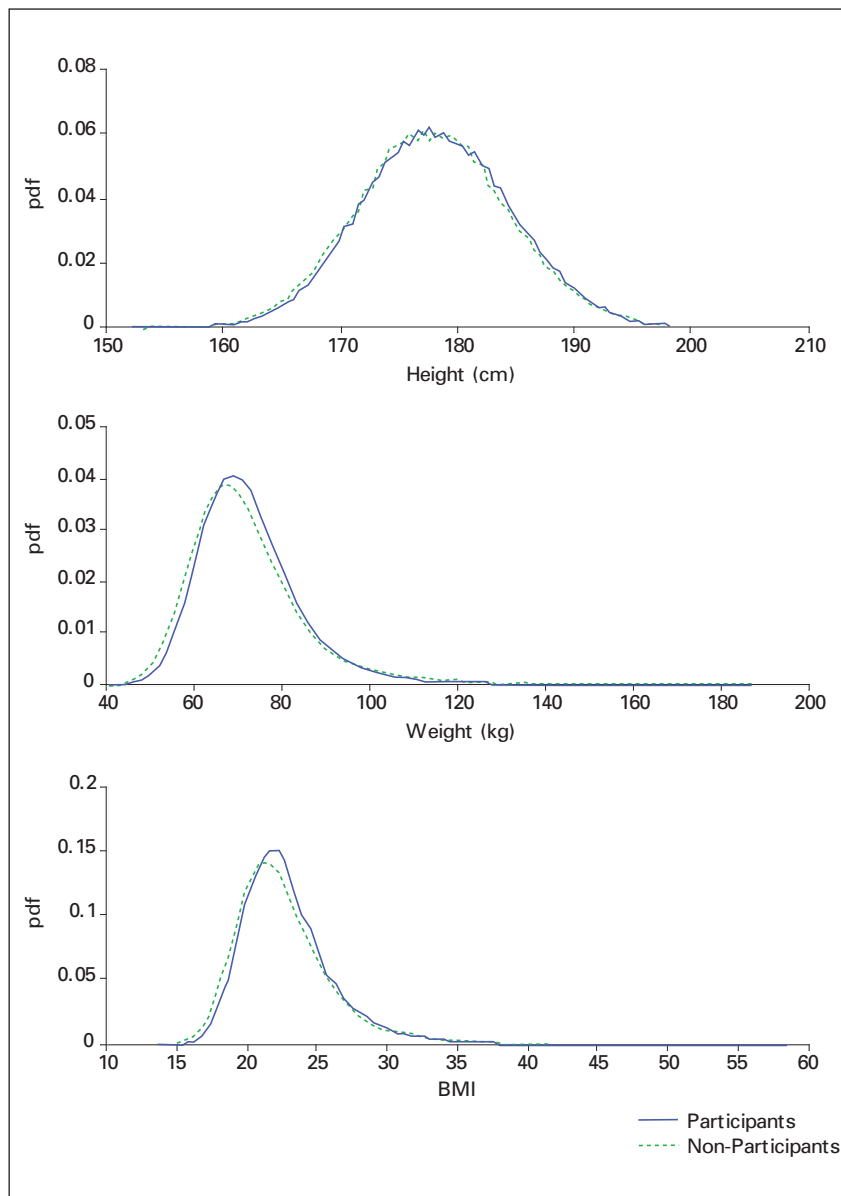
The results demonstrate that allowing for a changing impact dependent on the cholesterol level reveals information beyond what is possible in the usual linear regression context: while the impact of age and regional language is almost constant across quantiles, this is not true for sports performance and BMI, where intervention on the individual level is feasible.

Generally, such a screening programme offers a unique opportunity to target persons at high-risk for disease morbidity and mortality already early in their lives. For example, a possible correlation of individual stature morbidity and mortality risk has been addressed in studies of military personnel [15, 16]. Surprisingly, most data sets consist of biased samples, eg, with most of the conscripts data originating from volunteer army recruits, unlike the unbiased data of our study. The early detection of these risks should prompt

Figure 6

Distribution of Anthropometric Measures of Conscripts (Participants, $n = 19,271$; and Non-Participants, $n = 9287$). Medians: Height: 178 cm (both groups); Weight: 70 kg (Participants), 71 kg (Non-Participants); BMI: 22.0 (Participants), 22.3 (Non-Participants).

Note that there is a slight shift of the non-participant distributions of weight and BMI to the left.



more specific peer-group-oriented preventive measures and, thereby, prevent or at least delay more serious health complications such as stroke or myocardial infarction. Thus, society as a whole as well as public health programmes will benefit from such unbiased anthropometric information on possible groups at risk.

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Correspondence:

F. J. Rübli, MD, PhD

Institute of Anatomy

University of Zurich

Winterthurerstr. 190

CH-8057 Zurich

Switzerland

E-Mail: frank.rubli@anatom.uzh.ch

Appendix: quantile regression analysis

The method of ordinary least squares is a tool to estimate the parameters of the relationship between explanatory variables X_j , $j = 1, \dots, n$, and the expected value of a dependent variable Y , conditional on the realisations of the X_j 's. Changes in

the explanatory variables have an impact on the location of the distribution of Y by changing the conditional expected value. In applications where extremes are important, such as in the present study, the change in the expected value might not

be the most interesting issue. Quantile regression analysis allows modeling the relationship between the X_i 's and the quantiles of the distribution of Y , conditional on the realisations of the X_i 's. To illustrate the idea, consider the first, second, and third quartile of the cholesterol distribution,

conditional on high (above 90 percent quantile, 3050 m/12 min), medium (between 45 and 55 percent quantile, 2550 m/12 min and 2650 m/12 min), and low (less than 10 percent quantile, 2050 m/12 min) sports performance (table 1).

Table 1

Cholesterol Distribution (mmol/l) conditional on Sports Performance.

	Sports Performance		
	Low	Medium	High
First Quartile	3.6	3.5	3.5
Second Quartile	4.1	4.1	3.9
Third Quartile	4.7	4.5	4.3
n	1571	1669	1457

For the first quartile of the cholesterol distribution, improving sports performance does not have an effect on cholesterol levels. For the second quartile, moving from low to high sports performance induces a reduction in cholesterol level by 0.2 mmol/l (5%), while it is almost 0.4 mmol/l (9%) for the third quartile. Quantile regression allows detecting these effects, thus giving a more complete picture taking into account the effects of changes of explanatory variables on the entire shape of the distribution of the variable of interest: the result displayed in figure 5 shows clearly the increase in the impact of improving sports performance when moving to higher quantiles of the cholesterol distribution. Thus, the higher the individual cholesterol level, the stronger the effect of improving sports performance on reducing individual cholesterol level.

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