Changes in total cholesterol levels in Western societies are not related to statin, but rather dietary factors: the example of the Icelandic population

Bolli Thorsson1, Laufey Steingrimsdottir2, Sigrun Halldorsdottir1, Karl Andersen3,4, Gunnar Sigurdsson3,4, Thor Aspelund1,3, and Vilmundur Gudnason1,3*

1Icelandic Heart Association, Holtasmari 1, 200, Kopavogur, Iceland; 2Unit for Nutrition Research Reykjavik, University of Iceland, Reykjavik, Iceland; 3Faculty of Medicine, University of Iceland, Reykjavik, Iceland; and 4Landspitali University Hospital, Reykjavik, Iceland

Received 2 December 2011; revised 17 October 2012; accepted 31 October 2012; online publish-ahead-of-print 2 December 2012

Introduction

In a recent report by Farzadfar et al.,1 on global trends in serum total cholesterol (TC), it is suggested that HMG-CoA reductase inhibitors (statins) are important for lowering of average TC in high-income countries and that statin use is a likely driver of the polarized trend in average TC seen between low- and high-income countries. On the other hand, our results show that statins are not a key driver of lowering of average TC in the Icelandic population observed over the last decades. This is further supported by findings from USA,2 Scandinavia,3,4 and Czech Republic.5 Where the drop in cardiovascular mortality has been examined, by applying the IMPACT model, that examines the contribution of changes in various risk factors and interventions on cardiovascular mortality, the role of reduction in cholesterol levels has been demonstrated and largely shown to be related to other factors than intervention.6–9

The tendency to overestimate the impact of effective pharmacological intervention on the population cholesterol level calls for an understanding of which factors have led to the change in population TC. This applies to society at large, but especially to policy makers who need to allocate limited resources in health care and disease prevention in the most efficient way. Physicians have an important role to play to share their knowledge in this context. This is particularly important in the developing countries where cardiovascular diseases are on an increase.

Cholesterol trend

Total cholesterol levels have lowered considerably in most Western populations in the last decades.1,2,10,11 This is also the case in Iceland as shown in Figure 1A and B. Our results are based on eight cross-sectional studies with individual information on the cholesterol level and concurrent lipid-lowering medication during the period of 1967–2008 in males and females, residents of the Greater Reykjavik area in Iceland (n = 34 237).12 The figure shows data for individuals not taking lipid-lowering medication and thus reflects non-pharmacological effect. This entails information on the bulk of the population; close to 100% in the years 1967–92, 99.7% in 1993, and 93.3% in 2008. The data show that the population level of TC has been decreasing since the mid-1960s, with plateau in the 1980s and steeper fall in the 1990s and the first decade of this century. The drop in population cholesterol can be seen in all age groups and for both genders. The drop is parallel in all age groups. Thus, the driving factor behind these changes affects all generations in the population. These changes are not driven by pharmacological intervention. The mean drop in TC in the Icelandic population over four decades from 1967 to 2008 was 1.5 mmol/L in males and 1.6 mmol/L in females. This drop in the cholesterol level corresponds well with 0.3 mmol/L decrease per decade since 1980, recently reported in the Lancet in some other Nordic and European countries. In their important paper, Farzafar et al. estimate the trend in the mean serum TC in 199 countries in 3.0 million people from 1980 to 2008. Their results show a drop in TC in the high-income region in the world (~0.2 mmol/L per decade) but a slight increase in Southeast Asia and the Pacific (nearly 0.1 mmol/L per decade).1

Impact of cholesterol changes

The impact of this large decrease in cholesterol on public health is enormous. In Iceland the mortality rate from coronary heart disease declined by 80% between 1981 and 2006.13 Of this, 32%
is attributed to the simultaneous drop in population cholesterol levels.\textsuperscript{13} This estimate was based on the well-validated IMPACT model.\textsuperscript{6} In addition to cholesterol, other risk factors contributed to the drop in CHD mortality and this model addresses the contribution of changes in various cardiovascular risk factors and interventions long known to influence cardiovascular outcomes.

Table 1 gives overview of some of the countries where the IMPACT model has been applied. The drop in CHD deaths is $\approx 50\%$ in developed countries, but an increase of $50\%$ was seen in males in Beijing, China.\textsuperscript{14}

The change in cholesterol is smallest in England and Wales: 4.2\%.\textsuperscript{7} This drop in the cholesterol level was calculated to have prevented 9.6\% of CHD deaths. The drop in cholesterol was 6.1\% in USA\textsuperscript{8} and 6.2\% in Italy\textsuperscript{15} and 24 and 23\% of the lowering of CHD deaths, respectively, was attributed to this. In Iceland\textsuperscript{13} and Sweden,\textsuperscript{16} the lowering in cholesterol is somewhat more pronounced at 14.5 and 10\%, respectively, and the attribution to CHD deaths lowering was 32 and 40\%, respectively.

The reverse is seen for Beijing where cholesterol levels have increased since 1984. This coincides with an alarming 50\% increase in CHD in males in Beijing. This increase in cholesterol was considered consistent with the changes from a traditional diet to a Western diet in Beijing.\textsuperscript{14} Statin use in Beijing in the year 1999 was reported only as secondary prevention after myocardial infarction. The use was reported 23\% in 1999 in Beijing compared with 25\% in England and Wales and 36\% in the USA in the year 2000.

**Effect of statins on population cholesterol**

In the early 1990s, when statins were introduced, the population average TC was unaffected by statin use. The Icelandic population average in TC was 5.91 in males and females in the year 1993. In the year 2008, 4.6\% of females and 8.9\% of males 25–74 years of age used statins. For comparison, 7.6\% of females and 10.4\% of males aged 25–74 years in Sweden used statins the year 2004\textsuperscript{3} and in the same year 11.7\% of US population 20 years and older used statins.\textsuperscript{17}

The average cholesterol level for females in Iceland without statins in 2008 was 5.11 mmol/L and the population average (which includes also statin users) was 5.10 mmol/L. The average cholesterol level for males without statins was 5.18 mmol/L and the population average was 5.10 mmol/L. The fall in TC by statin use is also shown in Figure 2A and B. The trend for individuals not using statins is almost superimposable on the population.


### Table 1: Overview of the impact of population total cholesterol changes in different counties based on publications where the IMPACT model was used

<table>
<thead>
<tr>
<th>Study period (years)</th>
<th>Gender</th>
<th>England and Wales(^a)</th>
<th>USA(^b)</th>
<th>Italy(^c)</th>
<th>Iceland(^d)</th>
<th>Sweden(^e)</th>
<th>Beijing(^f)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHD deaths per 100 000 at beginning and end of study period</td>
<td>Both</td>
<td>25–84</td>
<td>25–84</td>
<td>25–84</td>
<td>25–74</td>
<td>25–84</td>
<td>35–74</td>
</tr>
<tr>
<td>Change in cholesterol levels (direction and %)</td>
<td>Male</td>
<td>↓6.2</td>
<td>↓4.7</td>
<td>↓79</td>
<td>↓53</td>
<td>↑10</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>↓4.5</td>
<td>↓51</td>
<td>↓82</td>
<td>↓52</td>
<td>↑127</td>
<td></td>
</tr>
<tr>
<td>TC (mmol/L) at beginning and end of the study period</td>
<td>Both</td>
<td>—</td>
<td>5.67–5.33</td>
<td>5.62–5.27</td>
<td>6.01–5.14</td>
<td>6.15–5.51</td>
<td>4.30–5.33</td>
</tr>
<tr>
<td>Change in population TC (%)</td>
<td>Both</td>
<td>4.2</td>
<td>6.1</td>
<td>6.2</td>
<td>14.5</td>
<td>10.4</td>
<td>24.0</td>
</tr>
<tr>
<td>Change in CHD death attributed to change in TC (%)(^g)</td>
<td>Both</td>
<td>9.6</td>
<td>24.2</td>
<td>23.4</td>
<td>31.6</td>
<td>39.5</td>
<td>76.7</td>
</tr>
<tr>
<td>Statin use secondary prevention (%)(^h)</td>
<td>Both</td>
<td>25</td>
<td>36</td>
<td>44</td>
<td>94</td>
<td>49</td>
<td>23</td>
</tr>
<tr>
<td>Statin use primary prevention (%)(^i)</td>
<td>Both</td>
<td>3</td>
<td>20</td>
<td>17</td>
<td>4</td>
<td>6</td>
<td>—</td>
</tr>
</tbody>
</table>

\(^a\)In the IMPACT papers a regression approach is taken to calculate the numbers of deaths prevented or postponed (NDPP) as a result of a change in risk factor. The formula is \( \text{NDPP} = \frac{\text{log-hazard rate of death for 1 unit change in the risk factor}}{\text{proportion of deaths prevented which is attributed to the risk factor}} \times \text{number of deaths prevented or postponed due to changes in disease rates} \).

\(^b\)Statin use at the end of the study period.

Trend. The steep fall in the mean TC seen in those taking statins most likely reflects more widespread use of statins in secondary prevention in patients with relatively normal cholesterol level. Given on average 30% effect of statins on individual cholesterol levels and the above mentioned prevalence of statin use in 2005, it can be estimated that the mean cholesterol level for England and Wales was 5.17 mmol/L in men and 5.10 mmol/L in women, which is lower than the average 25% on individual cholesterol levels and 10% prevalence of statin use in the population.\(^4\) In the Czech Republic the cholesterol levels dropped by 1.1 mmol/L between 1985 and 2007 (this was arrived to by estimating the effect of statins to be on average 25% on individual cholesterol levels and 10% prevalence of statin use in the population).\(^5\) In the Czech Republic the cholesterol levels dropped by 1.1 mmol/L between 1985 and 2007 (this was arrived to by estimating the effect of statins to be on average 25% on individual cholesterol levels and 10% prevalence of statin use in the population).\(^5\) In the Czech Republic the cholesterol levels dropped by 1.1 mmol/L between 1985 and 2007 (this was arrived to by estimating the effect of statins to be on average 25% on individual cholesterol levels and 10% prevalence of statin use in the population).\(^5\) In the Czech Republic the cholesterol levels dropped by 1.1 mmol/L between 1985 and 2007 (this was arrived to by estimating the effect of statins to be on average 25% on individual cholesterol levels and 10% prevalence of statin use in the population).\(^5\)

### Changes in consumption coincide with lowering cholesterol levels

We suggest that the large fall in cholesterol in Iceland between 1981 and 2008 is driven by major changes in the diet. Food supply data from the Public Health Institute of Iceland reveal that the diet in the 1970s was characterized by high consumption of whole milk and dairy products, stick margarine, butter, lamb, mutton, and fish. Between 1980 and 2006 there was a considerable drop in consumption of foods contributing most of the saturated fatty acid in the diet. Whole milk consumption dropped by 73%, from 238 kg/person/year to 64 kg, butter decreased by 44% from 3.9 to 2.2 kg/person/year and consumption of margarines made from hydrogenated fats decreased from 11.7 to 3.2 kg/person/year; the largest drop occurring in the 1990s, when the most significant drop in cholesterol is also seen. Margarine was mainly replaced by vegetable oils which showed an 88% increase, from 7.6 to 14.3 kg/person/year.
The lamb supply has been replaced by other meat products, mainly poultry and pork. From the 1990s the consumption of total fat in E% calculated from the food supply statistics has decreased from 40E to 35E%, but the composition of the fat has also changed from more saturated and trans-fatty acids to cis-unsaturated.

Similar trend in diet can be seen elsewhere. In Finland, consumption of high-fat milk products and butter decreased by 86 and 67%, respectively, in the period from 1982 to 2007 and consumption of skimmed milk increased by six-fold.4 The total fat intake in Finland decreased from nearly 40E% in the late 1960s to close to 30E% in 2007.20

The timing of the largest changes in both diet and cholesterol in Iceland coincides with the introduction of a national nutrition policy by the Icelandic government in the year 1987, where the reduction in saturated fat was greatly emphasized. Subsequently, the Icelandic Nutrition Council elaborated this further in Nutrition recommendations and Nutritional Goals, which had a great influence on nutrition education and awareness in the country. However, it is a limitation to not being able to address the effect of other potentially confounding factors that may have influenced the changes in cholesterol levels, such as physical activity.

**Conclusion**

The polarized trend in population TC in high- and low-income countries, recently described in the report on global trends lipids,1 is therefore likely to be driven by difference in awareness about healthy diet and the resulting dietary change rather than pharmacological intervention.

Our results demonstrate the importance of collaboration between health scientists, interest groups, and government, and setting and actively implementing nutritional goals at the population level, resulting in a profound impact on the population health.

**Authors’ contributors**

B.T., T.A., V.G., and L.S. drafted the manuscript. T.A. and S.H. did the data analysis. Data collection and preparation were done

---

**Figure 2** The total cholesterol age adjusted to the age of 50 in (A) men and (B) women from 1967 to 2008. Population average (boxes), individuals taking statins (triangles), individuals not taking statins (diamonds).
by B.T., T.A., S.H., L.S., K.A., G.S., and V.G. All authors contributed to the interpretation of the results, read, and commented on the manuscript and approved the final version.

**Funding**

This study was funded by Icelandic Heart Association.

**Conflict of interest:** none declared.

**References**


**Corrigendum**


Rianne M.F. van Schie, Judith A.M. Wessels, Saskia le Cessie, Anthonius de Boer, Tom Schalekamp, Felix J.M. van der Meer, Talitha I. Verhoeef, Erik van Meegen, Frits R. Rosendaal, and Anke-Hilse Maitland-van der Zee, for the EU-PACT Study Group

This paper was published with a wrong formula. The incorrect formula (1), which is on page 1911, is:

$$\text{MD} = \frac{D_1 \cdot e^{-2k} + D_2 \cdot e^k + D_3}{1 - e^k}$$

The correct formula is:

$$\text{MD} = \frac{1 - e^{-k}}{e^{-k}} \cdot D_1 \cdot e^{-2k} + D_2 \cdot e^k + D_3$$

The authors apologize for the error.

Published on behalf of the European Society of Cardiology. All rights reserved. © The Author 2013. For permissions please email: journals.permissions@oup.com