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Reply to: "Seasonal variations of lipid profiles in a French cohort"

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To the Editor,

We thank Nadif et al. for their interest in our paper [1] and for providing similar data from a French cohort. We read this letter with great interest.

Overall, it seems that the increases in levels of total cholesterol and low-density lipoprotein (LDL) cholesterol observed during winter, especially after the Christmas holidays, occur in both studies from Denmark and France. Nadif et al. state that the time of year with the highest concentrations differs between the two studies; however, both studies find the highest levels of total cholesterol and LDL cholesterol in winter: for the French study from November to January, and for the Copenhagen General Population Study (CGPS) from December to January.

The two studies do differ in other aspects, for example in the percentage of individuals with elevated cholesterol. The French study has a larger proportion of individuals with total cholesterol > 5 mmol/L (> 193 mg/dL) and LDL cholesterol > 3 mmol/L (> 116 mg/dL) during the entire year, compared to the CGPS study. In addition, the odds ratio of hypercholesterolemia (total cholesterol > 5 mmol/L (> 193 mg/dL) and/or LDL cholesterol > 3 mmol/L (116 mg/dL)) in the first week of January compared to summer is still significantly increased in the French study; however, it is substantially lower than in the CGPS.

Another difference between the two studies is that in the French study 54% of the individuals report high alcohol consumption while in the CGPS, 30% report a weekly alcohol intake above guideline limits. Nadif et al. do not specify exactly how much alcohol an individual should drink to have high alcohol consumption. Increasing alcohol intake increases mainly the levels of triglycerides [2] and not total and LDL cholesterol markedly. Surprisingly, however, we found that the mean level of triglycerides in the CGPS is substantially higher than in the French cohort: 1.64 mmol/L (145 mg/dL) in the CGPS *versus* 1.06 mmol/L (94 mg/dL) in the French study. Correspondingly, as shown in Table 1, a larger proportion of individuals in the CGPS have triglyceride levels above 1.7 mmol/L (151 mg/dL); ranging from 33 to 37% in the CGPS and 9.7 to 11.3% in the French study, respectively. In both studies, the proportion of individuals with elevated triglycerides is highest in October, November, December, and in the first week of January. The seasonal variation of triglycerides is not as consistent as for LDL and total cholesterol in the CGPS during the years 2014 through 2017 (Fig. 1); in some years the peak was observed in winter and in other years in summer.

Furthermore, individuals in the French cohort are on average 13 years younger; median age is 46 years in the French cohort *versus* 59 years in the CGPS. In general, both total and LDL cholesterol levels increase with age; however, there is often a decline in the very old. In individuals from the CGPS included in the paper, mean total cholesterol is 4.9 mmol/L (189 mg/dL) for individuals aged 40-49 and 5.4 mmol/L (209 mg/dL) for individuals aged 60-69, an increase also observed in other studies such as the Tromsø study [3]. Surprisingly, however, levels of total cholesterol and LDL cholesterol are higher in the French cohort *versus* the CGPS, 5.5 mmol/L (212 mg/dL) *versus* 5.3 mmol/L (205 mg/dL) for total cholesterol and 3.4 mmol/L (133 mg/dL) *versus* 3.0 mmol/L (116 mg/dL) for LDL cholesterol.

In the French cohort, individuals with non-fasting samples were excluded; however, as lipids and lipoproteins are shown to change only minimally in response to normal food intake and as non-fasting triglycerides have been shown to better predict cardiovascular risk [4–6], the rationale for this seems uncertain.

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Table 1
Proportion of individuals with triglycerides > 1.7 mmol/L (151 mg/dL) in percent, according to time of the year.

	January, February, March	April, May, June	July, August, September	October, November, December	First week of January
CGPS, Denmark	35	33	34	37	37
France	9.7	10	11	11	11

CGPS, Copenhagen General Population Study.

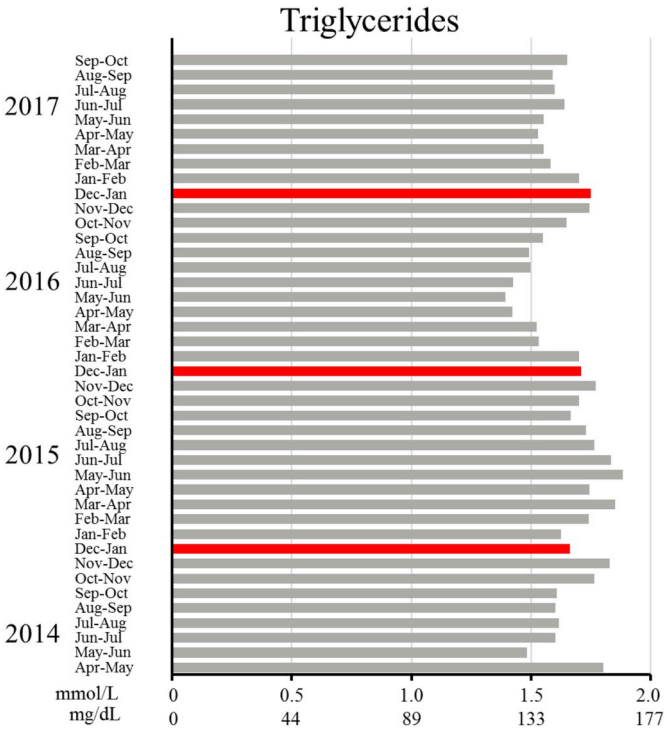

Fig. 1. Seasonal variation in triglycerides in individuals not on cholesterol-lowering therapy in the Copenhagen General Population Study.
Time is grouped from the 15th in the specific month to the 14th in the following month, to better capture the period surrounding the Christmas Holidays.

In general, besides stressing the need for a healthier Christmas celebration, and thereby endangering the "hygge" concept, the results from the CGPS and the French studies shed light on the variations throughout the year in lipid profile values. We would presume that the pathogenesis of cholesterol causing atherosclerosis is mainly due to a long exposure of high levels of cholesterol to the vessel wall, and consequently, the increase in cholesterol seen during the relative short period of Christmas celebration would have little impact on lifelong cholesterol exposure. We therefore recommend lipid testing for cardiovascular risk prediction and lipid-lowering medication control outside the Christmas period.

Conflicts of interests

The authors declared they do not have anything to disclose regarding conflict of interest with respect to this manuscript.

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