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The Christmas holidays are immediately followed by a period of hypercholesterolemia

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HIGHLIGHTS

- Celebrating Christmas is associated with higher levels of total and LDL cholesterol.
- Celebrating Christmas is associated with a higher risk of hypercholesterolemia.
- A diagnosis of hypercholesterolemia should not be made around Christmas.

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ABSTRACT

Background and aims: We aimed to test the hypothesis that levels of total and low-density lipoprotein cholesterol are increased after Christmas and that the risk of hypercholesterolemia is increased after the Christmas holidays.
Methods: We conducted an observational study of 25,764 individuals from the Copenhagen General Population Study, Denmark, aged 20–100 years. Main outcome measures were mean total and LDL cholesterol levels. Hypercholesterolemia was defined as total cholesterol > 5 mmol/L (> 193 mg/dL) or LDL-cholesterol > 3 mmol/L (> 116 mg/dL).
Results: Mean levels of total and LDL cholesterol increased in individuals examined in summer through December and January. Compared with individuals examined in May–June, those examined in December–January had 15% higher total cholesterol levels ($p < 0.001$). The corresponding value for LDL cholesterol was 20% ($p < 0.001$). Of the individuals attending the study during the first week of January, immediately after the Christmas holidays, 77% had LDL cholesterol above 3 mmol/L (116 mg/dL) and 89% had total cholesterol above 5 mmol/L (193 mg/dL). In individuals attending the Copenhagen General Population Study in the first week of January, the multivariable adjusted odds ratio of hypercholesterolemia was 6.0 (95% confidence interval 4.2–8.5) compared with individuals attending the study during the rest of the year.
Conclusions: Celebrating Christmas is associated with higher levels of total and LDL cholesterol and a higher risk of hypercholesterolemia in individuals in the general population. Thus, a diagnosis of hypercholesterolemia should not be made around Christmas, and our results stress the need for re-testing such patients later and certainly prior to initiation of cholesterol-lowering treatment.

1. Introduction

During December, Danes have numerous gatherings with family, friends, and colleagues to celebrate the upcoming Christmas holidays. Likewise, Christmas Eve and the following days are spent with family and friends to “hygge”, a special Danish term, which may be described as “spending cozy time together” [1]. At most of these gatherings, large amounts of food are consumed. Moreover, most individuals are seated for several hours, while eating and drinking, and generally spend sedentary time indoor during the cold and wet holiday season. Traditional Danish Christmas food contains large amounts of fat and sugar. Dishes such as roasted pork, rich sauces, sugar glazed potatoes, and desserts with whipped cream represent a main part of the food ingested.

A long-term high-fat diet has been associated with higher total and low-density lipoprotein (LDL) cholesterol compared with a low-fat diet, at least in overweight and obese individuals [2]. Thus, a month of

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"hygge" accompanied by a Danish Christmas diet could potentially influence patients' chance of a hypercholesterolemia diagnosis if cholesterol levels are determined immediately following the Christmas holidays. Indeed, in a study of 35 individuals 30 years ago, the UK Christmas feast was associated with both gain in weight and slight increases in levels of triglycerides and total and LDL cholesterol immediately following Christmas [3], therefore any hypercholesterolemia diagnosed around Christmas may not reflect the cholesterol levels during the rest of the year.

High cholesterol is a major causal risk factor for cardiovascular disease [4, 5] and targets for cholesterol-lowering therapy are to achieve total cholesterol ≤5 mmol/L (≤193 mg/dL) generally, and ≤4 mmol/L (≤155 mg/dL) in high risk individuals [5]. Likewise, LDL cholesterol should be ≤ 3 mmol/L (≤116 mg/dL) in low risk individuals, ≤2.5 mmol/L (≤97 mg/dL) in high risk individuals, and ≤1.8 mmol/L (≤70 mg/dL) in very high-risk individuals. As cholesterol-lowering therapy is often lifelong, the need to accurately identify individuals in true need of this treatment is pertinent. Thus, attention on possible seasonal variation in cholesterol levels is important.

We hypothesized that in individuals in the general population, levels of total and LDL cholesterol increase after Christmas and that the risk of hypercholesterolemia is increased after the Christmas holidays.

2. Materials and methods

2.1. Study population

We included individuals from the Copenhagen General Population Study (CGPS), a cohort study of the Danish general population of individuals living in Greater Copenhagen.[6, 7] At birth, all individuals in Denmark are assigned a unique identification number in the national Danish Civil Registration System. Using this number, individuals 20–100 years of age were randomly selected to reflect the adult Danish population. Importantly, people are invited randomly by age and sex, year around, securing that the characteristics of individuals examined at any time of year are similar. Also, only white individuals of Danish

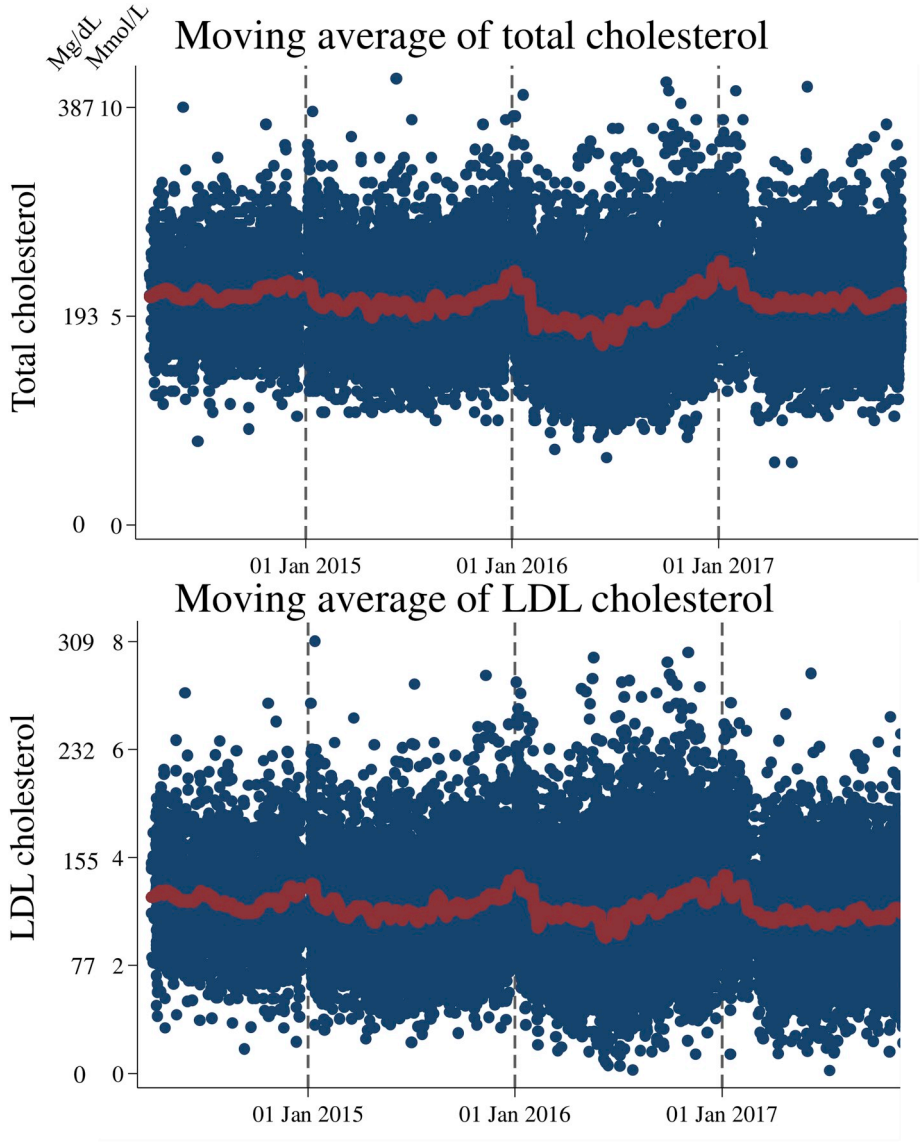

Fig. 1. Moving averages for total and LDL cholesterol from April 2014 to November 2017 in individuals not on cholesterol-lowering therapy in the Copenhagen General Population Study.
Moving averages of total and LDL cholesterol from April 2014 to November 2017. Each blue dot represents an individual measurement. Red dots represent moving average values as the average for 150 individuals before and 150 individuals following each individual person. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

descent mainly with a Christian upbringing are examined; naturally not all people of Danish descent are active Christians, but essentially all celebrate the Christmas holidays. The CGPS was initiated in 2003 with ongoing follow-up examinations started in 2014. Individuals were invited to participate from Monday through Thursday throughout the year, except for national holidays including the Christmas holidays. All participants completed a comprehensive questionnaire, underwent a physical health examination, and had blood drawn for biochemical tests. The study was conducted according to the Declaration of Helsinki, approved by the Ethics Committee of the Capital Region of Denmark (H-KF-01-144/01), and all individuals gave written informed consent. For this study, we included 25,764 individuals from the second examination of the CGPS not on cholesterol-lowering therapy and with total and LDL cholesterol measurements from April 2014 through November 2017, simply to focus on the individuals examined most recently.

2.2. Total and LDL cholesterol

For all subjects participating throughout the year, cholesterol levels were analyzed within 24 h on fresh samples using standard hospital assays. Nonfasting total and LDL cholesterol were measured using colorimetric assays; from 2014 to 2016 levels were determined using a Konelab autoanalyzer and from 2016 and onwards using a Roche Cobas 6000. Hypercholesterolemia was defined as total cholesterol > 5 mmol/L (> 193 mg/dL) or LDL cholesterol > 3 mmol/L (> 116 mg/dL). In 11,055 individuals, we had repeated measurements of total and LDL cholesterol approximately 10 years apart. Of these, 244 individuals participated in the first week of January in 2014–2016 and at another time of the year in 2004–2006 and 227 individuals participated in the first week of January in 2004–2006 and at another time of the year in 2014–2016. Additionally, as a negative control we included repeated measurements from 206 individuals who attended the CGPS in 2014–2016 in the first week of September but had also attended the study at another time of the year in 2004–2006.

2.3. Myocardial infarction

We included the number of first time myocardial infarctions according to time of the year in all 25,764 individuals. Information on myocardial infarction (World Health Organization International Classification of Diseases: ICD8: 410; ICD10: I21−I22) were obtained by linking the CGPS to the national Danish Patient Registry which record all discharge diagnoses from Danish hospitals. In total, we included 333 first time events of myocardial infarction.

2.4. Covariates

Measured weight (kg) and height (m) were used to calculate body mass index (kg/m^2). Diabetes mellitus was defined as self-reported disease, use of anti-diabetic medication, or a non-fasting plasma glucose above 11 mmol/L. Alcohol consumption was self-reported. Smoking was self-reported, and participants were grouped as never, former, or current smokers according to the questions “Do you smoke?” and “Have you previously smoked?“. Cholesterol-lowering therapy was self-reported.

2.5. Statistical methods

Analyses were done in Stata/SE version 13 for Windows.

Moving average was calculated for every individual (termed the “central individual”) by taking the mean of total and LDL cholesterol for the 150 individuals before and the 150 individuals after this central individual. P values for trends were estimated using Kruskal Wallis non-

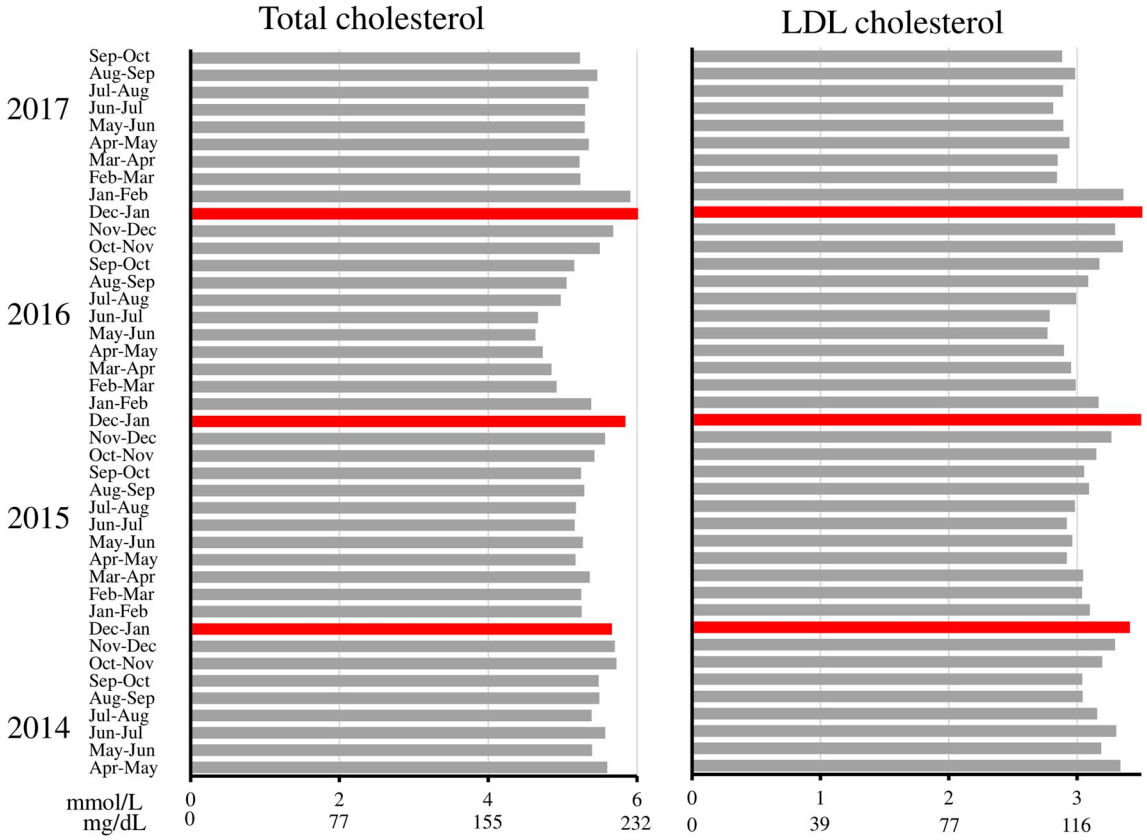

Fig. 2. Seasonal variation in mean total and LDL cholesterol in individuals not on cholesterol-lowering therapy in the Copenhagen General Population Study. Time is grouped from the 15th in the specific month to the 14th in the following month, to better capture the period surrounding the Christmas holidays.

parametric trend test or $\chi 2$ test. Comparison of total and LDL cholesterol levels by months were done using Wilcoxon rank-sum test. A logistic regression model with 95% confidence intervals was used to compare risk of hypercholesterolemia according to time in a model adjusted for possible confounders which were sex, age, body mass index, diabetes mellitus, alcohol consumption, and smoking status. All reported *p*-values are two sided.

3. Results

25,764 individuals not on cholesterol-lowering therapy with a median age of 59 years (interquartile range 50–69) were included in the study. Median total cholesterol in CGPS was 5.3 mmol/L (205 mg/dL) (interquartile range 4.6–6.0 mmol/L (178–232 mg/dL)). Mean LDL cholesterol was 3.0 mmol/L (116 mg/dL) (interquartile range 2.4–3.6 mmol/L (93–139 mg/dL)). Individuals attending the study in the first week of January had a mean total and LDL cholesterol of 6.2 mmol/L (240 mg/dL) (interquartile range 5.5–7.0 mmol/L (213–271 mg/dL)) and 3.7 mmol/L (143 mg/dL) (interquartile range 3.0–4.3 mmol/L (116–166 mg/dL)). In comparison, in June the mean total and LDL cholesterol were 5.1 mmol/L (197 mg/dL) (interquartile range 4.4–5.7 mmol/L (170–220 mg/dL)) and 2.8 mmol/L (108 mg/dL) (interquartile range 2.2–3.4 mmol/L (85–131 mg/dL)).

3.1. Possible confounders

Characteristics of individuals attending the CGPS in the first week of January following the Christmas holidays (N = 441) were similar to those of individuals attending during the rest of the year (Supplementary Table 1). We included possible confounders such as sex, age, body mass index, alcohol consumption, smoking status, and diabetes mellitus. We found no significant differences between individuals attending the CGPS in the first week of January and individuals attending in April, May, and June besides a slightly younger age of the individuals attending the CGPS just after the Christmas holiday.

3.2. Seasonal variation

The moving average of total cholesterol per 300 individuals from April 2014 through November 2017 was relatively stable just above 5 mmol/L (193 mg/dL) but showed a tendency toward increases during December and January and then returned to 5 mmol/L (193 mg/dL) shortly after January (Fig. 1). Likewise, moving average LDL cholesterol levels showed a tendency toward increases in the Christmas period and decreases shortly after.

There was a yearly trend towards higher and higher total cholesterol going from summer through to December and January (Fig. 2). The percentage change in total cholesterol from reference values in May–-June was +15% in December–January ($p < 0.001$) (Fig. 3). For LDL cholesterol, the corresponding change was +20% ($p < 0.001$). In contrast to cholesterol levels, a seasonal pattern was not observed for myocardial infarctions (Supplementary Fig. 1).

3.3. Hypercholesterolemia by season

Overall, 89% of individuals had total cholesterol levels above 5 mmol/L (193 mg/dL) in the first week of January, immediately following the Christmas holidays, compared with only 53% in April, May, and June combined ($p < 0.001$) (Fig. 4). The proportion of individuals with LDL cholesterol levels above 3 mmol/L (116 mg/dL) was 77% in the first week of January compared to 45% in April, May, and June, combined ($p < 0.001$).

For individuals attending the Copenhagen General Population Study in the first week of January, the multivariable adjusted odds ratio of hypercholesterolemia, defined by total cholesterol above 5 mmol/L (193 mg/dL) or LDL cholesterol above 3 mmol/L (116 mg/dL), was 6.0 (95% confidence interval 4.2–8.5).

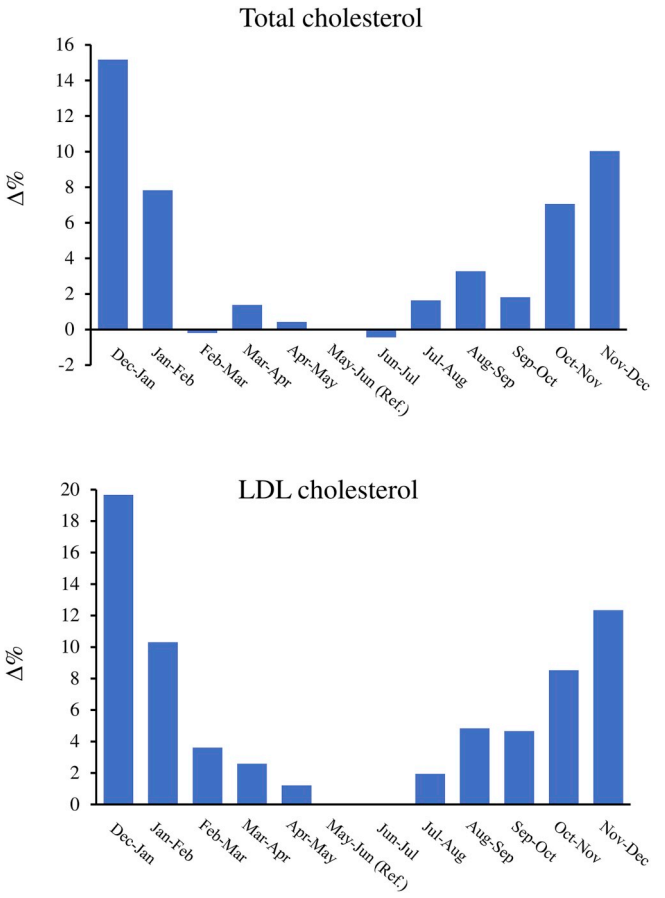

Fig. 3. Percent change in total and LDL cholesterol according to months of the year in individuals not on cholesterol-lowering therapy in the Copenhagen General Population Study.
Values are averaged from April 2014 through to November 2017. Time is grouped from the 15th in the specific month to the 14th in the following month, to better capture the period surrounding the Christmas holidays.

3.4. Repeated measurements of total and LDL cholesterol

For 244 individuals, we had repeated measurements of total and LDL cholesterol measured with a median of 10 years apart. Waterfall plots of the change in total and LDL cholesterol from the first week of January in 2014–2016 to other times of the year, 10 years earlier in 2004–2006, supported our overall findings of higher total and LDL cholesterol immediately following the Christmas holiday with a median change of −0.7 mmol/L (−27 mg/dL) (interquartile range −1.2;-0.5 mmol/L (-46;-19 mg/dL)) and −0.5 mmol/L (−19 mg/dL) (interquartile range −0.9; −0.1 mmol/L (−35;-4 mg/dL)), respectively (Fig. 5). As higher age might be a confounder in the assessment of longitudinal data, we also constructed waterfall plots for the change in total and LDL cholesterol in the other time direction, that is, from individuals attending the CGPS in 2004–2006 during the first week of January and again 10 years later at another time of the year. These data also showed a tendency towards higher total and LDL-cholesterol immediately following Christmas with a median change of 0.6 mmol/L (23 mg/dL) (interquartile range −0.1.; 1.3 mmol/L (−4; 50 mg/dL)) and 0.3 mmol/L (12 mg/dL) (interquartile range −0.2; 0.9 mmol/L (−8; 35 mg/dL)) (Supplementary Fig. 2). Additionally, waterfall plots of the difference in cholesterol levels from 2014 to 2016 to 2004–2006 in all 11,055 individuals with repeated measurements showed evenly

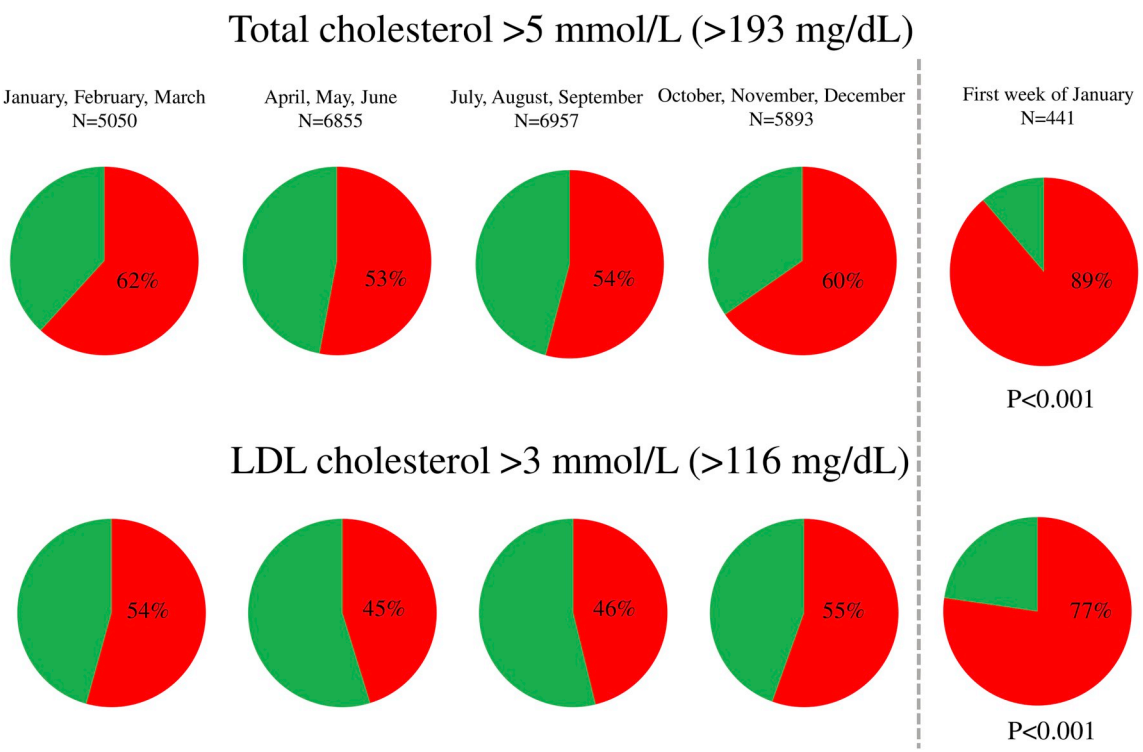

Fig. 4. Total and LDL cholesterol and hypercholesterolemia according to time of year in individuals not on cholesterol-lowering therapy in the Copenhagen General Population Study.
Green colour represent the fraction of individuals below the cut-off for hypercholesteolemia while red colour represent the fraction of individuals above the cut-off for hypercholesteolemia. *p*-values for comparison of the fraction of individuals with total and LDL cholesterol above the cut-off in the first week of January versus in April, May, and June (reference). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

distributed differences indicating a minor role of higher age in the observed change in cholesterol levels following the Christmas holiday (Supplementary Fig. 3). Also, as a negative control of our findings we did not observe similar differences over a decade when comparing a non-holiday season (Supplementary Fig. 4).

4. Discussion

In this study of 25,764 individuals from the general population, we found that levels of total and LDL cholesterol were higher during and immediately following Christmas. Additionally, the fraction of individuals with hypercholesterolemia was higher during Christmas and immediately after the holidays compared to the rest of the year with a 6.0 times higher risk of hypercholesterolemia in individuals attending the study in the first week of January compared to individuals attending the study during the rest of the year. These are novel findings.

Mechanistically, the observed variations in total and LDL cholesterol could be explained by intake of the high-fat diet traditionally consumed during Danish Christmas season spanning all of December until and including New Year's Eve. Furthermore, the corresponding lower levels observed in late winter could partly be due to the tendency to make New Year's resolutions and briefly engage in eating healthier following the Christmas holidays. If this is the case, such resolutions only last for a short period of time [8], as clearly supported by our study.

In support of our findings, in a UK study of 35 individuals with and without type 2 diabetes, the Christmas feast was associated with gain in weight and a slight increase in cholesterol levels immediately following Christmas [3]. The concept of seasonal variation in lipid levels has been documented in previous studies which have reported seasonal variation in cholesterol levels throughout the year [9–16]. In the SEASONS study of 476 healthy volunteers, women had higher total cholesterol, LDL cholesterol, and HDL cholesterol levels in winter compared to summer, whereas in men, this was only the case for HDL cholesterol [15]. Another study of 1446 hypercholesterolemic men with repeated cholesterol measurements found total cholesterol to be 0.19 mmol/L (7.3 mg/dL) higher in December–January than in June–July corresponding to 3% higher total cholesterol levels [10]. Also, in a study of 302 patients with type 2 diabetes mellitus 30% of the patients were within LDL cholesterol target of < 2.6 mmol/L (101 mg/dL) in summer and spring, whereas this was only the case for 22% during fall and winter [9]. Studies from the general population including over 200,000 measurements from routine health screening examinations in the UK and Japan likewise found evidence of a seasonal variation in plasma total cholesterol in both countries, with overall 3% higher cholesterol levels in winter than in summer [16] and seasonal variations in the general population have been confirmed by yet others.[13, 14] In the present study, we found that total cholesterol was 15% higher and LDL cholesterol 20% higher in the months of December–January compared with May–June, which are much higher levels than found in previous studies. In contrast, a study of 2245 healthy blood donors in Denmark found no distinct fluctuations in plasma cholesterol during the calendar year [12], similar to what a study including 304,156 serum cholesterol measurements from 14 Polish laboratories reported [11].

Apart from influencing the Christmas spirit, our results may also have clinical implications. It has been proposed that the seasonal variation in cholesterol levels could lead to failure to meet treatment goals if treatment is initiated in summer with repeated measurements carried out in winter [17]. Yet, the clinical importance of this depends on whether it is the actual plasma total and LDL cholesterol concentration at any given time that determines the rate of cholesterol deposition in the arteries, in which case the high post-Christmas feasting cholesterol levels are likely harmful, or if it is rather the long-term concentrations, making these temporary increases in cholesterol levels less important. In the present study, we observed no seasonal variation in first-time events of myocardial infarction which support the latter. The question

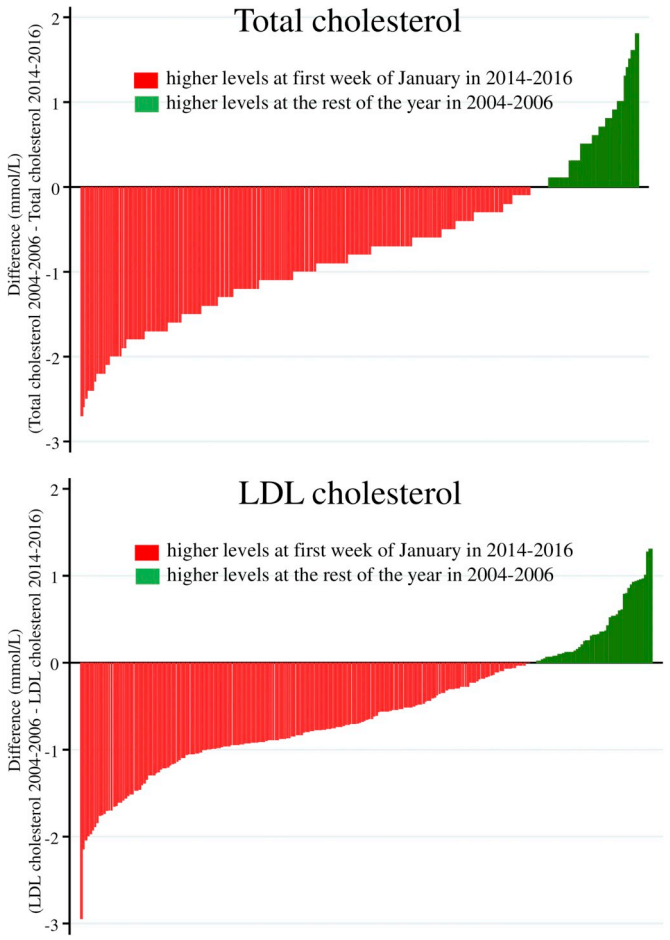

Fig. 5. Repeated measurements of total and LDL cholesterol according to time of year in individuals not on cholesterol-lowering therapy in the Copenhagen General Population Study.
Change from the first week of January in 2014–2016 to random day of the year in 2004–2006. Based on 244 individuals not on cholesterol-lowering medication with a measurement of total and LDL cholesterol in first week of January and a measurement approximately 10 years later at another time of year.

of therapeutic interest is whether these changes in cholesterol levels can be used as a rationale for being less aggressive with cholesterol-lowering therapy in winter; however, given the undertreatment with cholesterol-lowering therapy previously reported from our study [18] the opposite could be argued, that is, too few people are treated because of under-diagnosis in summer. Nevertheless, physicians should take these results into consideration when diagnosing hypercholesterolemia during December and January and, if the test has been done immediately following Christmas, consider the possibility of re-testing the patient some months later. Our study shows that lifestyle is an important basis of treating individuals with hypercholesterolemia. However, with an observed 15% change in total cholesterol going from summer to winter, the study also depicts the quantitatively small effects of extreme changes of diet and physical activity that cannot substitute for statins in high risk individuals.

Our study has several strengths such as the use of a large general population cohort of white individuals of Danish descent, essentially all of whom celebrate Christmas with a large amount of “hygge” [1] during all of December until and including New Year's Eve. Also, individuals in the Copenhagen General Population Study are invited randomly by age and sex throughout the year, securing that characteristics of those examined is similar from month to month.

Some limitations should also be considered. First, although repeated measurements from a relatively small subset of 244 individuals supported our main findings, only one measurement of cholesterol from each individual is included in the main analyses. While a design featuring repeated measurements is generally preferable to one with only a single measurement per subject, this may be compensated for by the large cohort size from a homogenous population. Second, we cannot exclude that individuals exhausted from celebrating Christmas and eating large amounts of food would choose not to participate in the CGPS, thereby introducing selection bias in the present study and a tendency to bias our results towards the null hypotheses. If this was the case, even larger increases in cholesterol levels may have occurred following Christmas. On the other hand, it is also possible that individuals who have been especially sedentary and eaten large amounts of food during Christmas are more prone to participate in a health examination following Christmas due to health concerns, in which case our results cannot be extrapolated to the whole population. However, we did not find major differences in characteristics between the individuals participating immediately following Christmas and those participating during the remaining part of the year, which does not suggest major biases. Third, as all individuals were of white Danish descent, our results may not necessarily apply to other ethnicities especially those unfamiliar to the Danish concept of “hygge” [1]. Holiday traditions have a strong cultural foundation and thus it is uncertain to what extent our findings might be generally applicable beyond a Scandinavian or Northern European population.

In conclusion, celebrating Christmas is associated with increased levels of total and LDL cholesterol in individuals in the general population and a higher risk of hypercholesterolemia. Thus, a diagnosis of hypercholesterolemia should not be made around Christmas and our results stress the need for re-testing such patients later and certainly prior to initiation of cholesterol-lowering treatment. Future research may elucidate whether writing and reading these current results will be associated with decreased Christmas spirit due to self-inflicted dietary restrictions when celebrating future Christmas holidays.

Conflicts of interest

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

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All authors had full access to all of the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

Author contributions

Signe Vedel-Krogh, Camilla Kobylecki, Børge G. Nordestgaard, and Anne Langsted designed the study together. Signe Vedel-Krogh, Camilla Kobylecki, and Anne Langsted analyzed the data. Børge G. Nordestgaard oversaw all analyses and contributed to the interpretation of data. Signe Vedel-Krogh, Camilla Kobylecki, and Anne Langsted wrote the first draft of the paper and Børge G. Nordestgaard edited the paper. All authors approved this paper in its final form.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.atherosclerosis.2018.12.011.

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