RESEARCH ARTICLE

Correlates of Untreated Hypercholesterolemia in Older Adults: A Community-Based Household Survey in China

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Abstract

Hypercholesterolemia is common in older adults and less treated, but little is known about correlates of untreated hypercholesterolemia. Using a standard interview method we examined a random sample of 7,572 participants aged ≥60 years in a community-based household survey across 7 provinces of China during 2007–2012, and documented 328 cases of hypercholesterolemia from self-reported doctor diagnosis. Compared to participants with normal cholesterol, older adults with hypercholesterolemia had higher socioeconomic position and larger body mass index. In patients with hypercholesterolemia, 209 were not treated using lipid-lowering medications (63.7%, 95% confidence interval (CI) 58.5%–68.9%). Untreated hypercholesterolemia was significantly associated with female sex (adjusted odds ratio 2.13, 95%CI 1.17–3.89), current smoking (3.48, 1.44–8.44), heavy alcohol drinking (3.13,1.11–8.84), chronic bronchitis (2.37,1.14–4.90) and high level of meat consumptions (2.85,1.22–6.65). Although having coronary heart disease exposed participants for treatment, half of participants with coronary heart disease did not receive lipid-lowering medications. Among hypercholesterolemia participants with stroke, hypertension or diabetes, more than half of them did not receive lipid-lowering medications. The high proportion of untreated hypercholesterolemia in older, high-risk Chinese adults needs to be mitigated through multi-faceted primary and secondary prevention strategies to increase population opportunities of treating hypercholesterolemia.
Introduction

Hypercholesterolemia is a major risk factor for cardiovascular disease. Clinical trials have repeatedly demonstrated that lipid-lowering medication, mainly in the form of statins, reduces future cardiovascular events. [1,2] This treatment effect is also true for older adults. [3] Serial health surveys conducted in European populations have documented a significant increase in the use of lipid-lowering medication in the general populations over time.[4,5] However, a substantial proportion of people with hypercholesterolemia remain untreated. [6,7] The reason remains unclear. Previous studies have shown that not receiving lipid-lowering medication for primary prevention is associated with younger age, male sex and smoking, [8] while for secondary prevention it is associated with older age and female sex. [9] These studies focused on young and middle aged populations, and the correlates of untreated hypercholesterolemia in older adults have not been well investigated.[10]

Current knowledge about the management of lipid lowering medication in people with hypercholesterolemia is predominately derived from studies undertaken in high-income countries, [7] [8] [9] thus limiting translation of findings to low and middle-income countries (LMICs) across the world. In LMICs, the number of people with hypercholesterolemia has increased over the last three decades, as countries undergo epidemiological transition. [11,12] Studying a population in LMICs may offer internationally applicable insights into the proportion and correlates of untreated hypercholesterolemia. China is the biggest among the LMICs, and the world’s most populous nation. Since the economic reform of the 1980s, China has had a rapid growth in income and increase in life expectancy. The number of older people in China, defined age of > = 60 years, [13] has increased in the past 3 decades. There is concomitantly an increasing prevalence of hypercholesterolemia in the Chinese population,[14] ensuing coronary heart disease and stroke.[6] In this paper we examine data from a community-dwelling based study of older adults in China [15] to identify proportion and correlates of untreated hypercholesterolemia.

Methods

The data were derived from a large-scale cross-sectional study in 2007–2011 across 7 provinces in China for this study. [15, 16]

Study populations

We included all participants in a four-province study, the Hubei province study and the Anhui province cohort 3rd wave study [15], and also Xinjiang Uyghur Autonomous Region study (rural areas) [16]. These studies were community-based household surveys, with a common research protocol which is derived from that in the four-province study [15]. Recruiting participants and collecting data were carried out in 2007–2011. The Four-Province Study: The sampling methods of the four-province study population have been fully described before. [15] In brief, we selected one rural and one urban community from each of four provinces (Guangdong, Heilongjiang, Shanghai and Shanxi–four research centres) as the study fields, aiming to recruit more than 500 participants in each community. We employed a cluster randomised sampling method to choose residential communities from each of the four provinces. The target population consisted of residents aged ≥60 years living in the area for at least five years. Ethical approval for the study was obtained from the Research Ethics Committee, University College London, UK, and from the Research Ethics Committee of Anhui Medical University and the local governments in China. Based on the residency list of the committees of the village and the district, we recruited a total of 4,314 participants with an overall response rate of 93.8%. The Hubei and Xinjiang studies: we extended the project to include in Hubei province...
and the Xinjiang Uyghur Autonomous Region, using the same protocol as in the four-province study. In Hubei, we selected one urban and one rural area to recruit 1,001 participants aged ≥ 60 years, and achieved a response rate of 91.8%. [15] In Xinjiang Uyghur Autonomous Region, we interviewed 500 participants in rural areas in Urumqi County, Lop county and Hami back to the urban and rural for this study, with a response rate of 91.3%. [16] The Anhui province cohort study—third wave survey: the methods of the Anhui cohort study has been fully described in previous publications.[15] In brief, in 2001–2003 we interviewed a random sample of 3,336 residents aged ≥ 60 years in urban and rural of Anhui province for mental health in older Chinese (wave 1). One year after the baseline investigation we re-examined 2,608 cohort members (wave 2). In 2007–2009 we successfully interviewed 1,757 survivors (wave 3), with a response rate of 82.4% of surviving cohort members.

Interview and data collection

Two researchers from each centre (province) team were trained at the Anhui Medical University, where we had previously completed several studies of mental illness in older people and had an experienced interview team.[17] The trained researchers cascaded skills to local research teams and trained the interviewers. The local survey teams from Anhui, Guangzhou (Guangdong), Harbin (Heilongjiang), Shanxi and Hubei Medical Universities, School of Public Health of Fudan University (Shanghai), and The People’s Hospital of Xinjiang Uyghur autonomous region interviewed the participants at home. Permission for interview and written informed consent were obtained from each participant or if that was not possible, from the closest responsible adult. Refusals were respected. In about 5% of the interviews, informed consent was impossible to elicit; in these cases, the nearest relative or carer was approached to provide assent to participation. The main interview included a general health and risk factors record,[17] the Geriatric Mental State (GMS) questionnaire,[18] and other components of the 10/66 algorithm dementia research package.[19]

In the general health and risk factors component we recorded details relating to sociodemography, social networks and support, and cardiovascular (CVD) and risk factors. Socioeconomic variables included rural/urban domicile area, educational level, occupational class, and annual personal and family incomes. Information about hobbies, physical activity and Daily Life Activity were documented. We asked participants (or their carers if the participant was unable to answer) if they had received a doctor’s diagnosis of heart disease (1.coronary heart disease—CHD, 2. valve disease, or 3. others), angina, stroke, diabetes, chronic bronchitis, chronic kidney disease, cancer, epilepsy, Parkinson’s disease, etc. We included a dietary intake questionnaire in the general health and risk factors record. We measured systolic and diastolic blood pressure, height, weight and waist circumference for all participants according to standard procedures. [20] The GMS questionnaire data were analysed by a computer program-assisted diagnosis, the Automated Geriatric Examination for Computer Assisted Taxonomy (AGECAT), to assess the principal mental disorders in the study participants. [18]

In the interview, we asked each participant for details of hypercholesterolemia. Participants with hypercholesterolemia were those who gave a positive answer to “Do you have a doctor-diagnosed hypercholesterolemia?”. If yes, they were asked how many years they had hypercholesterolemia and whether they took any lowering-lipids medication. We defined ‘untreated hypercholesterolemia’ as those who gave negative answers to the last enquiry.

Statistical analysis

The SPSS statistical package (Windows version 21.0; SPSS Inc, Chicago, Ill) was used for data analysis. Patient characteristics comparing treated and untreated using lipid-lowering
medications were tested by chi-square test. Using a logistic regression model we calculated odds ratios (ORs) and 95% confidence intervals (CIs) for untreated hypercholesterolemia in relation to individual characteristics, adjusted for age, sex and duration of hypercholesterolemia. Previous studies showed that age and sex were associated with taking lowering-lipid medications. [8, 9] In China, some older adults would not like to take medications immediately following the diagnosis of a chronic condition, which is not acute and serious. However in time they will eventually take medications for treatment. The time since hypercholesterolemia diagnosis would be also associated with other variables such as the consumption of meat and CHD. Therefore we took these 3 variables for adjustment in an initial logistic regression analysis. We employed a multivariate logistic model, which included urban-rural living and all variables with a p value < 0.1 in the above adjustment analysis, to assess the correlates for untreated hypercholesterolemia. We carried out a sensitivity analysis in participants who did not have chronic kidney disease (CKD) as the CKD may prevent from using lipid-lowering medications due to its metabolic issues. In the multivariate analysis we further used a stepwise method (forward: Wald) in the logistic model to examine the correlates.

Results
Of 7,572 participants, 328 (4.3%) were reported to have doctor-diagnosed hypercholesterolemia. Of these with hypercholesterolemia, the average age was 71.4 years (SD 7.1) with a range of 60–93, and 60.1% were women. They are not significantly different from those who were not reported to have hypercholesterolemia (age 72.0 (7.7), 54.9% women). However, they were more likely to have higher levels of education (>= high secondary school 34.1% versus 12.2%) and family income (RMB Yuan 17242 versus 11150), live in an urban area (79.6% versus 42.6%) and have a larger body mass index (BMI at 24.2 versus 22.8).

Among 328 participants with hypercholesterolemia (S1 Dataset included in Supporting Information), 209 were not treated (63.7% (95% CI 58.5%-68.9%)). The odds ratios for receipt of treatment for hypercholesterolemia stratified by individual characteristics in older Chinese adults are depicted in Table 1. Compared to those with treated hypercholesterolemia, patients who were untreated were more like to be current smokers, heavy alcohol drinkers, consume more meat, and have a shorter duration (<3years) of diagnosed hypercholesterolemia. Untreated hypercholesterolemia was inversely associated with coronary heart disease, but it was not significantly associated with other cardiovascular disease and risk factors in Table 1.

Table 2 shows ORs for the correlates of untreated hypercholesterolemia in a multivariate analysis. Being untreated was significantly associated with being female, current smoking, heavy alcohol drinking and more consumption of meat, and inversely with CHD. The association with chronic bronchitis was borderline significant. In the sensitivity analysis after excluding participants with chronic kidney disease, the findings of the associations were similar to those in the data analysis of all participants, but less significant probably due to a smaller number of participants.

In the stepwise regression analysis for all patients, the final-step results showed that being untreated was associated with female sex, current smoking, heavy alcohol drinking, CHD, chronic bronchitis and more consumption of meat (Table 3).

Discussion
In this community-based health survey of older adults in China we found that about two-thirds of patients who had self-reported doctor-diagnosed hypercholesterolemia were not on lipid-lowering medication. Untreated hypercholesterolemia was associated with female sex, current-smoking, heavy alcohol drinking, chronic bronchitis, and more consumption of meat.
Table 1. Characteristics of participants with hypercholesterolemia: frequencies and odds ratios for receipt of treatment for hypercholesterolemia in older adults.

| Variable                        | Treated | Untreated | Odds ratio adjusted for age, sex and duration of hypercholesterolemia |
|---------------------------------|---------|-----------|---------------------------------------------------------------------|
|                                 | n = 119 | n = 209 | Chi-square test p | OR† | 95%CI | P* |
| Basic characteristics           |         |          |                     |     |       |    |
| Age (years)                     |         |          |                     |     |       |    |
| 60–64                           | 28      | 44       | 21.1                | 0.060 | 1.11 | (0.60–2.06) |
| 65–74                           | 42      | 101      | 48.3                | 1.75 | (1.03–2.96) |
| ≥75                             | 49      | 64       | 30.6                | 1.00 |       | 0.089 |
| Sex                             |         |          |                     |     |       |    |
| Men                             | 52      | 79       | 37.8                | 1.00 |       | 0.495 |
| Women                           | 67      | 130      | 62.2                | 1.18 | (0.74–1.89) |
| Body mass index (kg/m²)         |         |          |                     |     |       |    |
| < 25                            | 80      | 131      | 63.6                | 0.685 |       | 0.717 |
| 25–30                           | 28      | 57       | 27.7                | 1.24 | (0.72–2.13) |
| ≥30                             | 9       | 18       | 8.7                 | 1.19 | (0.50–2.83) |
| Socio-economic status           |         |          |                     |     |       |    |
| Educational level               |         |          |                     |     |       |    |
| > = High Secondary Sch.         | 40      | 72       | 34.4                | 0.291 |       | 0.369 |
| Secondary school                | 30      | 38       | 18.2                | 0.68 | (0.36–1.29) |
| < = Primary Sch.                | 49      | 99       | 47.4                | 1.04 | (0.61–1.78) |
| Main occupation                 |         |          |                     |     |       |    |
| Official/teacher                | 46      | 65       | 31.1                | 0.117 |       | 0.268 |
| Businessmen, housewives and other | 15 | 44 | 21.1 | 1.82 | (0.87–3.83) |
| Manual labour or Peasant        | 58      | 100      | 47.8                | 1.11 | (0.66–1.87) |
| Annual personal income (RMB, Yuan) |       |           |                     |     |       |    |
| ≥20000                          | 44      | 82       | 39.2                | 0.750 |       | 0.438 |
| ≥10000–<20000                   | 54      | 86       | 41.1                | 0.70 | (0.41–1.21) |
| <10000                          | 21      | 41       | 19.6                | 0.86 | (0.44–1.70) |
| Averaged income of family member per year (RMB, Yuan) |       |           |                     |     |       |    |
| ≥20000                          | 38      | 66       | 31.6                | 0.982 |       | 0.867 |
| ≥10000–<20000                   | 57      | 99       | 47.4                | 0.88 | (0.52–1.51) |
| <10000                          | 24      | 44       | 21.1                | 0.85 | (0.43–1.67) |
| Urban-rurality                  |         |          |                     |     |       |    |
| Urban                           | 99      | 162      | 77.5                | 0.220 |       | 0.334 |
| Rural                           | 20      | 47       | 22.5                | 1.35 | (0.73–2.49) |
| Lifestyles                      |         |          |                     |     |       |    |
| Smoking status                  |         |          |                     |     |       |    |
| Never                           | 91      | 146      | 69.9                | 0.037 |       | 0.017 |
| Former                          | 18      | 24       | 11.5                | 1.21 | (0.55–2.62) |
| Current                         | 10      | 39       | 18.7                | 3.27 | (1.43–7.44) |
| Alcohol drinking/ month         |         |          |                     |     |       |    |
| No                              | 108     | 175      | 83.7                | 0.118 |       | 0.050 |
| 1–9 times                       | 5       | 9        | 4.3                 | 1.43 | (0.45–4.62) |
| 10–90 times                     | 6       | 25       | 12.0                | 3.32 | (1.26–8.77) |
| Favourite salt level in dishes   |         |          |                     |     |       |    |

(Continued)
| Variable                                      | Treated n = 119 | Untreated n = 209 | Chi-square test p | OR† 95%CI | P*  |
|----------------------------------------------|-----------------|-------------------|-------------------|----------|-----|
| Light                                       | 52 43.7         | 98 46.9           | 0.855             | 1.00     | 0.906 |
| Middle                                      | 42 35.3         | 70 33.5           |                   | 0.89     | (0.53–1.50) |
| Heavy                                       | 25 21.0         | 41 19.6           |                   | 0.98     | (0.53–1.83) |
| Consumption of meat in recent 2 years       |                 |                   |                   |          |      |
| < Once a week                               | 21 17.6         | 15 7.2            | 0.019             | 1.00     | 0.015 |
| Once a week                                 | 39 32.8         | 64 30.6           |                   | 2.67     | (1.20–5.94) @1 |
| > = Twice a week and < = once a day         | 30 25.2         | 71 34.0           |                   | 3.61     | (1.61–8.08) @2 |
| > = Twice a day                             | 29 24.4         | 59 28.2           |                   | 3.15     | (1.38–7.16) @2 |
| Consumption of fish in recent 2 years       |                 |                   |                   |          |      |
| < Once a week                               | 20 16.8         | 31 14.8           | 0.142             | 1.00     | 0.146 |
| Once a week                                 | 46 38.7         | 68 32.5           |                   | 0.91     | (0.45–1.82) |
| > = Twice a week and < = once a day         | 28 23.5         | 75 35.9           |                   | 1.69     | (0.82–3.49) |
| > = Twice a day                             | 25 21.0         | 35 16.7           |                   | 0.88     | (0.40–1.92) |
| Consumption of egg in recent 2 years        |                 |                   |                   |          |      |
| < Once a week                               | 11 9.2          | 25 12.0           | 0.272             | 1.00     | 0.297 |
| Once a week                                 | 29 24.4         | 39 18.7           |                   | 0.63     | (0.26–1.50) |
| > = Twice a week and < = once a day         | 28 23.5         | 66 31.6           |                   | 1.15     | (0.49–2.72) |
| > = Twice a day                             | 51 42.9         | 79 37.8           |                   | 0.76     | (0.34–1.73) |
| Consumption of vegetables in recent 2 years |                 |                   |                   |          |      |
| < Once a day                                | 5 4.2           | 12 5.7            | 0.749             | 1.00     | 0.569 |
| Once a day                                  | 54 45.4         | 88 42.1           |                   | 0.57     | (0.18–1.74) |
| > = Twice a day                             | 60 50.4         | 109 52.2          |                   | 0.65     | (0.21–1.99) |
| Consumption of fruits in recent 2 years     |                 |                   |                   |          |      |
| < Once a day                                | 57 47.9         | 90 43.1           | 0.693             | 1.00     | 0.726 |
| Once a day                                  | 51 42.9         | 97 46.4           |                   | 1.16     | (0.71–1.88) |
| > = Twice a day                             | 11 9.2          | 22 10.5           |                   | 1.34     | (0.59–3.04) |
| Do regular exercise                         |                 |                   |                   |          |      |
| No                                          | 75 63.0         | 125 59.8          | 0.566             | 1.00     | 0.597 |
| Yes                                         | 44 37.0         | 84 40.2           |                   | 1.14     | (0.71–1.83) |
| Walk often                                  |                 |                   |                   |          |      |
| No                                          | 22 18.5         | 42 20.1           | 0.724             | 1.00     | 0.661 |
| Yes                                         | 97 81.5         | 167 79.9          |                   | 0.88     | (0.49–1.57) |
| Social network and support                  |                 |                   |                   |          |      |
| Religious belief                            |                 |                   |                   |          |      |
| No                                          | 94 79.0         | 171 81.8          | 0.532             | 1.00     | 0.226 |
| Yes                                         | 25 21.0         | 38 18.2           |                   | 0.69     | (0.38–1.26) |
| Marital status                              |                 |                   |                   |          |      |
| Married                                     | 87 73.1         | 164 78.5          | 0.528             | 1.00     |      |
| Widow                                       | 29 24.4         | 40 19.1           |                   | 0.72     | (0.40–1.28) |
| Divorced/never married                      | 3 2.5           | 5 2.4             |                   | 1.00     | (0.22–4.49) |
| Living condition                            |                 |                   |                   |          |      |
| Live alone                                  | 17 14.3         | 23 11.0           | 0.383             | 1.00     | 0.423 |
| Live with somebody                          | 102 85.7        | 186 89.0          |                   | 1.33     | (0.66–2.65) |

(Continued)
Table 1. (Continued)

| Variable                                      | Treated n = 119 | Untreated n = 209 | Chi-square test p | OR† 95%CI | P*   |
|-----------------------------------------------|-----------------|-------------------|-------------------|----------|------|
| **Number of children**                        |                 |                   |                   |          |      |
| 0–1                                           | 20 16.8         | 25 12.0           | 0.367             | 1.00     | 0.332|
| 2–3                                           | 64 53.8         | 111 53.1          | 1.21 (0.61–2.42)  |          |      |
| ≥4                                            | 35 29.4         | 73 34.9           | 1.67 (0.80–3.51)  |          |      |
| **Frequency of visiting children/relatives**  |                 |                   |                   |          |      |
| Daily                                         | 26 21.8         | 37 17.7           | 0.618             | 1.00     | 0.715|
| <Daily and ≥ Monthly                          | 46 38.7         | 89 42.6           | 1.29 (0.68–2.44)  |          |      |
| < monthly                                     | 47 39.5         | 83 39.7           | 1.25 (0.66–2.36)  |          |      |
| **Help available when needed**                |                 |                   |                   |          |      |
| No                                            | 9 7.6           | 22 10.5           | 0.378             | 1.00     | 0.398|
| Yes                                           | 110 92.4        | 187 89.5          | 0.70 (0.30–1.61)  |          |      |
| **Health status and disease histories**        |                 |                   |                   |          |      |
| **Perception of self-health**                 |                 |                   |                   |          |      |
| Good                                          | 54 45.4         | 91 43.5           | 0.061             | 1.70     | (0.78–3.70)|
| Average                                       | 47 39.5         | 102 48.8          | 2.35 (1.08–5.11)  |          |      |
| Poor                                          | 18 15.1         | 16 7.7            | 1.00              | 0.080    |      |
| **Duration of hypercholesterolemia (years)**  |                 |                   |                   |          |      |
| <3 years                                      | 26 21.8         | 64 30.6           | 0.087             | 1.89     | (1.01–3.52)|
| 3–<10 years                                   | 52 43.7         | 94 45.0           | 1.41 (0.81–2.45)  |          |      |
| ≥ 10 years                                    | 41 34.5         | 51 24.4           | 1.00              | 0.132    |      |
| **Hypertension (BP ≥ 140/90 mm Hg or taking antihypertensive medication)** | 25 21.0         | 53 25.4           | 0.374             | 1.00     | 0.410|
| No                                            | 94 79.0         | 156 74.6          | 0.79 (0.45–1.38)  |          |      |
| Yes                                           | 79 66.4         | 167 79.9          | 0.007             | 1.00     | 0.010|
| **Coronary heart disease**                    |                 |                   |                   |          |      |
| No                                            | 40 33.6         | 42 20.1           | 0.51 (0.30–0.85)  |          |      |
| Yes                                           | 107 89.9        | 186 89.0          | 0.795             | 1.00     | 0.534|
| **Diabetes**                                  |                 |                   |                   |          |      |
| No                                            | 86 72.3         | 169 80.9          | 0.072             | 1.00     | 0.102|
| Yes                                           | 33 27.7         | 40 19.1           | 0.64 (0.37–1.09)  |          |      |
| **Chronic kidney disease (CKD)**              |                 |                   |                   |          |      |
| No                                            | 107 184         | 89.9 88.0         | 0.605             | 1.00     | 0.659|
| Yes                                           | 12 25           | 10.1 12.0         | 1.19 (0.56–2.52)  |          |      |
| **Chronic bronchitis**                        |                 |                   |                   |          |      |
| No                                            | 106 89.1        | 169 80.9          | 0.052             | 1.00     | 0.094|
| Yes                                           | 13 10.9         | 40 19.1           | 1.81 (0.90–3.61)  |          |      |
| **Vision problems**                           |                 |                   |                   |          |      |
| No                                            | 73 61.3         | 110 52.6          | 0.127             | 1.00     | 0.115|
| Yes                                           | 46 38.7         | 99 47.4           | 1.46 (0.91–2.33)  |          |      |
| **Hearing problems**                          |                 |                   |                   |          |      |

(Continued)
Table 1. (Continued)

| Variable | Treated | Untreated | Odds ratio adjusted for age, sex and duration of hypercholesterolemia |
|----------|---------|-----------|---------------------------------------------------------------|
|          | n = 119 | n = 209   | **OR† 95%CI**                                                 |
| No       | 95      | 158       | 1.00 (0.390)                                                |
| Yes      | 24      | 51        | 1.28 (0.73–2.25)                                            |
| Depression‡ |       |           |                                                                |
| No       | 102     | 184       | 1.00 (0.726)                                                |
| Subcase  | 5       | 9         | 0.99 (0.31–3.12)                                            |
| Case     | 12      | 16        | 0.72 (0.32–1.61)                                            |
| Dementia‡ |       |           |                                                                |
| No       | 113     | 193       | 1.00 (0.406)                                                |
| Subcase/Case | 6   | 16        | 1.52 (0.56–4.13)                                            |

† adjusted for age, sex and duration of hypercholesterolemia (model 1).
‡ diagnosed by the GMS-AGECAT.
*overall p value for each whole factor.
\( p < 0.100 \) and \( > 0.05 \)
\( \text{†} p < 0.05 \) and \( > 0.01 \)
\( \text{‡} p < 0.01 \) and \( > 0.001 \)
\( \text{††} p < 0.001 \)

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Strengths and weakness of study

Our study is the first to report correlates of untreated hypercholesterolemia in older adults in China. The studied participants are derived from a multi-province community-based survey and thus the data reflects ‘real-world’ older population. Our study investigated dietary intake factors and physical activities which were not investigated in previous studies. [7] [8] [9] When we examined correlates of untreated hypercholesterolemia, we carried out a sensitivity analysis by excluding participants with chronic kidney disease, a contra-indication to most lowering-lipid medications. Our study is cross-sectional, and thus the causal-result relationships between correlate factors and untreated require a large-scale cohort study to confirm. We do not have data on serum cholesterol from each patient as the hypercholesterolemia is self reported doctor-diagnosed and this may lead to an underestimate of the prevalence of hypercholesterolemia. A previous national survey in China used a cut-off point of \( > 5.72 \text{ mmol/L} \) in serum total cholesterol to produce a 6.1% prevalence of hypercholesterolemia in older adults aged 60 years or over. [21] Its prevalence rate would be closer to our study with its 4.3%, if a cut-off point of \( > 6.22 \text{ mmol/L} \) were used to define hypercholesterolemia according to the Chinese guidelines for management. [22] We acknowledge that participants with undetected hypercholesterolemia were mostly from lower socioeconomic groups, perhaps as they were less likely to undergo routine health screening, thus potentially resulting in the lack of association we note between socioeconomic deprivation and being untreated. However, missing such participants would not attenuate the significant associations we observe between untreated hypercholesterolemia and other individual characteristics in the analysis. Without data of serum cholesterol level from each patient we were unable to investigate whether the patients with very high hypercholesterolemia took medicines while and those with moderate to low levels of
Table 2. Multivariate logistic regression† to determine factors associated with untreated hypercholesterolemia in older adults.

| Variable                        | All participants |          | Participants without CKD |          |
|---------------------------------|------------------|----------|--------------------------|----------|
|                                 | OR               | 95%CI    | P*                       | OR       | 95%CI     | P*       |
| **Age (years)**                 |                  |          |                          |          |          |          |
| 60–64                           | 1.11             | (0.55–2.24) | 1.07                     | (0.51–2.22) |
| 65–74                           | 1.67             | (0.94–2.97) | 1.63                     | (0.89–2.98) |
| ≥75                             | 1.00             |          | 0.018                    | 0.000    |          |          |
| **Sex**                         |                  |          |                          |          |          |          |
| Men                             | 1.00             |          | 0.003                    | 1.00     |          |          |
| Women                           | 1.92             | (1.03–3.58) | 2.01                     | (1.03–3.90) | 0.041 |
| **Urban-rurality**              |                  |          |                          |          |          |          |
| Urban                           | 1.00             |          | 0.530                    | 1.00     |          |          |
| Rural                           | 1.25             | (0.62–2.53) | 1.24                     | (0.61–2.52) | 0.557 |
| **Smoking status**              |                  |          |                          |          |          |          |
| Never                           | 1.00             |          | 0.0055                   | 1.00     |          | 0.127   |
| Former                          | 1.22             | (0.52–2.83) | 1.06                     | (0.44–2.54) |
| Current                         | 3.05             | (1.22–7.59) | 2.54                     | (1.00–6.42) | 0.01   |
| **Alcohol drinking per month**  |                  |          |                          |          |          |          |
| No                              | 1.00             |          | 0.040                    | 1.00     |          | 0.051   |
| 1–9 times                       | 0.62             | (0.16–2.34) | 0.69                     | (0.18–2.73) |
| 10–90 times                     | 3.58             | (1.22–10.47) | 3.61                    | (1.20–10.80) | 0.01   |
| **Self-feeling health status**  |                  |          |                          |          |          |          |
| Good/very good                  | 1.32             | (0.57–3.04) | 1.55                     | (0.62–3.85) |
| Average                         | 1.88             | (0.81–4.36) | 2.05                     | (0.82–5.16) | 0.03   |
| Poor                            | 1.00             |          | 0.235                    | 1.00     |          | 0.273   |
| **Duration of hypercholesterolemia (years)** | 1.80             | (0.90–3.58) | 1.82                     | (0.88–3.76) | 0.01   |
| <3 years                        | 1.28             | (0.69–2.36) | 1.51                     | (0.78–2.91) |
| ≥10 years                       | 1.00             |          | 0.247                    | 1.00     |          | 0.250   |
| **Diabetic**                    |                  |          |                          |          |          |          |
| No                              | 1.00             |          | 0.327                    | 1.00     |          | 0.279   |
| Yes                             | 0.74             | (0.41–1.34) | 0.70                     | (0.37–1.33) |
| **Coronary heart disease**      |                  |          |                          |          |          |          |
| No                              | 1.00             |          | 0.007                    | 1.00     |          | 0.023   |
| Yes                             | 0.46             | (0.26–0.81) | 0.48                     | (0.26–0.91) | 0.01   |
| **Chronic bronchitis**          |                  |          |                          |          |          |          |
| No                              | 1.00             |          | 0.083                    | 1.00     |          | 0.058   |
| Yes                             | 1.95             | (0.92–4.15) | 2.21                     | (0.98–5.00) | 0.01   |
| **Meat**                        |                  |          |                          |          |          |          |
| < Once a week                   | 1.00             |          | 0.027                    | 1.00     |          | 0.111   |
| Once a week                     | 2.29             | (0.96–5.43) | 1.98                     | (0.81–4.85) |
| > = Twice a week and ≤ once a day | 3.65             | (1.53–8.73) | 2.96                     | (1.21–7.26) | 0.01   |
| > = Twice a day                 | 2.97             | (1.22–7.22) | 2.45                     | (0.96–6.23) | 0.01   |

† including the variables in model 1, factors with p value <0.10 in Table 1, and variables of urban-rurality and diabetes.

* overall p value for each whole factor.

** p<0.100 and >0.05

*** p<0.050 and >0.01

**** p<0.01 and >0.001

**** p<0.001

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hypercholesterolemia did not. Further research on determinants of untreated hypercholesterolemia in older adults is required.

Data from the World Health Organisation (WHO) showed that in China about 230 million people have cardiovascular disease and one in five adult Chinese have a cardiovascular disease. [23] Cardiovascular disease has been listed as one of top priority in China National Plan for NCD Prevention and Treatment (2012–2015).[23] High cholesterol is one of the main risk factors for cardiovascular disease leading to coronary heart disease, stroke and death. In 2007, before our survey started, the Chinese guidelines for prevention and treatment for hypercholesterolemia in adults was published[24] and stated that since the clinical benefits of lowering lipids on CHD incidence are seen for all ages of participants, treatment of hypercholesterolemia in older adults is indicated, and moreover there are no contraindications of the medication treatment. With the higher co-morbidity in older people such as a decline in renal function, however such treatment needs to be personalised and the initial dosage should start low. [24]

Apart from lipid-lowering medications, dietary intake control and physical activity also lower lipid levels. However, in the current study there is no evidence that not being on lipid-lowering medications was accounted for by dietary intake control and physical activity. In contrast, not

| Variable                                | OR    | 95%CI       | P*  |
|-----------------------------------------|-------|-------------|-----|
| Sex                                     |       |             |     |
| Men                                     | 1.00  |             |     |
| Women                                   | 2.13  | (1.17–3.89) | 0.014 |
| Smoking status                          |       |             |     |
| Never                                   | 1.00  |             |     |
| Former                                  | 1.17  | (0.51–2.67) | 0.019 |
| Current                                 | 3.48  | (1.44–8.44) |     |
| Alcohol drinking per month              |       |             |     |
| No                                      | 1.00  |             |     |
| 1–9 times                               | 0.58  | (0.16–2.10) | 0.054 |
| 10–90 times                             | 3.13  | (1.11–8.84) |     |
| Coronary heart disease                  |       |             |     |
| No                                      | 1.00  |             |     |
| Yes                                     | 0.41  | (0.24–0.72) | 0.002 |
| Chronic bronchitis                      |       |             |     |
| No                                      | 1.00  |             |     |
| Yes                                     | 2.37  | (1.14–4.90) | 0.020 |
| Meat                                    |       |             |     |
| < Once a week                           | 1.00  |             | 0.021 |
| Once a week                             | 2.21  | (0.98–4.99) |     |
| > = Twice a week and < = once a day     | 3.61  | (1.57–8.31) | 0.001 |
| > = Twice a day                         | 2.85  | (1.22–6.65) |     |

† all variables selected in the analysis were the same as those in Table 2.

*overall p value for each whole factor.

@ p = 0.100 and > 0.05
@1 p = 0.05 and > 0.01
@2 p = 0.01 and > 0.001
@3 p = 0.001

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Table 3. Stepwise logistic regression† to determine factors associated with untreated hypercholesterolemia in older adults.
being on lipid-lowering medication among hypercholesterolemia participants was significantly associated with smoking, which is consistent with the findings in previous studies in high income countries.[8] A more interesting finding was that those with untreated hypercholesterolemia had higher levels of alcohol drinking and meat consumption than treated participants. Thus there was no evidence that being untreated was due to other lifestyle interventions for controlling hypercholesterolemia, known to be effective in wider populations. [14]

We did not find that women with hypercholesterolemia had less treatment in the initial analysis. However, in the multivariate analysis including the smoking variable, being untreated was significantly associated with female sex as Chinese women rarely smoke. Sex inequality in treatment has also been found in other studies; in secondary prevention, women had less treatment than men. [9] Our data showed that women with hypercholesterolemia received less treatment than men. This would suggest an important inequality in health care as we found previously in mental health. [15] That hypercholesterolemia participants with chronic bronchitis had double the odds of not being treated with lipid-lowering medication may reflect a polypharmacy issue here, as participants may find it would be hard to cope with multiple medicines.

In this study we observed that more than half of those participants with CHD (51.2%), stroke (65.7%), hypertension (62.4%) or diabetes (54.8%) were not treated using lowering lipid medications (Table 1). Although the finding of a significant association between CHD and treatment for hypercholesterolemia is consistent with those in previous studies, [7] it should be noted that only about half of CHD patients had treated hypercholesterolemia in China. This is much lower than that in high income countries, e.g., 79% of CHD patients were on lipid-lowering medications in the EUROASPIRE III study.[25] Our data further showed that the proportions of participants with hypertension, diabetes and stroke who took lipid-lowering medications were significantly lower than the participants in high income countries.[5,26] These findings highlight that there is lack of awareness of major aetiologic and prognostic factors of cardiovascular disease, and the importance of secondary drug prevention for public health in China.

The low proportion of participants who were on lipid-lowering therapy could be also explained by their belief about the condition and medicines. Most Chinese people feel hypercholesterolemia is not a serious condition because there are no physical symptoms associated with this condition and thus complications may not occur. Furthermore, there is a common perception in the general population in China, particularly amongst older people, that any medicine has a side effect or toxicity, perhaps in part due to stories about the side-effects in Chinese medicine. [27,28] For instance some Chinese consider that in older people, treatment using medication is not merited because of a perceived lack of prognostic benefit and increased side effects. Therefore participants with hypercholesterolemia are more likely not to take medicine or take it intermittently until the disease progresses and complications appear. This may explain the finding that those with a good perception of self-health may have an increased risk of being untreated for hypercholesterolemia. Further study into health behaviour and belief about medicines would help to ascertain whether behaviour and belief play important roles in patient acceptance of chronic disease medication management. A health promotion program to manage these risk factors for cardiovascular disease and secondary prevention is perhaps part of the plan needed to tackle this growing public health problem.

In conclusion, more than two-thirds of older adults with hypercholesterolemia were not on lipid-lowering medication in China. Being untreated was positively related to being female, current smoking, heavy alcohol drinking, more consumption of meat, and chronic bronchitis. These participants with co-morbidities of coronary heart disease, stroke, hypertension or diabetes were given less treatment for hypercholesterolemia compared to those in high income countries. Qualitative research is needed to better understand why this occurs--from doctors,
patients and carers. Our research findings highlight a pressing need to tackle untreated hypercholesterolemia in older adults with hypercholesterolemia.

Supporting Information

S1 Dataset. “WJJ 328 RC sent to PLoS copied AAAA.sav” for analysis in this paper. (SAV)

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Dr Ruolding Chen has full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Author Contributions

Conceived and designed the experiments: RC ZH MJZ. Performed the experiments: RC ZH JW. Analyzed the data: JW ZH JLP RC. Contributed reagents/materials/analysis tools: RC JW JLP. Wrote the paper: ZH MJZ RC. Critically reviewed and revised the manuscript: ZH MJZ JW JLP RC.

References

1. Mihaylova B, Emberson J, Blackwell L, Keech A, Simes J, Barnes EH, et al. (2012) The effects of lowering LDL cholesterol with statin therapy in people at low risk of vascular disease: meta-analysis of individual data from 27 randomised trials. Lancet 380: 581–590. doi:10.1016/S0140-6736(12)60367-5 PMID:22607822
2. Gupta A, Guymard V, Zaman MJ, Rehman HU, Myint PK (2010) Systematic review on evidence of the effectiveness of cholesterol-lowering drugs. Adv Ther 27: 348–364. doi:10.1007/s12325-010-0033-6 PMID:20533012
3. Shepherd J, Blauw GJ, Murphy MB, Bollen EL, Buckley BM, Cobbe SM, et al. (2002) Pravastatin in elderly individuals at risk of vascular disease (PROSPER): a randomised controlled trial. Lancet 360: 1623–1630. PMID:12457784
4. Primatesta P, Poulter NR (2000) Lipid concentrations and the use of lipid lowering drugs: evidence from a national cross sectional survey. BMJ 321: 1322–1325. PMID:11090516
5. Primatesta P, Poulter NR (2006) Levels of dyslipidaemia and improvement in its management in England: results from the Health Survey for England 2003. Clin Endocrinol (Oxf) 64: 292–298.
6. Kotseva K, Wood D, De BG, De BD, Pyorala K, Keil U, et al. (2009) Cardiovascular prevention guidelines in daily practice: a comparison of EUROASPIRE I, II, and III surveys in eight European countries. Lancet 373: 929–940. doi:10.1016/S0140-6736(09)60330-5 PMID:19286092
7. Wu J, Zhu S, Yao GL, Mohammed MA, Marshall T (2013) Patient factors influencing the prescribing of lipid lowering drugs for primary prevention of cardiovascular disease in UK general practice: a national retrospective cohort study. PLoS ONE 8: e67611. doi:10.1371/journal.pone.0067611 PMID:23922649
8. Mantel-Teeuwisse AK, Verschuren WM, Klungel OH, de BA, Kromhout D (2004) Recent trends in (under)treatment of hypercholesterolaemia in the Netherlands. Br J Clin Pharmacol 58: 310–316. PMID: 15327591
9. Mantel-Teeuwisse AK, Verschuren WM, Klungel OH, Lindemans AD, Porsius AJ, et al. (2003) Undertreatment of hypercholesterolaemia: a population-based study. Br J Clin Pharmacol 55: 389–397. PMID: 12680888
10. Lemaitre RN, Furberg CD, Newman AB, Gordon DJ, Gottdiener JS, et al. (1998) Time trends in the use of cholesterol-lowering agents in older adults: the Cardiovascular Health Study. Arch Intern Med 158: 1761–1768. PMID: 9738605
11. Omran AR (2005) The epidemiologic transition: a theory of the epidemiology of population change. 1971. Milbank Q 83: 731–757. PMID: 16279965
12. Yang G, Wang Y, Zeng Y, Gao GF, Liang X, Zhou M, et al. (2013) Rapid health transition in China, 1990–2010: findings from the Global Burden of Disease Study 2010. Lancet 383: 1987–2015. doi: 10.1016/S0140-6736(13)61097-1 PMID: 23746901
13. Poston DL Jr, Duan CC (2000) The Current and Projected Distribution of the Elderly and Eldercare in the People's Republic of China. Journal of Family Issues 21: 714–732.
14. Mannu GS, Zaman MJ, Gupta A, Rehman HU, Myint PK (2013) Evidence of lifestyle modification in the management of hypercholesterolaemia. Curr Cardiol Rev 9: 2–14. PMID: 22998604
15. Chen R, Hu Z, Chen RL, Ma Y, Zhang D, Wilson K. (2013) Determinants for undetected dementia and late-life depression. Br J Psychiatry 203: 203–208. doi: 10.1192/bjp.bp.112.119354 PMID: 23888000
16. Feng L, Lu P, Lu C, Tang W, Mahapatra T, Wang Y, et al. (2014) Burden and correlates of geriatric depression in the Uyghur elderly population, observation from Xinjiang, China. PLoS One. 9:e114139. doi: 10.1371/journal.pone.0114139 PMID: 25437860
17. Chen R, Wei L, Hu Z, Qin X, Copeland JR, Hemingway H. (2005) Depression in older people in rural China. Arch Intern Med 165: 2019–2025. PMID: 16186473
18. Copeland JR, Prince M, Wilson KC, Dewey ME, Payne J, Gurland B. (2002) The Geriatric Mental State Examination in the 21st century. Int J Geriatr Psychiatry 17: 729–732. PMID: 12211122
19. Prince MJ, de Rodriguez JL, Noriega L, Lopez A, Acosta D, Albanese E, et al. (2008) The 10/66 Dementia Research Group's fully operationalised DSM-IV dementia computerized diagnostic algorithm, compared with the 10/66 dementia algorithm and a clinician diagnosis: a population validation study. BMC Public Health 24; 8:219.
20. Chen R, Tunstall-Pedoe H (2005) Socioeconomic deprivation and waist circumference in men and women: The Scottish MONICA surveys 1989–1995. Eur J Epidemiol 20: 141–147. PMID: 15792280
21. Zhang XH, Lu ZL, Liu L (2008) Coronary heart disease in China. Heart 94: 1126–1131. doi: 10.1136/ hrt.2007.132423 PMID: 18703693
22. The joint committee for guideline of prevention and treatment of lipid abnormality in Chinese adults. (2007) The guideline of prevention and treatment of lipid abnormality in Chinese adults. Chin J Cardiol 35: 390–413.
23. Region WWP (2013) Cardiovascular diseases. Available: http://www.wpro.who.int/china/mediacentre/ factsheets/cvd/en/index.html. Accessed 31 October 2013.
24. Hu DY, Ding RJ (2008) [Guidelines for management of adult dyslipidemia in China]. Zhonghua Nei KeZa Zhi 47: 723–724.
25. Kotseva K, Wood D, De Backer G, De Bacquer D, Pyorala K, Keil U, et al. (2009) EUROASPIRE III: a survey on the lifestyle, risk factors and use of cardioprotective drug therapies in coronary patients from 22 European countries. Eur J Cardiovasc Prev Rehabil 16: 121–137. doi: 10.1097/HJR. 0b013e3283294b1d PMID: 19287307
26. Sheng X, Murphy MJ, MacDonald TM, Wei L (2012) Effect of statins on total cholesterol concentrations and cardiovascular outcomes in patients with diabetes mellitus: a population-based cohort study. Eur J Clin Pharmacol 68: 1201–1208. doi: 10.1007/s00228-012-1234-5 PMID: 22354153
27. Chan TY, Chan JC, Tomlinson B, Critchley JA (1993) Chinese herbal medicines revisited: a Hong Kong perspective. Lancet 342: 1532–1534. PMID: 7902907
28. Wen CP, Cheng TY, Tsai MK, Chang YC, Chan HT, Tsai SP, et al. (2008) All-cause mortality attributable to chronic kidney disease: a prospective cohort study based on 462,293 adults in Taiwan. Lancet 371: 2173–2182. doi: 10.1016/S0140-6736(08)60952-6 PMID: 18586172