博士論文

The association between economic development, lifestyle differentiation and C-reactive protein concentrations within rural communities in Hainan Island, China

（中国海南省農村部コミュニティにおける

経済発展とＣ反応性タンパク質濃度に関する研究）

井 上 陽 介

Yosuke INOUE

Supervisor: Prof. Chiho Watanabe

Yosuke INOUE
School of International Health
Admission in April 2010

The association between economic development, lifestyle differentiation and C-reactive protein concentrations within rural communities in Hainan Island, China.

中国海南省農村部コミュニティにおける経済発展と
C 反応性タンパク質濃度に関する研究

Abstract

Objectives: Earlier fieldwork in rural Hainan, China demonstrated increasing differences emerging in lifestyles within each community. It is possible that these variations might have stratified residents into sub-populations with different health attributes. This study examined the association between C-reactive protein (CRP) concentration, a biomarker of future cardiovascular events, and personal lifestyle parameters and whether it differs according to the degree of community-level economic development among rural communities.

Methods: A cross-sectional field survey was undertaken in 19 rural communities in 5 regions in Hainan Island. Convenience sampling was used to collect dried blood spot samples to measure high-sensitivity CRP concentration from 1744 individuals. Logistic regression analyses were conducted to identify factors which contributed to an elevated CRP concentration (i.e., 3 – 10 mg/L) among the participants.

Results: CRP concentration was positively associated with the weekly consumption frequency of poultry (odds ratio [OR] = 1.36, 95% confidence interval [CI] 1.00 to 1.84) and experience of migratory work in the previous year (OR 1.79, 95% CI 1.18 to 2.72). CRP concentration was also positively associated with the degree of community-level economic development, indexed as the maximum income reported in each community (OR = 1.01, 95% CI 1.00 to 1.02). These associations were more pronounced among the female participants.

Conclusions: It is possible that the health impact of economic development may be more easily observed among female residents, who were previously isolated from market exposure. This study suggests that within these rural communities that once used to be homogeneous, economic development might have stratified people into different sub-populations with different CVD risks given that CRP concentration is a marker of future CVD risk.

Table of Contents

Appendices

Acknowledgements

First of all, I would like to express my gratitude to the local people in Hainan Island for participating in my study and accompanying me while I conducted fieldwork. My stay in Hainan was always fruitful as everyone treated me as if I were one of their community members. My thanks then go to Prof. Jianwei Du, Prof. Shanqing Wang, and Prof. Yan Chen of Hainan Center for Disease Control and Prevention, China, for providing practical support during my survey.

I also would like to express my deep gratitude to Prof. Chiho Watanabe and Dr. Masahiro Umezaki of the Department of Human Ecology, the University of Tokyo, whose comments and suggestions were of great value for my study. I am also indebted to Dr. Andrew Stickley of the Department of Human Ecology whose comments made an enormous contribution to my work. It should be noted that Prof. Toru Shinohara of the Lake Biwa Museum, Prof. Masaru Nishitani of the National Museum of Japanese History and Dr. Hongwei Jiang of the Research Institute for Humanity and Nature helped me initiate my research career.

My special appreciation goes to my research partners, Mr. Dandan Li of Hainan Provincial Center for Disease Control and Prevention, China, and Ms. Aki Yazawa of the Department of Human Ecology. Their intellectual curiosity and integrity in research activity have always inspired and motivated me. Finally, I would also like to express my gratitude to my family, especially to my wife, Kazuko, for their moral support and warm encouragement.

List of Tables and Figures

Tables:

Figures:

Abbreviations

ANOVA	analysis of variance
BMI	body mass index
CHD	coronary heart disease
CHNS	China Health and Nutrition Survey
CI	confidence interval
CRP	C-reactive protein
CV	coefficient of variation
CVD	cardiovascular disease
DBS	dried blood spot
EIA	enzyme immunoassay
GDP	gross domestic product
Hainan CDC	Hainan Provincial Center for Disease Control and Prevention
hs-CRP	high-sensitivity C-reactive protein
HDL	high-density lipoprotein
IL-1β	interleukin 1β
IL-6	interleukin 6
LDL	low-density lipoprotein
LOD	limit of detection
MIDUS	Survey of Midlife Development in the United States
MONICA	Monitoring Trends and Determinants in Cardiovascular Disease
NCD	non-communicable disease
NF-κB	nuclear factor – kappa B
NHANES	National Health and Nutrition Examination Survey
NSHAP	National Social Life, Health, and Aging Project
OR	odds ratio
RMB	ren min bi (Chinese Currency)

RR	relative risk
SD	standard deviation
SES	socioeconomic status
VIF	variance inflation factor
WHO	World Health Organization
WHR	waist-to-hip ratio

Chapter 1 Introduction

1.1. Economic development and health

The health status and disease profile of the human population have been linked to the level of economic development and societal organization (Yusuf et al., 2001a). In the initial stage of economic development (e.g., in urban settlements such as London in the 16th century), where sanitation, water treatment and other public health measures were lacking, people experienced infectious diseases resulting from an elevated degree of population concentration, and thus pathogen transmission among residents (Bogin, 1988). As societies became more economically developed, mortality from infectious diseases declined due to the implementation of public health measures while in the second half of the twentieth century people started to suffer more from non-communicable diseases (NCDs) than communicable diseases by adopting what has been termed a “modern” or “western” lifestyle (Yusuf et al., 2001a). This process has been termed the epidemiological transition (Omran, 1971).

Today, NCDs, such as cardiovascular diseases (CVDs), cancers, chronic respiratory diseases and diabetes mellitus, have a significant impact on human health, causing 35 million deaths each year, which equates to approximately 60 % of all deaths in the world. In particular, CVDs are the leading cause of death due to NCDs in the world. It has been estimated that 17.3 million people died from CVDs in 2008, which consisted of 7.3 million cases of death due to coronary heart disease (CHD) and 6.2 million due to stroke (Alwan, 2011). It has been estimated that this figure will rise to 23.3 million by 2030 (Alwan, 2011; Mathers & Loncar, 2006). As with NCDs in general (World Health Organization, 2008), low- and middle-income countries are disproportionally affected by CVDs with over 80 % of all CVD deaths taking place in these countries. The developing world is now home to the majority of global cases of CVDs (Kalache & Keller, 2004).

A growing body of research has focused specifically on the association between economic development and CVDs. A cross-country analysis found that, in general, economic development was associated with an increasing risk of CVDs in low-income countries and that CVDs were most prevalent in middle-income countries and then decreased in more developed countries (Monteiro et al., 2004). The increasing incidence of CVDs/CVD risks among low- and middle-income countries has been linked to increasing income; research on 37 developing countries, for instance, showed that almost two-thirds of the variation in female obesity, one of the major risk factors for CVDs, could be explained by differences in per capita gross domestic product (GDP) (Monteiro et al., 2004). This is the reason CVDs, or NCDs in general, are often referred to as the "diseases of affluence" or "Western disease" (Ezzati et al., 2005; McKeown, 1988; Trowell & Burkitt, 1981).

CVD is also related to the income level within each country (Fuster & Kelly, 2010). In lower-income countries, female obesity is almost twice as high (14.5 %) among the wealthiest 25 % of families than the poorest 25 % of families (7.7 %) while in higher-income countries female obesity is more common among the families in the poorest wealth quartile (14.1 %) than those in the highest wealth quartile (8.9 %) (Monteiro et al., 2004). Another example is the association between obesity and female formal education, indexed as a country-specific measure of socioeconomic status (SES); Monteiro et al. (2004) using data from 21 low-income countries showed that the risk of obesity was 5 to 10 times higher in the higher SES group than in the lower SES group, while in 12 lower middle-income countries the pattern of association between obesity and SES was mixed. Furthermore, in the upper middle-income economies (e.g., Turkey, South Africa, Brazil and Mexico), the risk of obesity was always significantly higher in the lower SES group than in the higher group. These results suggest that the SES group which has the highest risk of experiencing CVD might change during the process of economic development.

There are several explanations for the association between economic development and CVDs or CVD risks. Overall, economic development has been linked to a marked increase in the consumption of foods which are rich in energy and a decrease in energy expenditure through less physical activity; energy expenditure reduces due to increased use of public transportation, private automobiles and increased mechanization in agriculture, while increasing wealth and the development of commercial infrastructure enable people to consume more food items that are high in energy, fat and sodium (nutrition transition) (Popkin, 2004). Moreover, the spread of mass media means that global influences on the perception of what constitutes a desirable lifestyle are also changing the types of food consumed in both urban and rural areas (Yusuf et al., 2001a).

In high income countries the negative effects of these changes among those with a high SES may have been somewhat mitigated by changing lifestyle behaviors while those with a lower SES and less health-related knowledge have encountered greater difficulty in adapting to the changes brought about by economic development. They cannot afford to acquire healthier foods (e.g., fruits, vegetables, and whole-grain cereals) because of their expense and there are fewer opportunities for recreational exercise (Monteiro et al., 2004). Monteiro et al. (2004) pointed out that in high income countries the local environment associated with low SES may be more obesogenic. On the other hand, in low- and middle-income countries, recent economic development has provided richer people with an increased opportunity to adopt “western” lifestyles while, at the same time, they often have limited access to sufficient health education or effective health care services which enable the early detection of diseases and an emergency response to incidents when they manifest themselves (Ezzati et al., 2005). These conditions mean that richer individuals in the developing world are at higher risk of developing and dying from CVDs, compared to those who are poorer in society.

1.2. Transformation of the political system to a market economy in China and its health consequences

Perhaps no country exemplifies rapid economic development better than China.

Following political change and the creation of a market-oriented economy in the late 1980s, GDP increased more than 100-fold from 450,000 ren min bi (RMB) in 1980 to 52 million RMB in 2012. During this period of rapid economic growth, the urban population has increased at a staggering pace. The ratios of the urban population to the whole population were 11.8, 19.4, and 49.2 % in 1950, 1980 and 2010, respectively. And it has been estimated that by 2025 China will have more than 221 cities with a population in excess of 1 million people and more than 926 million people are expected to be living in cities (Woetzel et al., 2009).

The changes in the economic sphere in China in recent years have also been mirrored by those occurring in the health status of its population over time. As shown in Figure 1, life expectancy at birth has been increasing continuously since 1960 because of the successful control of infectious diseases and improvement in maternal and prenatal care (Yang et al., 2008). However, population ageing, which was further accelerated by the introduction of the country's one-child policy, has modified the disease profile of the country. While the proportion of deaths which resulted from communicable diseases and maternal and perinatal conditions decreased from 27.8 % of all deaths in 1973 to 5.2 % in 2005, an opposite trend was observed for chronic diseases, i.e.,

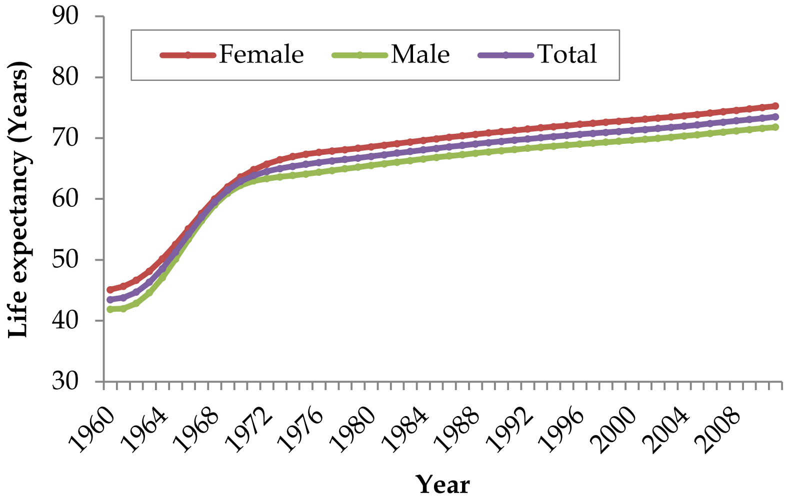


Figure 1 | Life expectancy at birth in China
Source: United Nations Population Division, World Population Prospects (2014)

cerebro-cardiovascular diseases, chronic obstructive pulmonary disease, and cancers, which increased from constituting 41.7 % of all deaths in 1973 to 74.1 % in 2005 (Yang et al., 2008). Data from the Chinese National Nutrition and Health Survey in 2002 showed that 14.7 % of Chinese were overweight (i.e., body mass index [BMI; kg/m^2] ≥ 25) and another 2.6 % were obese (i.e., BMI ≥ 30), which meant that 184 million people were overweight, and a further 31 million obese (Wu, 2006). As for hypertension in 2002, approximately 18 % of Chinese people older than 15 years of age had hypertension, corresponding to a population figure of 177 million people (Yang et al., 2008).

He et al. (2005) studied a nationally representative cohort of 109,871 men and women aged 40 years or older in China, following participants from 1991 up until 2000. They showed that the five leading causes of death for males were cancer (mortality, 374.1/100,000 person-years), heart disease (319.1), cerebrovascular disease (310.5), accidents (54.0) and infectious diseases (50.5) while among females, the corresponding causes were heart disease (268.5), cerebrovascular disease (242.3), cancer (214.1), pneumonia and influenza (45.9) and infectious diseases (35.3). The major diseases (i.e., heart disease, cancer, and cerebrovascular disease) accounted for 70.3 % of all deaths among urban residents and 61.7 % among rural residents.

1.3. Risk factors for CVDs in China

The increasing trend in chronic diseases, especially CVDs in China, has been underpinned by a dramatic increase in many of the risk factors for CVDs as societal change has continued. More specifically, diet, levels of physical activity, tobacco consumption and alcohol intake have all changed significantly in recent decades (Yang et al., 2008).

(i) Diet

According to a series of nation-wide nutritional studies conducted by the Chinese government (i.e., the China National Nutrition and Health Survey), the average daily calorie intake among both urban and rural Chinese has changed little over the past two decades; calorie intakes of 2,491–2,250 kcal per day were reported in 1982, 1992, and 2002. As a result of this Yang et al. (2008) concluded that the increase in the number of overweight and obese people has been mainly caused by a reduction in levels of physical activity. However, the composition of the diet has continued to change; in 1982, cereals constituted 65.0 % and 74.6 % of energy intake and fats 25 % and 14.3 % of energy intake in urban and rural areas. By 2002, cereals comprised 47.4 % and 60.7 % of energy intake, and fats 35.4 % and 27.7 % of energy intake in urban and rural areas (Yang et al., 2008). Du et al. (2004) studied the impact of income change on dietary behavior over time by using data from the China Health and Nutrition Survey (CHNS) from 1989 to 1997 and showed that the intake of animal food products increased as income increased. Since meat-derived saturated fat has been linked to CVD (de Oliveira Otto et al., 2012), the more frequent consumption of a diet high in fat against a backdrop of economic development may be leading to a worsening of CVD in China.

(ii) Physical activity/sedentary behavior

Monda et al. (2007) studied the impact of urbanization on physical activity by using the CHNS survey data. Men had 68 % and women 51 % higher odds of engaging in light versus heavy occupational activity given the mean change in community-level urbanization over the period between 1991 and 1997. Ng et al. (2009) also showed that in the period between 1991 and 2006, average weekly physical activity among those who participated in the CHNS fell by 32 %. Declining physical activity was strongly linked to factors associated with greater urbanization, such as the increased availability of educational institutions, housing infrastructure, sanitation improvements and the economic well-being of the community. Urbanization factors explained four-fifths of the decline in the level of occupational physical activity for the male participants and two-thirds of the decline for female participants.

(iii) Smoking/alcohol

Smoking is known to be associated with premature mortality and the overall disease burden from CVD (McBride, 1992). The proportion of Chinese men that smoke has been continuously high in the last two decades; their smoking prevalence was 61 % in 1984, 63 % in 1996, and 57 % in 2002. Passive exposure to tobacco smoke affects

52.2 % of the Chinese population, and this figure did not change between 1996 and 2002 (Yang et al., 2008).

Although the prevalence of liquor consumption has been declining over time, from over 50 % in 1993 to 41 % in 2006, the prevalence of beer consumption has risen by more than 50 % from only 20 % in 1993 and 32 % in 2006 (Tian et al., 2011). Millwood et al. (2013) showed the existence of an age-dependent trend in the consumption pattern by alcoholic beverage type while conducting research among 0.5 million people living in 10 cities in China; liquor is more frequently consumed by the older population while beer is consumed more frequently among the younger generation. Since liquors usually have an alcoholic content of more than 40 %, the declining consumption of liquor and growth in beer drinking would be beneficial to the well-being of the Chinese population if the overall volume of alcohol consumed remained constant. However, commercial alcohol production in China has increased more than 50-fold per capita since 1952 (Cochrane et al., 2003) and research suggests that the consumption of alcohol beverages is doing substantial damage to the health of the Chinese population (Hao et al., 2004).

1.4. Subclinical inflammation and cardiovascular disease

There have been a large number of epidemiological studies focusing on the association between C-reactive protein (CRP), a biomarker of subclinical inflammation, and CVD events or CVD risk factors, as it has been suggested that inflammation is predictive of a variety of diseases associated with ageing (McDade et al., 2011).

CRP is a plasma protein that is involved in the systemic response to inflammation. Plasma levels of CRP may rise rapidly and markedly, as much as 1000-fold or more, after an acute inflammatory stimulus, largely reflecting increased synthesis by hepatocytes (Black et al., 2004). Following the up-regulation of interleukin 6 (IL-6) or interleukin 1β (IL-1β) due to infection or inflammation, the transcription factor nuclear factor – kappa B (NF-κB) is activated and CRP is released into plasma (Rhodes et al., 2011).

In terms of the relationship with diseases associated with ageing such as CVD, the inflammatory process is initiated by the entrance of low-density lipoprotein (LDL) into the endothelial cells; macrophages then absorb these proteins, transforming themselves into foam cells. This process leads to modestly elevated levels of inflammation, i.e., CRP concentrations of 3 – 10 mg/L (Pearson et al., 2003).

The development of high sensitivity C-reactive protein (hs-CRP) assays (Ridker et al., 2003) has made it possible to evaluate variations in CRP concentration of less than 10 mg/L, which was previously regarded as meaningless subclinical inflammation. While agreement has not been obtained about the exact role of CRP in the development of CVD (whether it is a causal factor or just a marker of inflammation), this improvement in measurement technology has been important as it has been shown in numerous epidemiological studies that CRP concentration at a relatively low level (e.g., in the range between 3 and 10 mg/L) is associated with future CVD events (Koenig et al., 1999; Mendall et al., 2000; Ridker et al., 2002; Ridker et al., 2003; Sesso et al., 2007), type 2 diabetes mellitus (Pradhan et al., 2001; Thorand et al., 2003), late-life disability (Kuo et al., 2006), and mortality (Jenny et al., 2007; Tuomisto et al., 2006).

Koenig et al. (1999) studied CHD among initially healthy middle-aged men who participated in the Monitoring Trends and Determinants in Cardiovascular Disease (MONICA) Augsburg cohort during the period between 1984 to1992 in Germany. This study showed that the hazard ratio of CHD events associated with a 1-standard deviation (SD) increase in the log-CRP level was 1.60 after adjusting for age. Mendall et al. (2000) studied 1395 men from the Caerphilly Prospective Heart Study in South Wales, UK, with a follow-up period of 5 years and found that the odds ratio (OR) for the occurrence of ischemic heart disease (both fatal and non-fatal cases) among the highest quintile of CRP concentration versus the lowest was 2.11 (95% confidence interval [CI] 1.23 to 3.62) and that the OR for all-cause mortality was 2.32 (95% CI 1.47 to 3.67) for the highest versus lowest quintile of CRP concentration ($p < 0.0001$). There was a strong positive association between CRP concentration and fatal ischemic heart disease ($p = 0.0019$). Following up for 8 years, Ridker et al. (2003) studied the association between CRP concentration and cardiovascular events among 14,179 initial healthy American women. The study showed that the age-adjusted incidence rates of future CVD events were 3.4 and 5.9 per 1000 person-years of exposure for those with baseline CRP levels less than or greater than 3.0 mg/L, respectively. CVD event–free survival rates based on CRP levels above or below 3.0 mg/L were similar to survival rates based on having three or more metabolic syndrome characteristics, respectively. While undertaking separate analyses for CRP and LDL, Ridker et al. (2002) showed that the relative risk of initial CVD events rose in a linear fashion from 1.4 to 1.6, 2.0 and

2.3 in the lowest to the highest CRP quintiles, while the relative risk of LDL among quintiles 2 to 5 were 0.9, 1.1, 1.3 and 1.5, as compared to the participants in the lowest quintile. They pointed out that CRP is a stronger predictor of CVD events than LDL and that it adds prognostic information to that conveyed by the Framingham risk score, which was developed to estimate 10-year individual CVD risk (Albert et al., 2003b). Sesso et al. (2007) also showed that the relative risk of hypertension by CRP concentration was 1.00, 2.09, 2.51 and 2.44 (from the lowest to highest quartile) when using data from the Women's Health Study (USA) undertaken where participants were followed up for 10 years.

Pradhan et al. (2001) studied the association between CRP concentration and type 2 diabetes mellitus. Healthy middle-aged women, who participated in the Women's Health Study, were followed up for a period of 4 years and it was shown that the baseline level of CRP was higher among diabetic cases than among controls ($p < 0.001$). The relative risk (RR) for future diabetes mellitus in the highest quartile was significant (RR = 4.2) even after adjusting for BMI, family history, smoking, exercise, alcohol consumption and hormone replacement therapy. Thorand et al. (2003) also studied the association between CRP concentration and type 2 diabetes mellitus among those who participated in the MONICA study, focusing on middle-aged men aged 45 to 74 years old from 1984 to 1998 with an average follow-up period of 7.2 years. Men with CRP levels in the highest quartile (≥ 2.91 mg/L) had a 2.71 times higher risk of developing diabetes mellitus compared with the lowest (≤ 0.67 mg/L).

Kuo et al. (2006) studied the association between CRP at baseline and more general health attributes among those age 60 years or older who participated in the National Health and Nutrition Examination Survey (NHANES) from 1999 to 2002. Elevated CRP levels were significantly associated with disability in relation to instrumental activities of daily living, leisure and social activities, lower extremity mobility and general physical activities. The ORs for each SD increase in log-transformed CRP concentration were 1.18, 1.18, 1.17 and 1.17, respectively. Jenny et al. (2007) studied CRP in relation to near term death among older men from the Cardiovascular Health Study in the USA. When compared to participants in the lowest quartile, the hazard ratio for early death among those in the highest CRP quartile was 4.1, while the hazard ratio for early CVD death was 4.3.

Tuomisto et al. (2006) conducted their study in Finland among those aged 25 – 64 during the period 1992 – 2001. After adjusting for conventional CVD risk factors, such as the total to high-density lipoprotein (HDL) cholesterol ratio, systolic blood pressure, waist-to-hip ratio (WHR), diabetes mellitus and smoking, CRP remained statistically significantly associated with total mortality. The hazard ratio for total mortality was 3.48 while those for CHD and CVD were 2.39 and 2.42, respectively, when comparing those in the highest CRP quartile to people in the lowest quartile.

Based on the growing body of research evidence described above that subclinical inflammation, indicated as elevated CRP concentration at a lower level (e.g., in the range between 3 – 10 mg/L) is a significant predictor of future chronic diseases, especially CVDs, I decided to use CRP concentration as a surrogate endpoint of future CVD events in this study.

1.5. Lifestyle and socio-demographic determinants of elevated CRP concentration

Besides biological determinants of CRP concentration (i.e., age, sex, and BMI), several lifestyle factors have been associated with CRP concentration. These include smoking (Dietrich et al., 2007; O'Loughlin et al., 2008; Villegas et al., 2012a; Wannamethee et al., 2005), alcohol consumption (Imhof et al., 2004; Jellema et al., 2004), dietary patterns such as meat (Azadbakht & Esmaillzadeh, 2009; Esmaillzadeh et al., 2007) and fish consumption (Ciubotaru et al., 2003; Pischon et al., 2003; Trebble et al., 2003; Zampelas et al., 2005).

Smoking is a strong predictor of elevated CRP; a previous study showed that the ORs of elevated CRP were 1.43, 1.05, 1.36 and 1.51 among ex-smokers, and those who smoked 0 – 10, 10 – 20 and 20 cigarettes per day, respectively, compared with never smokers among urban Chinese males aged 40 – 74 years old (Villegas et al., 2012b). When adjusted for BMI, the association between smoking and CRP concentration was strengthened among them. Another study in Britain also showed that current cigarette smokers had significantly higher CRP concentrations (2.53 mg/L) compared to non-smokers (1.35 mg/L) after adjustment for other major cardiovascular risk factors (Wannamethee et al., 2005).

Previous studies have suggested that alcohol may be protective against cardiovascular mortality, in part, through an anti-inflammatory mechanism (Albert et al., 2003a; Imhof et al., 2004). Some studies have shown, for example, that a J-shape relationship exists between alcohol intake and CRP concentrations (Costanzo et al., 2011; Volpato et al., 2004).

Azadbakht and Esmaillzadeh (2009) studied Tehrani female teachers aged 40 – 60 years old in Iran and found that red meat intake was directly related to the plasma concentration of CRP. The concentrations of CRP were 1.34, 1.59, 1.75, 1.99 and 2.19 mg/L by increasing quintile of red meat intake. Studying food frequency data of the same participants, Esmaillzadeh et al. (2007) identified three dietary patterns by factor analysis, i.e., healthy, western and traditional dietary patterns and found that a healthy pattern (high in fruits, vegetables, tomatoes, poultry, legumes, tea, fruit juice, whole grains) was inversely associated with plasma CRP concentration even after adjusting for BMI and waist circumference. The western pattern score (high in refined grains [in contrast to whole grain], red meat, butter, processed meat, high-fat dairy products, sweets, pizza, potatoes, eggs, hydrogenated fats, and soft drinks) was positively associated with CRP concentration after adjusting for BMI and waist circumference ($p < 0.05$).

Ciubotaru et al. (2003) studied the effect of fish oil consumption on CRP concentration among postmenopausal women, who had their diets supplemented with the following composite for five weeks: either (1) 14 g safflower oil, (2) 7 g safflower oil and 7 g fish oil, and (3) 14 g fish oil. The results showed that IL-6 and CRP was lower among those whose diets were supplemented with fish oil, compared to those who only had safflower oil added to their diet. Zampelas et al. (2005) also showed that among those people who participated in the ATTICA study in Greece (1514 men and 1528 women aged 18 – 89), individuals who consumed > 300 g of fish per week had a concentration of CRP that was 33 % lower on average and a 33 % lower concentration of IL-6 when compared with non-fish consumers ($p < 0.05$).

Individual socio-economic position, such as educational attainment or income, has also been extensively studied in developed nations and shown to be inversely associated with CRP concentration. For example, a systematic review by Nazmi and Victora (2007) found that 19 studies out of 20 showed an inverse association between socio-economic position and CRP concentration. However, relatively little is known about the association between socioeconomic status and CRP concentration in developing nations. Nazmi et al. (2010) examined the association between socioeconomic position and CRP concentration in a Brazilian birth cohort where socio-economic position was assessed by four measures (i.e., family income at birth, maternal education, family income at age 23 [the age at which the survey was conducted] and participants' own education). They showed a positive association between family income at birth and CRP concentration among males and a negative association between maternal education and CRP concentration among females; this sex-related difference in the direction of the association between SES indicators and CRP concentration might be indicative of a complex mechanism linking SES and inflammatory/immune function in the context of rapidly developing regions.

As these lifestyle factors might have changed both in quantity and quality during the period of rapid economic development in China (Yang et al., 2008), I paid special attention to them as well as to migratory work as both might be linked to changes in consumption patterns of food items.

There are a number of studies which have shown that migrants to western countries had higher rates of CHD than the rates observed among their peers in their own country of origin. For example, it was reported that Japanese immigrants to the United States had higher rates of CHD and a higher concentration of risk markers for CHD (e.g., dyslipidemia and hypertension) (Kato et al., 1973). Subsequent research has also found similar increases in CHD among immigrants to western countries from China and South Asia, as well as among migrants who move from rural to urban settings within countries and adopt a more “western” lifestyle (Yusuf et al., 2001a, b). This parallels research on indigenous populations within western countries which has shown that significant increases in rates of CVD and its associated risk factors occur when such people abandon their traditional diets and way of life (Fuster & Kelly, 2010; Yusuf et al., 2001b). Now that people can migrate from rural to urban areas and from less developed to more developed regions on an unprecedented scale due to improved modes of transportation, it is essential to incorporate this aspect into any study on the association between economic development and health.

Holmes and Marcelli (2012) studied the CRP concentration of Brazilian migrants residing in the Northeastern United States (Boston-Cambridge-Quincy metropolitan statistical area) and found that unauthorized migrants were more likely to have a high CRP concentration than legal migrants ($p < 0.05$). However, to the best of my knowledge there is no study comparing the CRP concentration of returned migrants and that of non-migrants in the place of origin although Ullmann et al. (2011) showed that returned migrants in Mexico had a higher prevalence of heart disease ($p < 0.05$), hypertension ($p < 0.05$) and emotional/psychiatric disorders ($p < 0.001$) compared to non-migrants. This gives rise to the possibility that the experience of migratory work might result in elevated CRP concentration among returned migrants given that CRP concentration is a risk marker of future chronic diseases.

1.6. The impact of community-level economic development on CRP concentration

CVD events were associated with community-level indicators, such as rates of unemployment and poverty, the distribution of educational attainment, housing costs, rates of vehicle or home ownership, and median household income in the Atherosclerosis Risk in Communities Study, which was conducted in the United States (Borrell et al., 2004). As regards CRP concentration, Gallo et al. (2012) showed an inverse association between neighbourhood SES and CRP concentration. Specifically, a one-SD increase in neighborhood SES was associated with 23.56 % lower CRP concentration ($p < 0.01$). The neighbourhood SES measure was created by standardizing and summing up four SES indicators, namely household income, educational attainment, home ownership and public assistance.

In the context of developing countries, Thompson et al. (2014b) recently evaluated the impact of urbanization on CRP concentration in China, using data obtained from the CHNS. Their study revealed that a higher urbanicity score (Jones-Smith & Popkin, 2010) was positively associated with CRP concentration although this association differed by age and gender, which highlights the importance of understanding the effect of individual parameters and the community context simultaneously especially in the context of rapidly developing regions.

1.7. Study objectives

While the previous studies described above have identified determinants of elevated CRP concentration among the general population, usually in urban populations, little attention has been paid to inter-individual variation in lifestyles associated with economic development within rural communities and how it is associated with CRP concentration. One exception is a recent study conducted by Thompson et al. (2014b) that examined the impact of urbanization on this biomarker across all types of Chinese communities. However, as yet, there has been little focus on the way rural communities are being stratified into different population subgroups in the course of economic development or on how this might be being reflected in variations in CRP concentration within these communities. This may be an important research gap.

The results from a series of fieldwork studies undertaken in rural Hainan communities, China, between 2000 and 2010 by members of the Department of Human Ecology at the University of Tokyo showed that differences were rapidly emerging in SES and lifestyles within the study communities both in terms of inter-individual variation (Inoue et al., 2012) and inter-household variation (Jiang et al., 2006), as well as variation in the extent of economic development occurring across the island. Considering that in theory all of the island's residents lived an equally impoverished life in the era of the People's Commune (up until the late 1970s), when the means of production and community product were shared equally among commune members, I assumed that these inter-individual and inter-community variations may have emerged in the course of economic development since the late 1990s and might have stratified residents into different population subgroups with different health attributes. If this assumption is correct, it is of importance to describe their situation and identify the determinants of the association between different lifestyle parameters and CRP concentration, given its potential to impact detrimentally on future health outcomes.

Importantly, the Chinese rural communities focused on in this study are still in the initial stages of economic development and provide an ideal natural environment to examine the health impact of economic development.

The purpose of this research is therefore to elucidate the association between CRP concentration, a biomarker of future CVD events, and personal lifestyle parameters while determining the degree to which this relation is affected by the extent of community-level economic development in Hainan Island, China.

Chapter 2 Methods

2.1. Research location and historical background

Hainan Island is located to the south of mainland China. It lies between latitudes 18°10’ and 20°10’N and longitudes 108°37’ and 111°03’E. It has an area of 32,900 square kilometers and a subtropical and tropical climate (Köppen Climate Classification), with an average temperature of 22.8 – 25.8 °C and annual precipitation of 961 – 2439 mm (Hainan Provincial Bureau of Statistics, 2010). The population of the province was 8.8 million in 2010. The majority of the population belongs to the Han ethnicity (83 %), followed by ethnic minorities such as the Li (16 %) and the Miao (0.8 %).

Hainan Island, formerly part of Guangdong Province, became an independent province and was designated as a special economic zone in 1988. Since then, it has received large monetary investments from mainland China and overseas, especially to the agriculture and tourism sectors of the economy. Its subtropical climate is suitable for the cultivation of cash crops such as coffee, banana, litchi, mango, and longyan, and the island is well suited for tourism due to its extensive sandy beaches. The GDP of the island increased

21-fold from 7.7 billion RMB in 1988 to 165 billion RMB in 2009 (10 RMB is equivalent to 1.5 US dollars as of October 2010, when the survey was conducted) (Hainan Statistical Yearbook, 2010) (Figure 2). As shown in Figures 3 and 4, fruit production increased from 183,000 tons in 1988 to 4,037,000 tons in 2011 and the number of foreign visitor arrivals increased from 32,800 to 561,600 in the 21-year period between 1990 and 2011. Foreign exchange earnings from international tourism expanded from 27 million to 380 million US dollars in the same period. Most of the initial investment was focused on the coastal areas of the island, while later development, especially that since the year 2000 has occurred in the inland rural areas of the island, where I conducted my survey.

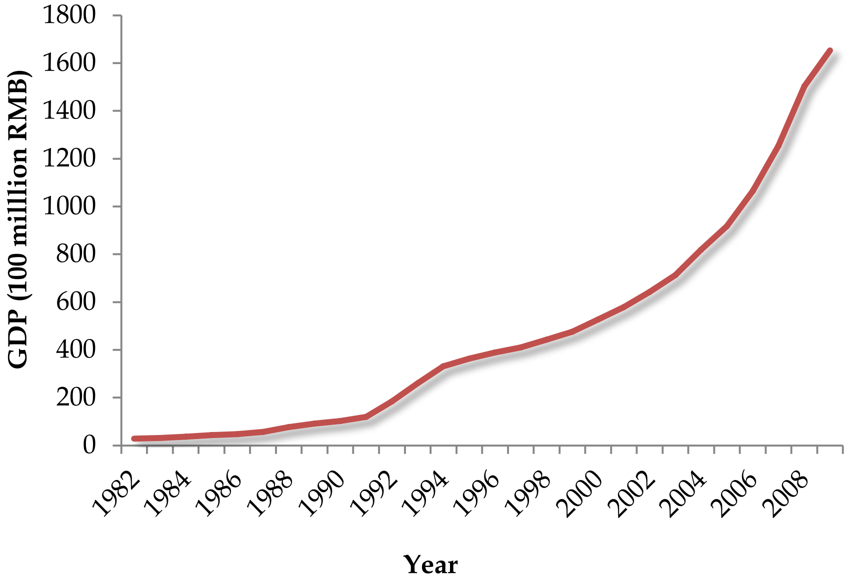


Figure 2 | GDP in Hainan Province
Source: Hainan Statistical Yearbook 2010

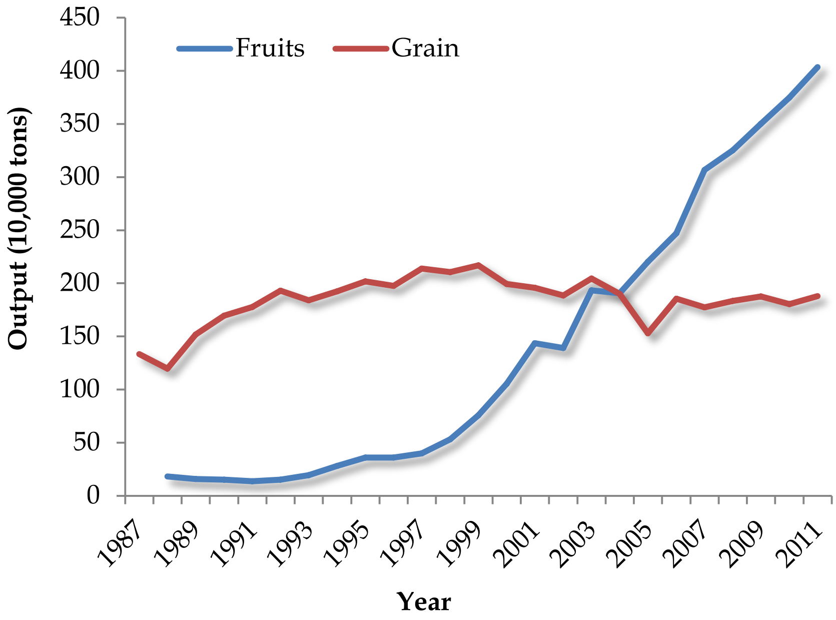


Figure 3 | Production of fruits and grains in Hainan Province
Source: National Bureau of Statistics of China (2013)

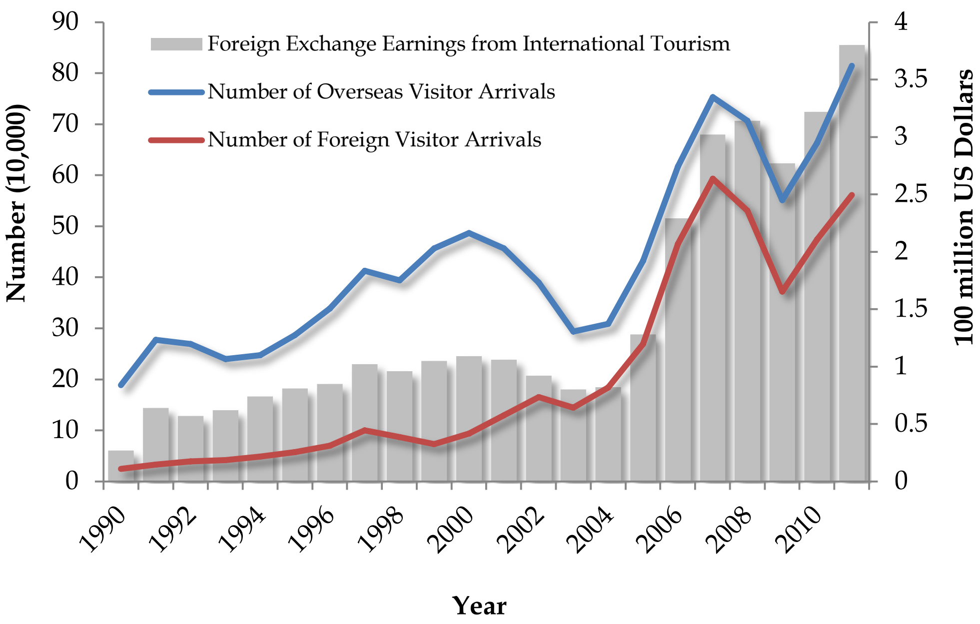


Figure 4 | Tourism in Hainan Province
Source: National Bureau of Statistics of China (2013)

The number of overseas visitor arrivals includes those from Hong Kong, Macau and Taiwan who visited Hainan Island and those who are foreign nationals (i.e., the number of foreign visitor arrivals).

Figure 5 shows the secular trend in population growth in Hainan Province since 1928. Except for the period during World War II, it shows a continuous increasing trend since that time. Figure 6 shows that between 1988 and 2000 the birth rate declined but it has been stable since 2000, while the death rate was stable in the period between 1988 and 2011.

These demographic changes, together with migration to the island, have contributed to population ageing. In 2000, the dependency ratio was 38.6 (the sum of the population aged 0 – 14 and population aged 65 or older divided by the number of people aged 15 to 64), the ratio of the young population (0 – 14) was 27.4, and the ratio of the old population was 11.2 (Figure 7). Although the ratio of the old population in China in 2014 is 13 and still lower than those recorded in developed countries (e.g., Japan: 41; Germany: 32; Italy: 33; Hong Kong: 19) (World Bank Group, 2014), one might expect that these numbers will increase at a quick rate as China has employed a one-child policy since 1979. Among rural communities, the impact should be especially quick and potentially more devastating considering the scale of current rural-urban migration, which is seeing many young people leaving their villages for cities.

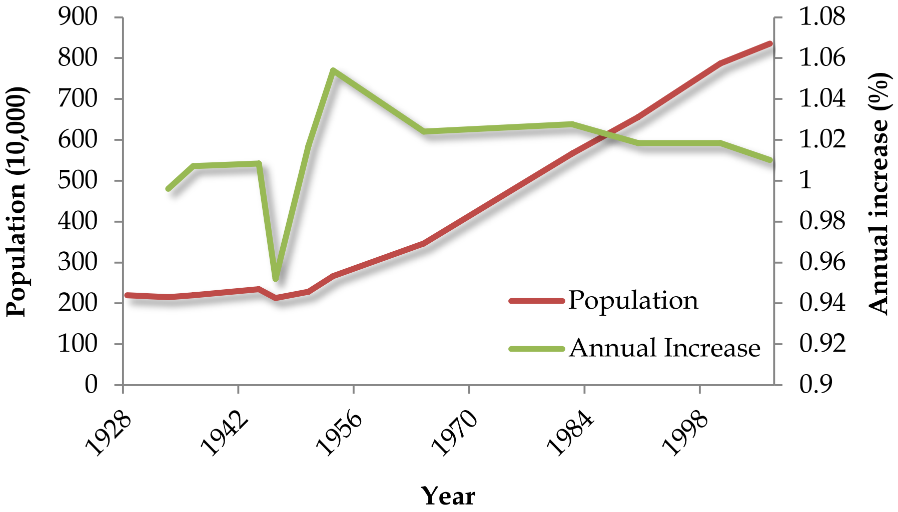


Figure 5 | Population trends in Hainan Province

Source: National Bureau of Statistics of China (2014)

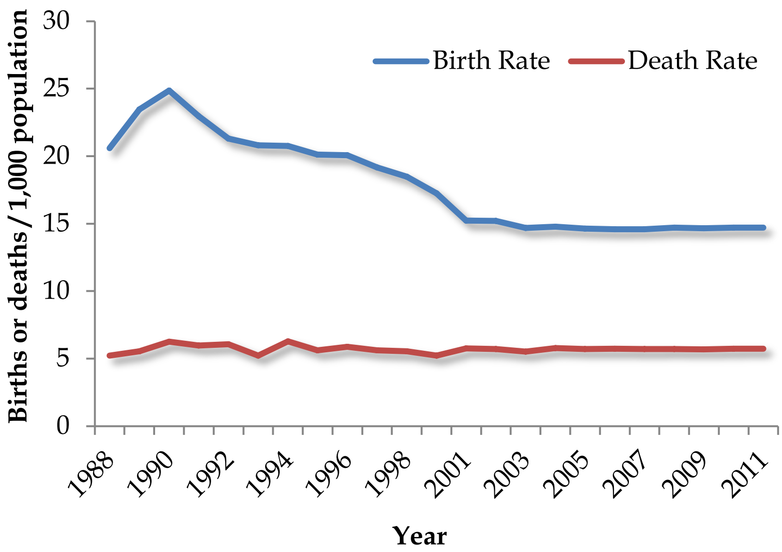


Figure 6 | Crude birth rate and death rate of the population in Hainan Province

Source: National Bureau of Statistics of China (2013)

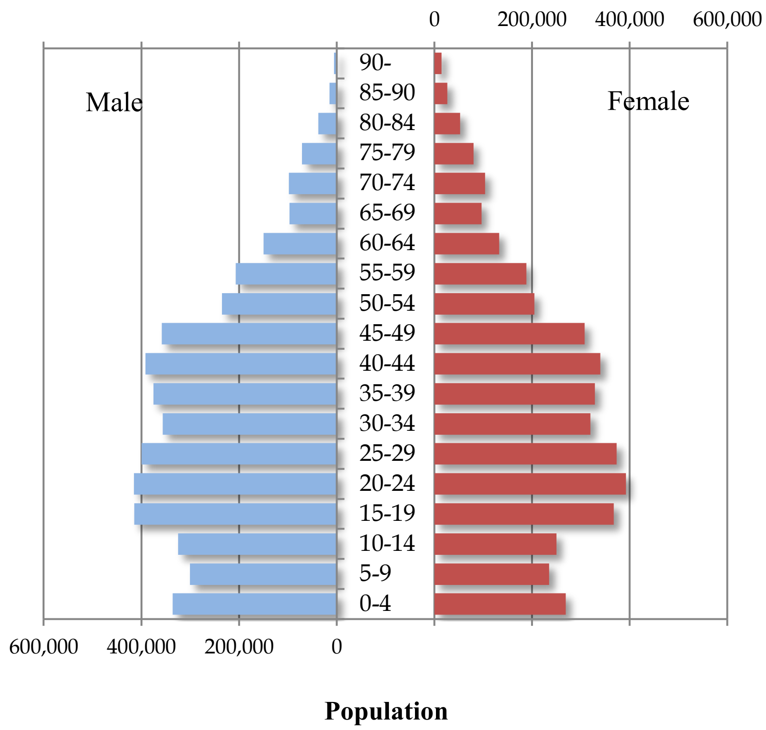


Figure 7 | Demographic structure of Hainan Province in 2000
Source: Population Census Office of Hainan Province (2002)

2.2. Study communities

For the present study, in order to identify the early onset of possible physiological consequences of economic development, rural communities were selected from 5 different regions in Hainan Island, which best represented the wide range of economic development across the island (Figure 8). These five regions had experienced different

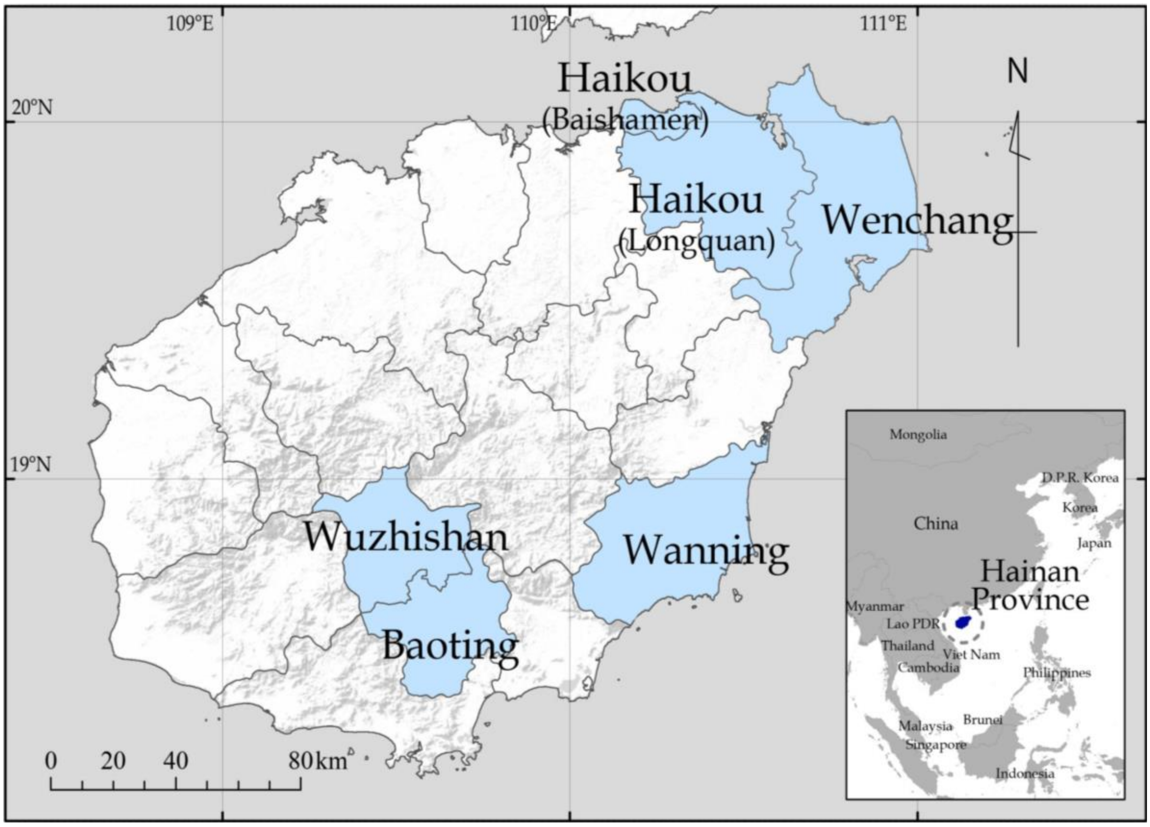


Figure 8 | Map of the study regions

levels of economic development as measured by the size of their GDP (Table 1); three regions (i.e., Haikou, Wenchang, and Wanning) were located in the coastal area, while the others (i.e., Wuzhishan and Baoting) were located inland. GDP was higher among those located in the coastal areas than those located inland.

Description of the study regions

I will briefly summarize the situation of the regions which were selected, according to the level of their regional GDP. The two municipalities of Wuzhishan City and Baoting Li and Miao Autonomous County are situated inland and have the lowest levels of regional GDP among all of the areas on the island (Table 1). Wuzhishan is the name of the highest mountain on Hainan Island; the municipality in which it is located includes Wuzhishan City at its center and Baoting County on its outskirts. These locations are a popular destination for tourists, as they can enjoy areas of tropical rainforest and hot springs. Many holiday condominiums are currently being constructed, but most of them are for the purpose of investment. Communities at lower altitudes cultivate cash crops, such as mango, betel nut, longyan, rubber, coconut and so on as their principal source of income (Jiang et al., 2006).

Wanning is situated on the eastern-south coastal line of the island and has the sixth highest level of regional GDP among Hainan's 18 areas. This location has an abundance of natural resources, such as titanium and zirconium. In terms of cash cropping, rubber, pepper, pineapple, coconut, betel nut, yizhi and coffee beans are all cultivated. This region is also noted for its coffee, Xinglong coffee, which was first cultivated in 1953

Table 1 | Characteristics of the municipalities in Hainan Province in 2009

Region	Population [10 thousands]	GDP [10,000 RMB]	GDP per capita [RMB]	Selected Region
Sanya	55.7	1,826,561	33,124	
Haikou	158.3	4,953,312	31,541	✔
Qionghai	48.8	885,125	18,235	
Wenchang	57.7	946,312	18,235	✔
Changjiang	26.0	439,285	17,061	
Chenmai	53.7	819,258	15,367	
Dongfang	43.5	634,018	14,708	
Wannning	60.1	768,007	12,886	✔
Lingao	48.4	578,008	12,075	
Lingshui	36.4	395,715	10,967	
Danzhou	105.5	1,092,846	10,962	
Baisha	19.9	194,333	9,840	
Wuzhishan	11.4	110,717	9,716	✔
Dingan	33.3	310,754	9,411	
Baoting	16.9	155,677	9,276	✔
Ledong	52.6	479,195	9,198	
Tunchang	29.5	267,404	9,149	
Qiongzhong	21.8	192,622	8,857	

Source: Hainan Statistical Yearbook 2010

Table 2 | Study participants in each region

	Baoting	**Wuzhishan**	**Wanning**	**Wenchang**	**Haikou**
Number of communities	3	4	3	6	3
Number of participants	230	367	372	389	386

and subsequently achieved commercial success. The fifth research region, Wenchang, has the fourth highest level of regional GDP on the island. Many of its inhabitants departed for overseas destinations such as Singapore, Thailand, Malaysia, as migrants, especially before the 1950s. As an illustration, Hainan chicken rice, which is sold in many Asian countries, was originally brought to those countries by Wenchang migrants. The effects of migration are still felt today as some families in Wenchang can receive financial support from those out-migrant families. Income is also obtained from cash cropping as the weather is suitable for cultivating tropical crops such as pepper, rubber and watermelon. Lastly, Haikou is the provincial capital of Hainan Province, situated in the north of the island. It is a center of business, politics, and culture and is the wealthiest region on Hainan Island. Most of its population resides in the city center and our survey was conducted in suburban rural villages. As they live close to Haikou city center, these rural residents have been exposed to the market economy for a longer period of time than those who live in ethnic minority communities in Wuzhishan or Baoting.

The number of communities I collected information from is shown in Table 2. These communities corresponded to "natural villages" ("zi ran cun" in Chinese) and were mainly composed of families based on paternal lines. The number of participants recruited within each study region is also shown in Table 2.

Based on my previous fieldwork undertaken among rural Hainan communities (Inoue et al., 2012), I identified rural-to-urban migrants as being one category of people, who are at higher risk of experiencing risk factors for CVDs in that they are experiencing rapid lifestyle change. In one of this study's community, I previously showed that the number of cash crops cultivated ($p = 0.003$) and consumption frequency of meat ($p = 0.03$) were different among those male participants who had paid jobs ($n = 21$) and those who did not ($n = 19$), where paid jobs included a tourism-related job in the village and migratory work in the previous month. Although BMI did not differ between the two groups (those who engaged in paid jobs and those who did not) at the time of my initial survey, these lifestyle variations in terms of the extent of exposure to the outside market economy (i.e., engagement in paid jobs) might be indicative of future health stratification within the community. Indeed, it can be speculated that this might be especially likely in an environment where access to health care or health-related information is not universal. As previous research has shown (Lu & Qin, 2014; Turra & Elo, 2008), migration can be a driving force that stratifies communities into different population subgroups.

2.3. Field survey

A cross-sectional field survey was conducted in November and December, 2010. I, together with trained local staff, collected dried blood spot (DBS) samples, which are drops of whole blood collected on filter paper following a simple finger prick, and questionnaire data from residents aged 15 years and above. All of the people residing in the study communities during our survey period were invited to participate in the study. The number of participants included in each region was the result of collecting as many participants as possible from the selected communities. All of the interviews were conducted individually at local health centers by trained interviewers in either Mandarin Chinese or the Hainan dialect.

Height was measured using a standard anthropometer (DKSH Switzerland, Ltd., Zurich, Switzerland) while weight was measured using a digital scale (HD-654, Tanita Corp., Tokyo, Japan); BMI was calculated by dividing weight (kg) by height squared (m^2). The mean systolic and diastolic blood pressures were calculated after they were measured twice using a sphygmomanometer (HEM-7000, OMRON Corp., Kyoto, Japan). Those who had a BMI of less than 15.0 were omitted from the analysis since these data might have resulted from measurement error (13 participants were removed).

Participants were asked to provide demographic and socioeconomic information about themselves (age, sex, marital status and educational attainment). Educational attainment was categorized into three groups according to years spent in school: less than 9 years (i.e., did not graduate from junior high school), 9 years (graduated from junior high school), and more than 9 years (obtained a higher education).

Lifestyle information was collected on (1) the weekly consumption frequency of various food items; (2) current smoking status (smoke/does not smoke); (3) alcohol consumption; and (4) experience of migratory work (paid work outside their own community for more than one month) in the previous year (yes/no). Information on the consumption frequency of various food items (sources of protein: pork, beef, poultry [chicken/duck/goose], marine fish, and freshwater fish) was obtained by the question, “How many days a week do you consume food items?” and was dichotomized at the median for statistical purpose (i.e., those whose consumption frequency was equal to or more than the median value and those whose consumption frequency was less). The weekly alcohol consumption (in mL of pure alcohol) was estimated by asking for information on the amount (in linag [Chinese unit equivalent to 50 mL]) and frequency of alcohol consumption by types of alcoholic beverage and dichotomized at the median for statistical purpose. This study assumed alcohol concentration to be 5% for beer, 15% for wine and 25% for home-distilled alcohol.

Household heads who participated in the survey were asked to provide information about their annual household income, which was estimated by summing up incomes obtained by subcategory, such as regular salary, pension, money from farming (rice, cash crops, and livestock), remittance from family members, and income earned from other small businesses based on questions used in the CHNS questionnaire (Popkin et al., 2010). To account for the number of household members which increase the needs of a household income at a diminishing rate due to the fact that household members can share their property or their livelihood (e.g., electricity or house), household income was divided by the square root of the number of household members (i.e., the square root scale) (OECD, 2011). The degree of community-level economic development was measured by using four measures, namely (1) the mean household income in each community, representing what members in each community are earning on average; (2) the median household income of the community, which might be more linked to what the majority of individuals in each community are earning than the mean income with distribution of household income skewed; (3) the maximum household income reported from each community, representing the extent of the distribution of wealth (income inequality); and (4) the number of items respondents had from 14 different assets, which represents cumulative wealth (i.e., a toilet, tractor, TV, video CD player, mobile phone, rice cooker, motorbike, personal computer, an Internet connection, car, refrigerator, air conditioner, washing machine and microwave oven). In a prior survey I conducted among these communities these items were considered to be those which could be purchased by the rural Hainan residents in the course of economic development.

2.4. Measurement of CRP concentration

The measurement of CRP concentration started with a minimally invasive method of blood collection. A disposable lancet was used to puncture participants' fingers, and blood was extracted and applied to validated filter paper (903 Protein Saver Cards, Whatman). Upon complete desiccation, DBS samples were stored at –20 °C for the first couple of days after collection near the field sites and later at –80 °C in the laboratory in Hainan Provincial Center for Disease Control and Prevention (Hainan CDC).

Following previous research (Brindle et al., 2010), duplicated DBS samples which were 1/8” punch in size were eluted in CRP assay buffer (0.01M phosphate buffer 0.5M NaCl, 0.1% Tween 20, pH 7.2 ± 0.3) and then assayed for CRP with a high-sensitivity sandwich enzyme immunoassay using polyclonal antibodies (Capture antibody: clone C5 anti-CRP MAb, cat.no. M86005M; and detection antibody: clone C6 anti-CRP MAb, cat.no. M86284M [Biodesign International, Maine, U.S.A.]). The secular change in the quality of DBS sample in relation to CRP concentration has been previously investigated by Brindle et al. (2010).

CRP concentrations were estimated with a four-parameter logistic calibration curve with standards at eight concentrations and three positive controls to check inter-assay variation. If the coefficient of variation (CV) between sets of the two absorbance data was greater than 10 %, the assay was rerun. Limits of detection were calculated by using the mean and SD of the absorbance of calibrators at the lowest (mean + 3 SD) and the highest (mean – 3 SD) concentrations.

To obtain serum-equivalent concentrations, I multiplied the value by 1.6, following a previously established protocol (Brindle et al., 2010). If serum-equivalent CRP concentration exceeded 10 mg/L, the participants were judged as experiencing inflammation due to acute infection. A CRP concentration greater than 3 mg/L was defined as “elevated” CRP and was regarded as being a marker for a potentially higher risk of developing CVD in the future, following a previous study which investigated the association between CRP concentration and CVD events (Yeh & Willerson, 2003). This value was also employed in previous studies conducted in China (Thompson et al., 2014a; Thompson et al., 2014b; Villegas et al., 2010).

2.5. Statistical analysis

Logistic regression analyses were conducted to identify factors which contributed to an elevated CRP concentration (i.e., 3 – 10 mg/L) among the rural population in Hainan Island. Results are presented in the form of OR. Models were developed following the procedure described below. The initial analytical model included age, sex and BMI variables (Model 1). Models were then adjusted for other explanatory variables: marital status, educational attainment and the experience of migratory work in the previous year (Model 2). Models 3, 5, 7, and 9 investigated the effect of the degree of community-level economic development on elevated CRP concentration. This was done by employing different indices of economic development, respectively, namely the mean household income of the community in Model 3, the median household income of the community in Model 5; the maximum household income reported from each community in Model 7; and the number of household assets in Model 9. In Models 4, 6 and 8, dietary pattern and alcohol consumption were incorporated in the models to see the change in the effect of the degree of community-level economic development. Some variables had to be deleted due to the issue of multicollinearity. This series of analyses (Model 1 – 9) was also conducted separately by sex. When examining the effect of these parameters among male participants, smoking status was included in the analyses in Models 4, 6 and 8.

Initial analyses showed that males and females were affected differently by the impact of economic development in terms of their CRP levels and that migratory status which might be one of the significant aspects of lifestyle change was also a predictor of subclinical inflammation. These results gave rise to the possibility that the impact of economic development on CRP concentration might differ by sex or migratory status. Thompson et al. (2014b) also reported heterogeneity in the impact of urbanization among their study communities by age group and sex. To examine the issue of heterogeneity, I created an interaction term between sex and the degree of community-level economic development and an interaction term between migratory status and the degree of community-level economic development and introduced them into the analyses (Tables 10 and 11). The degree of community-level economic development was examined by using three different measures, namely (1) the mean household income of the community; (2) the median household income of the community; and (3) the maximum household income reported from each community. The number of assets respondents possessed was removed from further analyses due to the issue of multicollinearity.

In trial analyses with a multilevel logistic regression model (Level 1: individual level; Level 2: community level), the likelihood ratio test indicated that the regression model which predicted elevated CRP concentration using the same set of explanatory variables with a single intercept was not rejected; thus I did not undertake a multilevel analysis.

A sensitivity analysis was conducted with (1) a cut-point of 2 mg/L of serum-equivalent CRP concentration and (2) using log-transformed CRP concentration as a continuous dependent variable (Appendix 2).

All statistical analyses were conducted using Stata 12.0. The statistical level of significance was set at the p-value of < 0.05.

2.6. Research ethics

The participation of the local residents was voluntary, using informed consent procedures. Respondents provided written consent after being informed that they could withdraw from the study at any time. The research protocol was officially approved by the appropriate sectors of the Chinese government. The field surveys were conducted after obtaining approval from the Research Ethics Committee at the Graduate School of Medicine at the University of Tokyo (No. 3406) and the Ethics Committee at Hainan CDC.

Chapter 3 Results

3.1. Characteristics of the study participants

The descriptive statistics of the participants are presented in Table 3. Of the 1731 participants included in the analysis, 51.0 % were female and 97.3 % of the participants had a CRP serum-equivalent concentration of less than 10 mg/L, which is the value conventionally used to judge the presence of acute inflammation. There were no significant differences in demographic and health attributes between the two groups categorized by using the CRP concentration of 10 mg/L as a cut-off point.

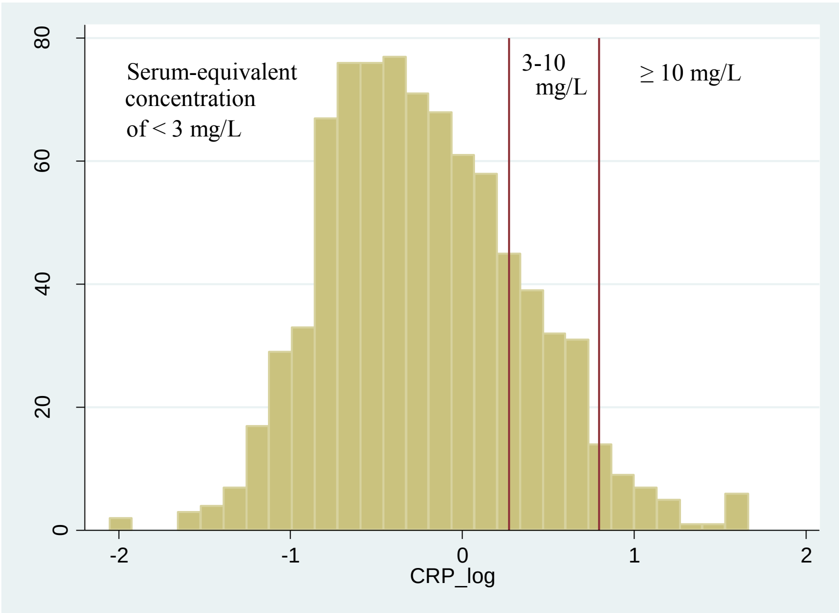
Among those without any obvious signs of clinical inflammation (i.e., the CRP concentration was < 10 mg/L), the average age was 45.0 (SD 17.4) for the male participants and 46.7 (SD 18.1) for the female participants. The average BMI scores were 21.3 (SD 2.8) and 21.2 (SD 3.0) for the male and female participants, respectively (results not shown); when using WHO criteria to determine overweight (i.e., a BMI score of equal to or greater than 25.0), 10.7 % of the male participants and 12.2 % of the female participants were categorized as being overweight. When hypertension was assessed using systolic blood pressure, 16.9 % and 14.3 % of the male and female participants were respectively judged as being hypertensive (≥ 140 mmHg), while 24.9 % and 26.4 % of the male and female participants were categorized as being hypertensive when using diastolic blood pressure (≥ 90 mmHg). There were sex differences in educational attainment, smoking status and alcohol consumption (higher in male participants) and BMI (higher in female participants) between the two groups categorized by using the CRP concentration of 10mg/L as a cut-off point.

Among those who had a CRP concentration of less than 10 mg/L, the average of the log-transformed CRP serum-equivalent concentration was −0.1 (SD 0.5) and −0.2 (SD 0.5) for the male and female participants, respectively (Table 3), while the median CRP values were 0.78 mg/L (inter-quartile range: 0.35 – 2.06 mg/L) for the male participants and 0.62 mg/L (inter-quartile range: 0.29 – 1.56 mg/L) for the female participants (data not shown). I converted the CRP variable into a binary variable dichotomized at the cut-off value of 3 mg/L CRP concentration (Thompson et al., 2014a; Thompson et al., 2014b; Villegas et al., 2012a) in the following analyses. The distribution of CRP concentration is shown in Figure 9.

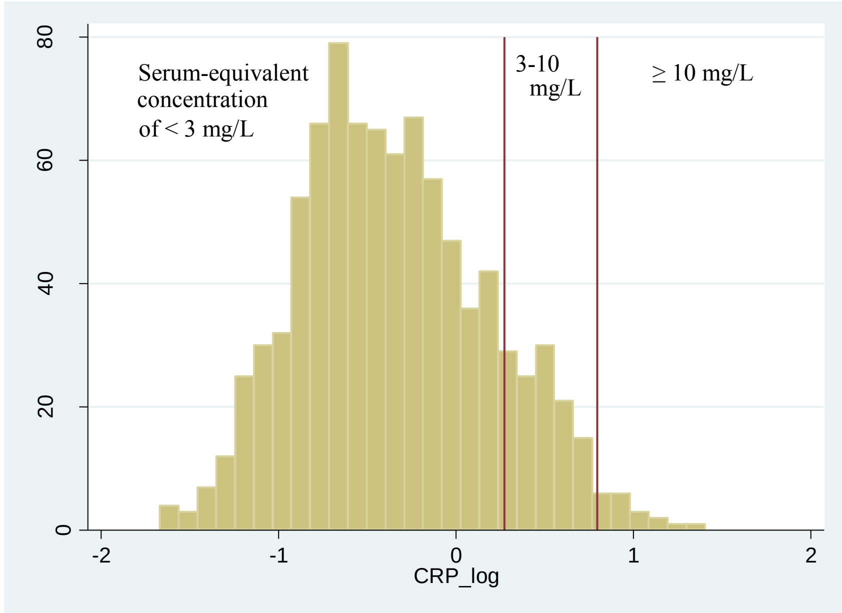
Table 3 | Descriptive statistics of the study participants

	CRP < 10 mg/L (N = 1684)				CRP ≥ 10 mg/L (N = 47)				Comparison [1]		
	Male (n = 807)		Female (n = 877)		Male (n = 32)		Female (n = 15)		CRP	Sex	Interaction
	Mean [SD]				Mean [SD]				p-value		
Age	45.0	17.4	46.7	18.1	51.3	18.7	45.9	17.0	0.326	0.512	0.206
C-reactive protein (log)	-0.1	0.5	-0.2	0.5	1.4	0.3	1.2	0.2	0.000	0.176	0.784
Alcohol (log, in gram)	1.8	1.5	0.5	1.1	1.6	1.5	0.4	1.0	0.390	0.000	0.957
	n (%)				n (%)						
Education attainment											
< 9 years	343	42.7	564	66.3	18	56.3	10	71.4	0.696	0.000	-
9 years	388	48.3	261	30.7	12	37.5	4	28.6			
> 9 years	73	9.1	26	3.1	2	6.3	0	0.0			
Smoking											
No	310	38.9	858	98.8	16	50.0	14	100.0	0.467	0.000	-
Yes	486	61.1	10	1.2	16	50.0	0	0.0			
BMI (kg/m^2) [2]											
< 18.5	119	14.7	178	20.3	7	21.9	2	13.3	0.232	0.007	-
18.5 - 24.9	602	74.6	592	67.5	19	59.4	10	66.7			
≥ 25.0	86	10.7	107	12.2	6	18.8	3	20.0			
Systolic blood pressure [3]											
≥ 140 mmHg	136	16.9	124	14.3	5	15.6	4	26.7	0.312	0.369	-
< 140 mmHg	668	83.1	746	85.7	27	84.4	11	73.3			
Diastolic blood pressure [3]											
≥ 90 mmHg	200	24.9	230	26.4	5	15.6	4	26.7	0.501	0.170	-
< 90 mmHg	604	75.1	641	73.6	27	84.4	11	73.3			

[1] A two-way ANOVA was conducted to compare continuous variables and Chi-squared tests were conducted to compare categorical variables.
[2] Body mass index (BMI) was used to categorize nutritional status by following WHO criteria: lean: < 18.5; normal: 18.5-24.9; and overweight: ≥ 25.
[3] People were judged as being hypertensive when systolic blood pressure was ≥ 140 mmHg or diastolic blood pressure was ≥ 90 mmHg.



Male



Female

Figure 9 | Histogram of CRP concentrations among the study participants

Table 4 presents details of the household-level living standard by region (i.e., household income and possession of 14 assets). There was a large variation in terms of income among the study communities both across the island and within each region; for example, the maximum annual household income observed in Haikou was 48,299 RMB, while that observed in Wanning was 9,000 RMB, which is still 15 times as much as the median income of that region. While some consumer durables were possessed comparatively little these in rural Hainan communities (e.g., personal computers, an Internet connection, cars, air conditioners and microwave ovens), other items such as toilets, TVs, mobile phones, rice cookers and motorbikes were owned more widely partially due to the fact that the local residents, especially the poor, are subsidized by the government when purchasing some of these items. Tractors were often purchased in Wuzhishan and Baoting, while this occurred less in Wenchang and Haikou. Refrigerators, washing machines and microwave ovens were more common possessions in Wenchang.

Table 5 shows the basic characteristics of the participants with a CRP concentration of less than 10 mg/L; the participants are stratified by sex and experience of migratory work in the previous year. More than 15 % of males (16.6 %) and 13.2 % of females were in a subclinical inflammatory state (i.e., had a CRP concentration of 3 – 10 mg/L) (data not shown). The results of a two-way analysis of variance (ANOVA) test showed that those who had experience of migratory work were younger (31.8 years old, SD 12.5) than those who did not (47.9 years old, SD 17.5). Hypertension was more frequently observed among those who did not have experience of migratory work in the previous year. Educational attainment and the prevalence of current smoking were higher among migrants (Education: $p < 0.001$; Smoking: $p = 0.002$) and males (Education: $p < 0.001$; Smoking: $p < 0.001$).

Table 6 presents descriptive statistics on dietary patterns (i.e., the weekly consumption frequency of selected food items) (See Appendix 1 for histograms of the consumption frequency of the food items). Pork was commonly consumed by the rural population in Hainan Island: the median consumption frequency of pork was 3 to 5 times a week. Further analyses will utilize information about the consumption frequency of pork, poultry, marine fish and freshwater fish. The consumption frequency of beef was excluded from subsequent analyses since it was not consumed sufficiently enough to be analyzed.

Table 4 | Participants' basic household characteristics in the regions

	Wanning (N = 125)		Wuzhishan (N = 153)		Wenchang (N = 121)		Baoting (N = 93)		Haikou (N = 144)	
Income (RMB)										
Mean [SD]	1190	[1581]	1732	[3460]	2066	[4065]	2127	[3521]	2699	[5800]
Median [IQR][1]	565	[0 - 2000]	577	[0 - 1789]	707	[0 - 1750]	894	[158 - 2121]	500	[0 - 2849]
Maximum	9000	-	25938	-	28800	-	20000	-	48299	-
	n	%	n	%	n	%	n	%	n	%
Toilet	91	72.8	80	52.3	96	79.3	38	40.9	82	56.9
Tractor	20	16.0	86	56.2	4	3.3	34	36.6	7	4.9
TV	101	80.8	132	86.3	114	94.2	70	75.3	90	62.5
Video CD player	32	25.6	54	35.3	25	20.7	28	30.1	35	24.3
Mobile phone	63	50.4	110	71.9	60	49.6	52	55.9	90	62.5
Rice cooker	96	76.8	83	54.2	113	93.4	60	64.5	70	48.6
Motorbike	75	60.0	86	56.2	80	66.1	64	68.8	61	42.4
Personal computer	2	1.6	3	2.0	7	5.8	4	4.3	9	6.3
Internet	1	0.8	1	0.7	8	6.6	1	1.1	8	5.6
Car	2	1.6	10	6.5	5	4.1	12	12.9	6	4.2
Refrigerator	0	0.0	8	5.2	25	20.7	4	4.3	10	6.9
Air conditioner	0	0.0	0	0.0	9	7.4	1	1.1	4	2.8
Washing machine	0	0.0	5	3.3	14	11.6	1	1.1	7	4.9
Microwave oven	1	0.8	2	1.3	7	5.8	2	2.2	4	2.8

Responses to the questions regarding household income and assets were obtained from household heads who participated in the present survey.
Regions are presented in the order of the amount of average household income in each region from left to right (i.e., from lowest to highest).
[1] IQR : inter-quartile range

Table 5 | Basic statistics of the participants whose CRP concentration was < 10 mg/L stratified by sex and migration status

	Male				Female				Comparison (1)		
	Returned migrant (n = 121)		Non-migrant (n = 686)		Returned migrant (n = 90)		Non-migrant (n = 787)		Migratory work	Sex	Interaction
	Mean [SD]				Mean [SD]				p-value		
Age	34.5	14.0	46.9	17.3	28.2	9.1	48.9	17.7	0.000	0.084	0.001
C-reactive protein	-0.1	0.5	-0.1	0.5	-0.2	0.5	-0.2	0.5	0.687	0.063	0.567
Alcohol (log, in grams)	1.9	1.4	1.7	1.5	0.3	0.8	0.6	1.1	0.708	0.000	0.012
	n [%]				n [%]				p-value		
Education attainment											
< 9 years	35	28.9	308	45.1	29	32.6	535	70.2	0.000	0.000	-
9 years	68	56.2	320	46.9	56	62.9	205	26.9			
> 9 years	18	14.9	55	8.1	4	4.5	22	2.9			
Smoking											
No	41	33.9	269	39.9	87	98.9	771	98.8	0.002	0.000	-
Yes	80	66.1	406	60.1	1	1.1	9	1.2			
BMI (2)											
< 18.5	11	9.1	108	15.7	22	24.4	156	19.8	0.707	0.004	-
18.5 - 24.9	94	77.7	508	74.1	60	66.7	532	67.6			
≥ 25.0	16	13.2	70	10.2	8	8.9	99	12.6			
Systolic blood pressure (3)											
< 140 mmHg	113	93.4	555	81.3	86	95.6	660	84.6	0.000	0.474	-
≥ 140 mmHg	8	6.6	128	18.7	4	4.4	120	15.4			
Diastolic blood pressure (3)											
< 90 mmHg	87	96.7	554	70.9	103	85.1	501	73.4	0.000	0.133	-
≥ 90 mmHg	3	3.3	227	29.1	18	14.9	182	26.6			

(1) A two-way ANOVA was conducted to compare continuous variables and Chi-squared tests were used to compare categorical variables.
(2) Body mass index (BMI) was used to categorize their nutritional status by following WHO criteria: underweight: < 18.5; normal: 18.5-24.9; and overweight: ≥ 25.
(3) People were judged as being hypertensive when systolic blood pressure was ≥ 140 mmHg or diastolic blood pressure was ≥ 90 mmHg.

Table 6 | Weekly food consumption frequency by sex and migration status

	Male		Female	
	Returned migrant (n = 121)	Non-migrant (n = 675)	Returned migrant (n = 90)	Non-migrant (n = 780)
	Median [IQR][1]	Median [IQR]	Median [IQR]	Median [IQR]
Pork	3 [2-7]	5 [3-7]	3 [1-5]	3 [2-7]
Beef	0 [0-0.25]	0 [0-0]	0 [0-0]	0 [0-0]
Poultry	1 [0-2]	1 [0-1] [2]	1 [0.25-2]	0.5 [0-1]
Marine Fish	2 [0-4]	2 [0-3.5] [2]	1 [0-3]	1 [0-3]
Freshwater Fish	1 [0-2]	1 [0-2] [2]	0.75 [0-2]	0.8 [0-1.5] [3]

* Participants were asked how many times a week they consumed food items.
[1] IQR: inter-quartile range.
[2] The number of participants is 674.
[3] The number of participants is 779.

3.2. Factors associated with subclinical inflammation (i.e., a CRP concentration of 3 – 10 mg/L)

Table 7 shows the results of the logistic regression analyses which investigated the associations between CRP concentration and demographic and socioeconomic variables among study participants in these rural Hainan communities. Model 1 shows that a higher CRP concentration was significantly associated with higher age (OR = 1.02, 95% CI 1.01 to 1.03, $p < 0.001$), sex (higher in males: OR = 1.35, 95% CI 1.03 to 1.78, $p = 0.031$) and BMI (OR 1.10, 95% CI 1.05 to 1.15, $p < 0.001$). BMI was removed in Models 2 – 9 due to multicollinearity (i.e., the uncentered variance inflation factor (VIF) was greater than 10 when it was in the models). The experience of migratory work in the previous year was significantly associated with CRP concentration (e.g., OR = 1.79, 95% CI 1.18 to 2.72, $p = 0.006$ in Model 2). The degree of community-level economic development was positively associated with CRP concentration when it was indexed as the maximum income reported in each community (OR = 1.01, 95% CI 1.00 to 1.02, $p = 0.013$ in Model 7), and it remained statistically significant after adjusting for the lifestyle variables in Model 8. Among the lifestyle variables, the frequency of consuming poultry was associated with a higher CRP concentration (e.g., OR = 1.36, 95% CI 1.00 to 1.84, p = 0.029 in Model 4). Alcohol consumption was not associated with CRP concentration. Some variables had to be removed due to multicollinearity in Model 9.

Table 8 shows the results of the logistic regression analyses which investigated the associations between CRP concentration and demographic and socioeconomic variables among male participants. Age and BMI were positively associated with CRP concentration (Model 1). Specifically, the ORs were 1.02 (95% CI 1.01 to 1.03, p = 0.002) for age and 1.09 (95% CI 1.02 to 1.16, p = 0.013) for BMI in Model 1, respectively. Those who graduated from junior high school (equivalent to 9 years of schooling) had significantly reduced odds of having subclinical inflammation (OR = 0.59, 95% CI 0.39 to 0.90, p = 0.014 in Model 2) than those who did not graduate from junior high school. The experience of migratory work in the previous year was not associated with CRP concentration. None of the indices of the degree of the extent of community-level economic development were associated with CRP concentration. None of the dietary patterns (i.e., the weekly consumption frequency of selected food items) was associated with higher CRP concentration among the male participants (Models 4, 6 and 8). Similarly, neither current smoking status nor alcohol consumption was associated with CRP concentration among the male participants.

As was observed for the male participants, among the female participants a higher CRP concentration was associated with increasing age and BMI (Table 9); specifically, the ORs were 1.02 (95% CI 1.01 to 1.03, $p = 0.003$) for age and 1.12 (95% CI 1.05 to 1.19, $p < 0.001$) for BMI in Model 1, respectively. Marital status was not associated with CRP concentration (Model 2). When adjusted for age and marital status, those who graduated from junior high school (equivalent to 9 years of schooling) had significantly higher odds of having subclinical inflammation (OR = 1.77, 95% CI 1.04 to 3.00, $p = 0.036$; results not shown) than those who did not graduate from junior high school. However, this association was attenuated and became non-significant in the following models (Models 2 – 9). Experiencing migratory work in the previous year more than doubled the odds of reporting a higher CRP concentration (OR = 2.05, 95% CI 1.05 to 4.01, $p = 0.035$ in Model 2). Adjustment for the extent of community-level economic development (Models 3 and 7) and the lifestyle variables (Models 4, 6 and 8) attenuated the association between the experience of migratory work in the previous year and the level of CRP concentration (e.g., OR = 1.91, 95% CI 0.97 to 3.80, $p = 0.063$ in Model 4). The degree of community-level economic development, indexed as the mean and maximum household income of the community, was also associated with a higher CRP concentration (mean: OR = 1.34, 95% CI 1.03 to 1.76, p = 0.032 in Model 3; maximum: OR = 1.02, 95% CI 1.01 to 1.03, p = 0.012 in Model 7). While the former was attenuated and became non-significant after adjusting for the lifestyle variables, the latter remained statistically significant (OR = 1.02, 95% CI 1.00 to 1.04, p = 0.014 in Model 8). The other indices of the extent of community-level economic development were not associated with CRP concentration. The frequency of consuming poultry was associated with a higher CRP concentration (OR = 1.71, 95% CI 1.08 to 2.69, p = 0.011 in Model 4). Alcohol consumption was not associated with CRP concentration.

The overall results did not change in the sensitivity analysis (Table 12 in Appendix 2).

Table 7 | Variables predicting elevated CRP concentrations (i.e., a CRP concentration of 3 – 10 mg/L) among study participants

		Model 1		Model 2		Model 3		Model 4		Model 5		Model 6		Model 7		Model 8		Model 9	
		OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Socio-demographic variables		(N = 1682)		(N = 1653)		(N = 1653)		(N = 1635)		(N = 1653)		(N = 1635)		(N = 1653)		(N = 1635)		(N = 1681)	
Age		1.02	[1.01, 1.03]	1.02	[1.01, 1.03]	1.02	[1.01, 1.03]	1.02	[1.01, 1.03]	1.02	[1.01, 1.03]	1.02	[1.01, 1.03]	1.02	[1.01, 1.03]	1.02	[1.01, 1.03]	1.02	[1.01, 1.03]
Sex (ref. female)		1.35	[1.03, 1.78]	1.35	[1.01, 1.80]	1.35	[1.01, 1.81]	1.36	[1.02, 1.82]	1.35	[1.01, 1.80]	1.36	[1.02, 1.82]	1.36	[1.02, 1.82]	1.36	[1.01, 1.82]	1.33	[1.01, 1.74]
BMI		1.10	[1.05, 1.15]	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Marital status (ref. not married)				0.79	[0.58, 1.09]	0.79	[0.57, 1.08]	0.75	[0.54, 1.04]	0.79	[0.58, 1.09]	0.76	[0.55, 1.04]	0.78	[0.56, 1.07]	0.73	[0.53, 1.01]	0.76	[0.55, 1.03]
Education (ref. < 9 years)	= 9 years			0.89	[0.64, 1.23]	0.86	[0.62, 1.20]	0.84	[0.60, 1.18]	0.89	[0.64, 1.23]	0.85	[0.61, 1.19]	0.85	[0.61, 1.19]	0.83	[0.59, 1.16]	-	-
	> 9 years			0.92	[0.51, 1.65]	0.90	[0.50, 1.61]	0.87	[0.48, 1.57]	0.92	[0.51, 1.65]	0.88	[0.49, 1.59]	0.89	[0.50, 1.60]	0.84	[0.47, 1.53]	-	-
Migration (1)				1.79	[1.18, 2.72]	1.77	[1.17, 2.69]	1.75	[1.15, 2.66]	1.79	[1.18, 2.72]	1.75	[1.15, 2.67]	1.68	[1.10, 2.55]	1.65	[1.08, 2.53]	-	-
Lifestyle variables																			
Alcohol (ref. < median) (2)	≥ median							0.95	[0.69, 1.31]			0.95	[0.69-1.31]			0.94	[0.68, 1.30]	-	-
Consumption frequency of (3)																			-
Pork (ref. < median)	≥ median							1.02	[0.76, 1.38]			1.03	[0.76, 1.38]			1.06	[0.78, 1.43]	-	-
Poultry (ref. < median)	≥ median							1.36	[1.00, 1.84]			1.40	[1.04, 1.88]			1.32	[0.98, 1.79]	-	-
Marine fish (ref. < median)	≥ median							1.11	[0.79, 1.54]			1.07	[0.77, 1.46]			1.25	[0.88, 1.77]	-	-
Freshwater fish (ref. < median)	≥ median							0.88	[0.66, 1.18]			0.88	[0.66, 1.18]			0.87	[0.65, 1.17]	-	-
Degree of economic development (4)																			
Mean income						1.12	[0.93, 1.34]	1.09	[0.90, 1.32]										
Median income										0.98	[0.63, 1.52]	0.96	[0.62, 1.49]						
Maximum income														1.01	[1.00, 1.02]	1.01	[1.00, 1.03]		
Assets																		1.09	[0.91, 1.32]

Results are presented in the form of odds ratios (OR).

(1) Migration included those who had experience of migratory work in the previous year outside of their own community.

(2) Alcohol consumption was calculated by the frequency, quantity and types of alcohol consumed and dichotomized at the median.

(3) The weekly consumption frequency of selected food items was dichotomized at the median.

(4) The degree of economic development was calculated at the community level by using the responses of household heads in each community.

Table 8 | Variables predicting elevated CRP concentrations (i.e., a CRP concentration of 3 – 10 mg/L) among male participants

		Model 1		Model 2		Model 3		Model 4		Model 5		Model 6		Model 7		Model 8		Model 9	
		OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Socio-demographic variables		(n = 807)		(n = 804)		(n = 804)		(n = 791)		(n = 804)		(n = 791)		(n = 804)		(n = 791)		(n = 804)	
Age		1.02	[1.01, 1.03]	1.02	[1.01, 1.03]	1.02	[1.01, 1.03]	1.02	[1.01, 1.03]	1.02	[1.01, 1.03]	1.02	[1.01, 1.03]	1.02	[1.01, 1.03]	1.02	[1.00, 1.03]	1.02	[1.01, 1.03]
BMI		1.09	[1.02, 1.16]	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Marital status (ref. not married)				0.75	[0.49, 1.17]	0.75	[0.49, 1.17]	0.73	[0.47, 1.13]	0.75	[0.49, 1.17]	0.73	[0.47, 1.13]	0.75	[0.49, 1.17]	0.72	[0.46, 1.12]	0.75	[0.49, 1.17]
Education (ref. < 9 years)	= 9 years			0.59	[0.39, 0.90]	0.60	[0.39, 0.91]	0.60	[0.39, 0.92]	0.59	[0.39, 0.90]	0.59	[0.39, 0.91]	0.57	[0.38, 0.87]	0.58	[0.38, 0.89]	0.59	[0.39, 0.90]
	> 9 years			0.63	[0.31, 1.27]	0.63	[0.31, 1.28]	0.65	[0.32, 1.32]	0.63	[0.31, 1.28]	0.64	[0.31, 1.31]	0.61	[0.30, 1.24]	0.63	[0.31, 1.29]	0.63	[0.31, 1.27]
Migration (1)				1.64	[0.96, 2.80]	1.65	[0.96, 2.81]	1.61	[0.94, 2.76]	1.63	[0.95, 2.78]	1.60	[0.93, 2.74]	1.56	[0.91, 2.68]	1.52	[0.88, 2.63]	1.64	[0.96, 2.80]
Lifestyle variables																			
Smoking (2)								1.13	[0.74, 1.71]			1.13	[0.74, 1.70]			1.14	[0.75, 1.72]		
Alcohol (ref. < median) (3)	≥ median							1.01	[0.66, 1.55]			1.02	[0.68, 1.55]			1.09	[0.71, 1.67]		
Consumption frequency of (4)																			
Pork (ref. < median)	≥ median							0.87	[0.58, 1.31]			0.87	[0.58, 1.32]			0.89	[0.59, 1.35]		
Poultry (ref. < median)	≥ median							1.15	[0.76, 1.76]			1.15	[0.76, 1.73]			1.10	[0.72, 1.66]		
Marine fish (ref. < median)	≥ median							1.07	[0.70, 1.62]			1.07	[0.71, 1.62]			1.16	[0.75, 1.80]		
Freshwater fish (ref. < median)	≥ median							0.80	[0.54, 1.19]			0.80	[0.54, 1.19]			0.80	[0.54, 1.20]		
Degree of economic development (5)																			
Mean income						0.98	[0.77, 1.26]	0.97	[0.74, 1.28]										
Median income										0.89	[0.50, 1.60]	0.93	[0.51, 1.69]						
Maximum income														1.01	[0.99, 1.02]	1.01	[0.99, 1.03]		
Assets																		0.99	[0.76, 1.30]

Results are presented in the form of odds ratios (OR).

(1) Migration included those who had experience of migratory work in the previous year outside of their own community.

(2) Current smoking status (either cigarette smoking or smoking by using a water pipe) was categorized using ‘yes’ or ‘no’ responses.

(3) Alcohol consumption was calculated by the frequency, quantity and types of alcohol consumed and dichotomized at the median.

(4) The weekly consumption frequency of selected food items was dichotomized at the median.

(5) The degree of economic development was calculated at the community level by using the responses of household heads in each community.

Table 9 | Variables predicting elevated CRP concentrations (i.e., a CRP concentration of 3 – 10 mg/L) among female participants

		Model 1		Model 2		Model 3		Model 4		Model 5		Model 6		Model 7		Model 8		Model 9	
		OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Socio-demographic variables		(n = 875)		(n = 849)		(n = 849)		(n = 843)		(n = 849)		(n = 843)		(n = 849)		(n = 843)		(n = 874)	
Age		1.02	[1.01, 1.03]	1.03	[1.01, 1.04]	1.02	[1.01, 1.04]	1.03	[1.01, 1.04]	1.03	[1.01, 1.04]	1.03	[1.01, 1.04]	1.03	[1.01, 1.04]	1.03	[1.01, 1.04]	1.02	[1.01, 1.03]
BMI		1.12	[1.05, 1.19]	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Marital status (ref. not married)				0.87	[0.53, 1.44]	0.83	[0.50, 1.39]	0.81	[0.48, 1.36]	0.87	[0.52, 1.44]	0.85	[0.51, 1.42]	0.83	[0.50, 1.39]	0.79	[0.47, 1.33]	0.79	[0.49, 1.29]
Education (ref. < 9 years)	= 9 years			1.70	[0.99, 2.91]	1.62	[0.94, 2.8]	1.50	[0.86, 2.61]	1.70	[0.99, 2.91]	1.55	[0.90, 2.69]	1.68	[0.98, 2.88]	1.52	[0.88, 2.64]	-	-
	> 9 years			2.10	[0.75, 5.92]	2.10	[0.74, 5.96]	2.03	[0.71, 5.77]	2.11	[0.75, 5.94]	2.01	[0.71, 5.72]	1.99	[0.70, 5.69]	1.87	[0.65, 5.40]	-	-
Migration (1)				2.05	[1.05, 4.01]	1.98	[1.01, 3.87]	1.91	[0.97, 3.80]	2.06	[1.06, 4.02]	1.93	[0.98, 3.82]	1.87	[0.95, 3.69]	1.81	[0.91, 3.62]	-	-
Lifestyle variables																			
Alcohol (ref. < median) (2)	≥ median							0.82	[0.47, 1.43]			0.75	[0.43, 1.30]			0.86	[0.49, 1.51]		
Consumption frequency of (3)																			
Pork (ref. < median)	≥ median							1.19	[0.76, 1.86]			1.19	[0.77, 1.86]			1.25	[0.80, 1.96]		
Poultry (ref. < median)	≥ median							1.71	[1.08, 2.69]			1.80	[1.14, 2.82]			1.73	[1.10, 2.72]		
Marine fish (ref. < median)	≥ median							1.14	[0.71, 1.84]			1.05	[0.66, 1.67]			1.30	[0.78, 2.15]		
Freshwater fish (ref. < median)	≥ median							0.97	[0.63, 1.50]			0.98	[0.63, 1.51]			0.94	[0.61, 1.46]		
Degree of economic development (4)																			
Mean income						1.34	[1.03, 1.76]	1.27	[0.95, 1.70]										
Median income										1.11	[0.58, 2.15]	1.05	[0.55, 2.04]						
Maximum income														1.02	[1.00, 1.03]	1.02	[1.00, 1.04]		
Assets																		1.28	[0.98, 1.68]

Results are presented in the form of odds ratios (OR).

(1) Migration included those who had experience of migratory work in the previous year outside of their own community.

(2) Alcohol consumption was calculated by the frequency, quantity and types of alcohol consumed and dichotomized at the median.

(3) The weekly consumption frequency of selected food items was dichotomized at the median.

(4) The degree of economic development was calculated at the community level by using the responses of household heads in each community.

3.3. Interaction between the degree of community-level economic growth and sex and migration status in relation to CRP concentration

Table 10 shows the results of the logistic regression analysis investigating the association between CRP concentration and the interaction terms between sex and the degree of economic development after adjusting for basic attributes (i.e., age, sex, marital status, educational attainment, experience of migration in the previous year and the degree of community-level economic development). The results in Model 10 indicated that the interaction term between sex and the mean household income of the community was statistically significant (OR = 0.68, 95% CI 0.47 to 0.98, p = 0.036 in Model 10), suggesting that the association between sex and CRP concentration was moderated by the extent of economic development. Figure 10A illustrates this result, by showing that the discrepancy in CRP concentration by sex narrows in the course of economic development and that males and females have the same CRP concentration when household income is around 2700 RMB (the square root scale) in each community. This trend was not observed when modeled with the median household income and maximum household income in Models 11 and 12, respectively. The main effects of migratory work in the previous year (OR = 1.75, 95% CI 1.14 to 2.65, p = 0.009) and the mean household income of the community (OR = 1.34, 95% CI 1.02 to 1.77, p = 0.036) were statistically significant in Model 10. The experience of migratory work in the previous year was also associated with CRP in Models 11 (OR = 1.74, 95% CI 1.14 to 2.66, p = 0.010) and 12 (OR = 1.67, 95% CI 1.09 to 2.56, p = 0.017), while the degree of economic development had a statistically significant result only when it was indexed by maximum income in Model 12 (OR = 1.02, 95% CI 1.01 to 1.04, p = 0.006).

Table 11 shows the result of a logistic regression analysis investigating the association between CRP and the interaction term between the degree of community-level economic development and migration status in the previous year after adjusting for the respondents' basic attributes. The results in Models 13 – 15 indicated that there was no statistically significant interaction between migratory status and the degree of community-level economic development, suggesting that the effect of migration on CRP was not conditioned by the degree of community-level economic development. These results are depicted in Figure 11.

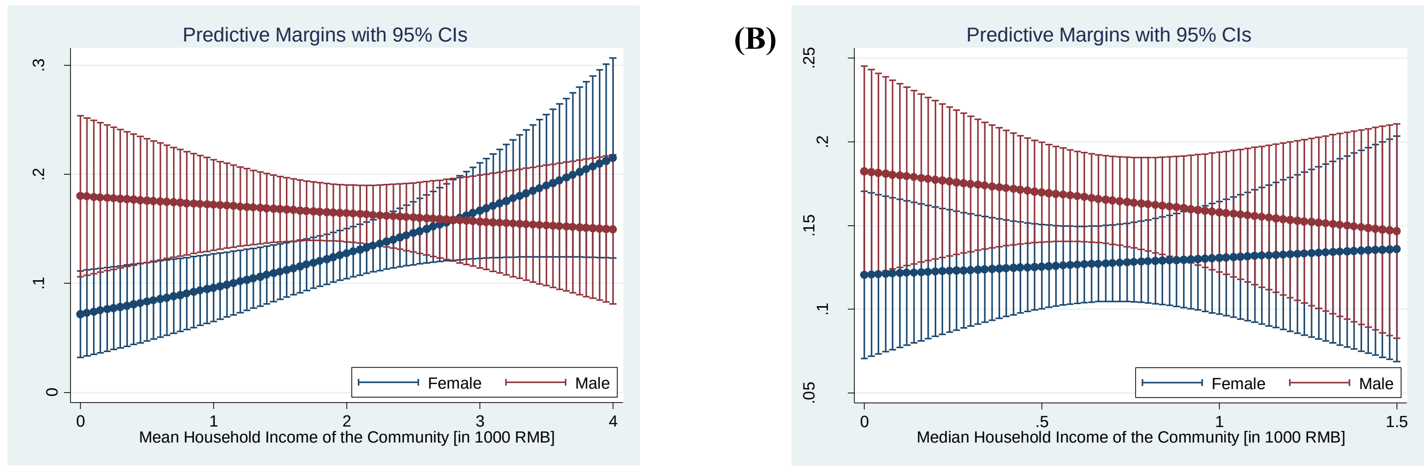
The overall results did not change in the sensitivity analysis (Tables 13 and 14 in Appendix 2).

Table 10 | The association between sex and community-level economic development and CRP concentration

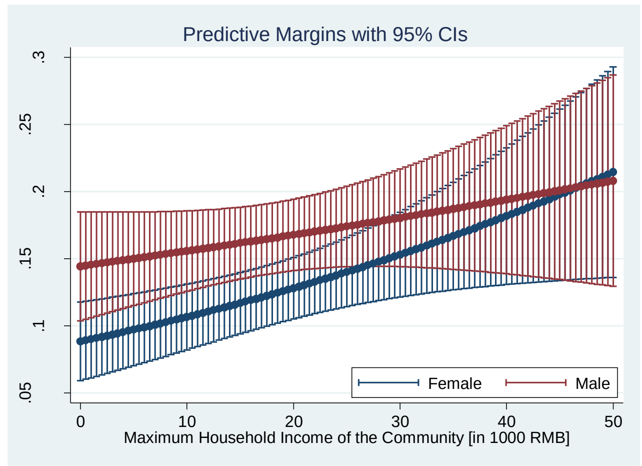
		Model 10		Model 11		Model 12	
		OR	95% CI	OR	95% CI	OR	95% CI
Basic variables		(N = 1653)		(N = 1653)		(N = 1653)	
Age		1.02	[1.01, 1.03]	1.02	[1.01, 1.03]	1.02	[1.01, 1.03]
Sex		2.96	[1.34, 6.54]	1.58	[0.82, 3.03]	1.78	[1.08, 2.95]
Marital status (ref. not married)		0.75	[0.54, 1.03]	0.75	[0.55, 1.04]	0.73	[0.53, 1.01]
Education (ref. < 9 years)	= 9 years	0.86	[0.61, 1.20]	0.85	[0.61, 1.19]	0.84	[0.60, 1.17]
	> 9 years	0.90	[0.50, 1.63]	0.88	[0.49, 1.59]	0.85	[0.47, 1.54]
Lifestyle variables							
Migration [(1)]		1.75	[1.15, 2.67]	1.74	[1.14, 2.66]	1.67	[1.09, 2.56]
Alcohol (ref. < median) [(2)]	≥ median	0.96	[0.69, 1.32]	0.95	[0.69, 1.31]	0.94	[0.68, 1.30]
Consumption frequency of [(3)]							
Pork (ref. < median)	≥ median	1.02	[0.76, 1.37]	1.03	[0.76, 1.38]	1.05	[0.78, 1.42]
Poultry (ref. < median)	≥ median	1.38	[1.01, 1.87]	1.40	[1.04, 1.88]	1.34	[0.99, 1.81]
Marine fish (ref. < median)	≥ median	1.10	[0.79, 1.53]	1.06	[0.77, 1.46]	1.25	[0.88, 1.77]
Freshwater fish (ref. < median)	≥ median	0.88	[0.66, 1.18]	0.88	[0.66, 1.18]	0.87	[0.65, 1.17]
Degree of economic development [(4)]							
Mean income		1.34	[1.02, 1.77]				
Median income				1.09	[0.57, 2.09]		
Maximum income						1.02	[1.01, 1.04]
Sex × Economic development [(5)]		0.68	[0.47, 0.98]	0.80	[0.33, 1.92]	0.99	[0.97, 1.01]

(1) Migration included those who had experience of migratory work in the previous year.
(2) Alcohol consumption was calculated by the frequency, quantity and types of alcohol consumed and dichotomized at the median.
(3) The weekly consumption frequency of selected food items was dichotomized at the median.
(4) The degree of economic development was calculated at the community level by using the responses of household heads in each community.
(5) Economic development in the interaction term refers to the type of economic development incorporated in the model (i.e., mean income (Model 10), median income (Model 11), and maximum income (Model 12).

(A) (B)



(C)



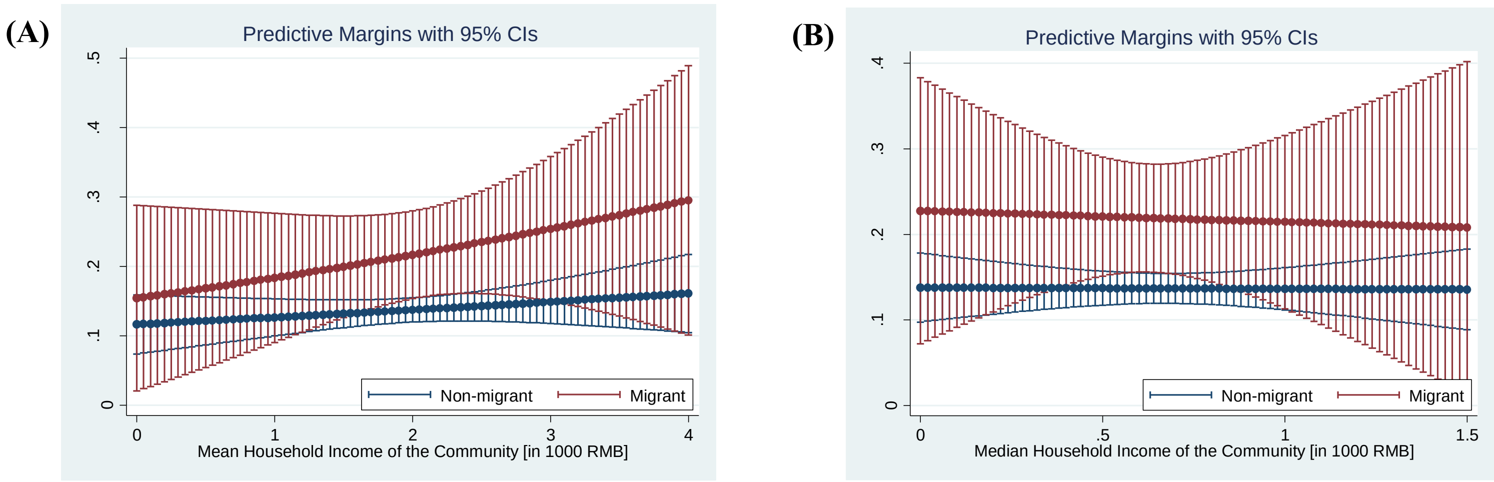
Each bar indicates the probability of a CRP concentration greater than 3 mg/L with 95% confidence intervals for sex and the degree of economic development indexed by the three measures (i.e., mean income (Fig. 10-A), median income (Fig. 10-B), or maximum income (Fig. 10-C)).

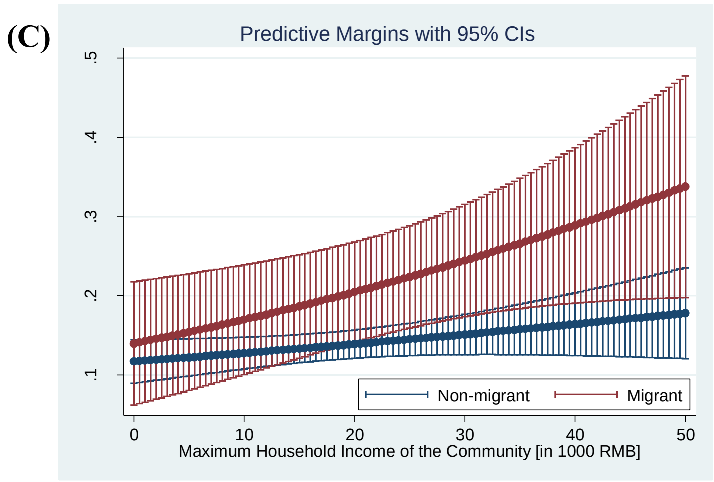
Figure 10 | Probability of a CRP concentration greater than 3 mg/L by the degree of community-level economic development and sex

Table 11 | The association between migratory status and community-level economic development and CRP concentration

		Model 13		Model 14		Model 15	
		OR	95% CI	OR	95% CI	OR	95% CI
Basic variables		(N = 1635)		(N = 1635)		(N = 1635)	
Age		1.02	[1.01, 1.03]	1.02	[1.01, 1.03]	1.02	[1.01, 1.03]
Sex		1.36	[1.02, 1.82]	1.36	[1.02, 1.82]	1.35	[1.01, 1.82]
Marital status (ref. not married)		0.75	[0.54, 1.03]	0.76	[0.55, 1.04]	0.73	[0.53, 1.01]
Education (ref. < 9 years)	= 9 years	0.84	[0.60, 1.18]	0.85	[0.61, 1.19]	0.83	[0.59, 1.16]
	> 9 years	0.87	[0.48, 1.58]	0.88	[0.49, 1.59]	0.85	[0.47, 1.54]
Lifestyle variables							
Migration [1]		1.33	[0.43, 4.16]	1.87	[0.70, 4.97]	1.20	[0.59, 2.48]
Alcohol (ref. < median) [2]	≥ median	0.95	[0.69, 1.32]	0.95	[0.69, 1.31]	0.95	[0.69, 1.31]
Consumption frequency of [3]							
Pork (ref. < median)	≥ median	1.02	[0.76, 1.38]	1.03	[0.76, 1.38]	1.06	[0.78, 1.43]
Poultry (ref. < median)	≥ median	1.35	[1.00, 1.84]	1.40	[1.04, 1.88]	1.31	[0.97, 1.78]
Marine fish (ref. < median)	≥ median	1.11	[0.80, 1.54]	1.07	[0.78, 1.47]	1.25	[0.88, 1.76]
Freshwater fish (ref. < median)	≥ median	0.88	[0.66, 1.18]	0.88	[0.66, 1.18]	0.87	[0.65, 1.17]
Degree of economic development [4]							
Mean income		1.07	[0.87, 1.31]				
Median income				0.97	[0.61, 1.55]		
Maximum income						1.01	[1.00, 1.02]
Migration × Economic development [5]		1.14	[0.69, 1.90]	0.91	[0.23, 3.65]	1.01	[0.99, 1.04]

(1) Migration included those who had experience of migratory work in the previous year.
(2) Alcohol consumption was calculated by the frequency, quantity and types of alcohol consumed and dichotomized at the median.
(3) The weekly consumption frequency of selected food items was dichotomized at the median.
(4) The degree of economic development was calculated at the community level by using the responses of household heads in each community.
(5) Economic development in the interaction term refers to the type of economic development incorporated in the model (i.e., mean income (Model 13), median income (Model 14), and maximum income (Model 15)).





Each bar indicates the probability of a CRP concentration greater than 3 mg/L with 95% confidence intervals for migratory status in the previous year and the degree of economic development indexed by the three measures (i.e., mean income (Fig. 11-A), median income (Fig. 11-B), or maximum income (Fig. 11-C)).

Figure 11 | Probability of a CRP concentration greater than 3 mg/L by the degree of community-level economic development and migratory status in the previous year

Chapter 4 Discussion

4.1. Summary of the study's main findings

The present study found a significant association between CRP concentration, a biomarker of future CVD events, and individual-level lifestyle patterns in rural Hainan Island, China. Specifically, CRP concentration was positively associated with the frequency of poultry consumption and experience of migratory work in the previous year. The extent of community-level economic development, as measured by the maximum household income reported in each community (i.e., a proxy of income inequality in each community), was significantly associated with elevated CRP concentration. When stratified by sex, these associations were more evident among female participants. That is, the frequency of poultry consumption and the extent of community-level economic development, as indexed by the mean and maximum household income reported in each community, was significantly associated with elevated CRP concentration among female participants. Among male participants, those with the equivalent of 9 years of schooling had significantly reduced odds of elevated CRP concentration.

4.2. Current health status of the rural Hainan population

At the time of the survey, those who were overweight (i.e., BMI $\geq$ 25.0) comprised 11.4 % of the subjects in these rural Hainan communities. Although this figure was still lower than the WHO estimates among Chinese representative samples (45.0 % and 32.0 % for males and females, respectively in 2010) (World Health Organization, 2010), efforts should be undertaken in order to avoid any future growth in the level of obesity. Hypertension was highly prevalent among the residents in these rural Hainan communities. Systolic blood pressure $\geq$ 140 mmHg was observed among 25.7 % of the participants and diastolic blood pressure $\geq$ 90 mmHg was observed in 15.5 % of them. These figures are similar to those previously reported among Chinese representative rural samples aged 35 – 74 years old (29.3 % and 26.9 % for males and females, respectively) (Reynolds et al., 2003). The high prevalence of hypertension might, in part, be due to the high sodium intake among residents as sodium intake is one of the biggest contributors in the development of hypertension (MacGregor et al., 1989; Sacks et al., 2001). Although economic development came late to Hainan Island compared to some other parts of the country, it now seems that this province's health problems mirror those in many other parts of the country.

4.3. Comparison with previous studies

4.3.1. Biological factors associated with variations in CRP concentration

Age:

In the present study, CRP concentration was positively associated with age (OR = 1.02, $p < 0.001$) (shown in Model 1 in Table 7). Previous studies also reported similar findings in terms of the association between CRP concentration and age; for example, Hutchinson et al. (2000) studied the concentration of CRP among the general adult population aged 25 to 74 years old in Augsburg, Germany, and Glasgow, Scotland and found that the median concentration of CRP doubled with increasing age from approximately 1 mg/L in the youngest age group (25 – 34 years) to approximately 2 mg/L among the oldest subjects (65 – 74 years), although this age-dependent relationship was only seen among male participants from Glasgow. They suggested that this age-related increase in CRP concentration might have resulted from the increasing prevalence of clinical and subclinical diseases, smoking or obesity among older individuals. Another study which focused on the Inuit population in Nunavik, Canada also showed that age was positively associated with CRP concentration; the ORs for having higher CRP concentration, defined as a CRP concentration of ≥ 2 mg/L, were

1.63 ($p = 0.003$) among those aged 30 – 49 years old and 4.93 ($p < 0.0001$) among those aged 50 years or older, compared to those who were less than 30 years of age (Labonté et al., 2012). Since it is known that age is associated with endothelial dysfunction (Celermajer et al., 1994), which leads to CRP production and that CVD is the leading cause of death among those who are aged 65 years old and above, this finding seems biologically plausible.

However, some exceptions have also been noted. For example, in a remote Aboriginal community in the Northern Territory of Australia, McDonald et al. (2004) examined CRP concentration together with other immunological attributes (e.g., fibrinogen, IgG, IgA and IgM). By categorizing their participants into 6 age groups (< 25; 25 – 34; 35 – 44; 45 – 54; 55 – 64; and ≥ 65), they showed that CRP concentration had a curvilinear trend where its concentration was highest among the 45 – 54-year age group. Friedman and Herd (2010) studied CRP concentration and other inflammatory markers among subjects who participated in the second wave of the Survey of Midlife Development in the United States (MIDUS) and found that age was not associated with CRP concentration, while IL-6, which stimulates CRP production, was positively associated with age ($p < 0.001$). McDade et al. (2011) studied an older population (aged 57 – 85 years old) drawn from the National Social Life, Health and Ageing Project in the USA. Although they found some evidence for an interaction between age, education and household wealth for CRP concentration, age itself was not associated with CRP concentration. One possible reason for the difference between these results and the findings from this study may emanate from differences in the age range of the study subjects; our participants had a much wider age range (15 – 92 years old). Other factors (e.g., such as the mixed race of the participants or the high prevalence of immune-related disease seen in the previous studies) might also help explain this difference.

Sex:

CRP concentration was significantly higher in males than in females in the present study. This contrasts with the results from several previous studies that have reported higher concentrations of CRP among female participants (Ford, 2003; Friedman & Herd, 2010; Geffken et al., 2001; Hutchinson et al., 2000; McDade et al., 2011; McDonald et al., 2004). Specifically, McDade et al. (2011) showed that female sex was positively associated with CRP concentration ($p < 0.05$) and McDonald et al. (2004) demonstrated that in terms of CRP concentration, the OR for males was 0.78 (95% CI 0.63 to 0.96, p

< 0.02). In addition, when using data from the MIDUS study, Friedman and Herd (2010) found that being female was positively associated with CRP concentration ($p < 0.01$) even after adjusting for educational attainment and pre-tax household income.

The association between sex and CRP concentration has also been studied among specific population groups. Geffken et al. (2001) studied CRP concentration in a healthy elderly population and showed that the mean value of CRP was higher in females (2.05 mg/L) than males (1.88 mg/L) ($p < 0.05$). Among the study participants examined by Hutchinson et al. (2000), females had a higher CRP concentration ($p = 0.0067$) in those subjects who were recruited from Augsberg, Germany. Ford (2003) studied children and young adults aged 3 – 19 years old who participated in the NHANES in the United States and showed that geometric mean CRP concentration was similar among male and female participants up until they reached 15 years of age, after which, female participants tended to have a higher concentration.

Given the fact that previous studies have shown that females usually have a higher CRP concentration than males and that this might result from sex-oriented differences in biological characteristics, the finding from the present study that males have a higher concentration of CRP than females might be due to their living environment and/or lifestyles, the details of which will be further discussed later.

BMI:

The positive association between CRP concentration and BMI (Models 1 in Tables 7 – 9) is in accordance with the results reported in most of the previous studies (Friedman & Herd, 2010; Rawson et al., 2003; Verdaet et al., 2004). Overweight and obese persons are at higher risk of elevated CRP concentration, compared to normal-weight persons; Visser et al. (1999) showed that the ORs for higher CRP concentration were 2.13 for obese males and 6.21 for obese females and also found that the WHR, indicative of the amount of abdominal visceral fat, was positively associated with CRP concentration even after adjusting for the effect of BMI. This may be due to the fact that abdominal visceral fat is the place where IL-6, which stimulates CRP production, is usually produced.

4.3.2. Educational attainment, marital status and CRP concentration

This study found that educational attainment was inversely associated with CRP concentration among male participants but positively associated with CRP concentration among female participants. Specifically, those males who finished junior high school (equivalent to 9 years of schooling) had a lower CRP concentration than those who did not (e.g., OR = 0.59, 95% CI 0.39 to 0.90, p = 0.014 in Model 2 in Table 8) while those females who finished junior high school had a higher CRP concentration than those who did not (results not shown; OR = 1.77, 95% CI 1.04 to 3.00, p = 0.036) when adjusting for age and marital status. The null findings among females in the subsequent analyses that adjusted for the lifestyle variables suggest that the association between CRP concentration and educational attainment among females might be explained by the dietary patterns of the residents.

As mentioned in the introductory section, in the early stages of economic development (in low- and middle-income countries) there is a positive association between SES and CVD risk factors (International Clinical Epidemiology Network, 1994) while in developed market economies there is a negative association between these factors (Smith et al., 1997). Given that Hainan Island is still in the initial stage of economic development and considering the context of these rural Hainan communities, those who attained a higher level of education could be expected to have a better living standard and, thus, a higher CRP concentration; however, in terms of risk factors associated with CVD, we witnessed the opposite trend among the male participants. One possible interpretation of this result is that the association between SES and economic development has already reversed among males and those (male participants) who are less educated might be more influenced by obesogenic factors.

A sex-related difference in the direction of the association between different SES indicators and CRP concentration were also reported by Nazmi et al. (2010) who found a positive association between SES and CRP concentration among males but an inverse association among females, which is opposite to what was found in this study. Future research should examine the effect of different individual-level SES indicators on CRP concentration, while paying special attention to dietary patterns in order to better understand the complex mechanisms linking SES and inflammatory/immune function.

In this study, marital status was not associated with CRP concentration. However, married males had lower odds of elevated CRP concentration than unmarried males when adjusting for only age and BMI (results not shown; OR = 0.60, 95% CI 0.38 to 0.94, $p = 0.027$). This is in line with the findings from previous studies that have reported the protective role of marriage on CRP concentration. For example, marriage remained statistically significant even after adjusting for demographic characteristics, subjective and objective health measures, and self-reported psychological distress among 838 males who participated in the National Social Life, Health, and Aging Project (NSHAP) in the U.S. (OR 0.56, 95% CI 0.39 to 0.79) (Sbarra, 2009). The difference between these results and the main non-significant result in this study might result from the difference in the age range of the participants; the effects of marital status might differ across different age ranges and this study had a relatively large age range (15 – 92 years old).

4.3.3. Diet, alcohol consumption, smoking and CRP concentration

Diet:

The consumption frequency of poultry was positively associated with CRP concentration among the study participants (Models 4 and 6 in Table 7 and Models 4, 6 and 8 in Table 9). Poultry was categorized as a “healthy food”, the consumption frequency of which was inversely associated with CRP concentration, in a study conducted by Esmaillzadeh et al. (2007) based on the result of a principal component analysis among Tehrani female teachers aged 40 – 60 years old. In contrast, this study has shown that CRP concentration was higher among those who consumed poultry more frequently. The consumption frequency of the other food items was not associated with higher CRP concentration. This contrasts with the results reported in several previous studies that revealed a positive association between CRP concentration and dietary patterns with a higher red meat intake (Azadbakht & Esmaillzadeh, 2009; Esmaillzadeh et al., 2007) and fish consumption frequency (Ciubotaru et al., 2003; Pischon et al., 2003; Trebble et al., 2003; Zampelas et al., 2005).

There are several factors that may underlie the association between higher CRP and the consumption frequency of poultry; first, there might be a direct causal linkage between CRP production and poultry consumption; for example, if the protein needed for CRP production is supplemented through poultry intake. However, the non-significant results regarding pork consumption and those among male participants make this unlikely. Second, the consumption frequency of poultry might be a surrogate indicator of a higher standard of living, which underpins higher CRP concentration. Studying a Chinese representative sample while using CHNS data, Du et al. (2004) showed that among all animal foods consumed, the difference in income elasticity in terms of the propensity to consume pork and the quantity of pork consumed did not differ between low-income and high-income people in China. On the other hand, people with a low income had a much higher income elasticity in terms of their propensity to consume poultry, beef and mutton. This suggests that the consumption of poultry might mirror individual variation in market exposure, especially among the rural Hainan population, whose income is well below the country average. Third, it is possible that infection due to Campylobacter or Salmonella bacterium might have elevated CRP concentration among those who consumed poultry more frequently. However, no data were available to test this hypothesis.

Smoking:

While smoking has been a strong predictor of higher CRP concentration in previous studies (Dietrich et al., 2007; O'Loughlin et al., 2008; Villegas et al., 2012b; Wannamethee et al., 2005), no association was observed between CRP and smoking in the present study (Models 4, 6 and 8 in Table 8). This finding is consistent with the result from a study by Thompson et al. (2014a) which used the CHNS data set, that is based on a longitudinal study of a representative Chinese population sample. There are several possible factors that may have blurred the difference in inflammatory status between smokers and non-smokers. One possibility is indoor air pollution due to cooking. Some households were still using wooden stoves, which can cause an elevated level of CRP concentration, and which is increasingly being recognized as a serious health concern in developing countries (Fullerton et al., 2008). Another possibility is that non-smokers are being exposed to second-hand smoke at tables where they socialize with others. Second-hand smoke has also been shown to be associated with CRP concentration (Wilkinson et al., 2007).

Alcohol:

Previous studies have suggested that alcohol may be protective against cardiovascular mortality, in part, through an anti-inflammatory mechanism (Albert et al., 2003a; Imhof et al., 2004). Some studies have shown a J-shape relationship between alcohol intake and CRP concentration (Costanzo et al., 2011; Volpato et al., 2004). However, a lack of variation in alcohol consumption levels among the participants in the current study did not enable me to examine whether the association was J-shaped. Furthermore, alcohol consumption dichotomized at the median was not associated with higher CRP concentration among either male or female participants. One of the possible reasons for this null finding, especially among the male participants, was that there were too few people who drank alcohol at an optimal level in terms of alcohol consumption being protective as reflected in CRP concentration. Another possible reason is that the respondents consumed spirits, which, unlike wine or beer, have not been shown previously to have a J-shaped relationship with cardiovascular events (Costanzo et al., 2011). People in Hainan Island, especially the elderly who live inland, overwhelmingly consume home-distilled alcohol beverages made from rice (Inoue et al., 2012; Umezaki, 2004).

4.4. Evaluating community-level economic development in relation to CRP concentration

This study evaluated the degree of community-level economic development by using information which was obtained from household heads who participated in the survey. Specifically, the household head provided information on their total household income and the number of assets the household possessed. The positive relationship between the maximum household income reported from each community and CRP concentration even after adjusting for major lifestyle variables, which have previously been reported as being strong predictors of elevated CRP in relation to CVD risk (Model 8 in Table 7) suggests that maximum income, which is a proxy of income inequality given that the minimum household income reported in every community was zero, elevated CRP concentration of the local residents. This finding is in line with Clark et al. (2012) who revealed an association between state-level income inequality as measured by the Gini coefficient and CRP concentration ($p < 0.01$) among 26,209 healthy U.S. women in the Women's Health Study. And the positive association between income inequality and CRP concentration might be mirroring the findings of many studies in social epidemiology that have revealed an adverse effect of income inequality on health (Kennedy et al., 1996; Kennedy et al., 1998; Kondo et al., 2009; Rodgers, 1979) although this study did not adjust for individual- or household-level income. For example, Kennedy et al. (1998) found that the self-rated health of those people who resided in states with the greatest level of income inequality was lower than that of those people who resided in states with the smallest degree of income inequality, even after adjusting for household-level income.

Knight et al. (2009) recently reported that in rural China dissatisfaction with life is not widespread, despite the relative poverty and low socio-economic status in Chinese society. They suggested that this might be because people in rural China had limited information sets and narrow reference groups, and expected their income to rise in the future, which kept them happy. However, the results from the present study indicate that this situation might already be changing. Specifically, now that people are more mobile and have the opportunity to be exposed to “modern” lifestyles with the differentiation that this is bringing in terms of increasing disparities in wealth, the authors’ assumption might no longer be valid.

In the context of Hainan, rapid economic development has affected individuals within each community unevenly and their subsistence and living standards have become increasingly stratified (Inoue et al., 2012; Jiang et al., 2006). Our earlier fieldwork has revealed that this differentiation in lifestyles was linked to psychological stress and the subjective well-being of the local residents (Inoue et al., 2014; Yazawa et al., 2014). An undesirable difference with his or her reference group (i.e., with those individuals whom a person believes him/herself to be comparable) does damage to the psychological well-being of the individual if he/she fares worse in the comparison (Festinger, 1954). This might be especially true among those who used to be equally impoverished at the time of the People’s Commune, when the means of production and community product were shared equally among community members (Inoue et al., 2012). This psychologically adverse situation might, in part, be linked to elevated CRP concentration due to psychological stress or unhealthy behaviors induced by psychological stress.

CRP concentration was positively associated with the mean household income in each community after adjusting for socio-demographic variables among female participants (Model 3 in Table 9) but the strength of this association was attenuated and it became non-significant when adjusting for the lifestyle variables (Model 4 in Table 9). This suggests that lifestyle factors which have been known to contribute to elevated CRP concentration might become increasingly important in the course of economic development. However, given that most of the lifestyle factors which were included in this study had little effect on CRP concentration, another possibility is that the components of economic development which were not included in the analysis, such as reduced physical activity levels (e.g., increased use of public transportation, private automobiles and increased mechanization in agriculture) and dietary components (such as refined sugar, sodium and carbohydrate) might also be affecting health outcomes. Future research should examine the effects of these variables.

The null findings regarding the association between CRP concentration and the median household income of each community as a proxy of the degree of community-level economic development suggests that if the overall level of wealth rises and it is distributed more evenly, then increasing wealth might not necessarily be detrimental in physiological terms at least after adjusting for socio-demographic variables and individual lifestyle variables. The community-level degree of economic development indexed as the number of household assets, was not significantly associated with CRP concentration which might be partially explained by the fact that the local residents, especially the poor, are subsidized by the government when purchasing some of their assets and so this index might not be a good marker of accumulated wealth in this context.

4.5. *Stratification of the community into population subgroups in relation to elevated CRP concentration*

This study showed that those who had experience of migratory work in the previous year were at a higher risk of having an elevated CRP concentration. This was especially true among the female participants while the association was only marginally significant among the male participants. This suggested that female participants were more likely to be affected by the degree of community-level economic development even though the overall CRP concentrations of females were still lower than those of males.

This sex-related difference in the association between the experience of migratory work and CRP concentration might be due to the differential impact of being migrants by sex in terms of certain cardiovascular risk factors. For example, men already had a chance to consume an “urban” diet (i.e., food items other than those tested in this study) outside of their community (e.g., during social gatherings in towns), irrespective of their engagement in migratory work, while females had less chance to do so; thus, the effect of being a migrant might be more apparent among the female population in this situation. Another possibility is that, among male participants, physical activity levels do not differ much, if at all, between those who engage in migratory work which requires a high level of physical activity (such as working on construction sites) and those who do not. Female participants who undertake migratory work often have jobs that require limited physical activity levels such as working in supermarkets or shops. In turn, this might have resulted in a difference in CRP concentration by migratory status.

From another perspective, it is possible that as regards CRP concentration the effect of community-level economic development might be more apparent among those who were previously more restricted to the community with a relatively small sphere of activities, such as the female participants. While males often had the opportunity to travel to other places (other communities, towns), and were exposed to urban lifestyles through eating and drinking practices even when they were from the least economically developed communities, females were more restricted to the community in which they were born and had relatively few opportunities to be exposed to an urban lifestyle. If women are more susceptible to the effects of community-level economic development, then this finding is in line with that of Vallée et al. (2011) who showed that a sex difference exists in the association between the neighbourhood environment and health. Specifically, they showed that females are more influenced by the place where they live since they spend longer hours in the community.

The variation in CRP concentration was more readily explained at the individual level in this study, in that I did not find a contextual effect when using a multilevel model (results not shown). Specifically, the likelihood ratio test indicated that the regression model in which a single intercept was estimated was not rejected. This finding supports the notion that the variation in socioeconomic status within each community (inter-individual or inter-household variations) is important in terms of determining CRP concentration as a result of heterogeneous exposure to “urban” lifestyles within these rural communities. In turn, this is causing differentiation between the local residents in terms of their potential risk of future CVD events. Since people in rural Hainan still cannot afford to pay high out-of-pocket costs for health services and are more vulnerable to disease in the course of economic development, the population might become increasingly stratified into sub-populations in terms of its health attributes and health disparities would emerge as a consequence.

4.6. How economic development is affecting the health of residents in rural Hainan communities

Economic development is a multifaceted phenomenon that affects all aspects of life both at an individual level (behavioral patterns such as diet, smoking, alcohol consumption and migration) and at a societal level (infrastructure development and social organization), which can impact on the health/physiology of local residents. This study revealed that those who had consumed poultry frequently and those who had experience of migratory work in the previous year potentially have a higher risk for future CVD as indicated by an elevated level of inflammation (i.e., CRP concentration of 3 – 10 mg/L), which was more apparent among female participants. Even after adjusting for socio-demographic and lifestyle variables, the maximum household income reported in each community, a proxy of income inequality, was positively associated with CRP concentration. This suggests that large differentiation in lifestyle as a consequence of exposure to a market economy in rural China has had an undesirable effect among the local residents, especially for those who have fared worse in the course of economic development, and are usually large in number due to the skewed nature of income distribution in these communities.

At the same time, biological traits (age, sex, or health status), marital status, and educational attainment or the experience of migratory work influence the degree to which each individual interacts with and is affected by the economic development that is taking place around them. For example, the stronger findings we observed for females than males may be indicative of the fact that rural males had been exposed to an “urban” lifestyle for a longer period of time, while females may have been more greatly affected by the development of a market economy in recent years. In contrast, the older population had, and still has, less opportunity to migrate to cities for work and also has a lower level of education.

To disentangle the complex effects of economic development as regards its impact on CRP concentration, future studies should examine how mobility brings about changes in lifestyles, and affects people’s life chances both within and outside of their own community.

4.7. Study strengths and limitations

There are several limitations to the study that should be borne in mind when interpreting the results. First, the group that was judged as being at higher risk of future CVD events (i.e., 3 – 10 mg/L of CRP concentration) might have included individuals who had elevated CRP concentrations because of other factors. Furthermore, applying a conversion rate of 1.6 to this population to calculate serum-equivalent CRP concentration might increase error; this population might have another conversion rate or this value might differ by sex. Second, the variables (smoking and the consumption frequency of alcohol and food) were dichotomized. The use of more detailed information (e.g., the number of cigarettes smoked or total energy intake) might have produced different results. I also lacked information about some important food components such as the consumption of sugar, salt and oil. Third, data on physical activity was not included in this study. Although Rawson et al. (2003) showed that physical activity was not associated with CRP after controlling for BMI, other studies have suggested that there is a negative association between physical activity and CRP concentration (Abramson & Vaccarino, 2002; Geffken et al., 2001; Villegas et al., 2012a; Wannamethee et al., 2002). In this study controlling for physical activity might have revealed a different association between migratory work and CRP concentration since males and females usually engage in different occupations with different levels of physical activity. However due to the problem of data availability, I used BMI as a summary measure of energy balance resulting from habitual patterns of physical activity and diet. Fourth, there was no information about the nature of migratory work. It is possible that males and females have very different migratory experiences which affect their well-being. There was no way to determine this from a simple 'yes' or 'no' question; the way migration is conceptualized (e.g., daily activity in the destination or reasons for the return of migrants) needs to be considered. Fifth, community-level economic development was only indexed by the annual household income or assets of each community. There are several other aspects of economic development, such as infrastructural development, type of residence, or types of work available to local residents. Built environment (e.g., walkability and the food environment) is also an important predictor of chronic diseases. Further research should incorporate such indicators to better describe the level of economic development of each community. Sixth, the design of the study was cross-sectional so causal relationships for the associations observed cannot be established. Seventh, this study did not employ a random sampling procedure. I collected data among the ethnic minority communities in Wanning, so those communities were not representative of the whole of the Wanning City reigon.

Despite these limitations, this study contributes to the literature on how economic development affects health. First, this study focused on communities at different stages of economic development and on the mechanisms that were stratifying rural populations into different subgroups with different health attributes. This information helps elucidate how economic development is not a heterogeneous phenomenon but can impact on different parts of a population in different ways. Second, this study was conducted among the rural Chinese population which has been comparatively little studied to date compared with the urban Chinese population despite the fact that it is extremely populous and currently undergoing a nutrition transition. Third, I used CRP concentration which is an important biomarker that has also been little studied in relation to economic development.

Chapter 5 Conclusions

CRP concentration was positively associated with the degree of community-level economic development, indexed as the maximum household income of each community (i.e., a proxy of income inequality), the experience of migratory work in the previous year and the consumption frequency of poultry. These associations were more evident among the female participants, which might be indicative of the fact that the health impact of economic development may be manifested more among female residents. In contrast to the male residents, who had prior opportunities to go outside of their own communities and be exposed to “modern” lifestyles, female residents seemed to have been more isolated from such lifestyles. This conclusion is supported by the fact that the impact of greater mobility as indicated by the experience of migratory work in the previous year was more apparent among females in terms of its contribution to an elevated CRP concentration. This study suggests that economic development within these rural Hainan communities might have stratified people into different sub-populations with different risks of CVD given CRP concentration is a marker of future CVD risk, although local residents within those villages were previously homogenous.

References

Abramson, J.L., & Vaccarino, V. (2002). Relationship between physical activity and inflammation among apparently healthy middle-aged and older US adults. *Archives of Internal Medicine,* 162, 1286-1292.

Albert, M.A., Glynn, R.J., & Ridker, P.M. (2003a). Alcohol consumption and plasma concentration of C-reactive protein. *Circulation,* 107, 443-447.

Albert, M.A., Glynn, R.J., & Ridker, P.M. (2003b). Plasma concentration of C-reactive protein and the calculated Framingham Coronary Heart Disease Risk Score. *Circulation,* 108, 161-165.

Alwan, A. (2011). *Global status report on noncommunicable diseases 2010.* Geneva: World Health Organization.

Azadbakht, L., & Esmaillzadeh, A. (2009). Red Meat Intake Is Associated with Metabolic Syndrome and the Plasma C-Reactive Protein Concentration in Women. *Journal of Nutrition,* 139, 335-339.

Black, S., Kushner, I., & Samols, D. (2004). C-reactive protein. *Journal of Biological Chemistry,* 279, 48487-48490.

Bogin, B. (1988). Rural-to-urban migration. In C. Mascie-Taylor, & G. Lasker (Eds.), *Biological Aspects of Human Migration* pp. 90-129). Cambridge: Cambridge University Press.

Borrell, L.N., Roux, A.V.D., Rose, K., Catellier, D., & Clark, B.L. (2004). Neighbourhood characteristics and mortality in the Atherosclerosis Risk in Communities Study. *International Journal of Epidemiology,* 33, 398-407.

Brindle, E., Fujita, M., Shofer, J., & O'Connor, K.A. (2010). Serum, plasma, and dried blood spot high-sensitivity C-reactive protein enzyme immunoassay for population research. *Journal of Immunological Methods,* 362, 112-120.

Celermajer, D.S., Sorensen, K.E., Spiegelhalter, D.J., Georgakopoulos, D., Robinson, J., & Deanfield, J.E. (1994). Aging is associated with endothelial dysfunction in healthy men years before the age-related decline in women. *Journal of the American College of Cardiology,* 24, 471-476.

Ciubotaru, I., Lee, Y.S., & Wander, R.C. (2003). Dietary fish oil decreases C-reactive protein, interleukin-6, and triacylglycerol to HDL-cholesterol ratio in postmenopausal women on HRT. *Journal of Nutritional Biochemistry,* 14, 513-521.

Clark, C.R., Ridker, P.M., Ommerborn, M.J., Huisingh, C.E., Coull, B., Buring, J.E., et al. (2012). Cardiovascular inflammation in healthy women: multilevel associations with state-level prosperity, productivity and income inequality. *BMC Public Health,* 12, 211.

Cochrane, J., Chen, H., Conigrave, K.M., & Hao, W. (2003). Alcohol use in China. *Alcohol and Alcoholism,* 38, 537-542.

Costanzo, S., Di Castelnuovo, A., Donati, M.B., Iacoviello, L., & de Gaetano, G. (2011). Wine, beer or spirit drinking in relation to fatal and non-fatal cardiovascular events: a meta-analysis. *European Journal of Epidemiology,* 26, 833-850.

de Oliveira Otto, M.C., Mozaffarian, D., Kromhout, D., Bertoni, A.G., Sibley, C.T., Jacobs, D.R., Jr., et al. (2012). Dietary intake of saturated fat by food source and incident cardiovascular disease: the Multi-Ethnic Study of Atherosclerosis. *The American Journal of Clinical Nutrition,* 96, 397-404.

Dietrich, T., Garcia, R.I., de Pablo, P., Schulze, P.C., & Hoffmann, K. (2007). The effects of cigarette smoking on C-reactive protein concentrations in men and women and its modification by exogenous oral hormones in women. *European Journal of Cardiovascular Prevention & Rehabilitation,* 14, 694-700.

Du, S., Mroz, T.A., Zhai, F., & Popkin, B.M. (2004). Rapid income growth adversely affects diet quality in China--particularly for the poor! *Social Science & Medicine,* 59, 1505-1515.

Esmaillzadeh, A., Kimiagar, M., Mehrabi, Y., Azadbakht, L., Hu, F.B., & Willett, W.C. (2007). Dietary patterns and markers of systemic inflammation among Iranian women. *Journal of Nutrition,* 137, 992-998.

Ezzati, M., Vander Hoorn, S., Lawes, C.M., Leach, R., James, W.P.T., Lopez, A.D., et al. (2005). Rethinking the “diseases of affluence” paradigm: global patterns of nutritional risks in relation to economic development. *PLoS Medicine,* 2, e133.

Festinger, L. (1954). A Theory of Social Comparison Processes. *Human Relations,* 7, 117-140.

Ford, E.S. (2003). C-reactive protein concentration and cardiovascular disease risk factors in children - Findings from the National Health and Nutrition Examination Survey 1999-2000. *Circulation,* 108, 1053-1058.

Friedman, E.M., & Herd, P. (2010). Income, education, and inflammation: differential associations in a national probability sample (The MIDUS study). *Psychosomatic Medicine,* 72, 290-300.

Fullerton, D.G., Bruce, N., & Gordon, S.B. (2008). Indoor air pollution from biomass fuel smoke is a major health concern in the developing world. *Transactions of the Royal Society of Tropical Medicine and Hygiene,* 102, 843-851.

Fuster, V., & Kelly, B.B. (2010). *Promoting cardiovascular health in the developing world: a critical challenge to achieve global health*. Washngton: National Academies Press.

Gallo, L.C., Fortmann, A.L., de los Monteros, K.E., Mills, P.J., Barrett-Connor, E., Roesch, S.C., et al. (2012). Individual and neighborhood socioeconomic status and inflammation in Mexican American women: what is the role of obesity? *Psychosomatic Medicine,* 74, 535-542.

Geffken, D.F., Cushman, M., Burke, G.L., Polak, J.F., Sakkinen, P.A., & Tracy, R.P. (2001). Association between physical activity and markers of inflammation in a healthy elderly population. *American Journal of Epidemiology,* 153, 242-250.

Hainan Provincial Bureau of Statistics. (2010). Hainan Statistical Yearbook. Beijing.

Hao, W., Su, Z., Liu, B., Zhang, K., Yang, H., Chen, S., et al. (2004). Drinking and drinking patterns and health status in the general population of five areas of China. *Alcohol and Alcoholism,* 39, 43-52.

He, J., Gu, D.F., Wu, X.G., Reynolds, K., Duan, X.F., Yao, C.H., et al. (2005). Major causes of death among men and women in China. *New England Journal of Medicine,* 353, 1124-1134.

Holmes, L.M., & Marcelli, E.A. (2012). Neighborhoods and systemic inflammation: High CRP among legal and unauthorized Brazilian migrants. *Health & Place,* 18, 683-693.

Hutchinson, W.L., Koenig, W., Frohlich, M., Sund, M., Lowe, G.D.O., & Pepys, M.B. (2000). Immunoradiometric assay of circulating C-reactive protein: age-related values in the adult general population. *Clinical Chemistry,* 46, 934-938.

Imhof, A., Woodward, M., Doering, A., Helbecque, N., Loewel, H., Amouyel, P., et al. (2004). Overall alcohol intake, beer, wine, and systemic markers of inflammation in western Europe: Results from three MONICA samples (Augsburg, Gtasgow, Lille). *European Heart Journal,* 25, 2092-2100.

Inoue, Y., Umezaki, M., & Watanabe, C. (2012). Emergence of income inequality and its impact on subjective quality of life in an ethnic minority community in Hainan Island, China. *Anthropological Science,* 120, 51-60.

Inoue, Y., Yazawa, A., Li, D., Du, J., Jin, Y., Chen, Y., et al. (2014). Epstein - Barr virus antibody titer and its association with the domain scores from the World Health Organization's Quality of Life questionnaire: Findings from Rural Hainan Province, China. *American Journal of Human Biology,* 26, 51-55.

International Clinical Epidemiology Network (1994). Socio-economic status and risk factors for cardiovascular disease: a multicentre collaborative study in the International Clinical Epidemiology Network (INCLEN). The INCLEN Multicentre Collaborative

Group. *Journal of clinical epidemiology,* 47, 1401-1409.

Jellema, A., Plat, J., & Mensink, R.P. (2004). Weight reduction, but not a moderate intake of fish oil, lowers concentrations of inflammatory markers and PAI-1 antigen in obese men during the fasting and postprandial state. *European Journal of Clinical Investigation,* 34, 766-773.

Jenny, N.S., Yanez, N.D., Psaty, B.M., Kuller, L.H., Hirsch, C.H., & Tracy, R.P. (2007). Inflammation biomarkers and near-term death in older men. *American Journal of Epidemiology,* 165, 684-695.

Jiang, H.W., Umezaki, M., & Ohtsuka, R. (2006). Inter-household variation in adoption of cash cropping and its effects on labor and dietary patterns: a study in a Li hamlet in Hainan island, China. *Anthropological Science,* 114, 165-173.

Jones-Smith, J.C., & Popkin, B.M. (2010). Understanding community context and adult health changes in China: Development of an urbanicity scale. *Social Science & Medicine,* 71, 1436-1446.

Kalache, A., & Keller, I. (2004). The WHO global strategy on diet, physical activity and health for older people. *Journal of Aging and Physical Activity,* 12, 248-248.

Kato, H., Tillotson, J., Nichaman, M.Z., Rhoads, G.G., & Hamilton, H.B. (1973). Epidemiologic studies of coronary heart disease and stroke in Japanese men living in Japan, Hawaii and California. *Am J Epidemiol,* 97, 372-385.

Kennedy, B.P., Kawachi, I., Glass, R., & Prothrow-Stith, D. (1998). Income distribution, socioeconomic status, and self rated health in the United States: multilevel analysis. *BMJ: British Medical Journal,* 317, 917-921.

Kennedy, B.P., Kawachi, I., & Prothrow-Stith, D. (1996). Income distribution and mortality: cross sectional ecological study of the Robin Hood index in the United States. *BMJ: British Medical Journal,* 312, 1004-1007.

Knight, J., Song, L.N., & Gunatilaka, R. (2009). Subjective well-being and its determinants in rural China. *China Economic Review,* 20, 635-649.

Koenig, W., Sund, M., Frohlich, M., Fischer, H.G., Lowel, H., Doring, A., et al. (1999). C-Reactive protein, a sensitive marker of inflammation, predicts future risk of coronary heart disease in initially healthy middle-aged men: results from the MONICA (Monitoring Trends and Determinants in Cardiovascular Disease) Augsburg Cohort Study, 1984 to 1992. *Circulation,* 99, 237-242.

Kondo, N., Sembajwe, G., Kawachi, I., van Dam, R.M., Subramanian, S., & Yamagata, Z. (2009). Income inequality, mortality, and self rated health: meta-analysis of multilevel studies. *BMJ: British Medical Journal,* 339.

Kuo, H.K., Bean, J.F., Yen, C.J., & Leveille, S.G. (2006). Linking C-reactive protein to late-life disability in the National Health and Nutrition Examination Survey (NHANES) 1999-2002. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences,* 61, 380-387.

Labonté, M.-E., Dewailly, E., Chateau-Degat, M.-L., Couture, P., & Lamarche, B. (2012). Population-based study of high plasma C-reactive protein concentrations among the Inuit of Nunavik. *International Journal of Circumpolar Health,* 71.

Lu, Y., & Qin, L. (2014). Healthy migrant and salmon bias hypotheses: A study of health and internal migration in China. *Social Science & Medicine,* 102, 41-48.

MacGregor, G., Sagnella, G., Markandu, N., Singer, D., & Cappuccio, F. (1989). Double-blind study of three sodium intakes and long-term effects of sodium restriction in essential hypertension. *The Lancet,* 334, 1244-1247.

Mathers, C.D., & Loncar, D. (2006). Projections of global mortality and burden of disease from 2002 to 2030. *PLoS medicine,* 3, e442.

McBride, P.E. (1992). The health consequences of smoking. Cardiovascular diseases. *The Medical Clinics of North America,* 76, 333-353.

McDade, T.W., Lindau, S.T., & Wroblewski, K. (2011). Predictors of C-Reactive Protein in the National Social Life, Health, and Aging Project. *The Journals of Gerontology. Series B, Psychological Sciences and Social Sciences,* 66, 129-136.

McDonald, S., Maguire, G., Duarte, N., Wang, X.L., & Hoy, W. (2004). C-reactive protein, cardiovascular risk, and renal disease in a remote Australian Aboriginal community. *Clinical Science,* 106, 121-128.

McKeown, T. (1988). *The origins of human disease continued*: Basil Blackwell.

Mendall, M.A., Strachan, D.P., Butland, B.K., Ballam, L., Morris, J., Sweetnam, P.M., et al. (2000). C-reactive protein: relation to total mortality, cardiovascular mortality and cardiovascular risk factors in men. *European Heart Journal,* 21, 1584-1590.

Millwood, I.Y., Li, L., Smith, M., Guo, Y., Yang, L., Bian, Z., et al. (2013). Alcohol consumption in 0.5 million people from 10 diverse regions of China: prevalence, patterns and socio-demographic and health-related correlates. *International journal of epidemiology,* 42, 816-827.

Monda, K.L., Gordon-Larsen, P., Stevens, J., & Popkin, B.M. (2007). China's transition: the effect of rapid urbanization on adult occupational physical activity. *Soc Sci Med,* 64, 858-870.

Monteiro, C.A., Conde, W.L., Lu, B., & Popkin, B.M. (2004). Obesity and inequities in health in the developing world. *International Journal of Obesity,* 28, 1181-1186.

National Bureau of Statistics of China (2013). *China Regional Dataset.* http://www.stats.gov.cn/english/. Accessed on 05/05/2014

Nazmi, A., Oliveira, I.O., Horta, B.L., Gigante, D.P., & Victora, C.G. (2010). Lifecourse socioeconomic trajectories and C-reactive protein levels in young adults: Findings from a Brazilian birth cohort. *Social Science & Medicine,* 70, 1229-1236.

Nazmi, A., & Victora, C.G. (2007). Socioeconomic and racial/ethnic differentials of C-reactive protein levels: a systematic review of population-based studies. *BMC Public Health,* 7, 212.

Ng, S.W., Norton, E.C., & Popkin, B.M. (2009). Why have physical activity levels declined among Chinese adults? Findings from the 1991-2006 China health and nutrition surveys. *Social Science & Medicine,* 68, 1305-1314.

O'Loughlin, J., Lambert, M., Karp, I., McGrath, J., Gray-Donald, K., Barnett, T.A., et al. (2008). Association between cigarette smoking and C-reactive protein in a representative, population-based sample of adolescents. *Nicotine & Tobacco Research,* 10, 525-532.

OECD. (2011). Divided we stand: Why inequality keeps rising. Paris: OECD Publishing.

Omran, A.R. (1971). The epidemiologic transition. A theory of the epidemiology of population change. *The Milbank Memorial Fund Quarterly,* 49, 509-538.

Pearson, T.A., Mensah, G.A., Alexander, R.W., Anderson, J.L., Cannon, R.O., Criqui, M., et al. (2003). Markers of inflammation and cardiovascular disease application to clinical and public health practice: a statement for healthcare professionals from the centers for disease control and prevention and the American Heart Association. *Circulation,* 107, 499-511.

Pischon, T., Hankinson, S.E., Hotamisligil, G.S., Rifai, N., Willett, W.C., & Rimm, E.B. (2003). Habitual dietary intake of n-3 and n-6 fatty acids in relation to inflammatory markers among US men and women. *Circulation,* 108, 155-160.

Popkin, B.M. (2004). The nutrition transition: an overview of world patterns of change. *Nutrition Reviews,* 62, S140-143.

Popkin, B.M., Du, S.F., Zhai, F.Y., & Zhang, B. (2010). Cohort Profile: The China Health and Nutrition Survey-monitoring and understanding socio-economic and health change in China, 1989-2011. *International Journal of Epidemiology,* 39, 1435-1440.

Population Census Office of Hainan Province (2002). *Tabulation on the 2000 population census of Hainan Province*. Beijing: China Statistics Press.

Pradhan, A.D., Manson, J.E., Rifai, N., Buring, J.E., & Ridker, P.M. (2001). C-reactive protein, interleukin 6, and risk of developing type 2 diabetes mellitus. *JAMA,* 286, 327-334.

Rawson, E.S., Freedson, P.S., Osganian, S.K., Matthews, C.E., Reed, G., & Ockene, I.S. (2003). Body mass index, but not physical activity, is associated with C-reactive

protein. *Medicine and Science in Sports and Exercise,* 35, 1160-1166.
Reynolds, K., Gu, D.F., Muntner, P., Wu, X.G., Chen, J., Huang, G.Y., et al. (2003). Geographic variations in the prevalence, awareness, treatment and control of hypertension in China. *Journal of Hypertension,* 21, 1273-1281.
Rhodes, B., Fürnrohr, B.G., & Vyse, T.J. (2011). C-reactive protein in rheumatology: biology and genetics. *Nature Reviews Rheumatology,* 7, 282-289.
Ridker, P.M., Buring, J.E., Cook, N.R., & Rifai, N. (2003). C-reactive protein, the metabolic syndrome, and risk of incident cardiovascular events. *Circulation,* 107, 391-397.
Ridker, P.M., Rifai, N., Rose, L., Buring, J.E., & Cook, N.R. (2002). Comparison of C-reactive protein and low-density lipoprotein cholesterol levels in the prediction of first cardiovascular events. *New England Journal of Medicine,* 347, 1557-1565.
Rodgers, G.B. (1979). Income and inequality as determinants of mortality: an international cross-section analysis. *Population Studies,* 33, 343-351.
Sacks, F.M., Svetkey, L.P., Vollmer, W.M., Appel, L.J., Bray, G.A., Harsha, D., et al. (2001). Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. *New England Journal of Medicine,* 344, 3-10.
Sbarra, D.A. (2009). Marriage protects men from clinically meaningful elevations in C-reactive protein: results from the National Social Life, Health, and Aging Project (NSHAP). *Psychosomatic Medicine,* 71, 828-835.
Sesso, H.D., Wang, L., Buring, J.E., Ridker, P.M., & Gaziano, J.M. (2007). Comparison of interleukin-6 and C-reactive protein for the risk of developing hypertension in women. *Hypertension,* 49, 304-310.
Smith, G.D., Hart, C., Blane, D., Gillis, C., & Hawthorne, V. (1997). Lifetime socioeconomic position and mortality: Prospective observational study. *British Medical Journal,* 314, 547-552.
Thompson, A.L., Houck, K.M., Adair, L., Gordon-Larsen, P., Du, S., Zhang, B., et al. (2014a). Pathogenic and obesogenic factors associated with inflammation in Chinese children, adolescents and adults. *American Journal of Human Biology,* 26, 18-28.
Thompson, A.L., Houck, K.M., Adair, L., Gordon-Larsen, P., & Popkin, B. (2014b). Multilevel examination of the association of urbanization with inflammation in Chinese adults. *Health & Place,* 28, 177-186.
Thorand, B., Lowel, H., Schneider, A., Kolb, H., Meisinger, C., Frohlich, M., et al. (2003). C-reactive protein as a predictor for incident diabetes mellitus among middle-aged men - Results from the MONICA Augsburg Cohort Study, 1984-1998. *Archives of Internal Medicine,* 163, 93-99.
Tian, S., Dong, G.H., Wang, D., Liu, M.M., Lin, Q., Meng, X.J., et al. (2011). Factors

associated with prevalence, awareness, treatment and control of hypertension in urban adults from 33 communities in China: the CHPSNE Study. *Hypertension Research,* 34, 1087-1092.

Trebble, T., Arden, N.K., Stroud, M.A., Wootton, S.A., Burdge, G.C., Miles, E.A., et al. (2003). Inhibition of tumour necrosis factor-alpha and interleukin 6 production by mononuclear cells following dietary fish-oil supplementation in healthy men and response to antioxidant co-supplementation. *British Journal of Nutrition,* 90, 405-412.

Trowell, H.H.C., & Burkitt, D.P. (1981). *Western diseases: their emergence and prevention*: Harvard University Press.

Tuomisto, K., Jousilahti, P., Sundvall, J., Pajunen, P., & Salomaa, V. (2006). C-reactive protein, interleukin-6 and tumor necrosis factor alpha as predictors of incident coronary and cardiovascular events and total mortality - A population-based, prospective study. *Thrombosis and Haemostasis,* 95, 511-518.

Turra, C.M., & Elo, I.T. (2008). The impact of salmon bias on the Hispanic mortality advantage: New evidence from social security data. *Population Research and Policy Review,* 27, 515-530.

Ullmann, S.H., Goldman, N., & Massey, D.S. (2011). Healthier before they migrate, less healthy when they return? The health of returned migrants in Mexico. *Social Science & Medicine,* 73, 421-428.

Umezaki, M. (2004). Alcohol and fieldwork. In T. Shinohara (Ed.), *The Death of Slash-and-Burn Agriculture on Hainan Island, China* pp. 25-50). Tokyo: The University of Tokyo Press.

Vallée, J., Cadot, E., Roustit, C., Parizot, I., & Chauvin, P. (2011). The role of daily mobility in mental health inequalities: the interactive influence of activity space and neighbourhood of residence on depression. *Social Science & Medicine,* 73, 1133-1144.

Verdaet, D., Dendale, P., De Bacquer, D., Delanghe, J., Block, P., & De Backer, G. (2004). Association between leisure time physical activity and markers of chronic inflammation related to coronary heart disease. *Atherosclerosis,* 176, 303-310.

Villegas, R., Xiang, Y.B., Cai, H., Elasy, T., Cai, Q., Zhang, X., et al. (2012a). Lifestyle determinants of C-reactive protein in middle-aged, urban Chinese men. *Nutrition Metabolism and Cardiovascular Diseases,* 22, 223-230.

Villegas, R., Xiang, Y.B., Cai, H., Elasy, T., Cai, Q., Zhang, X., et al. (2012b). Lifestyle determinants of C-reactive protein in middle-aged, urban Chinese men. *Nutr Metab Cardiovasc Dis,* 22, 223-230.

Villegas, R., Xiang, Y.B., Cai, Q., Fazio, S., Linton, M., Li, H., et al. (2010). Prevalence and determinants of hyperuricemia in middle-aged, urban Chinese men. *Metabolic Syndrome and Related Disorders,* 8, 263-270.

Visser, M., Bouter, L.M., McQuillan, G.M., Wener, M.H., & Harris, T.B. (1999). Elevated C-reactive protein levels in overweight and obese adults. *JAMA,* 282, 2131-2135.

Volpato, S., Pahor, M., Ferrucci, L., Simonsick, E.M., Guralnik, J.M., Kritchevsky, S.B., et al. (2004). Relationship of alcohol intake with inflammatory markers and plasminogen activator inhibitor-1 in well-functioning older adults: the Health, Aging, and Body Composition study. *Circulation,* 109, 607-612.

Wannamethee, S.G., Lowe, G.D., Shaper, A.G., Rumley, A., Lennon, L., & Whincup, P.H. (2005). Associations between cigarette smoking, pipe/cigar smoking, and smoking cessation, and haemostatic and inflammatory markers for cardiovascular disease. *European Heart Journal,* 26, 1765-1773.

Wannamethee, S.G., Lowe, G.D.O., Whincup, P.H., Rumley, A., Walker, M., & Lennon, L. (2002). Physical activity and hemostatic and inflammatory variables in elderly men. *Circulation,* 105, 1785-1790.

Wilkinson, J.D., Lee, D.J., & Arheart, K.L. (2007). Secondhand smoke exposure and C-reactive protein levels in youth. *Nicotine & Tobacco Research,* 9, 305-307.

Woetzel, J., Mendonca, L., Devan, J., Negri, S., Hu, Y., Jordan, L., et al. (2009). Preparing for China's urban billion. Shanghai: McKinsey Global Institute.

World Bank Group (2014). *World Development Indicators 2014.* Washington D.C.: World Bank Publications.

World Health Organization. (2008). 2008-2013 action plan for the global strategy for the prevention and control of noncommunicable diseases. Geneva: World Health Organization.

World Health Organization (2010). *WHO Global infobase 2010.* https://apps.who.int/infobase/. Accessed on September 3, 2014

Wu, Y. (2006). Overweight and obesity in China: the once lean giant has a weight problem that is increasing rapidly. *BMJ: British Medical Journal,* 333, 362.

Yang, G., Kong, L., Zhao, W., Wan, X., Zhai, Y., Chen, L.C., et al. (2008). Emergence of chronic non-communicable diseases in China. *The Lancet,* 372, 1697-1705.

Yazawa, A., Inoue, Y., Li, D., Du, J., Jin, Y., Chen, Y., et al. (2014). Impact of lifestyle changes on stress in a modernizing rural population in Hainan Island, China. *American Journal of Human Biology,* 26, 36-42.

Yeh, E.T., & Willerson, J.T. (2003). Coming of Age of C-reactive protein using Inflammation markers in cardiology. *Circulation,* 107, 370-371.

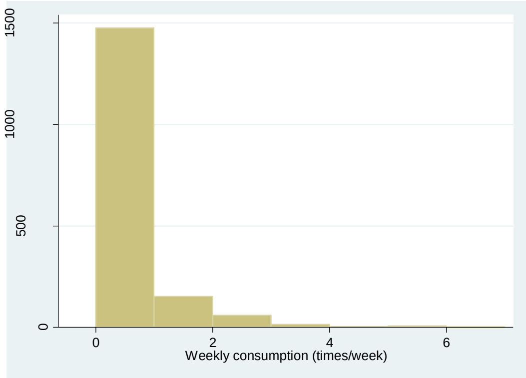
Yusuf, S., Reddy, S., Ôunpuu, S., & Anand, S. (2001a). Global burden of cardiovascular diseases part I: general considerations, the epidemiologic transition, risk factors, and impact of urbanization. *Circulation,* 104, 2746-2753.

Yusuf, S., Reddy, S., Ôunpuu, S., & Anand, S. (2001b). Global burden of cardiovascular diseases Part II: Variations in cardiovascular disease by specific ethnic groups and geographic regions and prevention strategies. *Circulation,* 104, 2855-2864.

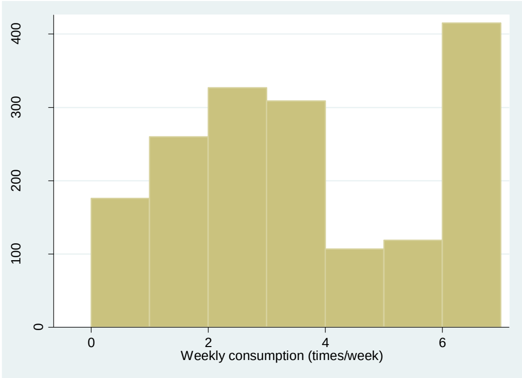
Zampelas, A., Panagiotakos, D.B., Pitsavos, C., Das, U.N., Chrysohoou, C., Skoumas, Y., et al. (2005). Fish consumption among healthy adults is associated with decreased levels of inflammatory markers related to cardiovascular disease - The ATTICA study. *Journal of the American College of Cardiology,* 46, 120-124.

Appendix 1 | Distribution of consumption frequency of major food items (sources of protein)

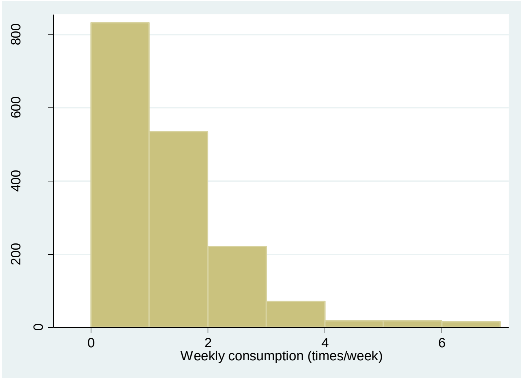
[1] Beef



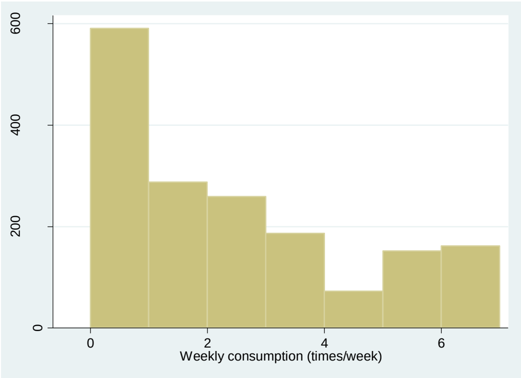
[2] Pork



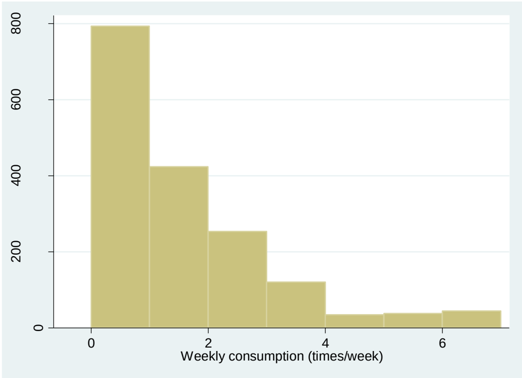
[3] Poultry



[4] Marine fish



[5] Freshwater fish



Appendix 2 | The results of sensitivity analyses

A sensitivity analysis was conducted since previous studies in other populations employed different cut-points and have had different results. It was conducted with (1) a cut-point of 2 mg/L of serum-equivalent CRP concentration and (2) using log-transformed CRP concentration as a continuous dependent variable. Generally speaking, the overall results did not change in the sensitivity analysis. The cut-off of 2 mg/L seemed to be less sensitive in terms of identifying factors associated with elevated CRP concentration.

Table 12 shows the results of the sensitivity analyses on the variables predicting CRP concentrations among the study participants, which were incorporated in Models 4, 6, 8 and 9 in Table 7. Findings regarding age, sex and BMI did not change. The degree of community-level economic development was positively associated with CRP concentration when maximum household income reported was incorporated into models with the two different CRP outcome variables. When CRP concentration was used as a continuous variable, the mean household income of each community was positively associated with CRP concentration (coefficient = 0.035, 95% CI 0.002 to 0.067).

Although some variables were deleted due to the issue of multicollinearity, the sensitivity analysis using 2 mg/L as a cut off revealed that household assets were positively associated with CRP concentration. The experience of migratory work in the previous year remained significantly associated with elevated CRP concentration.

The consumption frequency of poultry was not associated with elevated CRP concentration in some models using 2 mg/L of serum-equivalent concentration as a cut-off in Models 4 and 8. In contrast, the consumption frequency of freshwater fish was inversely associated with elevated CRP concentration in models which used CRP concentration as a continuous variable (Models 4, 6, 8 and 9) and the consumption frequency of marine fish was positively associated with CRP concentration (OR = 1.39, 95% CI 1.04 to 1.87) in Model 8.

A statistically significant interaction was found between sex and economic development (Table 13) when analyzing CRP concentration as a continuous variable. The other variables did not change in these sensitivity analyses. Table 14 shows the results of the association between CRP concentration and the interaction between migration and the degree of community-level economic development. No interaction term was statistically significant. Maximum household income in each community was also positively associated with CRP concentration when it was used as a continuous variable (Model 15 – S: coefficient = 0.004, 95% CI 0.002 to 0.006) and with the cut-off of 2 mg/L (Model 15 – S: coefficient = 1.01, 95% CI 1.00 to 1.02).

Table 12 | Sensitivity analysis using alternative CRP concentration predictors

		Model 4 - S				Model 6 - S				Model 8 - S				Model 9 - S			
		Cut-off: 2 mg/L		Linear Regression		Cut-off: 2 mg/L		Linear Regression		Cut-off: 2 mg/L		Linear Regression		Cut-off: 2 mg/L		Linear Regression	
		OR	95% CI	B	95% CI	OR	95% CI	B	95% CI	OR	95% CI	B	95% CI	OR	95% CI	B	95% CI
Socio-demogrpahic variables		(N = 1635)		(N = 1633)		(N = 1635)		(N = 1633)		(N = 1635)		(N = 1633)		(N = 1681)		(N = 1633)	
Age		1.02	[1.01, 1.03]	0.007	[0.005, 0.008]	1.02	[1.01, 1.03]	0.007	[0.005, 0.009]	1.02	[1.01, 1.03]	0.007	[0.005, 0.008]	1.02	[1.01, 1.02]	0.007	[0.005, 0.009]
Sex (ref. female)		1.35	[1.05, 1.72]	0.100	[0.051, 0.149]	1.34	[1.05, 1.72]	0.100	[0.051, 0.149]	1.34	[1.05, 1.72]	0.099	[0.050, 0.148]	1.41	[1.12, 1.77]	0.101	[0.052, 0.150]
BMI		-	-	0.038	[0.030, 0.047]	-	-	0.038	[0.030, 0.046]	-	-	0.037	[0.029, 0.045]	-	-	0.038	[0.030, 0.046]
Marital status (ref. not married)		0.82	[0.62, 1.09]	-0.055	[-0.113, 0.003]	0.83	[0.63, 1.1]	-0.052	[-0.110, 0.006]	0.81	[0.61, 1.07]	-0.059	[-0.117, -0.002]	0.83	[0.63, 1.09]	-0.053	[-0.111, 0.005]
Education (ref. < 9 years)	= 9 years	1.02	[0.77, 1.35]	-0.034	[-0.090, 0.021]	1.04	[0.78, 1.37]	-0.029	[-0.084, 0.026]	1.01	[0.76, 1.34]	-0.035	[-0.090, 0.020]	-	-	-0.030	[-0.085, 0.026]
	> 9 years	0.99	[0.60, 1.63]	-0.029	[-0.133, 0.075]	1.02	[0.62, 1.67]	-0.022	[-0.126, 0.081]	0.98	[0.59, 1.61]	-0.033	[-0.136, 0.070]	-	-	-0.022	[-0.126, 0.081]
Migration (1)		1.56	[1.08, 2.24]	0.035	[0.002, 0.067]	1.57	[1.09, 2.27]	0.092	[0.017, 0.166]	1.48	[1.03, 2.15]	0.076	[0.001, 0.150]	-	-	0.095	[0.021, 0.170]
Lifestyle variables																	
Alcohol (ref. < median) (2)	≥ median	0.94	[0.72, 1.23]	0.008	[-0.045, 0.062]	0.94	[0.72, 1.23]	0.007	[-0.047, 0.060]	0.93	[0.71, 1.22]	0.006	[-0.048, 0.059]	-	-	0.006	[-0.047, 0.060]
Consumption frequency of (3)																	
Pork (ref. < median)	≥ median	1.03	[0.81, 1.33]	-0.011	[-0.061, 0.040]	1.04	[0.81, 1.33]	-0.009	[-0.059, 0.042]	1.07	[0.83, 1.37]	-0.002	[-0.052, 0.048]	-	-	-0.013	[-0.064, 0.038]
Poultry (ref. < median)	≥ median	1.26	[0.98, 1.63]	0.071	[0.020, 0.122]	1.30	[1.02, 1.68]	0.083	[0.033, 0.133]	1.25	[0.97, 1.60]	0.068	[0.018, 0.118]	-	-	0.079	[0.029, 0.129]
Marine fish (ref. < median)	≥ median	1.27	[0.96, 1.68]	0.003	[-0.052, 0.058]	1.20	[0.92, 1.58]	-0.012	[-0.066, 0.041]	1.39	[1.04, 1.87]	0.029	[-0.028, 0.086]	-	-	-0.017	[-0.071, 0.037]
Freshwater fish (ref. < median)	≥ median	0.85	[0.67, 1.09]	-0.060	[-0.109, -0.011]	0.85	[0.67, 1.09]	-0.060	[-0.109, -0.010]	0.85	[0.66, 1.09]	-0.060	[-0.109, -0.012]	-	-	-0.059	[-0.108, -0.010]
Degree of economic development (4)																	
Mean income		1.12	[0.96, 1.32]	0.035	[0.002, 0.067]												
Median income						1.07	[0.74, 1.55]	-0.005	[-0.079, 0.068]								
Maximum income										1.01	[1.00, 1.02]	0.004	[0.002, 0.006]				
Assets														1.17	[1.00, 1.38]	0.019	[-0.017, 0.054]

(1) Migration included those who had experienced migratory work in the previous year outside of their own community.
(2) Alcohol consumption was calculated by the frequency, quantity and types of alcohol consumed and dichotomized at the median.
(3) The weekly consumption frequency of selected food items was dichotomized at the median.
(4) The degree of economic development was calculated at the community level by using the responses of household heads in each community.

Table 13 | Sensitivity analysis of the interaction term between sex and community-level economic development using alternative CRP concentration predictors

		Model 10 - S				Model 11 - S				Model 12 - S			
		Cut-off: 2 mg/L		Linear Regression		Cut-off: 2 mg/L		Linear Regression		Cut-off: 2 mg/L		Linear Regression	
		OR	95% CI	B	95% CI	OR	95% CI	B	95% CI	OR	95% CI	B	95% CI
Socio-demographic variables		(N = 1635)		(N = 1633)		(N = 1635)		(N = 1633)		(N = 1635)		(N = 1633)	
Age		1.02	[1.01, 1.03]	0.007	[0.005, 0.008]	1.02	[1.01, 1.03]	0.007	[0.005, 0.009]	1.02	[1.01, 1.03]	0.007	[0.005, 0.008]
Sex (ref. female)		2.18	[1.13, 4.20]	0.206	[0.079, 0.334]	1.27	[0.73, 2.19]	0.055	[-0.054, 0.165]	1.73	[1.13, 2.64]	0.167	[0.084, 0.250]
BMI				0.039	[0.031, 0.047]			0.038	[0.030, 0.047]			0.038	[0.030, 0.046]
Marital status (ref. not married)		0.82	[0.62, 1.08]	-0.055	[-0.113, 0.002]	0.83	[0.63, 1.10]	-0.052	[-0.110, 0.006]	0.81	[0.61, 1.07]	-0.060	[-0.117, -0.002]
Education (ref. < 9 years)	= 9 years	1.03	[0.78, 1.36]	-0.031	[-0.087, 0.024]	1.04	[0.78, 1.37]	-0.029	[-0.084, 0.026]	1.02	[0.77, 1.36]	-0.032	[-0.087, 0.023]
	> 9 years	1.02	[0.62, 1.67]	-0.023	[-0.127, 0.081]	1.01	[0.62, 1.67]	-0.023	[-0.127, 0.080]	0.98	[0.60, 1.62]	-0.030	[-0.134, 0.073]
Migration (1)		1.56	[1.08, 2.24]	0.090	[0.015, 0.164]	1.58	[1.09, 2.28]	0.093	[0.018, 0.167]	1.50	[1.04, 2.17]	0.078	[0.004, 0.153]
Lifestyle variables													
Alcohol (ref. < median) (2)	≥ median	0.94	[0.72, 1.24]	0.010	[-0.044, 0.063]	0.94	[0.72, 1.23]	0.007	[-0.047, 0.060]	0.93	[0.71, 1.22]	0.007	[-0.047, 0.060]
Consumption frequency of (3)													
Pork (ref. < median)	≥ median	1.03	[0.80, 1.33]	-0.011	[-0.061, 0.039]	1.04	[0.81, 1.33]	-0.009	[-0.059, 0.041]	1.06	[0.82, 1.37]	-0.003	[-0.053, 0.047]
Poultry (ref. < median)	≥ median	1.27	[0.98, 1.64]	0.073	[0.022, 0.123]	1.30	[1.02, 1.68]	0.083	[0.033, 0.133]	1.26	[0.98, 1.62]	0.070	[0.020, 0.120]
Marine fish (ref. < median)	≥ median	1.27	[0.96, 1.68]	0.002	[-0.053, 0.057]	1.21	[0.92, 1.58]	-0.012	[-0.065, 0.042]	1.39	[1.04, 1.87]	0.029	[-0.028, 0.086]
Freshwater fish (ref. < median)	≥ median	0.85	[0.67, 1.09]	-0.059	[-0.109, -0.010]	0.85	[0.67, 1.09]	-0.060	[-0.109, -0.011]	0.85	[0.66, 1.09]	-0.061	[-0.110, -0.012]
Degree of economic development (4)													
Mean income		1.28	[1.02, 1.61]	0.062	[0.018, 0.107]								
Median income						1.02	[0.59, 1.76]	-0.039	[-0.144, 0.066]				
Maximum income										1.02	[1.01, 1.03]	0.006	[0.003, 0.009]
Sex × Economic development (4)		0.78	[0.58, 1.07]	-0.055	[-0.116, 0.006]	1.09	[0.52, 2.27]	0.066	[-0.080, 0.212]	0.99	[0.97, 1.00]	-0.004	[-0.008, 0.000]

(1) Migration included those who had experienced migratory work in the previous year outside of their own community.
(2) Alcohol consumption was calculated by the frequency, quantity and types of alcohol consumed and dichotomized at the median.
(3) The weekly consumption frequency of selected food items was dichotomized at the median.
(4) The degree of economic development was calculated at the community level by using the responses of household heads in each community.

Table 14 | Sensitivity analysis of the interaction term between migration experience and community-level economic development using alternative CRP concentration predictors

		Model 13 - S				Model 14 - S				Model 15 - S			
		Cut-off: 2 mg/L		Linear Regression		Cut-off: 2 mg/L		Linear Regression		Cut-off: 2 mg/L		Linear Regression	
		OR	95% CI	B	95% CI	OR	95% CI	B	95% CI	OR	95% CI	B	95% CI
Socio-demogrpahic variables		(N = 1635)		(N = 1633)		(N = 1635)		(N = 1633)		(N = 1635)		(N = 1633)	
Age		1.02	[1.01, 1.03]	0.007	[0.005, 0.008]	1.02	[1.01, 1.03]	0.007	[0.005, 0.009]	1.02	[1.01, 1.03]	0.007	[0.005, 0.008]
Sex (ref. female)		1.34	[1.05, 1.72]	0.099	[0.051, 0.148]	1.34	[1.05, 1.71]	0.101	[0.052, 0.150]	1.34	[1.05, 1.72]	0.099	[0.050, 0.148]
BMI		-	-	0.038	[0.030, 0.046]	-	-	0.038	[0.030, 0.047]	-	-	0.037	[0.029, 0.045]
Marital status (ref. not married)		0.82	[0.62, 1.08]	-0.056	[-0.114, 0.002]	0.83	[0.63, 1.10]	-0.052	[-0.110, 0.006]	0.81	[0.61, 1.07]	-0.060	[-0.117, -0.002]
Education (ref. < 9 years)	= 9 years	1.02	[0.77, 1.35]	-0.035	[-0.090, 0.021]	1.04	[0.78, 1.37]	-0.028	[-0.083, 0.027]	1.01	[0.76, 1.34]	-0.035	[-0.090, 0.020]
	> 9 years	1.00	[0.61, 1.65]	-0.026	[-0.129, 0.078]	1.01	[0.61, 1.66]	-0.020	[-0.124, 0.083]	0.98	[0.59, 1.61]	-0.032	[-0.136, 0.071]
Migration [1]		1.06	[0.39, 2.87]	-0.065	[-0.262, 0.131]	2.02	[0.85, 4.78]	-0.019	[-0.200, 0.161]	1.37	[0.74, 2.52]	0.054	[-0.068, 0.175]
Lifestyle variables													
Alcohol (ref. < median) [2]	≥ median	0.94	[0.72, 1.24]	0.010	[-0.043, 0.064]	0.94	[0.72, 1.23]	0.006	[-0.048, 0.059]	0.93	[0.71, 1.22]	0.006	[-0.047, 0.059]
Consumption frequency of [3]													
Pork (ref. < median)	≥ median	1.04	[0.81, 1.33]	-0.010	[-0.060, 0.040]	1.04	[0.81, 1.34]	-0.010	[-0.06, 0.040]	1.07	[0.83, 1.37]	-0.001	[-0.051, 0.049]
Poultry (ref. < median)	≥ median	1.26	[0.97, 1.62]	0.070	[0.019, 0.121]	1.30	[1.01, 1.67]	0.083	[0.033, 0.133]	1.24	[0.97, 1.60]	0.067	[0.017, 0.117]
Marine fish (ref. < median)	≥ median	1.28	[0.96, 1.69]	0.004	[-0.051, 0.060]	1.21	[0.92, 1.58]	-0.013	[-0.067, 0.040]	1.39	[1.04, 1.87]	0.029	[-0.028, 0.086]
Freshwater fish (ref. < median)	≥ median	0.85	[0.67, 1.09]	-0.060	[-0.110, -0.011]	0.85	[0.67, 1.09]	-0.059	[-0.109, -0.010]	0.85	[0.66, 1.09]	-0.061	[-0.110, -0.012]
Degree of economic development [4]													
Mean income		1.10	[0.92, 1.30]	0.025	[-0.009, 0.059]								
Median income						1.11	[0.76, 1.64]	-0.021	[-0.098, 0.056]				
Maximum income										1.01	[1.00, 1.02]	0.004	[0.002, 0.006]
Migration × Economic development		1.21	[0.77, 1.88]	0.077	[-0.013, 0.168]	0.68	[0.20, 2.32]	0.173	[-0.084, 0.429]	1.00	[0.98, 1.03]	0.001	[-0.004, 0.006]

(1) Migration included those who had experienced migratory work in the previous year outside of their own community.
(2) Alcohol consumption was calculated by the frequency, quantity and types of alcohol consumed and dichotomized at the median.
(3) The weekly consumption frequency of selected food items was dichotomized at the median.
(4) The degree of economic development was calculated at the community level by using the responses of household heads in each community.

Appendix 3

中日合作研究项目

关于“中国海南省经济发展与农村居民健康转变的关系”的研究

中国海南省疾病预防控制中心
日本东京大学大学院医学系研究科

ID：________________________________

调查参加者：________________________________

小组：________________________________

电话号码：________________________________

调查人姓名：________________________________

调查日期：________ 年 ____ 月 ____ 日

使用的语言：普通话、海南话、黎话、苗话、其他（______）

第一部 – 第四部	第五部 – 第六部	第七部

第一部：基本信息（所有成人）

1. 身高 ____________ cm

2. 体重 ____________ kg

3. 血压 1st: ____________ / ____________
2nd: ____________ / ____________

4. 性别 ________
   1：男　　2：女

5. 民族 ________
   1：汉族　　2：黎族　　3：苗族
   4：回族　　5：其他

6. 生日（尽可能用阳历记录） ________ 年 ____ 月 ____ 日
6.1. 年龄(如果不知道生日，请填写大概的年龄) ____________ 岁

7. 婚姻情况 ____________
   1：未婚　　2：已婚　　3：离异/分居
   4：丧偶　　5：同居

8. 您的出生地 ____________
   1：本社区
   2：非本社区（出生地名：　　　　　　　　）

a：海口	b：文昌	c：五指山	d：琼海
e：儋州	f：万宁	g：东方	h：澄迈
j：定安	k：屯昌	m：临高	n：白沙
p：昌江	r：乐东	s：陵水	t：保亭
w：琼中	x：三亚	y：大陆	

9. 您是什么户口？ ________
   1：城镇　　2：农村

10. 文化程度 ________
   1：小学没毕业　　2：小学毕业　　3：初中及同等学历
   4：高中及同等学历　　5：大专及以上

11. 职业 ________

1：高级专业技术工作者(医生、教授、律师、建筑师、工程师等)
2：一般专业技术工作者(助产士、护士、教师、编辑、摄影师等)
3：管理者/行政官员/经理(厂长、政府官员、处长、司局长、行政干部及村干部等)
4：办公室一般工作人员(秘书、办事员)
5：农民、渔民、猎人
6：技术工人或熟练工人(工段长、班组长、工艺工人等)
7：非技术工人或熟练工人（普通工人、伐木工等）
8：军官与警官
9：士兵与警察
10：司机
11：服务行业人员(管家、厨师、服务员、看门人、理发员、售货员、洗衣工、保育员等)
12：运动员、演员、演奏员
13：学生
14：退休
15：待业/失业
16：其它（具体说明：________________________）
17：不知道

12. 你在此工作中是什么地位？ ________

1：有雇工的个体经营者
2：无雇工的个体经营者（包括农民）
3：为他人或单位工作的长期工(包括各级企、事业，大、中小集体企业，集体农场，私人企业）
4：为他人或单位工作(合同工)
5：临时工
6：领取工资的家庭工人
7：有报酬的家庭帮工
8：其它(具体说明:____________________)
9：不知道

13. 每周工作几天？ □天/周 ________ 天

14. 平均每天工作几小时？ □□小时/天 ________ 小时

（以下两题农民不需回答）

15. 不包括奖金和其他补助，一般每月工资有多少钱？ □□□□□元/月

16. 平均每月奖金及补贴多少钱？ □□□□元/月

第二部：个人经济情况（所有成人）

17. 过去 1 年的打工的情况 ________

0：不打　　　　　　1：打

18. 打工详细的信息

18.1.	第一次	____ 个月	地方：____	工作：____	工资：________	元/月
18.2.	第二次	____ 个月	地方：____	工作：____	工资：________	元/月
18.3.	第三次	____ 个月	地方：____	工作：____	工资：________	元/月
18.4.	第四次	____ 个月	地方：____	工作：____	工资：________	元/月
18.5.	一共多少个月	____ 个月				

地方

a：海口	b：文昌	c：五指山	d：琼海	e：儋州
f：万宁	g：东方	h：澄迈	j：定安	k：屯昌
m：临高	n：白沙	p：昌江	r：乐东	s：陵水
t：保亭	v：琼中	w：三亚	x：广东	y：大陆（填写具体省份）
z：国外（填写具体国家地名）				

工作类型

a：工厂　　b：建设（高层、水库、桥）　　c：其他建设（道路）
d：矿业　　e：农业　　f：林业　　g：厨师
h：司机　　j：酒店服务员　　k：商店
m：餐厅服务员　　n：保安　　p：其他服务

19. 上次您什么时候回来的？ ______ 前

20. 您回家的时候把工资给家人还是自己消费？ ________

1：全部自己消费
2：四分之一给家人，其他自己消费
3：一半给家人，一半自己消费
4：四分之三给家人，四分之一自己消费
5：全部给家人

21. 您回家的时候给家人买的礼物每年平均多少钱？ ____________ 元/年

22. 您对打工的收入满意吗？ ________

0：不满意　　　　　1：满意

23. 如果不考虑收入，您喜欢打工的生活吗？ ________

0：不喜欢　　　　1：喜欢

24.

24.1.　您打工的动机是因为您自己需要用钱吗？ ________

1：非常不同意　　2：有点不同意　　3：无所谓

4：有点同意　　5：非常同意

24.2.　您打工的动机是因为您要帮助家里减轻经济负担吗？ ________

1：非常不同意　　2：有点不同意　　3：无所谓

4：有点同意　　5：非常同意

24.3.　您打工的动机是因为您喜欢城市那边的生活吗？ ________

1：非常不同意　　2：有点不同意　　3：无所谓

4：有点同意　　5：非常同意

24.4.　您打工的动机是因为您不喜欢本地的生活吗? ________

1：非常不同意　　2：有点不同意　　3：无所谓

4：有点同意　　5：非常同意

25. 现在您是不是打算去外面打工？

0：不是

1：是（地方：__________ 从 a-z 中选择）

第三部：生活情况（所有成人）

26. 每天吃几顿饭？ ________顿/天

27. 每周吃几天肉？（请填写天数）

a：猪肉 ________天/周

b：牛肉 ________天/周

c：动物血（猪血、鸡血等） ________天/周

d：鸡肉、鸭肉、鹅肉 ________天/周

e：鸡蛋、鸭蛋 ________天/周

f：海鱼 ________天/周

g：河鱼 ________天/周

28. 每次吃猪肉/牛肉的类型 ________

1：大部分瘦肉　　2：一半瘦肉一半肥肉　　3：大部分肥肉

29. 每周吃几次方便面？ ________

30. 您用烟筒抽烟吗？ ________

1：从没用过

2：以前用过，现在不用了

3：现在使用烟筒抽烟（每月抽多少斤 □.□□斤）　　抽烟筒：________

31. 您抽过烟吗？ ________

1：从没抽过

2：抽过，但是现在（过去的一年）不抽

3：现在抽烟（每天抽多少支 □□□支）　　抽烟：________

32. 您抽的香烟一包多少钱？ □□□元/包

33. 您喝酒的频率： ________

0：不喝　　1：每天 2，3 顿　　2：每天 1 顿

4：每周 1-2 次　　5：每周 3-4 次　　6：每月 2-3 次

34. 您一般喝什么酒？

1：啤酒	平均每周/每月喝	□□瓶	（每周/每月）________瓶
2：葡萄酒	平均每周/每月喝	□□两	（每周/每月）________两
3：白酒	平均每周/每月喝	□□两	（每周/每月）________两
4：米酒	平均每周/每月喝	□□两	（每周/每月）________两

35. 您喝软饮料和含糖果汁饮料的频率： ________

0：不喝　　1：每天喝　　2：每周 1-2 次

3：每周 3-4 次　　4：　每月 2-3 次

36. 您平时上网吗？ ________

0：不上　　1：上

37. 您在哪里上网较多？ ________

1：网吧　　2：自己家　　3：朋友或亲戚家　　4：学校或单位

38. 如果您在网吧上网，每周花多少钱？ □□□元/周

39. 手机费（要求：调查人打电话查询）

上个月花多少钱？ □□□元/月

上月手机费免费短信查询号码
中国移动：125901863　中国联通：101561710　中国电信：118321103

第四部：健康情况（所有成人）

40. 您是否享有医疗保险？ ________

1：城镇职工基本医疗保险　　2：公费医疗　　3：城镇居民医疗保险

4：新农合　　5：其它社会医疗保险　　6：商业医疗保险

7：未参加任何医疗保险

41. 过去的四周中，您是否有下列症状（包括今天）？

a.	发烧、咽喉痛、咳嗽	0：无	1：不严重	2：一般	3：相当重
b.	腹泻、胃痛	0：无	1：不严重	2：一般	3：相当重
c.	头痛、眩晕	0：无	1：不严重	2：一般	3：相当重
d.	关节、肌肉酸痛	0：无	1：不严重	2：一般	3：相当重
e.	皮疹、皮炎	0：无	1：不严重	2：一般	3：相当重
f.	眼、耳疾病	0：无	1：不严重	2：一般	3：相当重
g.	心脏病、心口痛	0：无	1：不严重	2：一般	3：相当重
h.	其他疾病				注明:________________

42. 有没有得过大脖子病？ ________

0：没有（跳到第六部）

1：有

43. 如果得过大脖子病，是什么时候得的？ ________

□□□□年

大概□□岁的时候

☆请您用答题卡填写答案☆

第五部：WHOQOL-BREF（所有成人）

44. [1] 您如何评价您得生活质量？

1：很差　2：差　3：一般　4：好　5：很好

45. [2] 您对自己健康状况满意吗？

1：非常不满意　2：不满意　3：一般　4：满意　5：很满意

46. [3] 您因躯体疼痛而妨碍您去做需要做的事感到有多烦恼？

1：极其　2：很大　3：中等　4：有点　5：根本没有

47. [4] 您对保持日常生活的医学治疗的需求程度有多大？

1：极其　2：很大　3：中等　4：有点　5：根本没有

48. [5] 您觉得生活有乐趣吗？

1：根本没有　2：有点　3：中等　4：很大　5：极其

49. [6] 您觉得自己的生活有意义吗？

1：根本没有　2：有点　3：中等　4：很大　5：极其

50. [7] 您能集中注意力吗?

1：根本不　2：有点　3：中等　4：很大　5：极其

51. [8] 日常生活中您感觉安全吗？

1：根本不　2：有点　3：中等　4：很大　5：极其

52. [9] 您的生活环境对健康好吗？

1：根本不　2：有点　3：中等　4：很大　5：极其

53. [10] 您有充沛的精力去应付日常生活吗？

1：根本没有　2：有点　3：中等　4：多数有　5：完全有

54. [11] 您认为自己的外形过得去吗？

1：根本没有　2：有点　3：中等　4：多数有　5：完全有

55. [12] 您有足够的钱来满足您的需要吗?

1：根本没有　2：有点　3：中等　4：多数能　5：完全能

56. [13] 在日常生活中，您需要的信息都能得到吗？

1：根本没有　2：有点　3：中等　4：多数能　5：完全能

57. [14] 您有机会进行休闲活动吗？

1：根本没有　2：有点　3：中等　4：多数有　5：完全有

58. [15] 您行动的能力如何?

1：很差　2：差　3：一般　4：好　5：很好

59. [16] 您对自己的睡眠情况满意吗?

1：非常不满意　2：不满意　3：一般　4：满意　5：很满意

60. [17] 您对自己做日常生活事情的能力满意吗？

1：非常不满意　2：不满意　3：一般　4：满意　5：很满意

61. [18] 您对自己的工作能力满意吗?

1：非常不满意　2：不满意　3：一般　4：满意　5：很满意

62. [19] 您对自己满意吗?

1：非常不满意　2：不满意　3：一般　4：满意　5：很满意

63. [20] 您对自己的人际关系满意吗?

1：非常不满意　2：不满意　3：一般　4：满意　5：很满意

64. [21] 您对自己的性生活满意吗？

1：非常不满意　2：不满意　3：一般　4：满意　5：很满意

65. [22] 您对自己从朋友那里得到的支持满意吗?

1：非常不满意　2：不满意　3：一般　4：满意　5：很满意

66. [23] 您对自己居住地的条件满意吗?

1：非常不满意　2：不满意　3：一般　4：满意　5：很满意

67. [24] 您对您能享受到的卫生保健服务满意吗?

1：非常不满意　2：不满意　3：一般　4：满意　5：很满意

68. [25] 您对自己的交通情况满意吗?

1：非常不满意　2：不满意　3：一般　4：满意　5：很满意

69.［26］您有消极感受吗？如情绪低落、绝望、焦虑、忧郁

1：总是　2：经常　3：有时　4：很少　5：从不

第六部：其他（所有成人）

70.［27］与您的邻居相比，您觉得自己的生活怎么样？

1：很差　2：差　3：一般　4：好　5：很好

71.［28］与您的其他家人相比，您觉得自己的生活怎么样？

1：很差　2：差　3：一般　4：好　5：很好

72.［29］与您的邻居相比，您觉得自己的收入情况怎么样？

1：很差　2：差　3：一般　4：好　5：很好

73.［30］与您的其他家人相比，您觉得自己的收入情况怎么样？

1：很差　2：差　3：一般　4：好　5：很好

74.［31］您的生活 10 年前怎么样？

1：很差　2：差　3：一般　4：好　5：很好

75.［32］您的生活比较 10 年前改善了吗？

1：改善大　2：有点儿改善　3：没变化

4：变得一点儿差　5：变得非常差

76.［33］您觉得海南省国际旅游岛建设影响您的日常生产生活吗？

1：好的影响大　2：有一点好的影响　3：没有影响

4：有一点坏的影响　5：坏的影响大

☆ 请您用答案纸填写答案☆

第七部：家庭情况（户主）

77. 您是户主吗？ ________

0：否　　1：是

78. 您户口本里一共有多少人？　□□个人 ________

a. 现在多少个人住在您家　□□个人 ________

b. 外面打工/工作　□□个人 ________

c. 外面上学　□□个人 ________

d. 从军　□□个人 ________

e. 其他　□□个人 ________

79. 户口的经济来源

a：正规职业（不包括退休金）　□□□□□元/月 ________

b：退休金　□□□□□元/月 ________

c：农业（在外面卖的水稻）　□□□□□元/年 ________

d：农业（其他经济作物）　□□□□□元/年 ________

e：农业（家畜）　□□□□□元/年 ________

f：渔业　□□□□□元/年 ________

g：家人打工　□□□□□元/年 ________

80. 家里有经营家庭小手工业和小型家庭商业吗？如果家里有经营，那么一个月收入多少钱？

1：木工	0：没有	1：有	________ 元/月
2：鞋匠	0：没有	1：有	________ 元/月
3：保姆	0：没有	1：有	________ 元/月
4：裁缝	0：没有	1：有	________ 元/月
5：理发	0：没有	1：有	________ 元/月
6：电器修理	0：没有	1：有	________ 元/月
7：饭店	0：没有	1：有	________ 元/月
8：商店	0：没有	1：有	________ 元/月
9：家庭托儿所	0：没有	1：有	________ 元/月
10：家庭旅馆	0：没有	1：有	________ 元/月
11：家庭诊所	0：没有	1：有	________ 元/月
12：其他	0：没有	1：有	________ 元/月

81. 您家是否被列为本地的低保户或贫困户？ ________

0：否　　1：是

82. 您家承包的土地多少亩　　□□.□□亩　　________

83. 其中承包的水田多少亩　　□□.□□亩　　________

84. 其中承包的旱田多少亩　　□□.□□亩　　________

85. 今年使用的水田多少亩　　□□.□□亩　　________

86. 今年使用的旱田多少亩　　□□.□□亩　　________

87. 您家里有没有出售以下经济作物（可多选）：

1：芒果　2：槟榔　3：椰子　4：龙眼　5：香蕉
6：橡胶　7：菠萝　8：西瓜　9：益智　10：茶叶
11：荔枝　12：其他 ________

88. 是否从事以下活动：

a：抓鱼	0：否	1：是	________
b：打猎	0：否	1：是	________
[具体的名字：老鼠、松鼠、山猫、其他（　　　　　）]			
c：采集野生植物（山里）	0：否	1：是	________
d：采集野生植物（水田）	0：否	1：是	________
e：采集野生植物（其他）	0：否	1：是	________

89. 现代化生产生活方式的情况

1：耕地机	0：无	1：有	________
2：彩色电视	0：无	1：有	________
3：VCD	0：无	1：有	________
4：手机	0：无	一共多少	________
5：电脑	0：无	1：有	________
6：网络	0：无	1：有	________
7：电饭煲	0：无	1：有	________
8：摩托车/电动车	0：无	1：有	________
9：车/拖拉机	0：无	1：有	________
10：冰箱	0：无	1：有	________
11：空调	0：无	1：有	________
12：洗衣机	0：无	1：有	________
13：微波炉	0：无	1：有	________

90. 您家主要的建筑是什么样的建筑？ ________

1：草房　2：瓦房　3：平房　4：二层以上自建楼房　5：商品房

91. 该建筑是什么时候开始使用的？　□□□□年　__________ 年

92. 每月房租多少钱？　□□□□元/月　________ 元/月

93. 您们家的建筑属于扶贫吗？ ________

0：否　1：是

94. 吃水要交费吗？ ________

0：否　1：是

95. 您家的饮用水是通过什么方法来的？ ________

1：室内自来水
2：院内自来水
3：院内井水
4：周围的湖、河、泉等等

96. 是什么水源？ ________

1：井水　2：泉水　3：小溪
4：河水　5：湖泊　6：水厂

97. 您家的厕所是什么类型的？ ________

0：没有　1：室内冲水　2：室内马桶（无冲水）
3：室外冲水公厕　4：室外非冲水公厕　5：开放式水泥坑
6：开放式土坑　7：其他

98. 您家做饭通常用什么燃料？（最主要的） ________

1：木柴、柴草　2：木炭　3：煤　4：煤气（罐）
5：煤气（管道）　6：煤油　7：电　8：沼气　9：其他________

99. 使用碘盐吗？ ________

1：每次使用　2：有时使用碘盐　3：以前使用
4：没有使用过　5：没听说过