Urbanization and internal migration as risk factors for non-communicable diseases in Thailand

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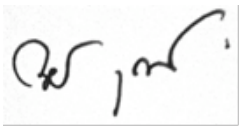
Declaration

I, Chaisiri Angkurawaranon, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

I acknowledge the use of a third party to edit and proof read the thesis. I confirm that the editing and proof reading has not introduced changes to the intellectual content and substance of the thesis.

Date: 12 April 2015

Signed: 

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To my Mom, Dad and sister—I wouldn't be where I am today without your love and support. Finally, Nook, your constant love, care, patience and encouragement were vital in the completion of the PhD.

Preface

This thesis is represented as a 'research paper' style thesis, which allows for work that has been published or prepared for publication to be included in the thesis. As each manuscript was prepared in a stand-alone format, there has, inevitably, been some repetition in the background and discussion section in some manuscripts. Due to the editorial and peer review process, there are some inconsistencies in terms of terminology and formatting. However, the linking text that I have provided should help draw each manuscript into one coherent body of work across chapters.

The thesis consists of six research papers, five of which have been published. I conceived all of the research papers presented in this thesis. I am the first and corresponding author for all these research papers. I wrote the first draft of each manuscript. I coordinated all co-authors' feedback and wrote all subsequent drafts. For the fieldwork presented in Chapter 4, I wrote the protocol, obtained ethical approval and supervised the day-to-day task of data collection and management. I analyzed all the data presented in this thesis.

As all manuscripts presented in the thesis are multi-authored works, a separate cover sheet for each manuscript, detailing my role in each research paper, is presented before each manuscript.

Abstract

Urbanization, which is driven mainly by the expansion of cities and urban migration, is considered one of the key drivers of non-communicable diseases (NCDs) in developing countries. This research aims to investigate the patterns and associations between different levels of urban exposures and NCD risk factors, NCD morbidity and NCD mortality in Thailand, to better understand the mechanisms underlying the link between urbanization and NCD in Thailand.

Using several study designs and analytical techniques, the research described in this thesis found that the process of migration and living in an urban environment were associated with lower social trust and higher levels of emotional problems. Urban environments were also associated with behavioural and physiological risk factors for NCDs, including smoking, heavy alcohol consumption, inadequate physical activity, inadequate fruit/vegetable consumption, high BMI, and high blood pressure. Both early life urban exposure and accumulation of urban exposure throughout life potentially play a role in these increases in behavioural and physiological risk factors for NCDs. Early life urban exposure was also found to be associated with an increased risk of developing obesity in adulthood.

Increased psychosocial, behavioural and physiological risk factors associated with living in an urban environment may not translate directly into increased prevalence of biological risk factors for NCDs (such as high cholesterol), the development of NCDs, or into NCD-related mortality. It is likely that biological risk factors for NCDs, as well as NCD incidence and mortality are more amendable to change from the positive influences of urbanization through higher socioeconomic status and potential access to better health care.

Table of contents

List of Tables

Chapter 5

Chapter 7

List of Figures

Chapter 6

Chapter 7

Chapter 8

Acronyms and Abbreviations

BMI	Body mass index
CMU	Chiang Mai University
CVD	Cardiovascular disease
DALYs	Disability-adjusted life years
DBP	Diastolic blood pressure
FBS	Fasting blood sugar
HAPIEE	Health, Alcohol and Psychosocial factors in Eastern Europe
HDL	High density lipoprotein
HT	Hypertension
IFG	Impaired fasting glucose
LDL	Low density lipoprotein
LMICs	low- and middle-income countries
LSHTM	London School of Hygiene and Tropical Medicine
NCD	Non-communicable disease
SBP	Systolic blood pressure
SES	Socioeconomic status
STOU	Sukhothai Thammathirat Open University
TCS	Thai Cohort Study
TG	Triglyceride
Urban HEART	Urban Health Equality Assessment and Response Tool
WHO	World Health Organization
95% CI	95% confidence interval

Chapter 1 : Introduction

Summary

In this chapter, I briefly introduce the definition and drivers of urbanization in developing countries such as Thailand. I then explain how the impact of living in urban environments or “urbanicity”, may impact on health in general and, particularly, in terms of susceptibility to non-communicable diseases. I summarize the current evidence and identify the gaps in evidence linking urbanization and non-communicable disease in Thailand. Lastly, I specify the aims and specific objectives of the research.

1.1 Urbanization and drivers of urbanization

The National Institutes of Health defines urbanization as "*The process whereby a society changes from a rural to an urban way of life. It refers also to the gradual increase in the proportion of people living in urban areas" (1)*. This concept refers to the social and economic shifts from agricultural to industrial societies, increasing educational level, occupational specialization, changes in family structure from extended families to nuclear families and decreasing fertility rates (2, 3)

In developing countries, the rate of urbanization has been more rapid than in developed countries. This rapid rate of urbanization corresponds to the rapid economic growth seen in many developing countries (4). Urbanization in Thailand, as in other developing countries, is driven by three main mechanisms: i) formation of new cities, ii) expansion of cities' fringes and urban populations, and iii) rural to urban migration. The latter is considered the key driver of urbanization in many developing countries such as Thailand and India (5, 6) since migration occurs more swiftly than the other two mechanisms.

1.2 Urbanization and health

"Urbanization and Health" was chosen as the theme for World Health Day 2010. It formally recognizes that urbanization has an effect on health globally and individually. It is estimated that, by 2050, the urban population of the world will have increased by 72%. This translates into seven out of ten people living in urban areas (7). When used within a public health context, the word urbanization often incorporates "urbanicity" or the impact of living in an urban environment into its conceptualization of urbanization and health.

The majority of research aimed at understanding the potential impact of urbanicity on health is conducted using simple "urban" versus "rural" comparisons. While such simple comparisons are useful, one major limitation is that there is no universally accepted definition of what is "urban" and "rural". Vlahov and Galea noted in the classification of urban areas in the United Nation's database varies greatly between countries. Many

countries use an administrative criterion such as living in the capital. Other countries use aspects of size and density, while 22 of the 228 nations in the database had no definition of what an urban was (8). Another limitation of the urban-rural dichotomy is that the patterns of urban-rural differences are likely to be changing overtime within a region as well as between regions (9).

Recent studies have explored the use of scales and indices to quantify urban environments based on factors such as population size and density, public transportation, provision of health services and education (9, 10). Generally in these scales, higher urbanicity values were assigned if there were higher levels of population density and size, higher economic output, higher levels of education, better sanitation, greater access to transport and health care. A recent systematic review, published in 2013, explored the validity of these urbanicity scales. The review found that eight of the eleven studies included in the review did not report the reliability and validity properties of urbanicity scales and concluded that more standardised measures of urbanicity are still needed. (11).

Despite these limitations, based on existing evidence in the literature, the key features of living in urban environments (or urbanicity), which can affect individual behaviours and health risks, can be considered under three main headings (8):

i) *Social environment:* This refers to sociocultural norms and stressors associated with an increased density and diversity of populations in urban environments. Features of an urban social environment (as opposed to a rural environment) may include socioeconomic development, lower social support, higher rates of crime and violence, and exposure to marginalized populations (such as drug addicts and sex workers).

ii) *Physical environment:* This refers to the built environment, transportation systems, sanitation services and the physical availability of resources (e.g. green spaces and healthy foods). It also incorporates aspects of pollution (air, water and noise).

iii) *Provision of Health and Social Services:* Aspects of this component are closely linked the previous two components. However, it has key distinct features, which mainly relate to accessibility, availability, acceptability and quality of health care along with social services and issues of health promotion.

Dr. Kumaresan, Director of the World Health Organization's (WHO's) Centre for Health Development, summarized the thinking around urbanization and health in a single statement:

> *"While urban living continues to offer many opportunities, including potential access to better health care, today's urban environments can concentrate health risks and introduce new hazards"* (7).

1.3 Urbanization as a potential driver of non-communicable diseases

Non-communicable diseases[1] (NCDs) are defined by WHO as diseases of long duration and generally slow progression (12). In 2008, 63% of global deaths were due to NCDs. Current projections estimate that, between 2010 and 2020, NCD deaths are expected to increase by 20% in low- and middle-income countries (LMIC), regions such as Africa and Southeast Asia (13, 14).

Urbanization is considered one of the key drivers of NCDs, especially in LMICs (15). The process of urbanization is a key determinant of two well described phenomena: the epidemiological transition (16) and the nutritional transition (17). Both of these transitions are linked with NCDs. The epidemiologic transition (18) describes the phenomenon whereby as societies progress and become developed, the population age structure and disease patterns change. In the early stages of the epidemiological transition, there is a high burden of diseases due to infectious agents, malnutrition and poor environmental hygiene. As societies progress, the

[1] The World Health Organization defines these conditions as "chronic diseases", while "non communicable diseases" are usually identified as "Group II Diseases", identified according to ICD-10 codes on causes of death. Group II disease (non-communicable disease) classification is used to differentiate illnesses from Group I diseases (communicable, maternal, perinatal and nutritional conditions) and Group III diseases (unintentional and intentional injuries) in the Global Burden of Disease (GBD) project.

high burden of mortality due to diseases of infectious origins, malnutrition and poor hygiene decreases and the life expectancy of the population increases. With increasing life expectancy, and as the population age structure matures, the major causes of death and morbidity shift towards chronic non-communicable disease.

Closely coinciding with this epidemiologic transition is the nutritional transition. The nutritional transition describes the process whereby traditional high fiber and low fat diets are replace by high fat, high sugar and low fiber diets, accompanied by increasing sedentary life styles (19). This leads to increased risk of nutritional-related chronic diseases described in the later stages of the epidemiological transition.

Literature on the subject also suggests that the association between urbanization and the increase in NCDs is causal and/or mediated through other risk factors, including environmental hazards, socioeconomic factors and individual lifestyle (behavioural) factors (20, 21).

Urban environmental hazards include air pollution or exposure to possible carcinogens (22). Urban socioeconomic environments are associated with lower social support and trust (23). At the individual level, urban environments can also promote unhealthy lifestyles in terms of diet and physical inactivity, smoking and alcohol consumption (24).

Due to the close relationship between urbanization and the nutritional transition, along with individual lifestyle risk factors described, the four main types of NCDs closely linked with urbanization are cardiovascular diseases (heart attacks and stroke), cancer, chronic respiratory diseases (such as chronic obstructed pulmonary disease and asthma) and diabetes. Although the symptoms may vary, behavioural risk factors such as unhealthy diet, physical inactivity, alcohol and tobacco use are common risk factors among the four major NCDs. These four behaviours lead to intermediate physiological and biological risk factors for NCD that include increased blood pressure, obesity, hyperlipidemia and hyperglycemia (13).

However, despite shared risk factors, there is heterogeneity among NCDs. Even if the association between urbanization and NCD risk factors are consistent, there can still be varying associations between urbanization and an NCD within the same group due to differences in underlying physiological mechanisms. One example is stroke. There are two main subtypes of stoke, ischemic stroke and hemorrhagic stroke. Evidence from the INTERSTROKE study has demonstrated variations in associations between the same NCD risk factor and these two subtypes of stroke (25). It is likely due to the different underlying physiological mechanisms. While hemorrhagic stroke is closely associated with high blood pressure, ischemic stroke is associated with atherosclerosis (narrowing of arteries due to accumulations of plaque, fatty substance and fibrins) (26).

Another example that may result in varying associations between urbanization within a major NCD is cancer. Cancers such as gastric cancers, cervical cancers and liver cancers have infectious origins. Others, such as lung cancer and breast cancers, are linked with individual lifestyles (27). Urbanization may decrease cancers of infectious origins due to improved sanitation, access to treatment of infectious agents and vaccination while increasing lifestyle associated cancers through increasing smoking and sedentary lifestyles (28).

1.4 Conceptual framework for urbanization and non-communicable disease

The conceptual framework for this thesis, adapted from the framework on globalization and health (29), considers the effect of urbanization on NCDs at two levels: the population level and the individual level (Figure 1.1).

At population level, the process of urbanization can influence health through changes in the built environment and sociocultural norms. An example of such influences from the built environment and social norms can be seen through the effects on secondhand smoking. Policies have reduced exposure to secondhand smoke in indoor and outdoor environments. It has also become more socially unacceptable to smoke in public places.

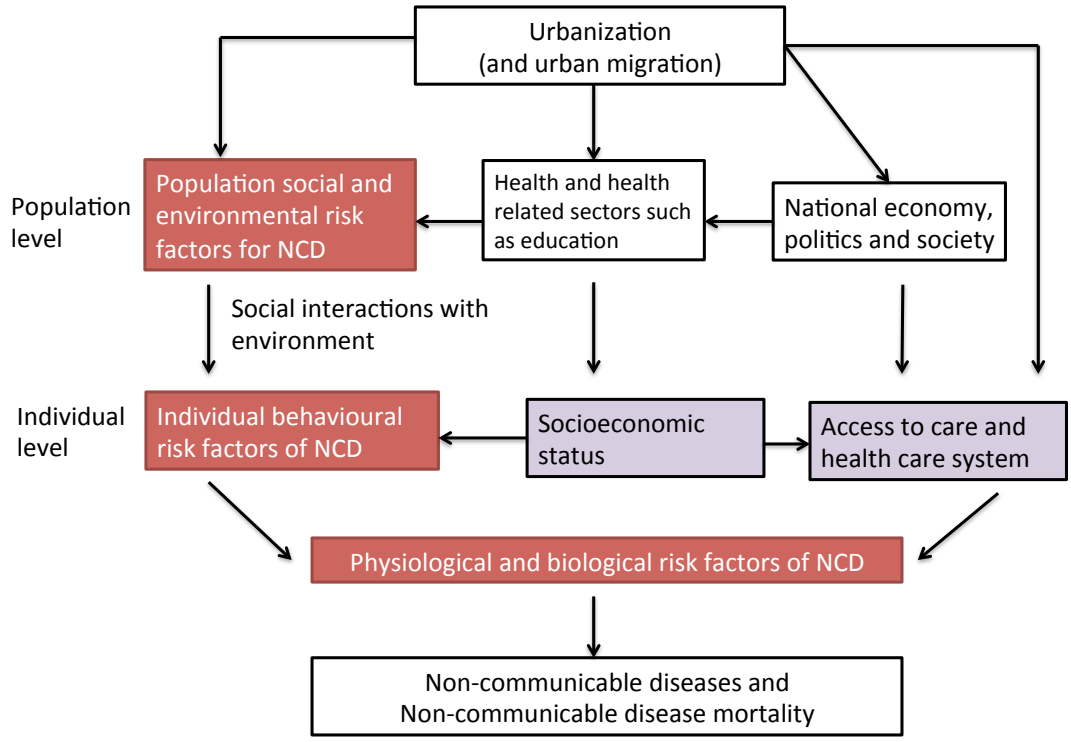
These environmental factors and sociocultural norms can influence an individual's health belief and behaviour. Urbanization can also influence other health and health-related sectors such as national provision of education and trade opportunities along with the changes in the national economy, politics and society.

Through the individual's social interactions with these environmental population-level factors, the process of urbanization affects the individual-level determinants of health. These individual-level determinants include the individual's behavioural determinants of health, the individual's household economy and the health care system that the individual can access. The health care system will reflect the individual's access to care and the availability of medication.

Ultimately, all these factors, along with the individual's behavioural, physiological and biological risk factor profiles are mediators on the pathway between urbanization and the development of NCD morbidity and mortality (8). In my conceptual framework, urbanization is considered the most distal environmental risk factor for NCD morbidity and mortality. The (causal) effect of urbanization is mediated through the individual's distal behavioural risk factors (inadequate physical activity, inadequate fruits and vegetable

consumption, smoking and heavy alcohol use) and more proximal physiological risk factors (increase body mass index and increase blood pressure) and biological risk factors (increase blood glucose, increase low density lipoprotein (LDL) cholesterol, decrease high density lipoprotein (HDL) cholesterol and increase triglycerides), which is depicted by the farthest left pathway in Figure 1.1.

Figure 1.1 Conceptual framework of factors linking urbanization and non-communicable disease (NCD)



Legend

Factors that are mediators on causal pathways between urbanization and NCD

Factors, which may introduce residual confounding in the association between individual behavioural risk factors and NCD risks

Adapted from Woodward D, Drager N, Beaglehole R, Lipson D. Globalization and health: a framework for analysis and action. *Bulletin of the World Health Organization*. 2001;79:875-81(29).

1.5 Review of current evidence from Thailand

Thailand's economic income category was recently upgraded from a lower middle income to an upper middle income economy by the World Bank in 2011 (30). Like many developing countries, Thailand has undergone rapid urbanization within the last few decades and, with it, there has been a growing burden of NCDs (31-33). Between 1987 and 1993, the burden of disease from NCDs increased by 36% (34). By 2004, NCDs accounted for 65% of disability-adjusted life years (DALY) lost in Thai people (35).

The majority of evidence examining the epidemiological transition and trends in chronic non-communicable disease in Thailand has been generated through the Thai Cohort Study (TCS). The TCS, funded by the Wellcome Trust and the Australian National Health and Medical Research Council (NHMRC), is a cohort of 87,142 students enrolled at the Sukhothai Thammathirat Open University (STOU) in 2005 and followed up in 2009.

Full details of the cohort profile and follow up methods have been published (36, 37). The cohort represented the Thai population well in terms of geographic (regional) and income distributions, median age and sex ratio (36, 38) but did not represented the Thai population well in terms of age structure. Members of the cohort tended to be younger than the Thai population (Figure 1.2). One of the main objectives of putting together the cohort was to study Thai epidemiological transition. The investigators of the TCS look a multi-level framework approach (Figure 1.3) to look at the determinants of health at different levels, similar to the framework introduced in section 1.4. Data were collected in seven major areas that included socio-demographic characteristics, income and work, food and physical activity, tobacco and alcohol use.

Six studies using this cohort examined health determinants with potential links between urbanization and health outcomes (36, 39-43). The main results from the six studies nested in the TCS are summarized in Table 1.1.

Figure 1.2 Baseline characteristic of the TCS-STOU cohort participants compared to the population of Thailand

	STOU Cohort	Thailand
Population	87 134	60 606 947
Median age (years)	29.0	29.2
Female (%)	54.3	51.2
Urban residence (%)	51.8	31.1
Buddhist religion (%)	94.5	94.2
Median income (US$)[a]	2 550	2 742
Region (% of population)[b]		
Bangkok	17.2	10.4
Central	30.6	23.3
North	18.2	18.8
Northeast	20.9	34.3
South	13.1	14.0
Age structure (% of population)[c]		
20–29	52.3	24.9
30–39	32.3	23.9
40–49	12.9	21.6
50+	2.5	30.5

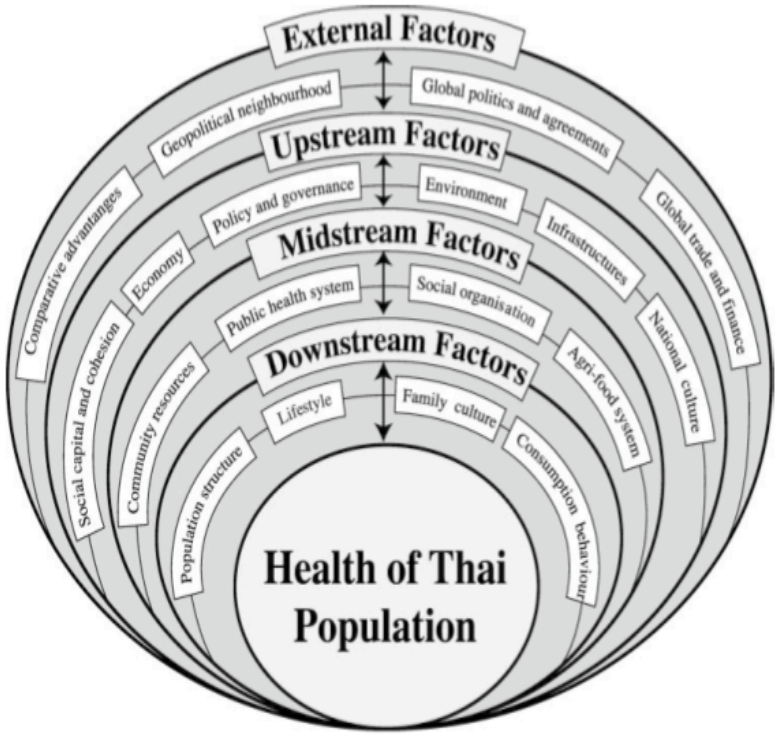
[a] Based on an exchange rate of 40 Baht per US dollar in 2005. Data for Thailand relates to 2004.

[b] Based on a cohort subset of 86,425 persons reporting geographical location. The eastern region is included with the central region in the Thai census and this analysis.

[c] Based on a cohort subset of 84,612 persons aged ≥20 years.

Source: Sleigh AC, Seubsman SA, Bain C: Cohort Profile: The Thai Cohort of 87 134 Open University students. *International Journal of Epidemiology* 2008, 37:266-272 (36).

Figure 1.3 Multi-level framework of factors in the epidemiological transition for the Thai Cohort Study (TCS)



Source: Sleigh AC, Seubsman SA, Bain C: Cohort Profile: The Thai Cohort of 87 134 Open University students**.** *International Journal of Epidemiology* 2008, 37**:**266-272 (36).

Table 1.1 Associations between factors related to urbanization[2] and health: summary of results from TCS studies

Determinant	Outcome	Key findings
Distal socioeconomic factors	Education, employment income, housing condition and household possession	Proportion of individuals with personal income greater than 10,000 baht increased with urbanization status (41). Increasing urbanization is associated with increased car ownership(39).
Mid-level environmental factors	Pollution, social and working conditions	Significantly higher proportion of urban than rural dwellers reported that air, water or noise pollution were “big problems” (41). Urbanization was associated with spending less time on social activities and having less social support (39, 40).
Proximal level behavioural factors	Diet, physical activity, smoking and alcohol	Intake of fast food and soft drinks rose with urbanization but intake of fruit and vegetables was lower. Exercise levels also fell with urbanization while smoking and drinking rose with urbanization (41).
Health status	Self-reported metabolic health status	Those growing up in urban settings were more likely to be overweight as young adults compared to those growing up in a rural setting (36, 44).
	General health	The general overall health deteriorated with an increasing level of urbanization (41).
	Self-reported doctor diagnosis of hypertension and dyslipidemia	Recent urban migrants were at higher risk of hypertension and dyslipidemia (43).

[2] Urbanization status was categorized according to self-classification of urban-rural status by location of residence at age 10-12 and in the years 2005 and 2009.

1.6 Gaps in evidence

As presented in Table 1.1, there is evidence to suggest that urbanization in Thailand is linked with a reduction of social support, with harmful behaviours such as decreased physical activity, increased consumption of junk food, fried food and drinking of alcohol, and with adverse health outcomes. Yet, there are still gaps to be filled in when trying to understand how urbanization determines non-communicable disease risk factors, morbidity and mortality:

1. It is unclear whether increased risk factors for NCDs, which are associated with urbanization, translate into corresponding changes in NCD morbidity and NCD mortality in Thailand.
2. As there are very few studies that have examined biological risk factors for NCDs (e.g. lipids), it is unknown whether the associations between changes in urbanization and corresponding risk factors for NCDs are uniform across behavioural, physiological and biological risk factors.
3. Literature has suggested that urban migrants may be at higher risk of NCDs and adverse health outcomes due to lower social support compared to non-migrants (45). However, few studies have explored the roles of 'migration' and 'urbanicity' as separate processes influencing psychosocial outcomes.
4. A life course approach (46), rather than the more simple urban-rural comparison, has been suggested as a useful way to improve understanding of the health effects of urbanization (47). However, limited evidence using this approach has been generated from Thailand, particularly in terms of changes to the levels of non-communicable disease risk factors and non-communicable disease development (43, 46).

1.7 Overall aim, objectives and structure of thesis

The aim of the research described in this thesis is to investigate associations between urban exposure and non-communicable disease (NCD) risk factors, NCD morbidity, and NCD mortality in Thailand in order to better understand the mechanisms underlying the link between urbanization and NCDs in Thailand.

Based on the conceptual framework proposed in Figure 1.1 and gaps in evidence identified, the objectives of the research and structure of the thesis begin from the association between urban environments and cause specific NCD mortality and work their way towards more distal risk factors for NCDs.

The specific objectives of the thesis are:

Objective 1: To investigate the association between urbanization and specific causes of NCD mortality in Thailand.

Objective 2: To carry out systematic reviews of existing literature on urbanization and NCDs (obesity and four major NCDs) in Thailand and Southeast Asia.

Objective 3: To investigate differences in NCD risk factors

- behavioural risk factors (physical activity, fruits and vegetable consumption, smoking and alcohol use)
- physiological risk factors (body mass index and blood pressure)
- and biological risk factors (fasting glucose, LDL cholesterol, HDL cholesterol and triglycerides)

among those with different urban exposures and to explore possible life-course mechanisms behind such associations.

Objective 4: To investigate the changes in body mass index (a physiological NCD risk factor) and fasting glucose (a biological NCD risk factor) and risk of developing obesity and impaired fasting glucose among those with different early life exposure.

Objective 5: (i) To investigate the influence of rapid changes in urbanicity (urban/rural location) and recent internal migration on psychosocial health and well-being (social trust, standard of living, safety and satisfaction with life) and (ii) To investigate whether lower levels of psychosocial health and well-being translate into an increase in body mass index (BMI).

Each objective stated above will have its own chapter. Each chapter will follow a similar pattern, beginning with a general introduction section, followed by a manuscript or draft of a manuscript prepared for publication. If required, additional results or discussion not included in the manuscript will

follow. Each chapter will end with a summary section detailing overall findings and conclusions.

Chapter 2 : Urbanization and non-communicable disease mortality in Thailand

Summary

Introduction: Urbanization has been linked with behavioural risk factors for NCDs such as inadequate physical activity and diets low in fruit and vegetables. It is unclear whether risk factors for NCDs, which are associated with urbanization, translate into corresponding changes in NCD mortality levels in Thailand.

Objective (1): To investigate the association between urbanization and specific causes of NCD mortality in Thailand

Study design: Ecological correlation study using aggregate data from all 76 provinces in Thailand

Exposures: i) Population density and ii) Proportion of population living in urban areas

Outcome: i) All-cause mortality, ii) Cardiovascular disease mortality, iii) Cerebrovascular disease mortality and iv) Cancer mortality

Key findings: Population density and the proportion of people living in an urban area were each independently associated with increased NCD mortality in Thailand. These associations remain significant despite adjustments for average household income and number of doctors per population. Further evaluation is warranted to understand the mechanisms underlying the link between urbanization, NCDs and NCD mortality on an individual level in Thailand.

2.1 Introduction

In this chapter, I describe an ecological study that was conducted in order to investigate whether there was any evidence linking urbanization with non-communicable disease mortality in Thailand. Ecological studies are considered a cost effective and convenient way to explore associations for population-level exposures (48). My exposures of interest for urbanization in this chapter, population density and proportion of population living in urban areas, are suited to an ecological study as both measures are considered exposures at the population-level.

Any associations found will provide evidence to further investigate these associations in greater detail at the individual level. Specifically, I assessed the associations between urbanization and the specific causes of non-communicable disease mortality (cardiovascular disease (CVD), cerebrovascular disease and malignant neoplasms), along with all-cause mortality in Thailand. In addition, using the conceptual framework discussed in section 1.4 above, I also investigated the influence on mortality of average monthly household income and the number of doctors per population, and how these factors relate to the association between urbanization and mortality.

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RESEARCH PAPER COVER SHEET

Urbanization and non-communicable disease mortality in Thailand: an ecological correlation study

PLEASE NOTE THAT A COVER SHEET MUST BE COMPLETED FOR EACH RESEARCH PAPER INCLUDED IN A THESIS.

SECTION A – Student Details

Student	Chaisiri Angkurawaranon
Principal Supervisor	Dorothea Nitsch
Thesis Title	Urbanization and internal migration as risk factors for non-communicable disease in Thailand

If the Research Paper has previously been published please complete Section B, if not please move to Section C

SECTION B – Paper already published

Where was the work published?	Tropical Medicine and International Health		
When was the work published?	February 2013		
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion			
Have you retained the copyright for the work?*	No, evidence of permission form the copyright holder is included as Appendix A	Was the work subject to academic peer review?	Yes

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Where is the work intended to be published?	
Please list the paper's authors in the intended authorship order:	
Stage of publication	

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	In consultation with my supervisors, I conceived the design of the study, collected and analyzed the data. I wrote the manuscript and coordinated all co-authors' feedback and comments. I wrote all subsequent drafts. I am first and corresponding author for the article

Student Signature: _____ **Date:** 13 April 2015

Supervisor Signature: _____ **Date:** 7/4/15

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Urbanization and Non-communicable disease mortality in Thailand: an ecological correlation study

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Abstract This study provides strong evidence from an LMIC that urbanization is associated with mortality from three lifestyle-associated diseases at an ecological level. Furthermore, our data suggest that both average household income and number of doctors per population are important factors to consider in ecological analyses of mortality.

keywords Urbanization, non-communicable disease, chronic disease, mortality, Thailand

Introduction

Urbanization is considered a determinant of health and one of the key drivers of non-communicable diseases (NCDs), especially in low- and middle-income countries (LMICs) (Boutayeb & Boutayeb 2005; Vlahov *et al.* 2007). In 2008, 63% of global deaths were due to NCDs. Current projections suggest that between 2010 and 2020, NCD deaths are expected to increase by 20% in LMIC regions such as Africa and South-East Asia (Mathers *et al.* 2008; World Health Organization 2010). Growing evidence from LMICs shows that urbanization is associated with increased prevalence of risk factors for non-communicable disease (Hernandez *et al.* 2012). There is some evidence for an urban advantage in NCD mortality in high-income countries, possibility due to higher income and better access to health care, but limited data have been published on the association between urbanization and non-communicable disease mortality in LMICs (Harpham *et al.* 2004; Allender *et al.* 2008; Leon 2008).

Thailand's income category was recently upgraded from lower-middle-income to upper-middle-income economy by the The World Bank (2011). Like many developing countries, Thailand has undergone rapid urbanization within the last decades and has a growing burden of NCDs (Viravaidya & Sacks 1997; Cohen 2004). Between 1987 and 1993, the burden of disease from NCDs increased by 36% (Samutaruk 1997). By 2004, NCDs accounted for 65% of disability-adjusted life years lost in Thai people. The emergence of NCDs in Thailand results from socioeconomic, environmental and lifestyle changes associated with urbanization (Yiengprungsawan *et al.* 2011a). Recently published studies from Thailand found geographical variations in all-cause and cause-specific NCD mortality, but did not investigate the role of urbanization (Faramnuayphol *et al.* 2008; Odton *et al.* 2010).

This study aimed to assess the association between urbanization and specific causes of non-communicable disease mortality (cardiovascular disease (CVD), cerebrovascular disease and malignant neoplasms) along with all-cause mortality, in Thailand. We also investigated the influence of average monthly household income and number of doctors per population on mortality, and how they relate to the association between urbanization and mortality.

Methods

This ecological correlation study used information from 76 provinces in Thailand in 2009, including data on demographic structure, population density, the proportion living in an urban area, the number of doctors per population, the average monthly household income and the top 10 known causes of death.

Vital registration in Thailand

A detailed description of the Thai vital statistics system has been published (Tangcharoensatien *et al.* 2002). By law, each death must be notified within 24 h to the Bureau of Registration and Administration (BORA). For deaths that occur in hospitals, and unnatural deaths outside hospitals, a physician records one cause of death in Thai that is sent electronically to the national registration database (Pattaraarchachai *et al.* 2010). For natural deaths outside hospitals, the local registrars record one cause of death in Thai after inquiring the cause of death

from the family. Mortality data from both systems are sent electronically to BORA to be complied into a database. Mortality is attributed to each province according to the deceased registered place of residence. The Ministry of Public Health is then responsible for coding the causes of death, which are specified in Thai, according to ICD-10 (Rao *et al.* 2010).

Outcome definitions

Cardiovascular disease mortality includes ICD codes, I05-I09, I120-I128 and I130-I152; cerebrovascular disease ICD codes, I10-I15 and I60-I69; and malignant neoplasms ICD codes, C00-C48.

Primary exposures

Population density is the number of (mid-year) population divided by the area (km2) for each province. The population in Thailand is defined using local administrative criteria (Archavanitkul 1988). Every person in Thailand must be registered under a household. People are classified as living in an urban area if the household they are registered at is under local municipality administration (Flood 2000). The *proportion of persons living in urban areas* within each province is defined as the urban population divided by total (mid-year) population of that province.

Other variables of interest

The province average monthly household income is derived from a survey carried out by the National Statistical Office annually using a stratified two-stage sampling technique. The 76 provinces are considered as individual strata, and each stratum is categorised into municipal areas and non-municipal areas. Villages are used as the primary sampling unit; individual households are the secondary sampling unit. (National Statistial Office of Thailand).

Number of doctors per population in a province is the number of medically licensed doctors registered to work in a hospital or clinic at the provincial public health office divided by the mid-year population of that province (Bureau of Policy & Strategy, Ministry of Public Health).

Data sources

Data are openly accessible from the National Statistical Office of Thailand and the Ministry of Public Health's website. Age and gender cause-specific mortality are tabulated for the National level data (http://service.nso.go.th/nso/thailand/thailand.jsp, http://service.nso.go.th/nso/nsopublish/BaseStat/tables/00000_Whole Kingdom/N28P02-income.xls and http://bps.ops.moph.go.th/Healthinformation/statistic50/statistic50.html).

Analysis

Each measure of urbanization was analysed separately. Age and gender were considered *a priori* as confounding factors. Indirect age-adjusted standardisation, using the country's age structure in 2009, was used to investigate the association between population density and the proportion living in an urban area with mortality. Scatter plots of standardised mortality ratios (SMRs) against measures of urbanization were used to graphically depict the relations between variables and to identify influential points and outliers. Pearson correlation coefficients were calculated to quantify associations between measures of urbanization and SMRs. Poisson regression models assessed the relationship between measures of urbanization and mortality after adjusting for age structure (10-year age bands) and the proportion of men, using the size of the population in each province as the offset variable. The Poisson models were adjusted further for the number of doctors per population and the average monthly household income. These variables are potential confounders (when trying to separate out the association between urbanization-induced life-style changes) and/or on the causal pathway between measures of urbanization and mortality outcomes. Sensitivity analysis was performed by removing the outlier, Bangkok, from the analyses. To explore the possible misclassification in causes of deaths, and to identify the main driver in all-cause mortality, further sensitivity analysis was performed by examining the other causes of death, which contribute to 55% of all-cause mortality.

Results

In 2009, the population in Thailand was 63 525 062 with an overall population density of 123.8 people per km^2. Within the 76 provinces, the population varied from 181 754 people in Ranong Province to 5.7 million people in Bangkok (median = 634 202, IQR = 462 520–1033 997). The proportion living in an urban area ranged from 6.9% in Surin Province to 100% in Bangkok (median = 23.1%, IQR = 18.5–33.8%), whilst the population density varied from 19.1 people per km^2 in Mae Hong Sorn Province to 3635.2 people per sq.km.in Bangkok (median = 121.9, IQR = 78.9–163.2). The average monthly household income across

the 76 provinces was 18 805 baht (approx. £ 375) (median = 17, 537; IQR = 14 545–22 174). The average number of doctors per 10 000 population across the 76 provinces was 2.55 (median = 2.29; IQR = 1.82–3.12). There was a strong positive correlation between population density and proportion living in an urban area ($r = 0.72$, $P < 0.01$). There was a positive correlation between the two primary measures of urbanization and the average household income and number of doctors per population ($r > 0.6$ and $P < 0.001$ in all analysis). Of the two, the proportion living in an urban area showed a stronger correlation with average household income and number of doctors per population than population density (Figure 1).

Urbanization and mortality

The all-cause mortality rate was 6.2 per 1000. The leading known causes of deaths and their contribution to all mortality were as follows: malignant neoplasms, 14.1%; accidents and poisoning, 8.9%; cerebrovascular disease, 5.0%; and CVD, 4.6%. The top 10 known causes of deaths accounted for 45% of all mortality. The rest were classified as other causes.

There was a weak negative correlation between population density and the SMRs (Figure 2). For every increase of 100 people per km^2 in population density, there was a 0.2% decrease in overall mortality rate after adjustment for age and gender. Additional adjustments for numbers of doctors per population and average household income strengthened the association (Table 1).

In contrast, for the proportion living in an urban area, there was a positive correlation with mortality ($r = 0.29$, $P = 0.01$) (Figure 2). In the age- and gender-adjusted Poisson regression model, every ten per cent increase in the proportion living in an urban area was associated with a 0.3% increase in overall mortality rate (95% CI 0.1–0.6). Adjusting for number of doctors per population and average household income strengthened the association. (Table 1)

In both models, increasing average household income was associated with a decrease in mortality rate, whilst increasing number of doctors per population was associated with an increased mortality.

Urbanization and cardiovascular mortality

The overall cardiovascular mortality rate was 28.9 per 100 000. Across provinces, there was a positive correlation between both measures for urbanization and the SMR for cardiovascular disease (Figure 3).

Every increase of 100 people per km^2 was associated with a 2.2% increase in cardiovascular mortality rate (95% CI 2.0–2.5) in age- and gender-adjusted analyses. Additional adjustment for numbers of doctors per population and average household income attenuated the association (Table 2). On its own, average household income had a negative confounding effect and the number of doctors had a positive confounding effect (data not shown).

The correlation coefficient between the proportion living in an urban area and the SMR for CVD was 0.43 ($P < 0.001$). Adjusting for age and gender, every ten per cent increase in proportion living in urban area was

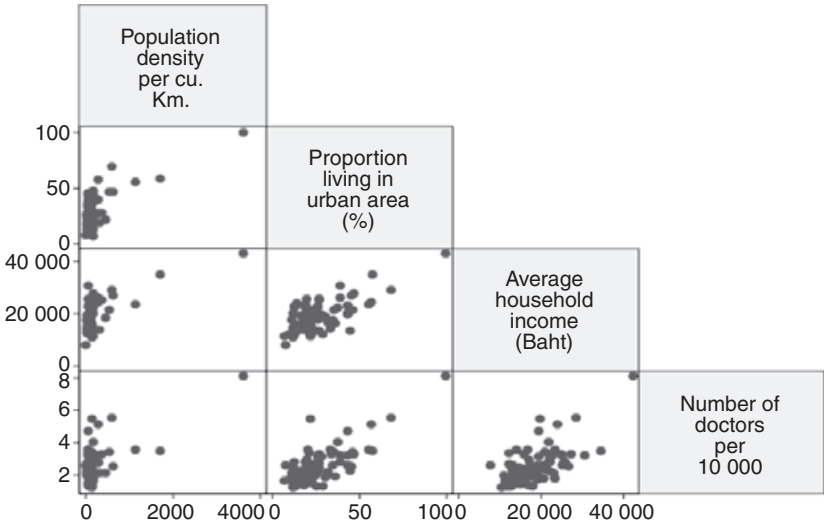

Figure 1 Matrix scatter plots of population density, proportion living in urban area, average household income and number of doctors per population using aggregate data across 76 provinces in Thailand.*Note: the outlier at the upper right represents Bangkok.

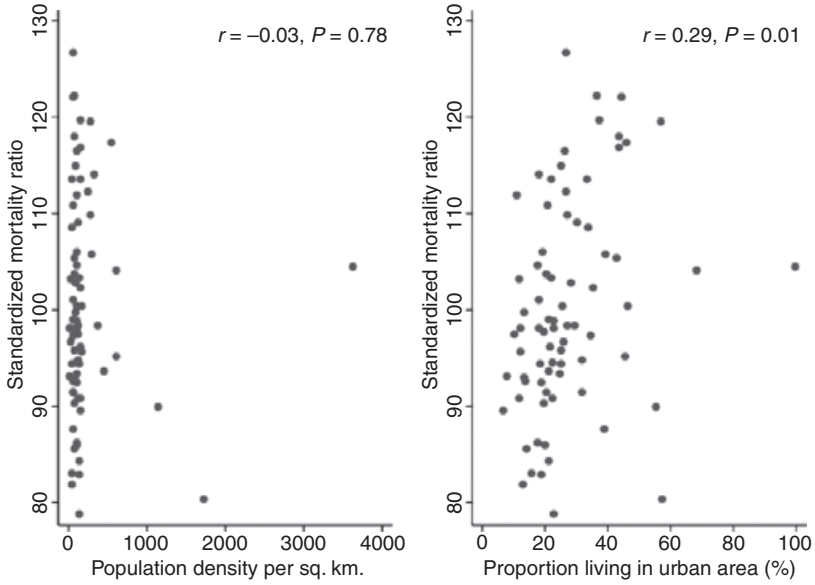

Figure 2 Correlation between proportion living in urban area and population density with standardised mortality ratio using aggregate data across 76 provinces in Thailand.

Table 1 Estimated associations between measures of urbanization and percentage increase in all-cause mortality rate and their 95% confidence intervals (CI) using aggregate data across 76 provinces in Thailand

		Model 1	Model 2	Model 3	Model 4
	Measures of urbanization in each province (Units)	Percentage increase in rate per unit increase (95% CI)	Percentage increase in rate per unit increase (95% CI)	Percentage increase inrate per unit increase (95% CI)	Percentage increase in rate per unit increase (95% CI)
All-cause mortality	Population density (100 people per population)	−0.15 (−0.20 to −0.11) $P < 0.001$	−0.28 (−0.39 to −0.18) $P < 0.001$	—	—
	Proportion living in urban area (10 per cent)	—	—	0.34 (0.12 to 0.55) $P = 0.002$	1.87 (1.41 to 2.34) $P < 0.001$
	Average monthly householdincome (1000 baht)	—	−0.68 (−0.80 to −0.56) $P < 0.001$	—	−1.12 (−1.22 to −1.02) $P < 0.001$
	Number of doctors per population (Doctors per 10 000)	—	4.11 (3.70 to 4.52) $P < 0.001$	—	2.79 (2.34 to 3.25) $P < 0.01$

Model 1 exposure variables in model: population density, age and gender.
Model 2 exposure variables in model: population density, age, gender, average monthly household income and number of doctors per population.
Model 3 exposure variables in model: proportion living in urban area, age and gender.
Model 4 exposure variables in model: proportion living in urban area, age, gender, average monthly household income and number of doctors per population.

associated with a 10.5% increase in cardiovascular mortality rate (95% CI 9.5–11.6), which attenuated to 6.6% (95%CI 4.3–9.0) after adjustments for average household income and number of doctors per population (Table 2). There was a positive association between number of doctors and cardiovascular mortality rates.

Urbanization and cerebrovascular mortality

The overall cerebrovascular mortality rate was 24.6 per 100 000. There was a positive correlation between both measures for urbanization and the SMR for cerebrovascular disease (Figure 4), but the correlation between

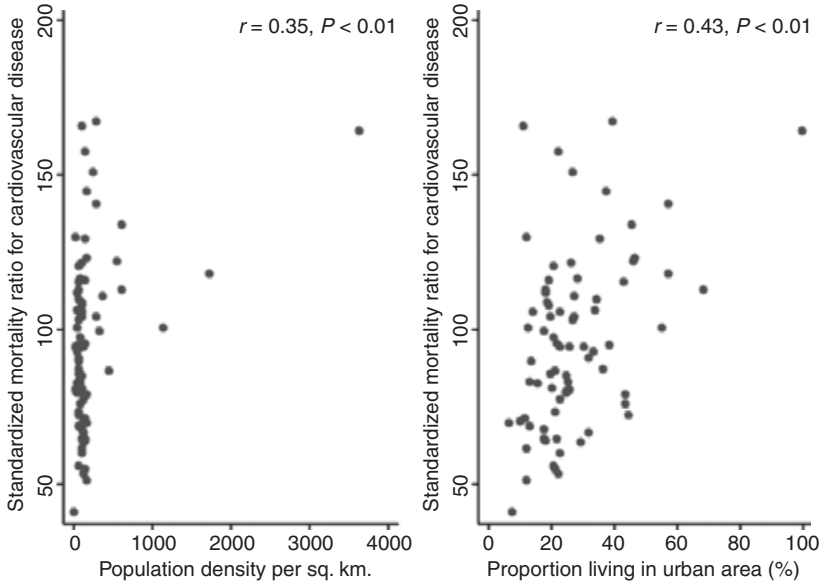

Figure 3 Correlation between proportion living in urban area and population density with standardised mortality ratio for cardiovascular disease using aggregate data across 76 provinces in Thailand.

Table 2 Estimated associations between measures of urbanization and percentage increase in cardiovascular mortality rate and their 95% confidence intervals (CI) using aggregate data across 76 provinces in Thailand

		Model 1	Model 2	Model 3	Model 4
	Measures of urbanization in each province (Units)	Percentage increase in risk per unit increase (95% CI)	Percentage increase in risk per unit increase (95% CI)	Percentage increase in risk per unit increase (95% CI)	Percentage increase in risk per unit increase (95% CI)
Cardiovascular mortality	Population density (100 people per population)	2.25 (2.04 to 2.46) $P < 0.001$	1.97 (1.48 to 2.46) $P < 0.001$	—	—
	Proportion living in urban area (10 per cent)	—	—	10.52 (9.48 to 11.58) $P < 0.001$	6.63 (4.32 to 9.00) $P < 0.001$
	Average monthly household income (1000 baht)	—	−0.57 (−1.12 to −0.01) $P = 0.047$	—	0.29 (−0.19 to 0.76) $P = 0.236$
	Number of doctors per population (Doctors per 10 000)	—	4.53 (2.61 to 6.49) $P < 0.001$	—	3.36 (1.20 to 5.57) $P = 0.002$

Model 1 exposure variables in model: population density, age and gender.
Model 2 exposure variables in model: population density, age, gender, average monthly household income and number of doctors per population.
Model 3 exposure variables in model: proportion living in urban area, age and gender.
Model 4 exposure variables in model: proportion living in urban area, age, gender, average monthly household income and number of doctors per population.

population density and SMR for cerebrovascular mortality did not reach statistical significance (r = 0.14, $P = 0.244$). The regression models, adjusting for population age structure and gender, suggested that every increase of 100 people per km^2 in population density was associated with a 1.0% increase in cerebrovascular mortality rate. (95% CI 0.8–1.2) Additional adjustments for numbers of doctors per population and average household income attenuated the association to a small degree (Table 3).

The correlation coefficient for the proportion living in an urban area and SMR for cerebrovascular disease was 0.42 ($P < 0.001$) (Figure 4). In the age- and gender-adjusted model, every ten per cent increase in propor-

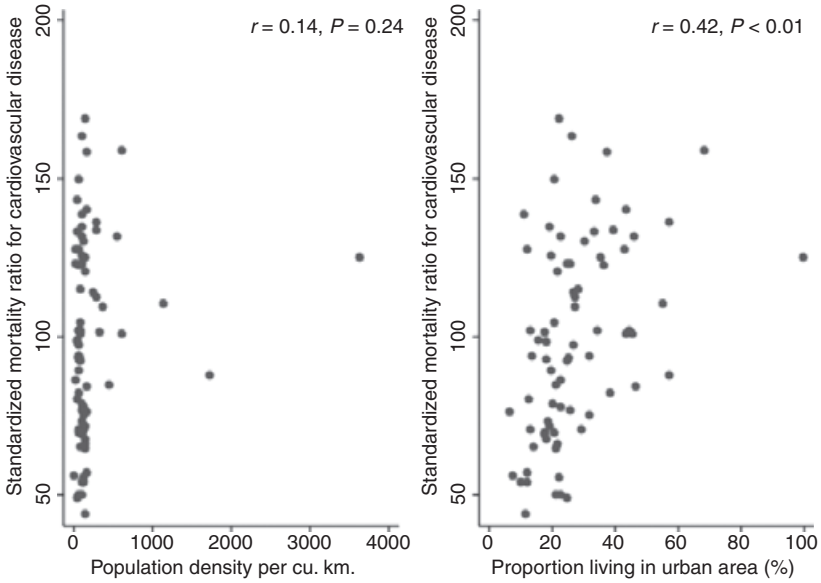

Figure 4 Association between proportion living in urban area and population density with standardised mortality ratio for cerebrovascular disease using aggregate data across 76 provinces in Thailand.

Table 3 Estimated associations between measures of urbanization and percentage increase in cerebrovascular mortality rate and their 95% confidence intervals (CI) using aggregate data across 76 provinces in Thailand

		Model 1	Model 2	Model 3	Model 4
	Measures of urbanization in each province (Units)	Percentage increase in risk per unit increase (95% CI)	Percentage increase in risk per unit increase (95% CI)	Percentage increase in risk per unit increase (95% CI)	Percentage increase in risk per unit increase (95% CI)
Cerebrovascular mortality	Population density (100 people per population)	0.99 (0.76 to 1.22) $P < 0.001$	0.93 (0.41 to 1.46) $P < 0.001$	—	—
	Proportion living in urban area (10 per cent)	—	—	5.81 (4.72 to 6.92) $P < 0.001$	5.24 (2.78 to 6.92) $P < 0.001$
	Average monthly household income (1000 baht)	—	−2.27 (−2.86 to −1.67) $P < 0.001$	—	−2.09 (−2.59 to −1.59) $P < 0.001$
	Number of doctors per population (Doctors per 10 000)	—	12.02 (9.86 to 14.22) $P < 0.001$	—	10.11 (7.66 to 12.60) $P < 0.001$

Model 1 exposure variables in model: population density, age and gender.
Model 2 exposure variables in model: population density, age, gender, average monthly household income and number of doctors per population.
Model 3 exposure variables in model: proportion living in urban area, age and gender.
Model 4 exposure variables in model: proportion living in urban area, age, gender, average monthly household income and number of doctors per population.

tion living in an urban area was associated with a 5.8% increase in cerebrovascular mortality rate (95% CI 4.7–6.9), with little attenuation after further adjustments for average household income and number of doctors per population. Average household income was negatively associated with cerebrovascular mortality, whilst number of doctors showed a strong positive association (Table 3).

Urbanization and malignant neoplasms mortality

The overall mortality rate from malignant neoplasms was 88.3 per 100 000. There was a positive correlation between population density and SMR for malignant neoplasm (Figure 4). In the adjusted regression model, every increase of 100 people per km^2 in population density was associated with a 1.0% increase in malignant neoplasm mortality rate (95% CI 0.9–1.1) (Table 4).

There was very weak evidence for a positive correlation between the proportion living in an urban area and SMR for malignant neoplasm. ($r = 0.20$, $P = 0.086$) (Figure 5). The age- and gender-adjusted model suggests that every 10% increase in the proportion living in an urban area is associated with a 5.5% increase in malignant neoplasm mortality rate (95% CI 4.9–6.1). Additional adjustment for numbers of doctors per population and average household income strengthened the association (Table 4).

Sensitivity analyses

Removing Bangkok as the outlier did not materially change the correlations between urbanization and all-cause mortality, cardiovascular mortality and cerebrovascular mortality.

Population density was associated with a decrease in rate from other causes of death (Appendix 1). The proportion of those living in an urban area was negatively associated with the rate of other causes of death in the age- and gender-adjusted model, but this association completely attenuated after adjusting for average household income and number of doctors per populations.

Further analysis including additional adjustments for number of hospitals in each province did not change the direction of association between the two measures of urbanization and the four types of mortality. The distribution of the proportional mortality between NCD and other causes of death did not differ by number of hospitals within province (Appendix 2).

Discussion

This study found that that urbanization, measured by population density and the proportion of people living in an urban area, was associated with increased NCD mortality in Thailand. Increasing average monthly household income in each province was associated with lower NCD mortality, whilst higher density of doctors appeared to be associated with higher NCD mortality.

We found that population density was negatively associated with all-cause mortality, whilst the proportion of people living in urban area was positively associated with all-cause mortality. Discrepancy in the effects of the two measures could be due to the capture of different aspects of urbanization. Population density by definition captures crowding. The urban proportion in Thailand, by virtue of

Table 4 Estimated associations between measures of urbanization and percentage increase in malignant neoplasm mortality rate and their 95% confidence intervals (CI) using aggregate data across 76 provinces in Thailand

		Model 1	Model 2	Model 3	Model 4
	Measures of urbanization in each province (Units)	Percentage increase in risk per unit increase (95% CI)	Percentage increase in risk per unit increase (95% CI)	Percentage increase in risk per unit increase (95% CI)	Percentage increase in risk per unit increase (95% CI)
Malignant neoplasm mortality	Population density (100 people per population)	1.00 (0.88 to 1.12) $P < 0.001$	0.96 (0.69 to 1.23) $P < 0.001$	—	—
	Proportion living in urban area (10 per cent)	—	—	5.46 (4.86 to 6.07) $P < 0.001$	6.27 (5.01 to 7.55) $P < 0.001$
	Average monthly household income (1000 baht)	—	−0.93 (−1.26 to −0.60) $P < 0.001$	—	−0.89 (−1.17 to −0.60) $P < 0.001$
	Number of doctors per population (Doctors per 10 000)	—	4.58 (3.49 to 5.68) $P < 0.001$	—	2.74 (1.57 to 3.92) $P < 0.001$

Model 1 exposure variables in model: population density, age and gender.
Model 2 exposure variables in model: population density, age, gender, average monthly household income and number of doctors per population.
Model 3 exposure variables in model: proportion living in urban area, age and gender.
Model 4 exposure variables in model: proportion living in urban area, age, gender, average monthly household income and number of doctors per population.

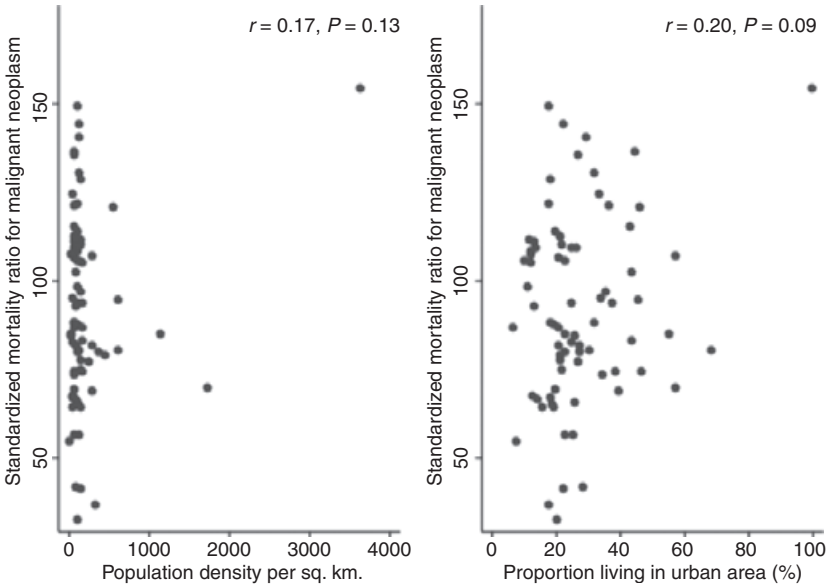

Figure 5 Association between proportion living in urban area and population density with standardised mortality ratio for malignant neoplasms using aggregate data across 76 provinces in Thailand.

the criteria for becoming a municipality, captures some aspects of density but will also include access to high-tech health facilities and equipment, and to public health interventions such as sanitation and waste management. This notion is supported by the observation that in comparison with population density, the proportion living in an urban area shows a stronger correlation with the number of doctors per population and average household income.

All-cause mortality is made up of a variety of underlying causes of death. Apart from the top 10 causes of deaths, a variety of other causes of mortality accounted for 55% of total mortality. Each of the specific causes of death might have different associations with urbanization. For example, the association between population density and all-cause mortality was flat or slightly negative, whilst the association between population density and all NCD causes of death was positive. The sensitivity analyses showed that this different directionality of association is likely to be driven by other causes of mortality.

Our findings are consistent with other ecological studies considering urbanization and NCD mortality (Schorr *et al.* 1989; Smith *et al.* 1995; Pritchard & Evans 1997; Yang & Hseigh 1998). Petcharoen *et al.* carried out a similar ecological study using the same databases in 2000 to assess the relationship between socioeconomic status and cardiovascular mortality in Thailand (Petcharoen *et al.* 2006). In their study, the correlation between the proportion living in urban area and age-standardised cardiovascular mortality rate was 0.41, similar to the correlation found in our study (0.43). There are several plausible explanations for the associations seen between urbanization and NCD mortality. Although one must be careful not to imply causation from such a study design, it is possible that the association between urbanization and mortality is causal and mediated through other risk factors, such as individual life-style factors, social support/access to care and environmental hazards such as air pollution or exposures to possible carcinogens (Yang & Hseigh 1998; Maheswaran & Elliott 2003). Several studies have found links between urbanization and many individual risk factors for NCDs (Sleigh *et al.* 2008; Allender *et al.* 2010; Hernandez *et al.* 2012). Evidence from Thailand suggests that negative health behaviours such as decreasing physical activity, increasing consumption of junk food and fried food, smoking and drinking are associated with urbanization (Young 2001; Kosulwat 2002; Banwell *et al.* 2009; Lim *et al.* 2009; Yiengprungsawan *et al.* 2011b). Thus, it is feasible that the association between urbanization and increasing prevalence of risk factors for NCD could result in increasing NCD mortality, although these may be masked by changes in socioeconomic status. Other studies, using individual level data, found that higher socioeconomic status was associated with lower mortality in Thailand, possibly due to better health behaviour in terms of less smoking and drinking and better access to care (Sethapongkul 1992; Vapattanawong *et al.* 2008).

A recent meta-analysis provides evidence that fewer social relationships, whether structural or functional, lead to higher mortality (Holt-Lunstad *et al.* 2010). In Thailand, social relationships such as trust, support and interactions are less strong in urban environments (Yiengprungsawan *et al.* 2011b).

Reverse causality proposes that severely ill patients with chronic non-communicable disease are more likely to relocate to a more urban area, where it is assumed there will be better access to care (Bentham 1988; Phillips 1993). Although this could be possible for diseases such as cancer, it is less likely for cardiovascular mortality and cerebrovascular mortality because in Thailand the time from event to death is short (Venketasubramanian 1998; Srimahachota *et al.* 2007).

The positive association we found between number of doctors per population and increasing mortality is consistent with past literature, and several explanations have been offered (Cochrane *et al.* 1978; Young 2001). One is the fact that urban areas are able to attract more doctors, and the urban populations have higher risk factors. The association seen is not, therefore, causal in either direction. It is interesting to note that adjustment for average household income and number of doctors alters the association between urbanization and NCD mortality differently, depending on cause and which measure of urbanization is being considered, even though the direction of association remains consistent.

There were several limitations to our study. The urban proportion in 1999 was dramatically increased due to a decentralising act, which upgraded existing rural sanitation districts to urban municipalities. This resulted in transformation of more than 700 areas to "urban" overnight, even though their lifestyle and environmental surroundings could be considered rural. This misclassification could lead to underestimation of true associations. There is also potential for uncontrolled confounding by other factors, which we have not been able to adjust for. However, it is unlikely that these issues explain the direction of the findings reported here. Regarding accuracy of death registration, a medical records review for hospital deaths suggested that around 9% of deaths were unregistered (Porapakkham *et al.* 2010), and for vital registration records, the positive predict values for ischaemic heart disease, cerebrovascular disease, lung cancer and liver cancer (leading causes of deaths from malignant neoplasms for men and women in Thailand) were 65%, 77%, 83% and 86%, respectively (Pattaraarchachai *et al.* 2010). We found no clear evidence of pronounced differential misclassification at provincial level by numbers of hospitals. Because the symptoms of cardiovascular and cerebrovascular disease are relatively clear and distinguishable from other conditions, we do not consider misclassification of outcome a major problem in this study.

A major strength of this study was the use of national data. This provided consistency in measures of urbanization as well as homogeneity in terms of national culture and lifestyle. The study was also able to adjust for important potential confounders or mediators of urbanization.

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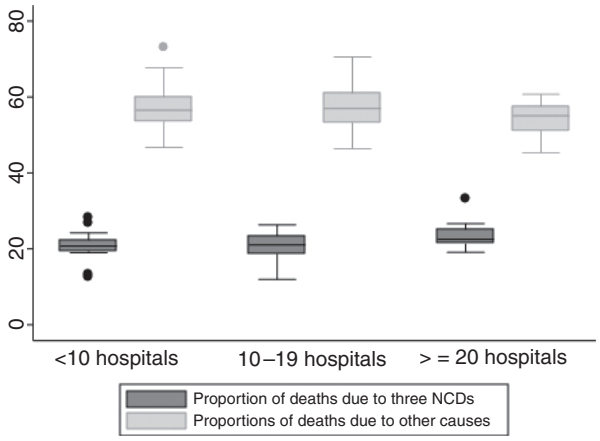
Appendix 1 Estimated associations between measures of urbanization and percentage increase in other causes of mortality rate and their 95% confidence intervals (CI) using aggregate data across 76 provinces in Thailand

		Model 1	Model 2	Model 3	Model 4
	Measures of urbanization in each province (Units)	Percentage increase in risk per unit increase (95% CI)	Percentage increase in risk per unit increase (95% CI)	Percentage increase in risk per unit increase (95% CI)	Percentage increase in risk per unit increase (95% CI)
Other causes of mortality	Population density (100 people per population)	−0.88 (−0.95 to −0.82) $P < 0.001$	−0.79 (−0.93 to −0.66) $P < 0.001$	—	—
	Proportion living in urban area (10 per cent)	—	—	−2.83 (−3.12 to −2.54) $P < 0.001$	0.26 (−0.35 to 0.87) $P = 0.413$
	Average monthly household income (1000 baht)	—	−0.57 (−0.73 to 0-.41) $P < 0.001$	—	−1.19 (−1.33 to −1.05) $P < 0.001$
	Number of doctors per population (Doctors per 10 000)	—	2.13 (1.58 to 2.68) $P < 0.001$	—	0.99 (0.38 to 1.60) $P = 0.001$

Model 1 exposure variables in model: population density, age and gender.
Model 2 exposure variables in model: population density, age, gender, average monthly household income and number of doctors per population.
Model 3 exposure variables in model: proportion living in urban area, age and gender.
Model 4 exposure variables in model: proportion living in urban area, age, gender, average monthly household income and number of doctors per population.

Appendix 2 Proportional mortality by number of hospitals across 76 provinces in Thailand



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1

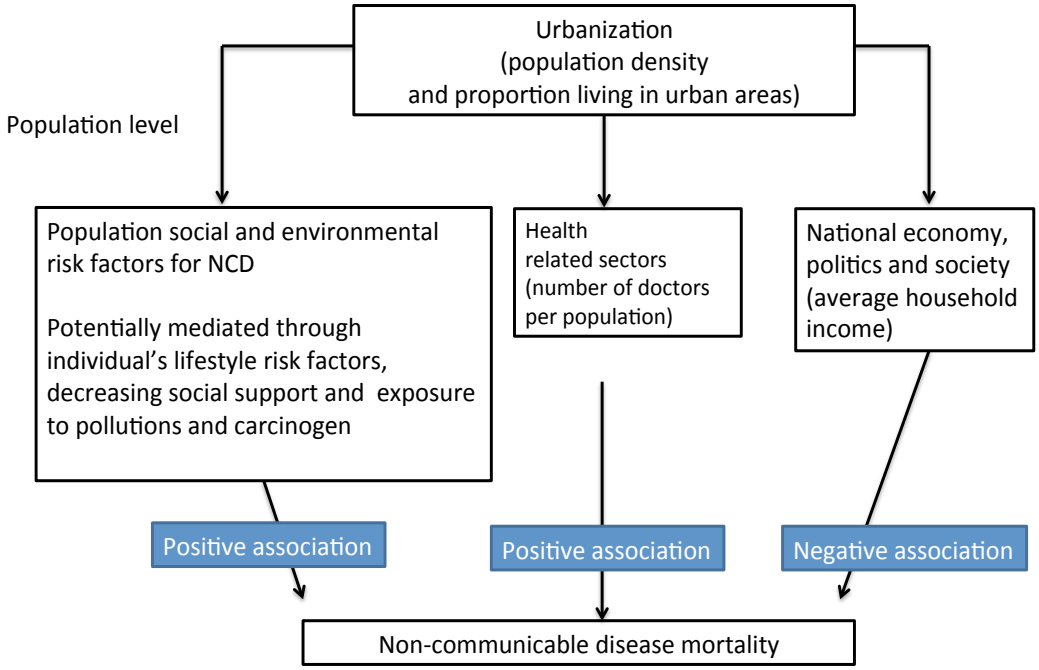
2.3 Summary and conclusion

The study found that increasing population density and increasing proportions of people living in urban areas were positively associated with mortality from three lifestyle associated NCDs: cardiovascular disease, cerebrovascular disease and malignant neoplasms (cancers). However, the strength of association was weakest for cancer mortality.

Cancers with infectious origins, such as gastric, liver and cervical cancer, are common in Thailand (49). Urbanization could be associated with better hygiene and access to immunization, which may have weakened the positive association seen for cancer mortality. Increased average household income was associated with lower NCD mortality rate and an increased number of doctors per population was associated with a higher NCD mortality rate (Figure 2.1).

Causal interpretation and extrapolation of findings to individual-level associations must be made with caution. However, our data suggest that both environmental socioeconomic development (as measured by average household income) and public health services (as measured by number of doctors per population) are important factors on the pathway between urbanization and non-communicable disease development in Thailand. Further evaluation is warranted to understand the mechanisms underlying the link between urbanization with NCDs and NCD mortality at the individual level in Thailand.

Figure 2.1 Conceptual framework of this thesis with adaptations to incorporate findings from Chapter 2



Chapter 3 : Urban environments, obesity, and non-communicable diseases in Thailand and Southeast Asia

Summary

Introduction: Existing literature suggests an association between urbanization and obesity, as well as some non-communicable diseases (NCDs). It is not known whether such associations are uniform across age, gender and across different major NCDs in Thailand and Southeast Asia.

Objective (2): To carry out systematic reviews of existing literature on urbanization and NCDs in Thailand and Southeast Asia. The reviews will focus on the associations between i) urbanization and obesity and ii) urbanization and four major NCDs. The reviews will also explore potential sources of heterogeneity in reported associations.

Study design: Systematic review, meta-analysis and meta-regression

Exposure: Urban environments versus rural environments

Outcomes: Obesity and four major NCDs (cardiovascular disease, diabetes, chronic respiratory disease and cancer)

Key findings: Urban (vs. rural) environments are associated with obesity in countries in Southeast Asia. This association is consistent across ages, gender and countries in Southeast Asia. Stages of economic development, as measured by per capita gross national income, modified the association between urbanization and obesity as well as diabetes. There is pronounced heterogeneity among the results examining urbanization and NCDs. Urban (vs. rural) environments are positively associated with coronary heart disease, diabetes and negatively associated with rheumatic heart disease. No evidence for associations was found for cancer and cerebrovascular disease.

3.1 Introduction

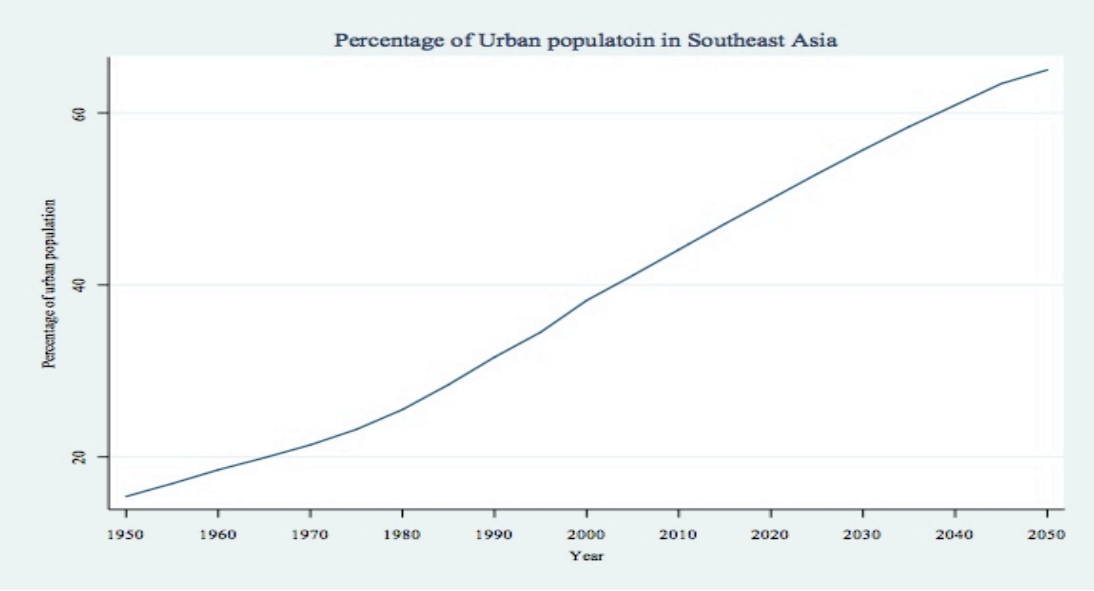
Results from the ecological study in chapter 2 suggest that there are associations between levels of urbanization and specific causes of NCD mortality in Thailand. My initial literature review found that literature on the issue of urbanization and its association with major NCDs in Thailand was limited; thus, I extended my systematic reviews to other countries in Southeast Asia.

I will begin the chapter by giving a general summary of urbanization and the non-communicable disease burden within the Southeast Asian region. This will be followed by two manuscripts representing findings from two systematic reviews. Specifically, the first systematic review focused on the association between urbanization and obesity, and the second on urbanization and four major NCDs. The systematic reviews explored potential sources of heterogeneity in reported associations.

3.1.1 Urbanization in Southeast Asia

Southeast (SE) Asia has undergone a rapid change in its patterns of urbanization in recent decades. The United Nations estimated that between 1950 and 1990, the proportion of the population living in an urban area rose from 15.4% to 31.6%. By 2010, about 50% of the 600 million people in Southeast Asia were living in an urban area and it is projected that almost two thirds (65%) will be living in an urban area by 2050 (50) (Figure 3.1).

Figure 3.1 Percentage of population living in urban environments in Southeast Asia



Source: United Nations, Department of Economic and Social Affair (51)

Within the eleven countries that make up the Southeast Asia region, the rate of urban growth and the proportion of the population living in urban areas varied between countries. Singapore has had a 100% urban population since the 1950s. In less developed countries such as Cambodia, Laos, Vietnam and Thailand, the populations in 2010 remained predominantly rural (Table 3.1).

These differences are due to each country's historical development, western colonization and also different classifications of urban populations (52, 53). Table 3.2 summarizes the definitions used for classifying urban populations in Southeast Asian countries according to the United Nations' World Urbanization prospects. Despite these differences, the key drivers of urbanization in this region, as in many low and middle income countries, are rural to urban migration and the expansion of urban areas (54, 55). It is projected that almost every country, except for Cambodia and Timor-Leste, will be more urban than rural by 2050.

Table 3.1 Proportion of urban inhabitants in Southeast Asian countries

	Percentage of Urban population			
Country	1990	2000	2010	2050
Brunei	65.8	71.2	76.5	85.9
Cambodia	15.5	18.6	19.8	37.6
Indonesia	30.6	42.0	49.9	72.1
Laos	15.4	22	33.1	64.6
Malaysia	49.8	62.0	72.0	86.0
Myanmar	24.6	27.2	32.1	56.8
Philippines	48.6	48.0	48.6	65.6
Singapore	100	100	100	100
Thailand	29.4	31.1	33.7	55.7
Timor-Leste	20.8	24.3	28.0	44.2
Vietnam	20.3	24.4	30.4	55.9
Southeast Asia	31.6	38.2	44.1	65

Source: United Nations, Department of Economic and Social Affair (51)

Table 3.2 Urban definitions currently used in Southeast Asian Countries

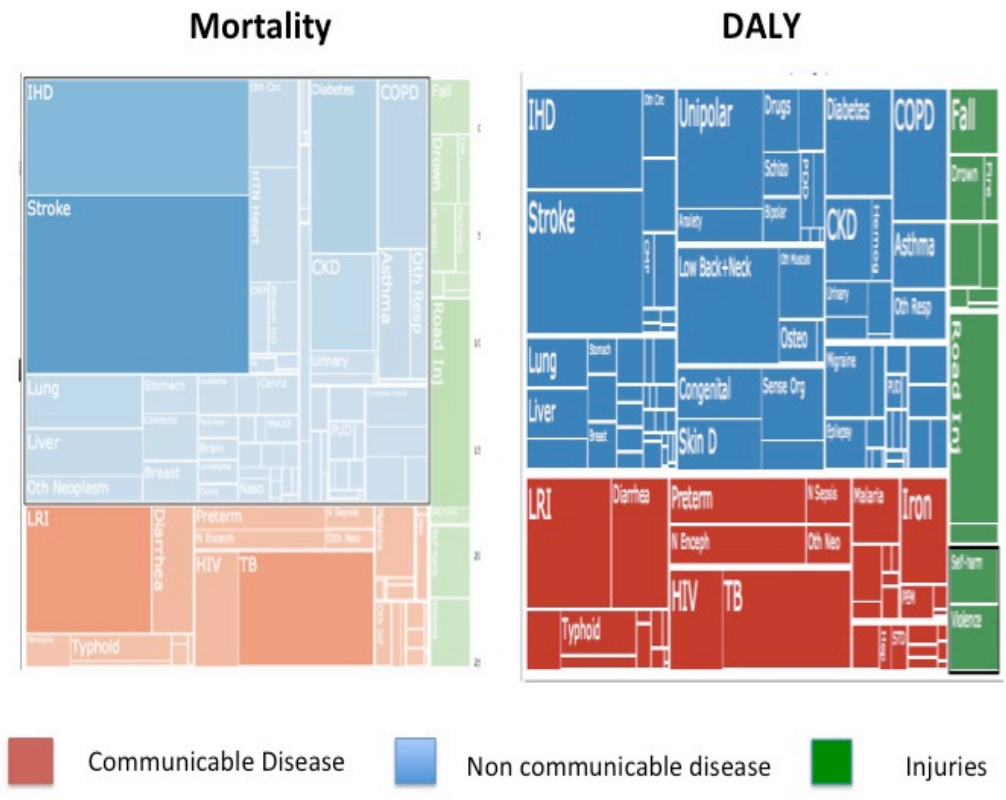
Country	Urban definition
Brunei Darussalam	Municipalities and areas having urban socio-economic characteristics.
Cambodia	Up to 1998 census: the designation of places as urban was based only on administrative criteria (e.g., municipalities of Phnom Penh, Bokor and Kep and 13 additional urban centres). Since 2005: every commune that meets at least one of the following criteria: (a) population density exceeding 200 per km, (b) percentage of male employment in agriculture below 50 percent, or (c) total population of the commune exceeding 2,000. To improve time trend comparability, the proportion urban for the 1998 census was recalculated based on the revised classification of urban areas adopted in the 2008 census.
Indonesia	Municipalities 'kotamadya', regency capitals 'kabupaten' and other places with urban characteristics.
Lao People's Democratic Republic	Urban villages were defined in the 2005 census as areas within municipal vicinity with the center of that municipality having more than 600 residents or more than 100 households. Further, the areas have to have certain urban characteristics (roads, electricity, market function, tap water supply).
Malaysia	Gazetted areas with their adjoining built-up areas and with a combined population of 10,000 persons or more. Built-up areas were areas contiguous to a gazetted area and had at least 60 per cent of their population (aged 10 years and over) engaged in non-agricultural activities. Areas had also modern toilet facilities in their housing units.
Myanmar	Not available.
Philippines	All cities and municipalities with a density of at least 1,000 persons per square kilometre; administrative centres, 'barrios' of at least 2,000 inhabitants, and 'barrios' of at least 1,000 inhabitants which are contiguous to the administrative centre, in all cities and municipalities with a density of at least 500 persons per square kilometre; and all other administrative centres with at least 2,500 inhabitants.
Singapore	City of Singapore, including residents and non-residents.
Thailand	Municipalities. In 1999, 981 sanitary districts were reclassified as 'Tambon' municipalities and data for proportion urban were adjusted retrospectively.
Timor-Leste	Dili (capital) and other small settlements (sucos) defined as urban. For 2004, the functional definition of urban of the National Statistics Directorate of Timor-Leste was used.
Vietnam	Places with 4,000 inhabitants or more.

Source: United Nations, Department of Economic and Social Affair (56).

3.1.2 Burden of non-communicable disease in Southeast Asia

During periods of increasing urbanization in Southeast Asia, the burden of non-communicable disease has also increased. According to the Global Burden of Disease (GBD) project, between 1990 and 2010, the proportion of deaths and disability-adjusted life years (DALYs) due to NCDs in this part of the world has increased from 47.9% to 65.2% for mortality and 40.3% to 59.1% for DALYs (Figure 3.2).

Figure 3.2 Proportion of deaths and DALYs due to NCDs as estimated in 2010 for Southeast Asia using data from the Global Burden of Disease Study



Source: Institute for Health Metrics and Evaluation (57)

In 1990, data from the Global Burden of Disease Study estimated that only two of the top ten leading causes of DALYs were NCDs. Three of the four major NCDs (cardiovascular disease, chronic pulmonary disease and diabetes) ranked in the top 10 causes of DALYs in the 2010 Global Burden of Disease report. Diabetes was the 18th ranked cause in 1990 but became the 10th ranked cause in Southeast Asia (Table 3.3). Six of the top ten leading causes of DALYs in Southeast Asia were NCDs in the 2010 report.

Table 3.3 Leading causes of DALYs in Southeast Asia between 1990 and 2010 using data from the Global Burden of Disease Study

1990	
Rank	Disease
1	Lower respiratory infection
2	Diarrheal Disease
3	Tuberculosis
4	Stroke
5	Preterm birth complications
6	Ischemic heart disease
7	Malaria
8	Road injury
9	Congenital anomalies
10	Iron deficiency anemia
11	Major depressive disorder
13	COPD
14	Low back pain
18	Diabetes

2010	
Rank	Disease
1	Stroke
2	Tuberculosis
3	Ischemic heart disease
4	Lower respiratory infection
5	Road Injury
6	Major depressive disorders
7	Low back pain
8	Diarrheal disease
9	COPD
10	Diabetes
11	Preterm birth complication
14	Iron deficiency anemia
16	Congenital anomalies
27	Malaria

Source: Institute for Health Metrics and Evaluation (57)

Not surprisingly, if we look at the leading risk factors that contribute to DALYs in the Southeast Asian region, they are common risk factors for multiple NCDs. At the top of the list in 2010 were high blood pressure, smoking, low fruit and vegetable intake and high plasma glucose. Obesity, a key risk factor for diabetes and other major NCDs, jumped from the 23rd ranked risk factor in 1990 to 9th in 2010 (Table 3.4).

Table 3.4 Leading risk factors based on DALYs in Southeast Asia between 1990 and 2010 using data from the Global Burden of Disease Study

1990	
Rank	Risk factors
1	Household air pollution
2	Childhood underweight
3	Smoking
4	Suboptimal breast feeding
5	High blood pressure
6	Low fruit
7	Iron deficiency
8	High fasting plasma glucose
9	Alcohol use
10	Ambient particular matter (PM) pollution
11	High sodium
12	Low vegetables
23	High body mass index

2010	
Rank	Risk factors
1	High Blood pressure
2	Smoking
3	Household air pollution
4	Low fruit
5	High fasting plasma glucose
6	Alcohol use
7	High sodium
8	Physical inactivity
9	High body mass index
10	Low vegetables
11	Ambient particular matter (PM) pollution
12	Iron deficiency
13	Childhood underweight
14	Suboptimal breast feeding

Source: Institute for Health Metrics and Evaluation (57)

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LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

RESEARCH PAPER COVER SHEET

Urban environments and obesity in Southeast Asia: A systematic review, meta-analysis and meta-regression

PLEASE NOTE THAT A COVER SHEET MUST BE COMPLETED FOR EACH RESEARCH PAPER INCLUDED IN A THESIS.

SECTION A – Student Details

Student	Chaisiri Angkurawaranon
Principal Supervisor	Dorothea Nitsch
Thesis Title	Urbanization and internal migration as risk factors for non-communicable disease in Thailand

If the Research Paper has previously been published please complete Section B, if not please move to Section C

SECTION B – Paper already published

Where was the work published?	PloS One		
When was the work published?	August 2013		
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion			
Have you retained the copyright for the work?*	Yes	Was the work subject to academic peer review?	Yes

**If yes, please attach evidence of retention. If no, or if the work is being included in its published format, please attach evidence of permission from the copyright holder (publisher or other author) to include this work.*

SECTION C – Prepared for publication, but not yet published

Where is the work intended to be published?	
Please list the paper's authors in the intended authorship order:	
Stage of publication	

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	Details of contribution are stated in the manuscript. In consultation with my supervisors, I conceived the design of the review, screened abstracts, extracted the data and analyzed the data. I wrote the manuscript and coordinated all co-authors' feedback and comments. I am first and corresponding author for the article

Student Signature: _____ **Date:** 13 April 2015

Supervisor Signature: _____ **Date:** 9/4/15

The evidence presented in Figure 3.1 and Table 3.1 above suggests that the Southeast Asian region is becoming more urbanized. During such a period of urbanization, the burden from risk factors for NCDs, as well as NCDs themselves, has increased according to the Global Burden of Disease Study.

However, based on the conceptual framework proposed in section 1.4 above, and the findings described in Chapter 2, urbanization may also lead to an increase in environmental factors that may have a protective effect on the population against NCDs, such as increasing socioeconomic development and better access to care. While research from developing countries, including countries in Southeast Asia, has suggested that urbanization is associated with an increased prevalence in many risk factors for NCDs, and some NCDs themselves, (58) it is uncertain whether these associations are uniform across the Southeast Asian region (59, 60).

3.2 Research articles

My review of the literature resulted into two separate publications:

1. Urban Environments and Obesity is Southeast Asia: A Systematic review, Meta-analysis and Meta-regression
2. Urbanization and non-communicable disease in Southeast Asia: a review of current evidence

Both publications shared the same protocol for abstract screening, inclusion and exclusion criteria and methods of quality of appraisal, which are described in each manuscript. Due to the peer review process, the search procedure (duration of review and number of databases used) differed slightly between the two publications. The search strategy, flow charts, characteristics of studies, funnel plots and summary of bias within studies were submitted as supporting documents in both publications and can be found in Appendices B and C of this thesis.

PLOS ONE

RESEARCH ARTICLE

Urban Environments and Obesity in Southeast Asia: A Systematic Review, Meta-Analysis and Meta-Regression

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Competing Interests: The authors have declared that no competing interests exist.

Abstract

Many environmental factors contribute to the rise in prevalence of obesity in populations but one key driver is urbanization. Countries in Southeast (SE) Asia have undergone rapid changes in urbanization in recent decades. The aim of this study is to provide a systematic review of studies exploring the relationship between living in an urban or rural environment (urbanicity) and obesity in Southeast Asia. In particular, the review will investigate whether the associations are uniform across countries and ages, and by sex. The literature search was conducted up to June 2014 using five databases: EMBASE, PubMed, GlobalHealth, DigitalJournal and Open Grey. Forty-five articles representing eight of the eleven countries in SE Asia were included in the review. The review found a consistent positive association between urbanicity and obesity in countries of Southeast Asia, in all age groups and both genders. Regional differences between the associations are partly explained by gross national income (GNI). In countries with lower GNI per capita, the association between urbanicity and obesity was greater. Such findings have implications for policy makers. They imply that population level interventions need to be country or region specific, tailored to suit the current stage of economic development. In addition, less developed countries might be more vulnerable to the negative health impact of urbanization than more developed countries.

Introduction

The increasing prevalence of obesity is a phenomenon happening worldwide, with global prevalence almost doubling since 1980 [1]. Previously considered an epidemic of developed countries, in recent years the growing burden of obesity has affected most regions, including Southeast Asia [2]. In Southeast Asia, like other parts of the world, obesity is considered one of the key risk factors for chronic and non-communicable disease [3, 4]. Its burden on health is reflected by the Global Burden of Disease project report [5]. In 1990, high BMI was ranked the 23rd most important risk factor for SE Asia, and by 2010 it was 9th [6].

Many environmental factors contribute to the rise in prevalence of obesity, but one key driver is urbanization [7]. The National Institute of Health defines urbanization as "the process whereby a society changes from a rural to an urban way of life. It refers also to the gradual increase in the proportion of people living in urban areas" [8].

The framework proposed by the International Obesity Taskforce has outlined possible causal pathways between urbanization and obesity [9]. In short, factors operating at the national and international level, such as urbanization, will influence the environment of the individual at the community and family level. Such environmental influences are likely to result in lower levels of physical activity and energy expenditure, coupled with a high energy and high fat diet [10].

Countries in Southeast (SE) Asia have undergone a rapid increase in urbanization in recent decades. The proportion living in an urban area rose from 15% to 32% between 1950 and 1990. By 2010, about 50% of the 600 million people in SE Asia were living in an urban area [11].

Since most studies on the impact of urbanization on health have focused on urban-rural differences [12], the aim of this study is to provide a systematic review of studies exploring the relationship between urban and rural environments (urbanicity) and obesity in Southeast Asia. In particular, the review will investigate whether the associations are uniform across countries and ages, and by sex.

Methods

Search strategies and procedures

The literature search was conducted up to June 2014 using five databases. Three standard international databases in the field of medicine, epidemiology and public health were used: EMBASE (from 1974), PubMed (from 1946), GlobalHealth (from 1910). We used one regional database: DigitalJournal (from 2007), which is an electronic journal database from SE Asian member countries and currently health science journals from Indonesia, Myanmar and Thailand can be searched electronically [13]. We used one database for grey literature and unpublished research: Open Grey (from 1980) [14]. Full articles of relevant abstracts were retrieved through the London School of Hygiene and Tropical Medicine and

Chiang Mai University's network. We also conducted an additional cited-reference search from articles included in the review to pick up relevant published and unpublished articles. The search strategy using EMBASE can be found in the supporting document. (Table S1 in File S1)

Inclusion and exclusion criteria

Criteria for articles to be included in the review were that they must:

i) Have a clearly defined measure for an urban environment
ii) Have a defined measure of obesity
iii) Have a direct control group or comparison group such as a semi-urban or rural comparison group
iv) Report (or have data to be able to calculate) quantitative measures for the association between urban/non-urban environments and obesity
v) Be published in English.

The eleven countries in SE Asia included in the review were Brunei Darussalam, Cambodia, Indonesia, Laos PDR, Malaysia, Myanmar, Philippines, Thailand, Timor-Leste, and Vietnam and Singapore. However, studies from Singapore were not expected, as the entire country was considered urban. As long as the inclusion criteria were met, we did not have restrictions on the type of study design included. We excluded any studies conducted outside the SE Asian region or studies with historical controls where the prevalence of obesity was measured at different time points within the same study.

Screening and data extraction

Titles and abstracts were screened independently by two reviewers (CA and WJ) and classified into three subgroups:

i) Clearly not relevant,
ii) Potentially relevant, and
iii) Relevant to review.

Studies that were classified as 'clearly not relevant' by both reviewers were excluded during the initial abstract screening process. Full text articles, which were classified as 'potentially relevant' or 'relevant articles' by one of the reviewers, were retrieved and reviewed by the lead author (CA). Reasons for exclusion (if relevant) were documented (Table S2 in File S1). Authors were contacted if full text articles were not retrievable or if additional information was needed to make a decision on inclusion or exclusion.

A small sample of literature included in the review was used to derive a standard data abstraction form. Information was collected on the lead author's name and year of publication, country and year of fieldwork, study design and sample size, characteristics of the study population (such as age and gender distribution), the definition of urban and non-urban/rural environment, and how the outcome of interest was defined and measured. In addition, the per capita

Gross National Income (GNI) corresponding to the country and year of fieldwork was included. If year of fieldwork was not stated, it was assumed to be three years prior to year of publication. For the results section, prevalence and odds ratios were considered to be the main summary measures of interest. Information was also collected on which factors were controlled for if adjusted ratio measures of effect were reported. (Tables S3–S15 in File S1)

Definition of variables for meta-regression

For each observation included in the meta-regression, the following definitions were used to define six variables:

1) Country of conduct: Based on the total number of observations from each country, the variable ''country of conduct'' was grouped according to geographical proximity and level of per capita GNI into four groups. They consisted of i) Malaysia and Philippines, ii) Thailand, iii) Vietnam and Laos, and iv) Indonesia and Timor-Leste
2) Per capita GNI (US dollar) corresponding to year of field work and county of conduct, as reported by the United Nations was obtained [15]. This was categorized into three groups: i) $<$1,500 dollars, ii) 1,500–2500 dollars iii) $>$2,500 dollars
3) Year of fieldwork was categorized into two groups, whether the study was conducted within i) ten years (2004–2013) or ii) earlier (up to 2003)
4) Age of study population was categorized into two groups: i) children ($<$18 years old) or ii) adults ($\geqslant$18 years old)
5) Sex of study population was categorized into three groups: i) men only, ii) women only, or iii) both (results adjusted for sex)
6) Obesity classification: The obesity definition differed between individual studies. To explore the different obesity classifications as a source of heterogeneity, the variable ''obesity classification'' was categorized into three groups according to whether the study used a i) non BMI classification (using waist circumference), ii) a BMI classification (or corresponding percentiles) defining obesity as $\geqslant$23 kg/m^2 or $\geqslant$25 kg/m^2, or iii) a BMI classification (or corresponding percentiles) defining obesity as $\geqslant$30 kg/m^2.

Quality appraisal

The risk of bias within individual studies was assessed according to the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach [16] as recommended by the Cochrane handbook [17]. In summary, information was collected on potential risk of i) selection bias, ii) confounding and residual confounding, and iii) information bias in the classification of an urban environment status and in the measurement of obesity. Information bias in exposure and outcome variables was also further assessed as likely to be differential or non-differential. Additional limitations of each study were

recorded. We used the Preferred Reporting Items for Systematic Review and Meta-Analysis: The PRISMA statement as guidelines for reporting our results [18]. (Table S16 in File S1)

Data analysis

For the results (odds ratios) of an individual article to be included in the meta-analysis, it must have been adjusted for age and sex, or stratified by sex and adjusted for age. If an article presented additional results adjusting for other covariates (such as socioeconomic status), we used the age and sex adjusted results. Additional adjustments could be considered over-adjustments for factors on the causal pathway between urbanicity and obesity.

We took the effect size (odds ratio) as reported by each article. If an article reported summary measures for more than one independent dataset, all available summary measures were used. If there was more than one summary measure reported from a single dataset, such as reporting by different gradients of urbanicity or with additional stratification by sex, we used the most reliable estimate (largest sample size) and the most conservative definition of obesity using BMI classifications. If odds ratios were not directly reported, when possible, we calculated crude odds ratios and CIs based on the proportions provided. However, crude odds ratios were not included in the meta-analysis, as these were not adjusted for age and sex.

High degrees of heterogeneity among studies were expected due to differences in the age distribution and regions of the study populations. Three main subgroup meta-analyses were pre-specified: i) analysis in children; ii) analysis in adult populations; and iii) analysis by country or countries.

In the absence of statistical heterogeneity, the fixed effect model using the inverse variance method was use to summarize the measures of effect. If there was evidence for heterogeneity, the DerSimonion and Laird approach for random effect models was used [19]. Heterogeneity was evaluated using Cochran's Q and I^2 statistics. Combining results with high heterogeneity may lead to misleading results [20]. If there was high heterogeneity, $I^2>80\%$, the summary measures were displayed using Forest plots without combining effects. Funnel plots were used to evaluate publication bias for the meta-analyses.

Sensitivity Analyses

Random effect meta-regression [21] was used to explore the role of age, gender, time periods, obesity classification, country of conduct, and stage of economic development as measured by per capita GNI as sources of heterogeneity for the association between urban/rural environment and obesity. In presence of potential publication bias, the trim and fill technique was used to explore the its impact [22]. Stata 12 was used in all analyses.

Results

Characteristics of studies

Forty-five studies met the inclusion criteria, and all were cross sectional in design (Figure 1). Eight of the eleven countries in SE Asia were covered by these 45 studies. Thirteen studies were from Malaysia, twelve from Vietnam, nine from Thailand, six from Indonesia, two from Laos, and one each from Philippines, Myanmar and Timor-Leste. Countries for which we found no studies were Brunei Darussalam, Cambodia and Singapore. Twenty-seven studies focused only on adults, seventeen focused only on children and/or adolescents (age <18 years old), and one study included both children and adults but reported estimates separately [23]. Two studies were published in1988 and 1992, the rest were published after 2000. Detailed characteristics of each study can be found in Tables S3–S8 in File S1.

The urban environment and obesity in children

Eighteen studies included children, whose ages ranged between 2 and 18. Of these studies, six were from Vietnam [23, 24, 25, 26, 27, 28], six from Malaysia [29, 30, 31, 32, 33, 34], three from Thailand [35, 36, 37], two from Indonesia [38, 39] and one from Laos [40]. All classifications of obesity were age-and-gender specific, but studies differed in the criteria and the cutoff points used for obesity. Six studies used the International Obesity Task Force definition [24, 27, 29, 30, 38, 40], eleven studies used the World Health Organization's standard [23, 24, 25, 28, 31, 32, 33, 34, 35, 37, 39], and one study from Thailand used its own National standard [36].

Sixteen studies, consisting of at least one from each of the five countries presented, reported a significant association between an urban environment and obesity in children [23, 24, 25, 26, 27, 28, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40]. The two studies that did not find a significant association were from Malaysia [29, 30]. Two studies explored a gradient effect between urbanicity and obesity. The study by Julia et al, conducted in Indonesia compared children in three different exposure groups: i) urban, ii) urban poor and iii) rural. The study found that although there were differences in obesity between urban and rural children, these differences were less pronounced when urban poor children were compared with rural children [38]. A gradient effect was also seen in the study by Tang et al, conducted in Vietnam [27]. The adjusted odds ratio for the wealthy urban population compared to the semi-rural and rural population was 5.53 (95% CI 2.42 to 14.16), and the odds ratio for less wealthy urban versus the semi-rural and rural population was 3.82 (95% CI 1.73 to 9.56). Individual results for each of the eighteen studies in children can be found in Tables S9–S11 in File S1.

Sixteen of the eighteen studies were included in the meta-analysis [24, 25, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40]. The random effect estimates gave a pooled odds ratio of 1.34 (95% CI 1.12 to 1.59) in studies from Malaysia and 2.68 (95% CI 1.98 to 3.63) in studies from Thailand. The pooled

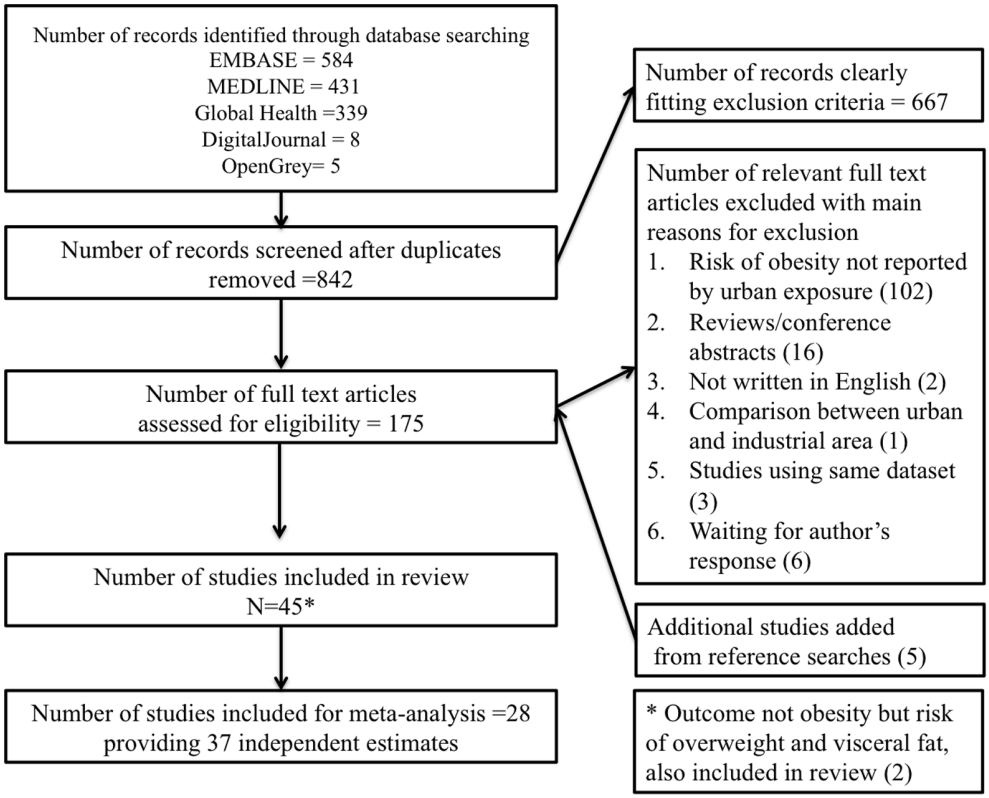

Figure 1. Flow chart of articles included in the review.

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odds ratio was 3.66 (95% CI 2.12 to 6.30) in studies from Indonesia and 4.16 (95% CI 2.51 to 6.91) in studies from Vietnam and Laos (Figure 2).

The urban environment and obesity in adults

Twenty-eight studies included adults, whose ages ranged between 18 to over 80. Of these studies, seven each were from Vietnam [23, 41, 42, 43, 44, 45, 46] and Malaysia [47, 48, 49, 50, 51, 52, 53], six were from Thailand [54, 55, 56, 57, 58, 59], four from Indonesia [60, 61, 62, 63] and one each from the Philippines [64], Timor-Leste [65] and Myanmar [66] and Laos [67]. Twelve studies, representing Vietnam [23, 41, 44], Thailand [54, 55, 56, 57, 59], Malaysia [47, 49, 50] and Timor-Leste [65], were considered nationally representative of the adult population of these nations. Other study populations which were not considered representative of the national populations included an indigenous population in Malaysia [48], Thai university students [58] and an elderly Malaysian and Laotian populations [51, 67].

Most studies reported obesity as measured by BMI, although using different cut-off points to define obesity. Two reported waist circumference as the only measure of obesity [49, 54]. Fuke et al studied visceral fat in adults from Indonesia

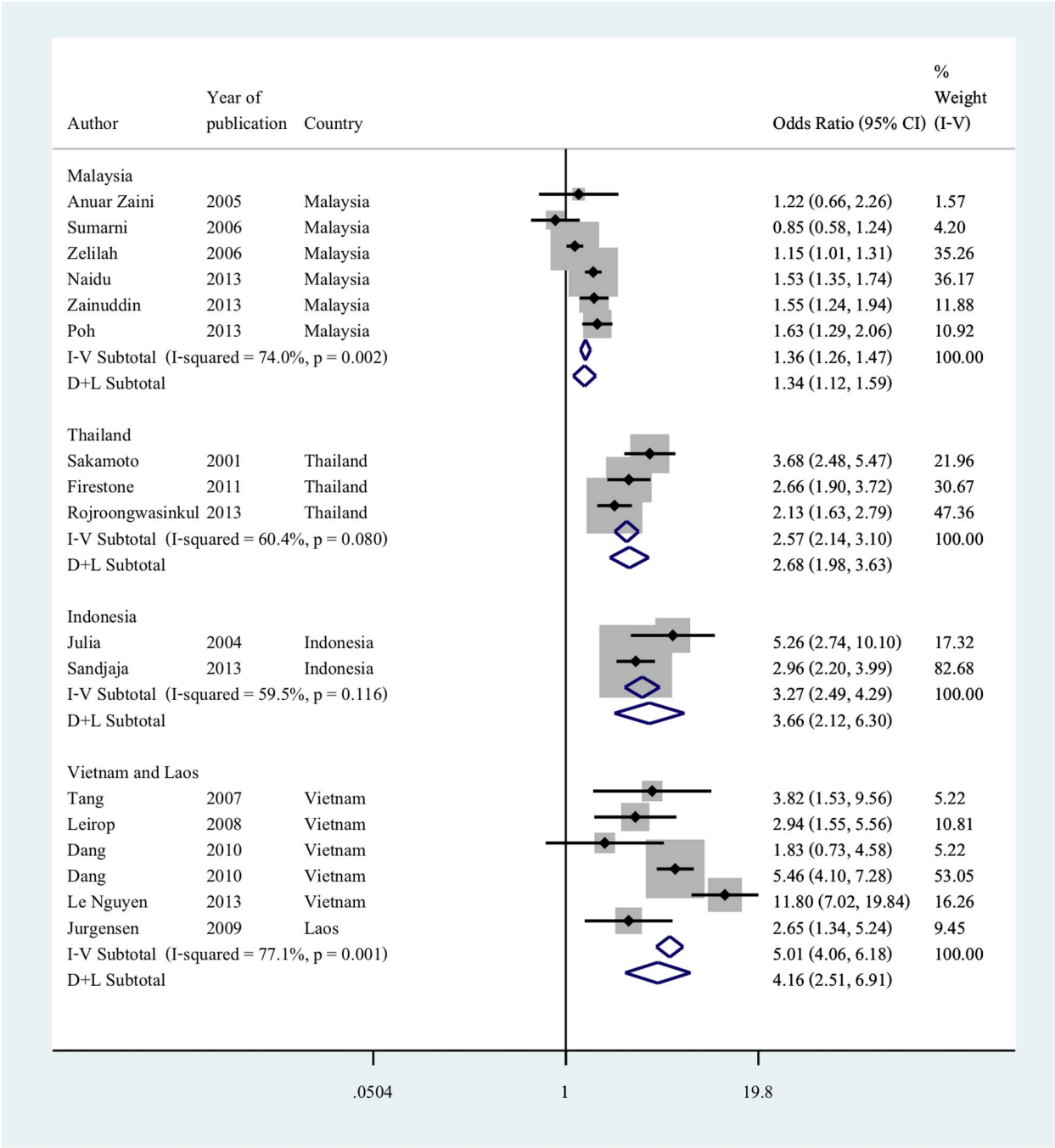

Figure 2. Adjusted odds ratio for living in an urban environment and obesity in children by country or countries. Reference group is living in a rural environment; Odds ratios are adjusted for age and sex; countries are grouped according to geographical proximities and gross national income per capita.

doi:10.1371/journal.pone.0113547.g002

with normal BMI and did not find an association between urban-rural differences and visceral fat [62]. Seven studies did not find an association between an urban environment and obesity in adults, four from Malaysia [47, 49, 52, 53] and one each from Vietnam [43], Indonesia [63] and Philippines [64]. Of these seven studies, only two studies were adjusted for both age and gender [53, 64]. Rasiah et al additionally adjusted for level of education [53]. Dahly et al used an urbanicity score as their exposure rather than directly comparing outcomes by urban and rural status [64]. Four studies looked for a gradient effect between urbanicty and obesity in adults [42, 43, 60, 64], all of which reported higher prevalence of obesity in populations with greater levels of urbanization. Results for each of the twenty-eight studies in adults can be found in Tables S12–S15 in File S1.

Twelve studies, from six nations, met the criteria for meta-analysis by reporting age and sex adjusted odds ratio. The six nations represented were grouped into four groups taking into consideration geographical proximities and/or similar gross national income level: i) Malaysia and Philippines, ii) Thailand, iii) Indonesia and Timor-Leste and iv) Vietnam (Figure 3). In studies from Malaysia and Philippines, there was no heterogeneity between the results (I^2=0, p=0.836). The pooled random effect estimates gave an odds ratio of 1.20 (95% CI 1.10 to 1.32). All adjusted estimates between urbanicity and obesity from Thailand were statistically significant, but had very high heterogeneity (I^2=93.3, p<0.001). The results from Indonesia and Timor-Leste showed moderate heterogeneity (I^2 46.7, p=0.153), the random effect model gave an adjusted odds ratio of 3.0 (95% CI 2.17 to 4.14). There was moderate heterogeneity between the results from Vietnam (I^2=59.2, p=0.044), and the pooled random effect odds ratio was 2.12 (95% CI 1.68 to 2.69).

Sources of heterogeneity: Results from Meta-regression

Twenty-eight studies, contributing thirty-seven independent age and sex-adjusted estimates, were included for meta-regression. Exploring six potential sources of heterogeneity separately, results suggested that there was heterogeneity in the association between urbanicity and obesity both within country and between countries of SE Asia (Table 1). Country setting drove much of the heterogeneity in these estimates, which in turn may be related to the economic output of that country at the time the studies were conducted. The pooled measure of association between urbanicity and obesity in countries such as Malaysia and Philippines (OR 1.29, 95% CI 1.14 to 1.45) was smaller than the association seen in lower income countries such as Indonesia and Timor-Leste (OR 3.14, 95% CI 2.22 to 4.46) (Table 1). Figure 4 presents the association between urbanicity and obesity by GNI per capita. There was strong evidence that the association is greater when GNI per capita was smaller. No other sources of heterogeneity were statistically significant but there was some weak evidence that effect size in children may be larger than adults (p=0.07) (Table 1). When including per capita GNI, country/countries of conduct, and other possible sources of heterogeneity (age and sex of study population, whether the study was conducted within the

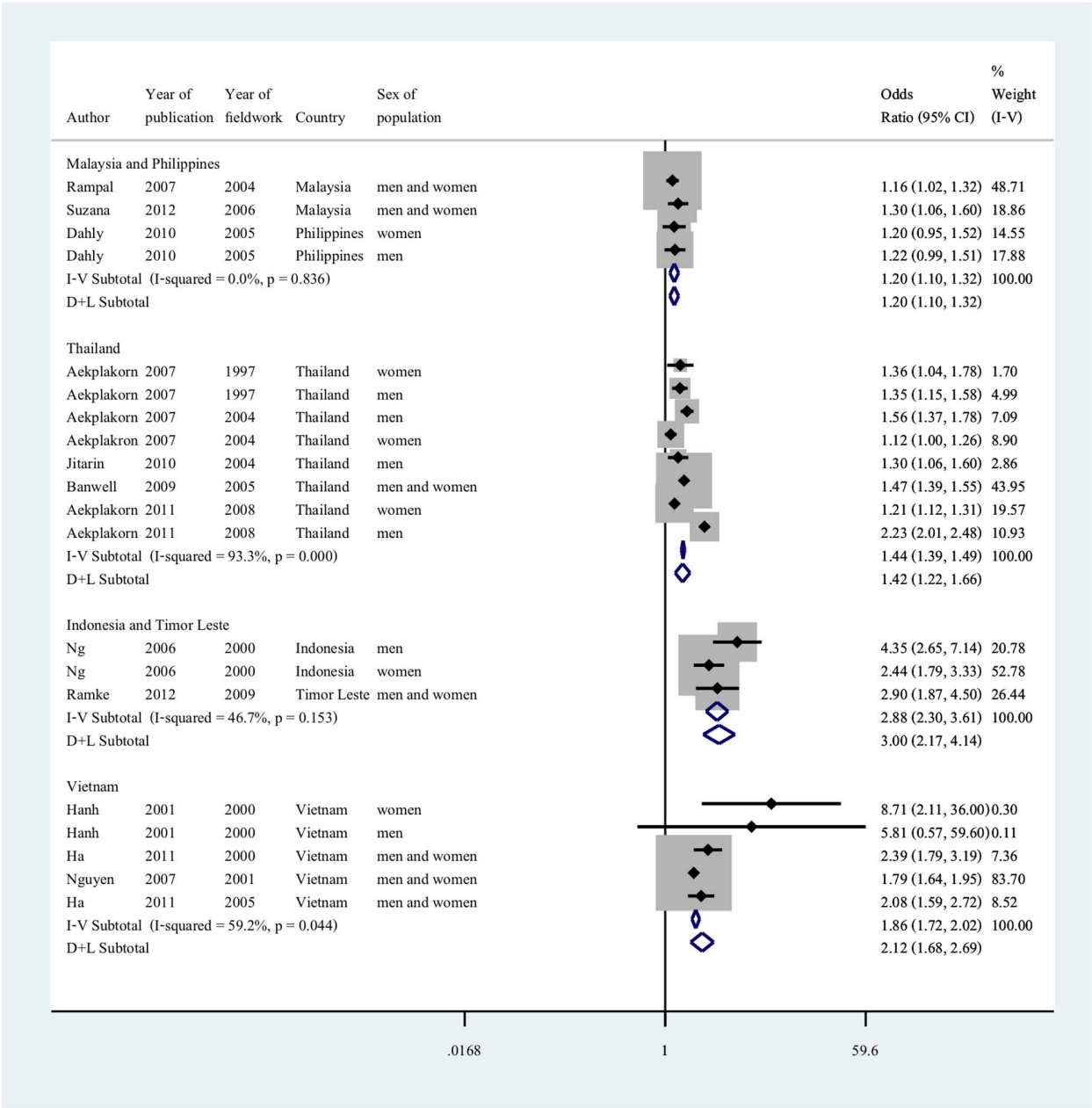

Figure 3. Adjusted odds ratio for living in an urban environment and obesity in adults by country or countries. Reference group is living in a rural environment; Odds ratios are adjusted for age and sex (or adjusted for age if stratified by sex); countries are grouped according to geographical proximities and gross national income per capita.

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past ten years or before, and the type of BMI classification for obesity used), these six variables together were able to explain 22.4% of the heterogeneity between results.

Table 1. Adjusted odds ratios (OR) for living in an urban environment and obesity using stratification by country/countries, per capita GNI, year of fieldwork, sex, age of study population and criteria for obesity.

Stratification	Number of observations	OR for living in an urban environment (95% CI)	P-value	I^2	p-values*	F-ratio (p-value)**
None	37	1.99 (1.64 to 2.41)	<0.001	92.1%	<0.001	–
Country/countries						12.16 (<0.001)
Philippines and Malaysia	10	1.29 (1.14 to 1.45)	0.001	62.8%	<0.001	
Thailand	11	1.66 (1.30 to 2.11)	0.001	93.2%	<0.001	
Vietnam and Laos	11	3.36 (2.14 to 5.27)	<0.001	90.6%	<0.001	
Indonesia and Timor-Leste	5	3.14 (2.22 to 4.46)	0.001	40.4%	<0.001	
Per capita GNI (US dollars)						12.00 (<0.001)
<1,500	14	3.42 (2.42 to 4.84)	<0.001	89.4%	<0.001	
1,500–2,500	10	1.62 (1.20 to 2.18)	<0.001	86.7%	<0.001	
>2,500	13	1.50 (1.23 to 1.82)	0.01	91.9%	<0.001	
Year of field work						0.78 (0.383)
2004 to 2013	20	1.85 (1.45 to 2.37)	<0.001	92.4%	<0.001	
Up to 2003	17	2.22 (1.60 to 3.09)	<0.001	91.9%	<0.001	
Sex of study population						0.94 (0.407)
Men only	7	1.76 (1.14 to 2.73)	0.020	90.8%	<0.001	
Women only	6	1.47 (0.89 to 2.43)	0.106	82.8%	<0.001	
Both	24	2.19 (1.70 to 2.81)	<0.001	92.2%	<0.001	
Age of population						3.57 (0.067)
Children	17	2.43 (1.72 to 3.43)	<0.001	92.9%	<0.001	
Adults	20	1.65 (1.36 to 1.99)	<0.001	90.9%	<0.001	
Obesity classifcation						1.18 (0.318)
Non BMI classifciation (using WC)	3	2.10 (0.53 to 8.28)	0.145	98.0%	<0.001	
Obesity defined BMI⩾23 or 25	29	2.13 (1.69 to 2.67)	<0.001	91.1%	<0.001	
Obesity defined as BMI⩾30	5	1.39 (0.90 to 2.16)	0.104	80.9%	<.0.001	

Twenty eight studies contributed to 37 independent age and sex adjusted estimates (Figure 1); Reference group is living in a rural environment; GNI gross national income; WC waist circumference;
* p-value for heterogeneity chi-square;
** Likelihood ratio test for heterogeneity between subgroup by meta-regression, providing F-ratio and p-values.

doi:10.1371/journal.pone.0113547.t001

Sensitivity analysis

The funnel plots suggested that there was potential for publication bias (Figure S1 and Figure S2). However, sensitivity analysis using the trim-and fill technique did not materially alter any of the results seen. (Table S17 in File S1)

Discussion

To our knowledge, this is the first systematic review to examine the association between living in an urban environment and obesity in SE Asia. The review found consistent positive associations between urbanicity and obesity in countries of Southeast Asia, in both genders and all age groups. We found that different

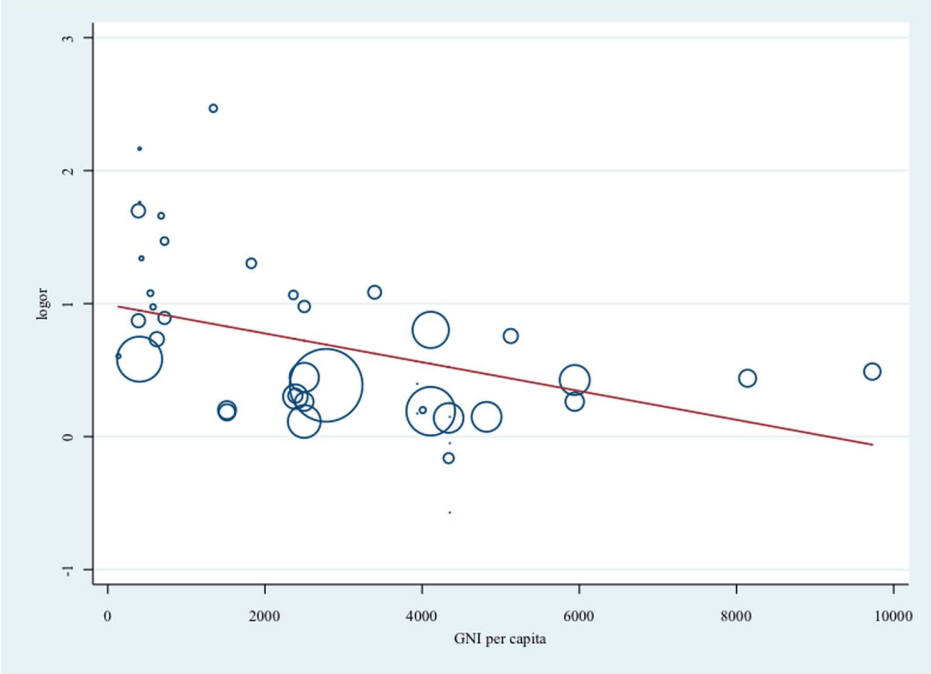

Figure 4. Association (log odds ratio) between living in an urban environment and obesity by GNI per capita. Size of circles reflects sample size. Higher log odds ratio (logor) reflect larger effect size for living in an urban environment and obesity; gross national income (GNI) per capita in US dollar corresponding to year and country of fieldwork; Reference group is living in a rural environment.

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country settings contributed strongly to the source of heterogeneity between the estimates. There was strong evidence that the association between urban environments and obesity is modified by the country's GNI per capita and this partly explained the observed heterogeneity of the estimates.

Sources of Heterogeneity: Regional differences

Associations between urban environments and obesity were expected to vary between countries because of different cultures, and varying political and socioeconomic environments. When the data were grouped according to country or countries with close geographic proximity and similar economic status, some of the observed heterogeneity decreased. The notable exception was Thailand. However, these studies differed in other ways: one was conducted in university students [58], one used abdominal obesity [56] and another used a cut of point of BMI$\geqslant$23 kg/m^2 [33] as the outcome.

A systematic review from developed countries exploring the role of geographic environment on cardiometabolic risk factors, such as obesity, was conducted by Leal and Chaix [68]. The review found that living in a rural environment and areas with lower socioeconomic level was associated with higher BMI but did not look at the effect modification between these two exposures. The review by Leal

and Chaix may not be generalizable to developing countries of SE Asia which may explain why we found the opposite, i.e. that the association between living in an urban environment and obesity was positive. Monteiro et al combined nationally representative data on women from 37 developing countries to examine the association between obesity and inequality [69]. The study found that there was interaction between the women's socioeconomic status (SES) and the country's Gross Nation Product (GNP), which was seen as a measure of the environmental level of economic development. Specifically, if the country's GNP per capita was less than 2,500 dollars, high SES was positively associated with obesity. If the country's GNP was greater than 2,500 dollars, the risk of obesity was highest for the poor. These observations support the findings of our review.

One explanation for an interaction between income (or SES) and urbanization (as a development process) on obesity could be sociocultural and behavioral in nature. It could be that in less developed countries people with higher incomes have easier access to a plentiful food supply. Whereas in more developed countries, people with higher income have options to counter-balance the impact of an obesogenic environment [70]. The 'developmental origins' theory [71] can also be used to help explain such interactions. If early life under-nutrition is associated with rapid weight gain in childhood and risk of obesity in adults, less developed countries would be more vulnerable to the obesogenic impact of urbanization.

Other sources of heterogeneity between studies

This review also examined whether the association between urban environment and obesity differed between children and adults, and by gender. We found some very weak evidence that the effects were more pronounced in children than in adults. Literature has suggested that for childhood obesity, growth and puberty may interact with the obesogenic environment associated with urbanization [72]. The size of the effect may be reduced for children around puberty as they experience a growth spurt. In SE Asia where the prevalence of obesity is relatively low, there could be a cultural expectation for women to remain slim [2]. However, we did not find evidence that gender modified the association between urban environment and obesity. The current meta-analysis may be underpowered to detect an interaction with gender, and the high heterogeneity between studies could limit generalization of a potential finding.

Strengths and limitations

The review had several limitations. It is possible that not all relevant articles on urban environment and obesity in SE Asia were included in the review. Omitted studies could have been published in other formats such as country reports or could have been published in other databases or in other languages. All studies were of cross-sectional design which, in principle, is susceptible to reverse causality. However, it is difficult to imagine how obesity would drive

urbanization. All studies, except one [64], included in this review examined the association between an urban environment and obesity through comparing outcomes in rural and urban settings. Such comparisons do not reflect urbanization as a process, and offer little insight into the underlying mechanisms for the associations found. The failure to account for length of stay in an urban area, transient migration (urban migration to work during parts of the year) and economic diversity within urban areas may have caused bias in the estimates and limit the interpretation of findings. However, even if these biases existed, they are likely to lead to an underestimate of the association between exposure to an urban environment and obesity.

The strengths of the study include conducting the literature search using a regional SE Asian database and exploring the sources of heterogeneity using meta-regression. There was good inter-rater agreement between the reviewers (Kappa 0.85) (Table S18 in File S1). We also reviewed all articles classified as 'potentially relevant' or 'relevant' irrespective of agreement between the reviewers. Although there was potential for publication bias, our results did not materially alter in the sensitivity analysis. The evidence for interactions between urban living and obesity with the country's GNI per capita was unlikely to be spurious effects due to poorly conducted studies as most studies included in the meta-analysis were assessed to be at low risk of bias (Table S19 and Table S20 in File S1).

Unanswered questions and future research

A better quantification of specific environmental characteristics, carrying out migrant studies, and taking a life-course approach to examine the development of obesity within individuals over time would be useful to enable understanding of the mechanisms underlying the link between urban environments and obesity in this region [72, 73].

Conclusions and Policy Implications

This systematic review found a consistent positive association between living in an urban environment and obesity in countries of Southeast Asia, across all age groups and both genders. Regional differences between the associations are partly explained by gross national income (GNI). The association between urban environments and obesity was stronger in countries with lower GNI per capita. Exposure to an urban environment was associated with 29% higher odds of obesity in Malaysia and Philippines (pooled OR 1.29, 95% CI 1.14 to 1.45). In countries with lower GNI such as Vietnam and Laos, exposure to urban environment was associated with a three-fold increase in obesity (pooled OR 3.36, 95% CI 2.14 to 5.27).

Our findings imply that population level interventions need to be country or region specific, tailored to suit the stage of economic development [74]. Developing countries such as those in SE Asia may be more vulnerable to the

negative health impacts of urbanization than more developed countries. A recent report from Malaysia in 2013 highlighted that economic growth has accelerated the problem of obesity though availability of high calorie diets and decreased physical activity in the population. The authors suggested that the creation of healthy infrastructure for active transportation, protection of natural environment, along with healthy and affordable food resources are vital for sustainable economic development [75]. Environmental interventions are recognized as a promising strategy to combat obesity and other obesity-related conditions [76, 77]. School based interventions have been successful in reducing obesity in Singapore [78].Other countries in SE Asia, such as Thailand and Indonesia, have also made progress by adopting population approaches to prevent and control obesity [79].

Supporting Information

Figure S1. Funnel plots of results included in meta-analysis.
doi:10.1371/journal.pone.0113547.s001 (TIFF)

Figure S2. Funnel plots of results included in meta-analysis by country/ countries.
doi:10.1371/journal.pone.0113547.s002 (TIFF)

Data S1. Data extraction worksheet.
doi:10.1371/journal.pone.0113547.s003 (XLSX)

File S1. Supporting tables. Table S1: Search strategy using EMBASE. Table S2: List of excluded articles by main reasons for exclusion. Table S3: Study characteristics of studies conducted in children (<18) from Malaysia, Thailand and Indonesia. Table S4: Study characteristics of studies conducted in children (<18) from Laos and Vietnam. Table S5: Study characteristics of studies conducted in adults from Malaysia and Philippines. Table S6: Study characteristics of studies conducted in adults from Thailand. Table S7: Study characteristics of studies conducted in adults from Indonesia and Timor-Leste. Table S8: Study characteristics of studies conducted in adults from Laos, Vietnam and Myanmar. Table S9: Results of studies conducted in children from Malaysia. Table S10: Results of studies conducted in children from Thailand and Indonesia. Table S11: Results of studies conducted in children from Laos and Vietnam. Table S12: Results of studies conducted in adults from Malaysia and Philippines. Table S13: Results of studies conducted in adults from Thailand. Table S14: Results of studies conducted in adults from Indonesia and Timor-Leste. Table S15: Results of studies conducted in adults from Laos, Vietnam and Myanmar. Table S16: PRISMA checklist. Table S17: Sensitivity analysis: Results from random effect meta-regression and trim and fill technique. Table S18: Inter-rater agreement from abstract screening. Table S19: Summary of potential biases within studies among children. Table S20: Summary of potential biases within studies among adults.
doi:10.1371/journal.pone.0113547.s004 (DOCX)

Author Contributions

Conceived and designed the experiments: CA PD DN. Performed the experiments: CA WJ BC. Analyzed the data: CA. Wrote the paper: CA. Revised and approved the final version: CA WJ BC PD DN.

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Urbanization and non-communicable disease in Southeast Asia: a review of current evidence

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Student	Chaisiri Angkurawaranon
Principal Supervisor	Dorothea Nitsch
Thesis Title	Urbanization and internal migration as risk factors for non-communicable disease in Thailand

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Review Paper

Urbanization and non-communicable disease in Southeast Asia: a review of current evidence

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ABSTRACT

Objective: Non-communicable diseases (NCDs) have been highlighted as a major public health issue in the Southeast (SE) Asian region. One of the major socio-environmental factors that are considered to be associated with such a rise in NCDs is urbanization. Urbanization is associated with behavioural changes such as eating an unhealthy diet, and a decrease in physical activities, which may result in associated obesity. The SE Asian region also has a substantive burden of infectious disease such as HIV and malaria, which may modify associations between urbanization and development of NCDs.
Study design: A systematic review was conducted until April 2013.
Methods: Using four databases: EMBASE, PubMed, GlobalHealth and DigitalJournal, the systematic review pools existing evidence on urban-rural gradients in NCD prevalence/incidence.
Results: The study found that in SE Asia, urban exposure was positively associated with coronary heart disease, diabetes and respiratory diseases in children. Urban exposure was negatively associated with rheumatic heart diseases. The stages of economic development may also modify the association between urbanization and NCDs such as diabetes.
Conclusion: There was pronounced heterogeneity between associations. It is recommended that future studies examine the major constituents of NCDs separately and also focus on the interplay between lifestyle and infectious risk factors for NCDs. Prospective studies are needed to understand the diverse causal pathways between urbanization and NCDs in SE Asia.

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Introduction

In 2011, The Lancet launched a series of articles on 'Health in Southeast Asia', one of which highlighted non-communicable diseases (NCDs) as a major public health issue in the region.[1] Under the World Health Organization's framework, one of the major upstream socio-environmental factors considered to be associated with such a rise in NCDs is urbanization.[2] Urbanization is associated with increased downstream behavioural risk factors such as unhealthy diets and decreases in physical activity which is thought to result in obesity. All of these risk factors are seen as shared causes for NCDs which are classified into four main groups: cardiovascular disease (mainly ischaemic heart disease and cerebrovascular disease), cancer, chronic respiratory disease and diabetes.

The associations between urbanization, risk factors for NCDs and development of NCDs are established in western countries, but evidence from low- and middle-income countries are often based on extrapolation from large population surveys.[3,4] Furthermore, many low- and middle-income countries face the double burden of infectious and non-infectious diseases.[5] A subset of infectious agents are thought to be associated with the development of some NCDs such as cancer[6] and rheumatic heart disease.[7] The interplay between socio-environmental and behavioural risk factors, along with the potential modifying role of infectious risk factors, may result in variations in the association between urbanization and different NCDs which may differ from what is seen in more developed countries.[8]

The aim of this study is to provide a systematic review of studies exploring the relationship between urban exposure and the four major groups of NCDs in Southeast (SE) Asia. In particular, the review will investigate whether the associations are consistent across i) different countries, ii) different subtypes of diseases classified within the same group of NCDs and iii) across different groups of NCDs. Due to different underlying causes/mechanisms for developing NCDs along with possible interplay between infectious and non-infectious causes of NCDs, the authors hypothesized that the association between urban exposure and NCDs is likely to vary by country and across NCD subtypes.

Methods

Search strategies and procedures

Four databases were used for searches: EMBASE, PubMed, GlobalHealth and DigitalJournal until April 2013. DigitalJournal is a database which contains electronic health science journals from SE Asia.[9] Separate searches for each of the four main groups of NCDs had been conducted. The search strategies using EMBASE can be found in Appendix 1. For DigitalJournal, only simple keyword searches were possible. The search terms for urban exposure only were used. An additional cited-reference search from articles included in the review was also conducted.

Inclusion and exclusion criteria

Criteria for articles to be included in the review were that they must:

i) have a defined measure of one of the main group of NCDs; cardiovascular disease, cancer, chronic respiratory disease (including asthma and allergies) and diabetes;
ii) have a clearly defined measure for urban exposure;
iii) have a direct control group or comparison group such as a semi-urban or rural group;
iv) report (or have data to able to calculate) quantitative measures for association between urban exposure and one of the NCD groups or individual diseases; and
v) be published in English or Thai.

The studies that were conducted outside the SE Asian region or studies with historical controls were excluded, where the prevalence/odds/incidence of NCDs were measured at different time points. SE Asia countries included in the review were Brunei Darussalam, Cambodia, Indonesia, Laos PDR, Malaysia, Myanmar, Philippines, Singapore, Thailand, Timor-Leste, and Vietnam. And also the articles that were classified as reviews by their respective journals and articles that were not full reports such as conference abstracts or editorials had been excluded. There were no restrictions on the type of designs as long as the inclusion criteria were met.

Screening and data extraction

Article abstracts were screened by two independent reviewers and classified into three subgroups:

i) clearly not relevant
ii) potentially relevant
iii) relevant to review

All articles initially classified as clearly not relevant were reviewed by a third reviewer to double-check for potentially relevant articles initially excluded. All articles identified as potentially relevant and relevant were retrieved and reviewed by the lead author. If full-text articles were not retrievable or additional data was required to make a decision on inclusion or exclusion of a study, the corresponding authors were contacted.

Standard data extraction forms, one for each type of study design, were derived from a small sample of articles included in the review. Article information such as the author's name, country of conduct, year of fieldwork and publication, sample size, definition of urban and rural exposure and how the NCD of interest was defined and diagnosed were recorded. The Gross National Income (GNI) per capita, as reported by the United Nations,[10] corresponding to the country and year of fieldwork was also included. Depending on the type of study design, the main measures of disease frequency were the prevalence/odds/risk of the NCD along with the corresponding crude and adjusted measures of relative effect. Information was also collected on which factors were controlled for if adjusted relative risks were reported.

Quality appraisal

As recommended by the Cochrane handbook,[11] the risk of bias was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.[12] A different bias assessment form was used depending on the type of study design, but in general the studies were assessed for three main potential types of bias. The first was selection bias. The second was information bias for potential misclassification of exposure and/or outcome. Information bias was also assessed as likely to be differential or non-differential. Lastly, the results were assessed for confounding and residual confounding. For cohort studies, the potential impact due to loss of follow-up (selection bias) was also considered.

Data analysis

Data were analysed separately for the four main groups of NCDs. Within each group of NCDs, data were categorized according to disease. For chronic respiratory diseases, the results were further categorized according to the age group of the study population (children or adults). The authors calculated confidence intervals if obtainable from the available data.

For the meta-analysis, age and/or gender adjusted measures of association were given first priority but crude measures of association were included if adjusted measures of association were not available. For studies reporting more than one summary measure from multiple independent datasets, all available summary measures were used. For studies reporting multiple outcomes, such as reporting results on both ischaemic heart disease and cerebrovascular disease, both results were included but were analysed separately according to disease. If a study reported summary measures by different gradients of urban exposure (such as urban, semi-urban and rural), the estimates with the largest sample size were used as it is considered most reliable. Cochran's Q and I^2 statistics were used to evaluate heterogeneity among results. The DerSimonion and Laird approach for random effect models[13] was used if there was evidence for heterogeneity, otherwise, the inverse-variance fixed effect model was used. If there was high heterogeneity (I^2>85%), summary measures for each study were displayed without combining the effects.

Funnel plots were used to assess publication bias. Random effect meta-regression was used to explore potential variability due to different country settings, such as differences in classification of urban exposure or sociocultural environment. GNI per capita, which represents stages of economic development, was also explored as a factor that may explain the variability due to different country settings.

Results

Three hundred and six abstracts were screened and 14 articles were assessed for cardiovascular disease. Four hundred and fifty nine abstracts were screened and 24 articles were assessed for cancer. One hundred abstracts were screened and 15 articles were assessed for chronic respiratory disease. Three hundred and sixteen abstracts were screened and fifty articles were assessed for diabetes. The flow charts for the number of articles included in the review can be found in Appendix 2. After assessing for eligibility, seven articles were included in the review for urban exposure and cardiovascular disease. Five were included for urban exposure and cancer, nine for urban exposure and chronic respiratory disease and sixteen for urban exposure and diabetes. The definition of urban exposure varied by articles and by different countries of conduct. Some used classification according the country's official classification. Some compared results between two different locations. The study characteristics and detailed summary of the results from these articles can be found in Appendix 3 and 4.

Urban exposure and cardiovascular disease

The seven studies, representing five nations, explored the association between urban exposure and cardiovascular diseases (Fig. 1). Two articles each were conducted in Vietnam[14,15] and Myanmar.[16,17] One article each was from Malaysia,[18] Thailand[19] and Indonesia.[20] All were cross sectional in design. The sample sizes ranged from 387 participants to 2611 participants. One study[18] used medical records from hospitals while other studies used population surveys to obtain data. The associations between urban exposure and cardiovascular disease can be sub-classified into two major groups, stroke (cerebrovascular disease) and heart disease.

Five studies explored the association between urban exposure and stroke (cerebrovascular disease) and one for symptoms of stroke.[15] Urban exposure was significantly associated with higher odds of stroke in a study from Malaysia.[18] One study from Vietnam reported that urban exposure was significantly associated with lower odds of symptoms of stroke.[15] There was inconclusive evidence for the remaining four articles. In the meta-analysis, there was presence of high heterogeneity (I^2 = 64.8%) and the random effect model gave a pooled odds ratio of 1.01 (95% CI 0.56–1.82).

Six articles explored the association between urban exposure and heart disease. The results could be categorized into three subgroups, coronary heart disease (ischaemic heart disease), rheumatic heart disease and non-specific heart disease. Two studies from Myanmar[16] and Malaysia[18] reported results specifically for coronary heart disease. The study from Malaysia showed strong evidence of an association, but the study from Myanmar showed no evidence for an effect. The results from the random effect meta-analysis gave a pooled odds ratio of 2.48 (95% CI 1.20 to 5.11, I^2 = 0.47) for urban exposure and coronary heart disease. Rheumatic heart disease was reported in only one study from Myanmar.[16] The results suggested that urban exposure was significantly associated with lower odds of rheumatic heart (pooled OR = 0.31, 95% CI 0.13–0.76). Four studies, from Thailand, Vietnam, Indonesia and Myanmar, were conducted in the elderly aged over 60.[14,17,19,20] All reported results for non-specific cardiovascular disease. Most reported inconclusive evidence except for one study from Indonesia which suggested that urban exposure was inversely associated with

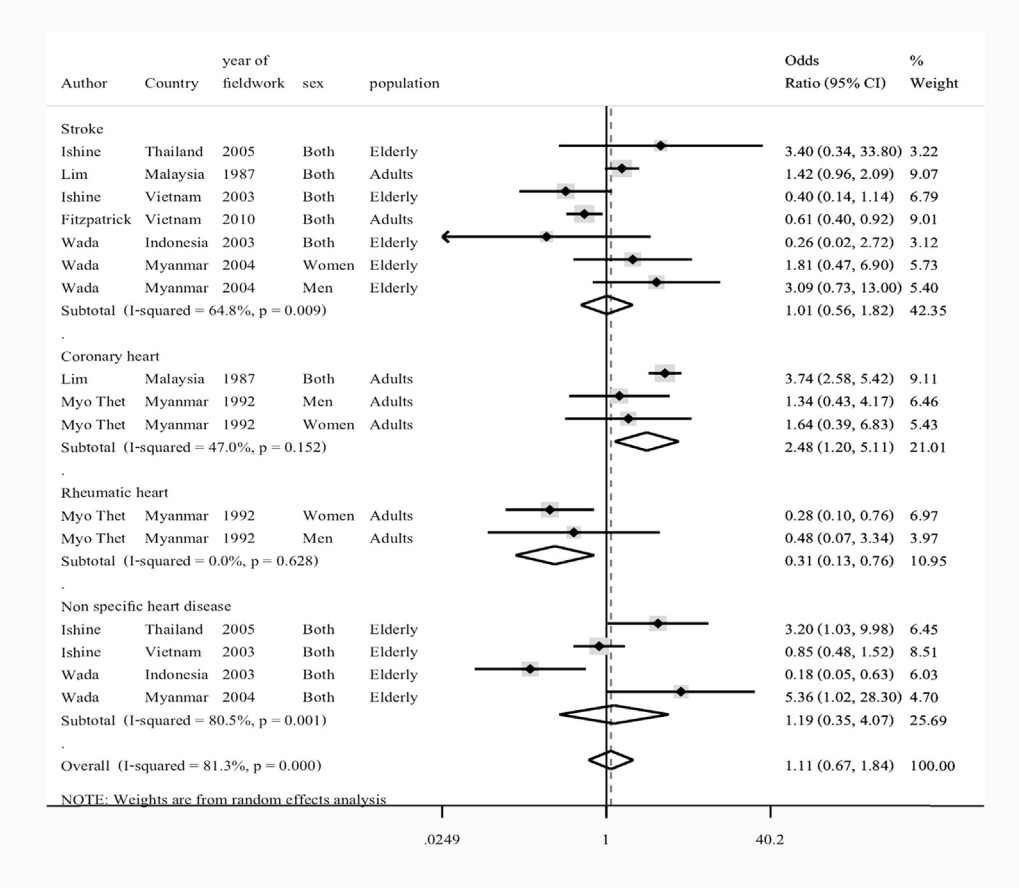

Fig. 1 – Meta-analysis of associations between urban exposure and cardiovascular disease in seven studies.

non-specific cardiovascular disease in the elderly.[20] In the meta-analysis, there was evidence for heterogeneity between the four studies ($I^2 = 80.5\%$). The random effect odds ratio for urban exposure and non-specific heart disease in the elderly was 1.19 (95% CI 0.35 to 4.07) (Fig. 1).

Urban exposure and cancer

Five articles, three from Thailand and two from Malaysia, were included in the review. Three early studies were reported in 1975, 1977 and 1979.[21–23] The more recent studies, both from Thailand, were published in 2009 and 2011.[24,25] Four types of cancer were reported, head and neck cancer,[22,23] lung cancer,[22] breast cancer[24] and osteogenic sarcoma.[21] One article did not specify the type/site of cancer.[25] A summary of results is presented in Table 1. There was some evidence that urban exposure was positively associated with osteogenic sarcoma[21] and lung cancer[22] but was inversely associated with oropharyngeal cancer.[22] With sparse data across and within each type of cancer, meta-analysis was not performed.

Urban exposure and chronic respiratory disease

Nine studies were included in the review for urban exposure and chronic respiratory diseases. Three were conducted in adults and six were conducted in children. All were cross sectional studies, published between 1986 and 2012.

Of the three studies conducted in adults (data not shown), a study from the Philippines reported that urban exposure was inversely associated with rhinitis (OR 0.80, 95% CI 0.68–0.94).[26] Another from Vietnam found very weak evidence that urban exposure was associated with chronic bronchitis (OR 1.34, 95%CI 0.98–1.83).[27] Two studies reported on asthma, but did not find conclusive evidence.[18,27]

Six articles were included in the review of urban exposure and chronic respiratory disease in children, which includes asthma and allergies. Two articles each were from Malaysia[28,29] and Thailand.[30,31] One article each was from Singapore[32] and Vietnam.[33] Four studies reported evidence that urban exposure was associated with asthma and allergic symptoms such as rhinitis and conjunctivitis.[30–33] One article reported that urban exposure was associated with increasing asthma severity among children with asthma (OR 2.58, 95% CI 1.16–5.77).[28] One article reported that urban exposure was positively associated with otitis media with effusion (OR 2.08, 95% CI 1.43–3.04),[29] which is associated with allergic rhinitis.[34] These findings also suggested that the association between urban exposure and chronic respiratory disease might be modified by age. The association was more pronounced in younger children than in older children (Fig. 2).

Table 1 – Summary of results for association between urban exposure and cancer.

Type of cancer	Author (year of publication)	Country (year of conduct)	Definition	ES* for urban exposure (95% CI)	ES for comparison	ES ratio (95% CI)	Note
Head and neck cancer	Armstrong (1977)	Malaysia (1968 to 1974)	Histologically confirmed diagnosis of Nasopharyngeal cancer	Incidence of 10.2 per 100,000 person/year in men	Incidence of 8.9 per 100,000 person/year in men	1.15 in men	Cumulative incidence per population at risk
				Incidence of 5.4 per 100,000 person/year in women	Incidence of 3.5 per 100,000 person/year in women	1.54 in women	
	Simarak (1979)	Thailand (1971)	Presumptive hospital diagnosis of Oral and oropharynx cancer	---	---	0.38 (0.13 to 0.93) in men	Age and sex matched hospital based case-control study
				---	---	0.39 (0.13 to 0.99) in women	
			Presumptive hospital diagnosis of Larynx and hypo pharynx	---	---	0.94 (0.53 to 1.61) in men	
Lung cancer	Simarak (1979)	Thailand (1971)	Presumptive hospital diagnosis of lung cancer	---	---	1.40 (0.76 to 2.53) in men	
				---	---	2.03 (1.10 to 3.72) in women	
Breast cancer	Jordan** 2009	Thailand 2005	Self reported of diagnosis of breast cancer by doctor	---	---	0.84 (0.43 to 1.67)	Exposure is current urban residence.
				---	---	1.56 (0.80 to 3.04)	Exposure is urban residence at age 10 to 12.
Osteogenic sarcoma	Bovill 1975	Malaysia (1969 to 1972)	Biopsy confirmed diagnosis	Incidence of 0.29 per 100,000 person/year	Incidence of 0.12 per 100,000 person/year	2.53 (1.48 to 4.34)	Cumulative incidence per population at risk
Non-specific	Phomphet 2011	Thailand 2009	Self report of diagnosis by doctor	0 (0.0 to 5.3) in urban group	1.4 (0.3 to 4.0) in semi-urban group / 0 (0.0 to 6.4) in remote rural group	---	Cross sectional study

*ES= effect size which differs by study design, ** Age matched, population based case-control design

Urban exposure and diabetes

Sixteen articles were included in the review for urban exposure and diabetes. All were cross sectional in design, conducted in adults (age >18) and published between 1991 and 2012. Half of the articles were from Thailand.[19,25,35–40] Three were from Malaysia[18,41,42] and one each from the Philippines,[43] Vietnam,[14] Cambodia,[44] Myanmar[17] and Indonesia.[20] There were variations in the methods and definition used to define diabetes. Most articles used a self-reported history of previous diagnosis by a doctor or a history of taking medication for diabetes as part of their criteria. For objective measurements, some articles used fasting glucose level, some used an oral glucose tolerance test (OGTT) and others used casual (non-fasting) blood glucose. Five studies used standardization as methods for analysis and found that the prevalence of diabetes in the urban exposure group was higher than the comparison group.[35–37,41,43] The results from the remaining articles, except one[39] where the odds ratio could not be calculated, are presented in Fig. 3. There was evidence for high heterogeneity between the results ($I^2 = 84.1\%$). In the meta-regression, including country of conduct as an exploratory variable explained about 26.1% of the variability in the estimates but it did not reach statistical significance (P-value = 0.142). In comparison, per capita GNI corresponding to country and year of fieldwork helped explain 39.0% of the variability between the estimates and was significant (P-value = 0.048). Moreover, there was evidence that GNI per capita modified the association between urban exposure and diabetes. In countries with lower GNI per capita, the association between urban exposure and diabetes is greater than in countries with higher per capita GNI (Fig. 4).

Discussion

The review found evidence for associations between urbanization and NCDs in SE Asia. However, these associations were variable between countries and also between diseases classified within the same group of NCDs and across different groups of NCDs. Different pathways between urban exposure and types of NCDs should be considered to explain these variations.

Variations across countries

Urbanization has been shown to be associated with risk factors for NCDs within countries of SE Asia.[45] The INTERHEART[46] and INTERSTROKE[47] studies have shown that for some NCD risk factors, such as high blood pressure and obesity, their association with coronary heart disease and stroke can vary by regions. Thus it is perhaps not surprising to see variations in the association between urbanization and NCDs across countries in SE Asia. The findings for urban exposure and diabetes suggested that the variation across countries of conduct could be partly explained by GNI per capita which could be considered a proxy to the stage of economic development. Individual level data from other studies also support these findings. In developing countries, diabetes is associated with higher socio-economic status (SES).[48] In developed countries, diabetes is inversely associated with higher SES.[49] It is likely that in developing countries (less urbanized), higher SES is associated with greater access to food and exposure to unhealthy lifestyles and environment. In developed countries (more urbanized), people with higher

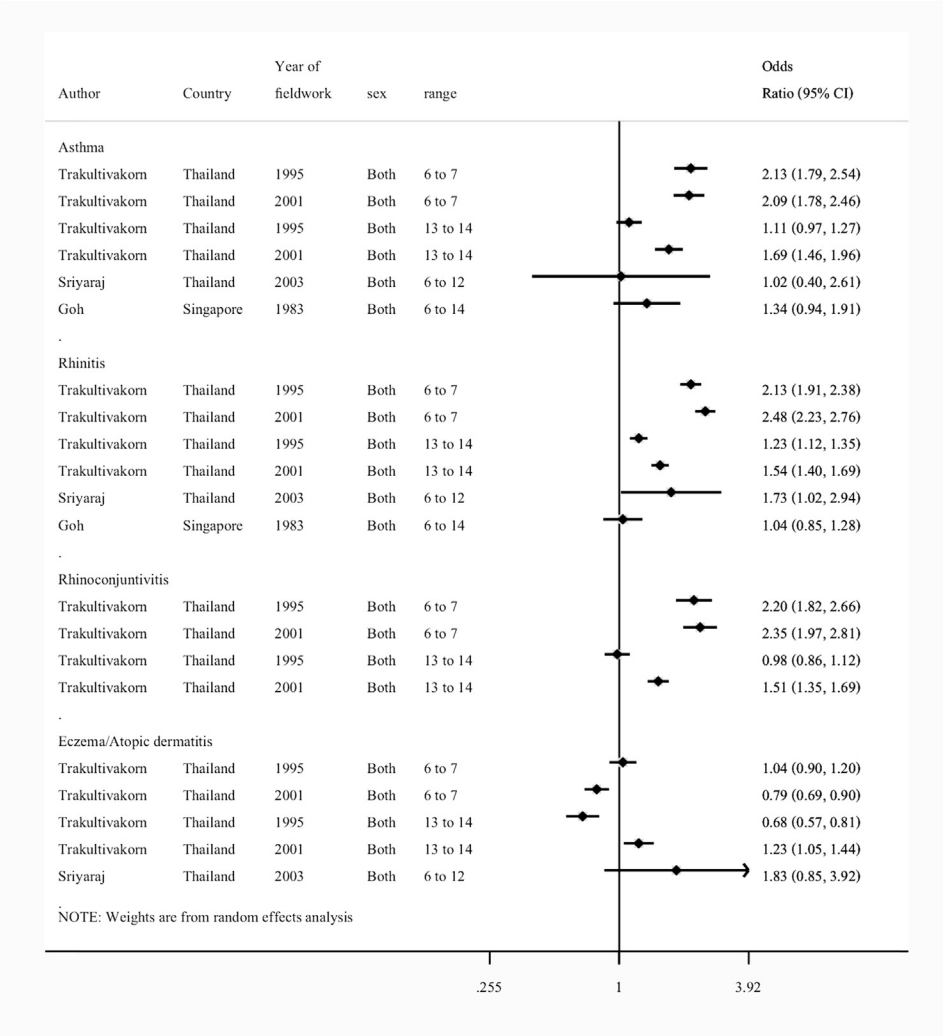

Fig. 2 – Associations between urban exposure and chronic respiratory diseases (asthma, rhinitis, rhinoconjunctivitis, exzema/atopic dermatitis) in children taken from three studies.

SES can counteract such environments through access to healthier life choices and utilization of medical systems.[50,51] The 'developmental origins' may also help explain such findings.[52] If maternal and childhood malnutrition is associated with greater risk of NCDs in adulthood, as countries rapidly become more urbanized, people from less developed countries would be at greater risk of developing diabetes and coronary heart disease later in life.

Variations within and across groups of NCDs

The review also found variations in the effect of urban exposure within the same group of NCDs, as well as across major groups of NCDs. To help explain such variations, two different pathways between urbanization and the different types of NCDs should be considered.

Urbanization and lifestyle risk factors for NCDs

In SE Asia, evidence has suggested that urbanization is associated with many lifestyle risk factors for NCDs such as low physical activity, unhealthy diet, obesity and high blood pressure.[53–55] At an ecological level, urbanization was shown to be associated with lifestyle related mortality from heart disease, stroke and cancer in Thailand.[56] The review found positive associations between urban exposure and lifestyle-associated disease such as coronary heart disease, diabetes and lung cancer. There was inconclusive evidence for other lifestyle-associated diseases such as stroke and breast cancer. Coronary heart disease and stroke share common risk factors and are grouped within the same NCD group, but their epidemiology is known to differ.[57] The main mechanism for coronary heart disease revolves around atherosclerosis.[58] Although sharing many underlying mechanisms, stroke may be due to different mechanisms such as atrial fibrillation or severe hypertension.[59,60] This suggests that different causal pathways exist between diseases within the same group.

Role of urbanization and infectious risk factors for NCDs

It is known that non-communicable diseases such as rheumatic heart disease, liver and cervical cancer have infectious

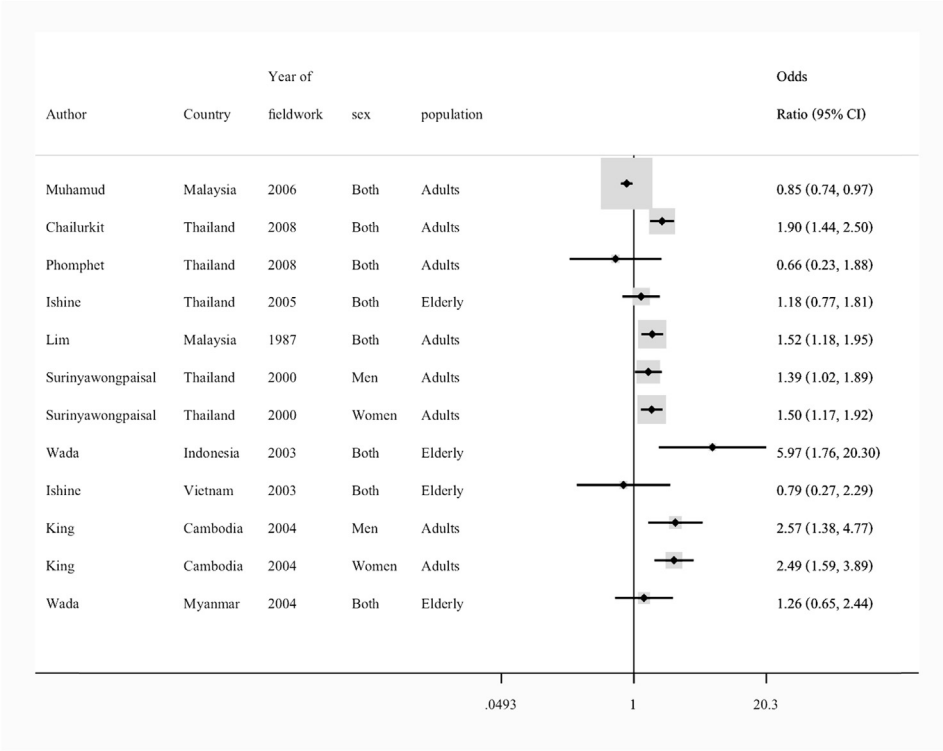

Fig. 3 – Associations between urban exposure and diabetes in ten studies.

causes. A number of autoimmune diseases also have infectious agents as an initiating risk factor.[61] There is evidence that urban exposure is associated with better access to health care, immunization and better hygiene and sanitation.[8,62] Hence urban exposure, via improved hygiene, could be protective against NCDs of infectious origin. The review found a negative association between urban exposure and rheumatic heart disease in Myanmar. Global patterns also suggest that the burden of cancers related to infectious diseases are lower in more developed (urbanized) countries.[63]

It is also possible that urban exposure, due to population growth and crowding, could increase the risk of some vector borne infections. There is evidence from the region that urbanization plays a role in the spread of dengue infection and increasing incidence of tuberculosis[62,64] but their causal roles in development of NCDs are not well established in SE Asia.

The authors have argued that an urban environment can lower the risk of NCDs with infectious origins. But evidence has also supported the notion that a lack of infection can disrupt the development of the normal immune response system that can lead to increased susceptibility to some chronic diseases. This is called the 'hygiene hypothesis'.[65] This hypothesis proposes that the reason allergic diseases such as asthma, hay fever and rhinitis are more common in urban (or more developed) settings lies in the lack of previously common, low grade infections.[66] This theory could be the explanation for the positive association between urban exposure and chronic respiratory disease in children within SE Asia. It is also possible that urban exposure is associated with increased exposure to pollution and allergens which drive the associations seen.[67]

Strength and limitations

The review had several limitations. There was sparse data exploring the impact of urbanization on NCDs within the region, thus limiting any definitive conclusions on the association between urban exposure and NCDs in SE Asia. It was also difficult to assess publication bias due to limited data (Appendix 5). The number of studies with similar methodology was few. However, the findings and discussion in the review were based on prespecified analysis and observed results from individual studies. Diagnosis and confirmation of the different types of NCDs are methodically challenging. To minimize its potential impact, results were considered for each group and subgroup of NCDs separately. Information bias may be an issue in many of the studies, but most were likely to be non-differential within studies (Appendix 6). Many of the results seen in the review were unadjusted results. Depending on the type of disease, especially cardiovascular disease and cancer, results can be prone to confounding by age and sex. When possible, the results by age group and sex were presented but there was still potential for residual confounding due to broad age groupings.

Conclusion

Although the upstream and downstream risk factors for NCDs are common worldwide, the pathways between upstream causes (such as urbanization) and NCDs may differ by country and type of disease. The study found that in SE Asia, urban exposure was positively associated with coronary heart disease, diabetes and respiratory diseases in children and

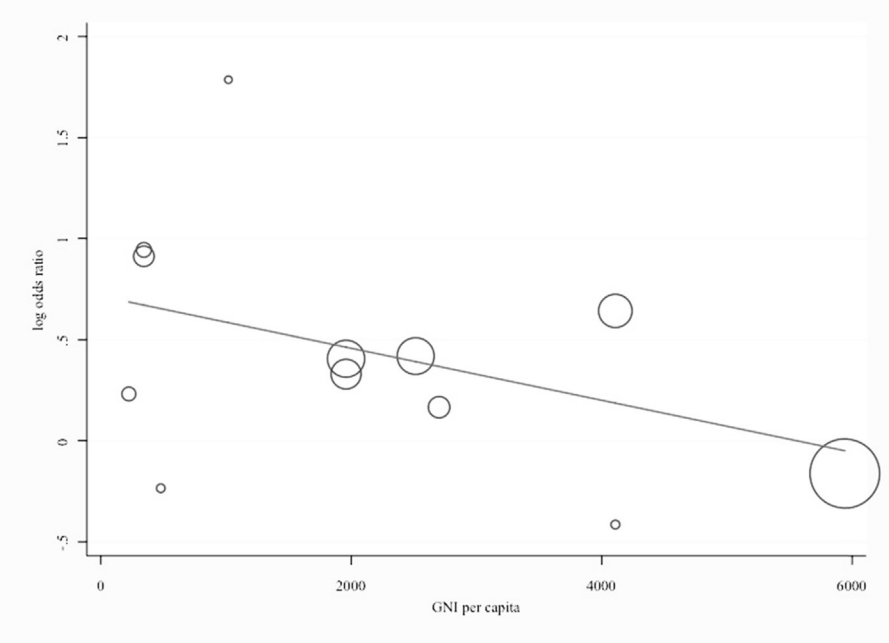

Fig. 4 – Association (log odds ratio) between urban exposure and diabetes by gross national income per capita.

negatively associated with rheumatic heart diseases. The stages of economic development may also modify the association between urbanization and NCDs such as diabetes.

Author statements

Ethical approval

Ethical approval was not sought, as it was not required for conducting a systematic review.

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Competing interests

None declared.

Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.puhe.2014.08.003.

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3.3 Summary and conclusion

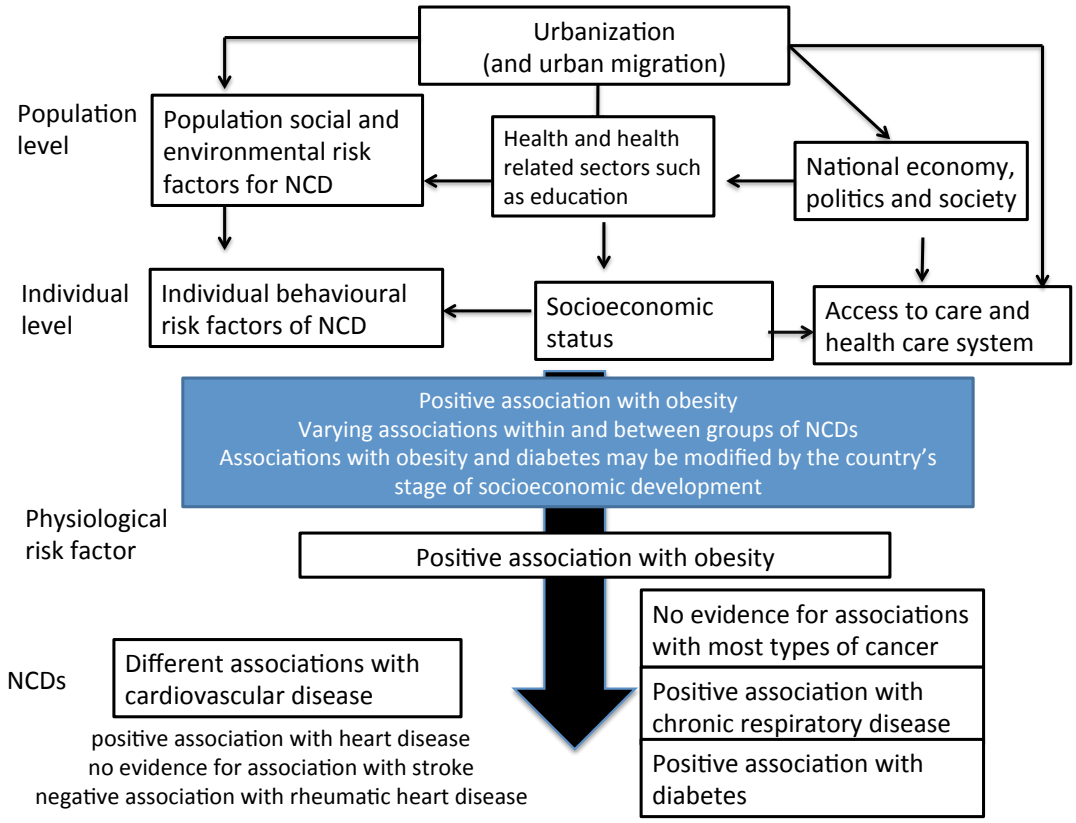
Urban environments were found to be associated with obesity in Thailand and other countries in Southeast Asia. This association was consistent across ages, gender and countries in Southeast Asia. Within the countries of Southeast Asia, there was pronounced heterogeneity in the results of studies examining urbanization and specific NCDs.

Urban environments (versus rural environments) were positively associated with coronary heart disease, diabetes and chronic respiratory disease in children and, in one study, negatively associated with rheumatic heart disease. No evidence for an association between urban environments and cancer or cerebrovascular disease (stroke) was found. Stages of economic development, as measured by per capita GNI, modified the association between urbanization and obesity and diabetes (Figure 3.3).

The findings from these systematic reviews of the literature suggest that the association between urban environments and obesity is consistent in terms of direction of association within Thailand and across Southeast Asian countries. However, the effect size of the association between urbanization and NCDs is likely to differ across countries and in terms of type of NCD. Stages of economic development, along with the interplay between lifestyle risk factors and infectious risk factors for NCDs (61), may help explain the diverse pathways between the relationship of urbanization to NCDs in Thailand and that in the rest of Southeast Asia.

A better understanding of the links between urbanization with more distal individual risk factors for NCDs (such as body mass index) and more proximal biological risk factors (such as blood glucose and lipid profiles) would be useful in helping to explain the association between urbanization and NCDs in Thailand.

Figure 3.3 Conceptual framework of this thesis with adaptations to incorporate findings from Chapter 3



Chapter 4 : Field work and data collection

Summary

In this chapter, I summarize the rationale and advantages for further data collection. Prior to coming to LSHTM, I was part of the research team that conducted a health survey among health care workers at Chiang Mai University's (CMU) Hospital in 2008. Taking advantage of this earlier data collection, I proposed that new data collected from amongst health care workers (as part of my PhD) could be used to generate two related datasets.

The first is a cross-sectional study with comprehensive and detailed measurement of NCD risk factors. This is essential in order to address Objective 3 (to investigate the difference in behavioural, physiological and biological risk factors for NCD among those with different urban exposures). By linking the results of the 2008 survey with the new data collection, I was able to generate a cohort dataset. This is essential in order to address Objective 4 of the thesis (to investigate the changes in physiological and biological NCD risk factors and the risk of developing obesity and impaired fasting glucose among those with different urban exposures).

To demonstrate the feasibility of the proposed new data collection, I showed some results of the survey in 2008 and sample size calculations. A detailed cohort description with rationale and cohort profile has been published and is included in this chapter. I end the chapter with a discussion of how I planned initially to address the limitations in the data within the context of each of the above study objectives.

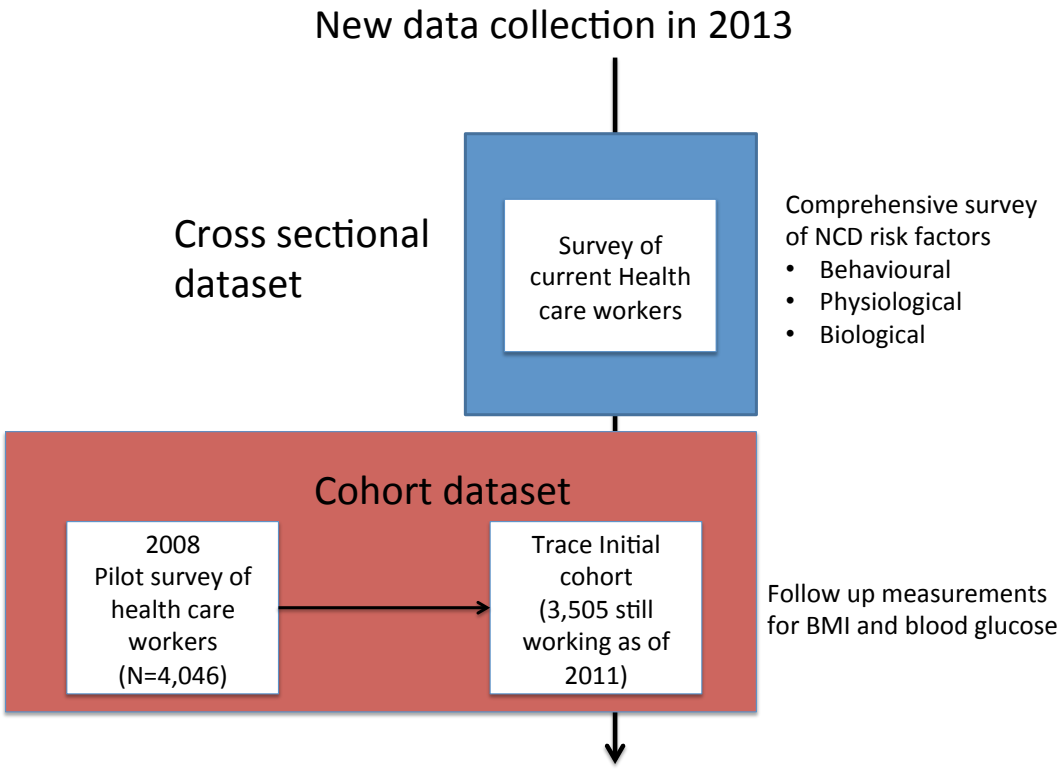
4.1 Introduction

The previous two chapters have presented results suggesting that living in urban environments is associated with obesity, some NCDs, and NCD mortality in Thailand. A better understanding of the link between urban environments and shared NCD risk factors, especially biological risk factors such as high glucose and high cholesterol, is needed in order fill in the gaps along the pathway proposed in my conceptual framework (Figure 1.1). In this chapter I present the rationale for new data collection that would address some of these gaps in knowledge.

In 2008, prior to coming to LSHTM, I was part of the research team that conducted a health survey among health care workers at Chiang Mai University's (CMU) Hospital in 2008 (62). Data were collected on self-reported health risk factors and the prevalence of common diseases such as hypertension and diabetes. In accordance with the Thai National guidelines (63), laboratory investigations, including fasting glucose and lipid profiles, were only offered to those aged 35 or above. Thus only a subpopulation of all health care workers was available for laboratory investigations in 2008.

I considered that I could take advantage of this previous data collection to generate further evidence relating to the association between urban and rural living environments and pathways to NCDs. This new health survey, which would allow for data collection from all workers irrespective of age, would include a detailed history of past migration along with comprehensive measurements of current behavioural, physiological and biological risk factors. In carrying out this data collection, my intention was to generate two related datasets (Figure 4.1). The first was to be a cross-sectional dataset of current health personnel in CMU Hospital. The second was to be a cohort dataset of health personnel in CMU hospital (using data from both 2008 and 2013).

Figure 4.1 New data collection



Behavioral risk factors consisted of inadequate physical activity, inadequate fruit and vegetable consumption, smoking and alcohol consumption.

Physiological risk factors consisted of high blood pressure and high body mass index.

Biological risk factors consisted of high blood glucose, high low-density lipoprotein (LDL) cholesterol, high triglyceride and low high-density lipoprotein (HDL) cholesterol.

All hospitals in Thailand require a 13-digit National ID number for each person to register with the hospital databases. All health workers are registered to received care at the hospital where they work, thus making records within the hospital traceable and linkable.

4.2 Rationale and potential advantages of the new data collection

New cross-sectional data collection was essential in order to obtain a complete history of urban exposure and migration along with detailed measurements of risk factors for NCDs to address Objective 3 (to investigate the difference in behavioural, physiological and biological risk factors for NCD among those with different urban exposures).

The cohort dataset was essential to complete Objective 4 (to investigate the differences in changes in body mass index and fasting glucose and risk of developing obesity and impaired fasting glucose among those with different urban exposures).

This new occupational dataset derived from health care workers has other potential advantages that can help in the achievement of these objectives. Firstly, a new definition of urbanicity could improve the validity of the assessment of urban exposure compared to the commonly use “urban” classification in Thailand. Secondly, since health care workers are likely to have migrated since birth, whether for educational or employment purposes (64), a study that assessed internal migration would become possible. Lastly, an occupational cohort could help to limit potential confounding factors associated with socio-demographic status and health-seeking behaviours, information bias due to loss to follow up, and could also allow for life course models to be examined.

4.2.1 Advantages of using a new definition of urbanization

Classifying an area as “urban” poses many challenges (21). For most studies conducted in Thailand, two main issues arise. The first issue relates to how an urban population is classified in Thailand. Every person in Thailand must be registered under a household. People are classified as living in an urban area if the household they are registered in is under local municipality administration.

This classification is for administrative and legislative purposes, but does not reflect the changes in urbanization over time (urban-rural interactions and urban expansion taking place). A point of particular concern is that, in 1999, there was a sudden change in the definition of what constitutes “urban” status in Thailand. This decentralizing act upgraded existing rural sanitation districts to urban municipalities and accorded over 700 areas “urban” status overnight, even though their lifestyle and environmental surroundings could more rightly be considered rural.

The second issue is that the duration of rural or urban exposure of the study participants has not been adequately recorded in previous Thai studies. For example, the authors of the TCS asked participants to self-identify whether they were living in a ‘countryside (rural)’ or ‘city/town (urban)’ and did not record the ages at which any moves took place from rural to urban locations, and vice versa. This limits the possible interpretation and causal inference within the TCS.

The United Nations defines an urban agglomeration as “a built-up or densely populated area containing the city proper, suburbs and continuously settled commuter areas. It may be smaller or larger than a metropolitan area; it may also comprise the city proper and its sub-urban fringe or thickly settled adjoining territory” (65). As earlier stated, the classification of urban areas in Thailand is defined using government administrative criteria largely driven by population density. In 1970, only three areas were considered ‘cities’: Bangkok, Thonburi (a suburb of Bangkok) and Chiang Mai (66).

I decided that for my new study, all districts in Bangkok/Thonburi and the ten districts in the Chiang Mai Metropolitan Area, consisting of Muang (Chiang Mai Province), Sarapi, Sanpatong, Hang Dong, Mae Rim, Sansai, Doi Saket, Mae On, Sang Kampang, Muang (Lumphun Province), would be considered urban. The remaining districts in Thailand outside Bangkok/Thonburi and Chiang Mai Metropolitan Area are classified as rural for the purposes of the study. As only limited areas were to be considered urban, it was unlikely that I would substantially misclassify urban exposure.

Using this classification, at any two time points, I was able to categorize whether participants could be considered rural to urban migrants (or vice versa), rural dwellers (at both time points) or urban dwellers. By tracking the area of residence during crucial development points, I could also estimate "years of urban exposure" for each individual.

It is likely that the rate of urban development is higher in existing urban areas in developing countries compared to rural areas (32) and, given the historical context in Thailand, this "urban" indicator, which better captures "urban patterns of life" than the classification based purely on municipality or subjective self-classification of urban exposure, allows for years of urban exposure to be calculated; it was expected that this would provide improved measures of urbanicity than those available in existing literatures from Thailand. The consequence would be improved interpretation of results for both studies.

4.2.2 Advantages of a study that assesses migration

Early studies of urbanization and health focused on cross-sectional urban-rural comparisons. The use of such comparisons is limited for two main reasons. The first is that such crude comparisons would not allow any study of the mechanisms or pathways by which the difference in urban exposure influences NCD risks factors (47). Moreover, Ebrahim et al. point out that *"Migration studies are powerful means of identifying environmental causes of common diseases as changes in environment are large and occur at a known time, making causal inferences more feasible"* (6).

Secondly, urbanization in Thailand, as in many LMICs, is driven by the expansion of urban boundaries as well as rural-urban migration (39). Thus a study investigating migration might be more relevant than simple urban-rural comparisons given the rural-urban migration context in Thailand and the aim to understand mechanisms behind potential differences between those with different gradients of urban exposure.

4.2.3 Advantages of a cohort among health care workers

A cohort of health care workers would also provide several unique advantages. From a practical standpoint, as suggested in the 2008 survey, the compliance rate is likely to be very high. With proper recruitment, this could help limit the bias from loss to follow up. Furthermore, conducting research in a university hospital would allow for physiological and biological markers to be easily collected and processed.

A cohort study design allowed me to explore life course models in order to help understand the mechanisms by which urban environments influence NCD risk factors. In recent decades, a life course approach to chronic disease epidemiology (46) has been suggested as a way forward in the understanding of urbanization and health (47). A life course approach considers the effect of an exposure (such as urban environments) during different periods of life (from gestation to adult life) on later health-related risks and outcomes. Two main conceptual life-course models exist (67).

The first is the critical period or sensitive period model. This model emphasizes the importance of the timing of the exposure. It is based on theories that there may be a limited period in which an exposure may affect structural or functional development (the critical period model) or that there is a time period when an effect of an exposure may be stronger than during other time periods (the sensitive period model). An example of the critical period/sensitive period model is the developmental origins hypothesis (68). This suggests that those spending early life in rural areas could have an increased susceptibility to risk factors for NCD in adulthood due to inadequate nutrition in early life. They could be physiologically maladapted to urban environments (59, 69).

The second main conceptual life course model is the accumulation of risks model. This model emphasizes the importance of cumulative exposure over time. An example of an accumulation model is one in which the risk of obesity and diabetes rises with the time spent in an urban environment (70).

The cohort design, looking at level and changes in NCD risk factors, made it possible to explore these models. For the developmental (early-life exposure) hypothesis, one would expect that those who spent their early life in a rural area would have greater changes in NCD risks than those who spent their early life in urban areas, irrespective of later subsequent rural or urban exposures. For the accumulation of risk model, one would expect the level and changes in risk factors to become more similar as the years of urban exposure increase.

When exploring the above models, the conceptual framework of the PhD (Figure 1.1) was be used to identify potential confounders. Furthermore, as suggested in previous chapters, any further data collection would need to take into account the economic environment and access to health care as key factors and potential confounders when interpreting the relationship between urban environments and NCDs in Thailand.

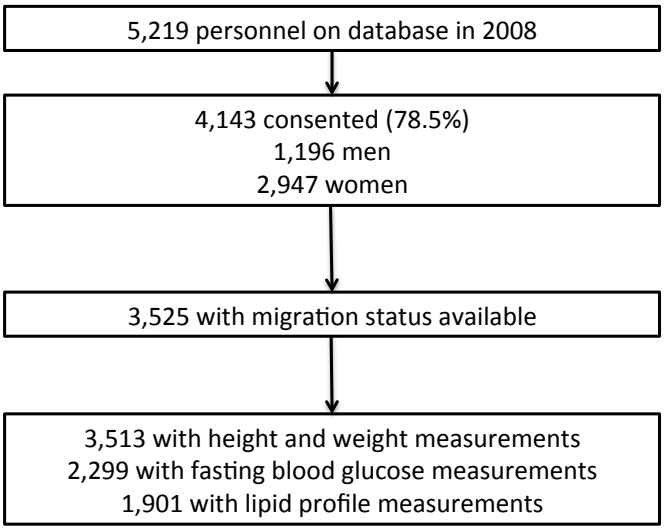
An occupational cohort of health personnel would allow me to control for such potential confounders. Since all participants were to be health personnel, they would have good and similar access to health care. In this occupational cohort, the participants' socioeconomic status (SES) would be less diverse than would be the case for a general population study. Furthermore, controlling for household income in a health worker study may deal with confounding for SES in a more stringent way than doing the same in a general population study.

4.3 Health survey results (2008)

A health survey among health care workers from the Faculty of Medicine, CMU Hospital was conducted in early 2008. Personnel were requested to complete an online electronic questionnaire. The survey achieved an over 75% compliance rate (Figure 4.2). The topics in the survey included history of chronic diseases, lifestyles and behaviour, plus exposure to occupational hazards. Participants were also requested to enter their own body weight, height and blood pressure measurements.

According to the Thai National guideline (63), laboratory investigations (fasting glucose and lipid profiles) were only offered to those ages 35 and above or those at high risk of developing diseases based on age, gender, family history and self-reported behavioural and occupational risk factors. Over 3,500 personnel came for further laboratory investigations.

Figure 4.2 Enrolment flowchart for 2008 survey of Chiang Mai University Health worker



As migration status was not available in the initial survey, a request and ethical approval (Appendix E) was obtained from the Faculty of Medicine to acquire records for the address (only district and province) of the household where personnel were registered in 2011. The address was used to classify whether participants were rural-urban migrants or urban dwellers as earlier defined in section 4.2.1.

Those with a current address outside Chiang Mai metropolitan area were classified as rural-urban migrants and those with a current address within Chiang Mai metropolitan area were classified as urban dwellers (Table 4.1).

Table 4.1 Number and percentages of rural-urban migrants and urban dwellers by age group using address data from all health care workers at CMU in 2011

	Age Group									
	<25	25-29	30-34	35-39	40-44	45-49	50-54	55-59	>=60	Total
Rural-urban Migrants (N)	110	219	185	179	72	63	33	16	2	879
(%)	65.9	30.7	28.5	27.2	11.8	7.3	4.5	3.1	2.2	17.6
Urban dwellers (N)	57	494	465	480	538	798	702	496	90	4,120
(%)	34.1	69.3	71.5	72.8	88.2	92.7	95.5	96.9	97.8	82.4
Total	167	713	650	659	610	861	735	512	92	4,999

Classification was carried out using a current address in 2011. Those with a current address outside Chiang Mai metropolitan area were classified as rural-urban migrants and those with a current address within Chiang Mai metropolitan area were classified as urban dwellers.

The 13 digit national ID was then used to link the 2008 survey results and migration status based on current address in 2011. Of the 4,143 included in the 2008 survey, the address migration status was available for 3,525 records (85%).

All subsequent results represented in this section of the thesis utilized the 3,525 records from the 2008 health survey with available migration status. Of the 3,525 participants, 481 personnel (13.6%) were classified as rural-urban migrants. The average age of the sample was 40.0 years old of which, 71% were female.

In the age and gender adjusted analysis, these data suggested that urban dwellers had higher levels of NCD risk factors than rural-urban migrants. Urban dwellers had higher BMI, waist circumference, SBP and lower HDL (Table 4.2). The odds of having hypertension and being overweight

(BMI>23) were 94% and 33% higher in urban dwellers than in rural-urban migrants after adjustment for age and sex (Table 4.3).

Table 4.2 Association between migration and NCD risk factors in 2008 using linear regression

NCD risk factors	Differences (Urban vs. rural-urban Migrant)*		p-value	Number of observations
BMI (kg/m^2)	0.47	0.14 to 0.81	0.006	3513
Waist circumference (cm)	1.90	0.99 to 2.82	<0.001	3513
FBS (mg/dL)	1.47	-1.23 to 4.17	0.286	2299
SBP (mmHg)	1.37	0.16 to 2.59	0.026	3513
DBP (mmHg)	0.40	-0.56 to 1.37	0.415	3513
Total cholesterol units (mg/dL)	-3.36	-10.06 to 3.35	0.326	1901
LDL (mg/dL)	1.00	-4.99 to 7.00	0.330	1901
HDL (md/dL)	-2.33	-4.39 to -0.26	0.028	1901

Migration classification was carried out using current address in 2011. Those with a current address outside Chiang Mai metropolitan area were classified as rural-urban migrants and those with a current address within Chiang Mai metropolitan area were classified as urban dwellers. BMI refers to body mass index; FBS is fasting blood glucose; SBP is systolic blood pressure; DBP is diastolic blood pressure: LDL refers to low density lipoproteins and HDL refers to high density lipoprotein. The differences are adjusted for age and sex.

Table 4.3 Association between migration and NCD risk factors in 2008 using logistic regression

NCD risk factors	Odds Ratio (urban vs. rural-urban migrant)		p-value	Number of observations
Overweight (BMI>23 kg/m^2)	1.33	1.06 to 1.66	0.014	3513
Obesity (BMI>25 kg/m^2)	1.19	0.90 to 1.56	0.214	3513
HT (SBP≥140 or DBP ≥ 90 mmHg)	1.94	1.23 to 3.06	0.004	3513
IFG (FBS≥110 mg/dL)	2.66	0.96 to 7.29	0.059	2299
DM (FBS≥126 mg/dL)	2.04	0.48 to 8.61	0.330	2299
High LDL (>130mg/dL)	0.94	0.67 to 1.31	0.717	1901
Low HDL (<40 mg/dL in male, <50 mg/dL in female)	1.40	0.91 to 2.14	0.122	1901

Migration classification was carried out using current address in 2011. Those with a current address outside Chiang Mai metropolitan area were classified as rural-urban migrants and those with a current address within Chiang Mai metropolitan area were classified as urban dwellers. HT refers to hypertension; IFG is impaired fasting glucose; DM is diabetes; FBS is fasting blood glucose; LDL refers to low density lipoprotein and HDL is high density lipoprotein. The odds ratios are adjusted for age and sex. Obesity is defined using the BMI criteria for Asians provided by the Regional Office for the Western Pacific Regions of the World Health Organization (71).

The results from the health survey in 2008 provided some evidence that there were likely to be differences in NCD risk factors between urban dwellers and rural-urban migrants. However, these results were prone to biases. A particular concern was information bias in terms of 1) misclassification of exposure because current address in 2011 was used rather than place of birth or information on another critical period of life and 2) missing data from non-respondents and those who were lost to follow up.

The Faculty of Medicine provides some housing within the hospital area for those from outside the province. Using current address to classify migration

status, it is estimated that about 30% of personnel aged below 40 can be considered rural-urban migrants (Table 4.1). This percentage dropped drastically amongst the older age groups. It is very likely that, as members of the population get older and settle to live in one place, they move permanently to the Chiang Mai metropolitan area.

As stated earlier, rural-urban migration status is likely to have been underestimated when using current address to define migration status. With this misclassification, the effect sizes seen are likely to have been conservative estimates. Additional analysis (Appendix F), comparing those who were still working in 2011 (n=3,525) with those who were lost to follow up (n=618), revealed that the lost to follow up group was younger compared to those still working in 2011 but did not differ in terms of gender.

Some NCD risk factors, such as diastolic blood pressure and the prevalence of obesity, were lower in the lost to follow up group, which is possibly attributable to the difference in age. The results reported in the previous section were already adjusted for age and gender. If loss to follow is unlikely to be differential by migration status, it would also dilute the associations seen.

4.4 Power calculations for new cross-sectional health worker study

Based on 2008 data using current address in 2011 to classify urban and migration status, the ratio between urban dwellers and rural-to-urban migrants is approximately 4:1. There are approximately 5,000 employees at the CMU Hospital. The results from 2008 showed that around 80%, or 4,000 personnel, would be willing to respond to surveys.

Assuming the same compliance rate of 80%, it was estimated that 3,200 participants would be classified as urban and 800 participants classified as rural-to-urban migrants. Given the assumed number of participants and point estimates of the preliminary results from 2008 (Tables 4.2 and 4.3), I performed power calculations as seen in Table 4.4.

All power calculations assumed a two-sided α value of 0.05, the number of urban dwellers as 3,200, and the number of migrants as 800. I assumed that my new data collection would be conducted in 2013.

For changes in BMI, most participants would have likely to gained weight since 2008. However, I hypothesized that the weight gain (on average) would be greater in the migrant group as migrants are likely to have increased susceptibility to risk factors for NCD in adulthood due to inadequate nutrition in early life (outlined in section 4.2.3).

Thus, while the average BMI in both groups would have increased by 2013, the absolute difference in BMI between the two groups would decrease after 5 years of additional time in urban environments. Assuming that the absolute difference in BMI between urban dwellers and migrants would decrease by half from 0.47 kg/m^2 to 0.235 kg/m^2 after 5 years and the correlation between changes in BMI in a similar time period for each individual is 0.88 (72), it was estimated that I would have 95% power to detect such absolute differences in BMI.

Similarly, for changes in blood pressure, I hypothesized that change would be greater in the migrant group, and the absolute difference between the two groups (on average) would decrease after 5 years. Assuming the absolute difference in systolic blood pressure between urban dwellers and migrants would decrease by half from 1.37 mmHg to 0.685 mmHg after 5 years of additional urban exposure and the correlation between changes in systolic blood pressure in a similar time period for each individual is 0.37 (73), it was estimated that I would have 76% power to detect such absolute differences in systolic blood pressure.

Table 4.4 Power calculations

Outcomes	Estimated effect size	Power
Absolute difference (Urban – Migrant) in BMI in 2008	0.47 kg/m2	92%
Absolute difference (Urban – Migrant) in BMI in 2013 (after 5 years of additional urban exposure)	0.235 kg/m2	95%
Odds ratio of being overweight (BMI > 25) using migrants as reference group	1.33	90%
Absolute difference (Urban – Migrant) in SBP in 2008	1.37 mmHg	85%
Absolute difference (Urban - Migrant) in SBP in 2013 (after 5 years of additional urban exposure)	0.685 mmHg	76%

BMI - body mass index; SBP - systolic blood pressure

4.5 New data collection

I obtained ethical approval for the proposed research from Chiang Mai University in March 2012 (Appendix G) and London School of Hygiene and Tropical Medicine (LSTHM) ethical approval in October 2012 (Appendix H). In September 2012, I returned to Thailand to secure additional funding for the fieldwork and laboratory investigations, recruited local collaborators, trained research staff, developed the materials and the online data entry system to be used for data collection.

My colleagues added two additional objectives for the new data collection. These objectives consisted of exploring the potential role of occupational shift work on burnout, and exploring patterns of substance misuse among health care workers. Together with my supervisor and local colleagues, we conducted two practice data collection runs in November 2012. The actual survey started in January 2013 and ended in June 2013.

The study methods and description of the recruited study population has been published. Additional materials such questionnaires, record forms for physical examination and materials used during interview of non-communicable disease risk factors can be found in Appendix I.

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RESEARCH PAPER COVER SHEET

Chiang Mai University Health Worker Study aiming towards a better understanding of non-communicable disease development in Thailand: methods and description of study population

PLEASE NOTE THAT A COVER SHEET MUST BE COMPLETED FOR EACH RESEARCH PAPER INCLUDED IN A THESIS.

SECTION A – Student Details

Student	Chaisiri Angkurawaranon
Principal Supervisor	Dorothea Nitsch
Thesis Title	Urbanization and internal migration as risk factors for non-communicable disease in Thailand

If the Research Paper has previously been published please complete Section B, if not please move to Section C

SECTION B – Paper already published

Where was the work published?	Clinical Epidemiology		
When was the work published?	August 2013		
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion			
Have you retained the copyright for the work?*	Yes	Was the work subject to academic peer review?	Yes

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Where is the work intended to be published?	
Please list the paper's authors in the intended authorship order:	
Stage of publication	

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	In consultation with my supervisors, I conceived the design of the study and wrote the protocol. I managed the day-to-day responsibility of data collection and analyzed the data. I wrote the manuscript and coordinated all co-authors' feedback and comments. I am first and corresponding author for the article. The detailed contribution of each author is given in the manuscript

Student Signature: _____ **Date:** 13 April 2015

Supervisor Signature: _____ **Date:** 9/4/15

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ORIGINAL RESEARCH

Chiang Mai University Health Worker Study aiming toward a better understanding of noncommunicable disease development in Thailand: methods and description of study population

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Background: Urbanization is considered to be one of the key drivers of noncommunicable diseases (NCDs) in Thailand and other developing countries. These influences, in turn, may affect an individual's behavior and risk of developing NCDs. The Chiang Mai University (CMU) Health Worker Study aims to provide evidence for a better understanding of the development of NCDs and ultimately to apply the evidence toward better prevention, risk modification, and improvement of clinical care for patients with NCDs and NCD-related conditions.

Methods: A cross-sectional survey of health care workers from CMU Hospital was conducted between January 2013 and June 2013. Questionnaires, interviews, and physical and laboratory examinations were used to assess urban exposure, occupational shift work, risk factors for NCDs, self-reported NCDs, and other NCD-related health conditions.

Results: From 5,364 eligible workers, 3,204 participated (59.7%). About 11.1% of the participants had high blood pressure (systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg) and almost 30% were considered to be obese (body mass index ≥25 kg/m^2). A total of 2.3% had a high fasting blood glucose level (≥126 mg/dL), and the most common abnormal lipid profile was high low-density lipoprotein (≥160 mg/dL), which was found in 19.2% of participants.

Discussion: The study of health workers offers three potential advantages. The first is that the study of migrants was possible. Socioenvironmental influence on NCD risk factors can be explored, as changes in environmental exposures can be documented. Second, it allows the investigators to control for access to care. Access to care is potentially a key confounder toward understanding the development of NCDs. Lastly, a study of health personnel allows easy access to laboratory investigations and potential for long-term follow-up. This enables ascertainment of a number of clinical outcomes and provides potential for future studies focusing on therapeutic and prognostic issues related to NCDs.

Keywords: urbanization, noncommunicable disease, risk factors, Thailand

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Background

Thailand, like many middle-income countries, has undergone rapid sociocultural and environmental changes within the last decades, and with them there has been a growing burden of noncommunicable diseases (NCDs).[1] Sociocultural changes thought to be associated with urbanization, globalization, and an aging population are considered potential drivers for the growing burden of NCDs.[2] At an ecological level, there is

evidence from Thailand that urbanization is associated with NCD mortality.[3] At an individual level, there is further evidence that current sociocultural and environmental changes in Thailand are associated with many behavioral changes, such as consumption of fatty food and lack of exercise.[4] In turn, these behavioral changes may lead to increases of some physiological risk factors for NCDs, such as obesity and high blood pressure.[5] However, there is still limited evidence on whether urbanization leads to biomarker changes preceding the development of NCDs, and the mechanisms behind such susceptibility to NCDs in Thailand remain unknown. Evidence from Western countries suggests that although socioeconomic and cultural changes may lead to increased risk of developing NCDs, the same socioeconomic and cultural changes may also be associated with higher income and better access to care and life choices that may decrease risk of developing NCDs.[6]

Conceptual framework of study

The conceptual framework for this research was adapted from the framework on globalization and health (Figure 1).[7] In this study we considered urbanization as the key driver of sociocultural and environmental change in Thailand. The effect of urbanization on the development of NCDs was considered at two levels: the population level and the individual level. At the population level, urbanization could influence health through environmental and sociocultural norms, and could also influence other health-related sectors such as education and trade, along with the national economy, politics, and society. These population level factors could subsequently influence an individual's health beliefs and behavior. For individual level factors, the risk factors for NCDs were taken from the World Health Organization's (WHO) framework.[8] The individual level determinants included the individual's behavioral risk factors for NCDs, the individual's socioeconomic status, and the health care system that the individual is in. Health care systems would reflect the individual's access to care and availability of medication. Ultimately, all these pathways would be expected to mediate changes in an individual's biological/physiological risk factor profile, which is depicted by the farthest left pathway in Figure 1.

Aim of the Chiang Mai University Health Worker Study

The overall aim of the Chiang Mai University (CMU) Health Worker Study is to provide evidence for a better

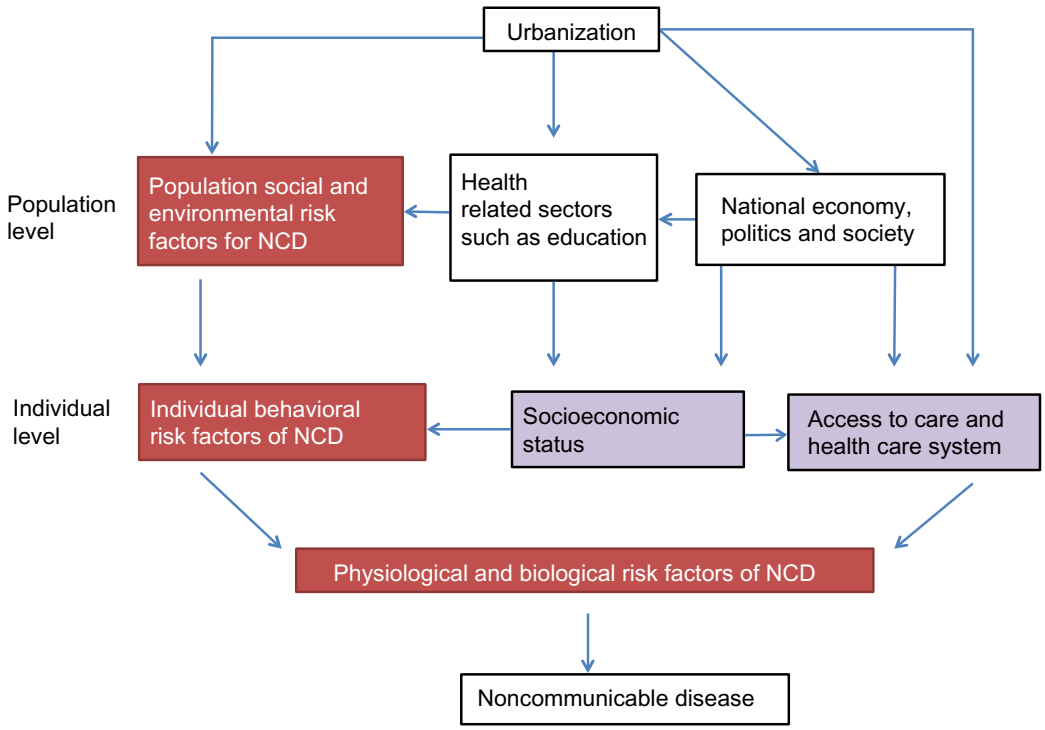

Figure 1 Conceptual framework for drivers of noncommunicable disease (NCD).
Notes: Factors that are mediators on causal pathways between urbanization and NCD. More distal risk factors that may introduce residual confounding in the association between individual behavioral risk factors and NCD risk.

understanding of the development of NCDs in contemporary Thailand, and ultimately to apply the evidence toward better prevention, risk modification, and improvement of clinical care for patients with NCDs and NCD-related conditions.

The specific objectives of the study are:

1. To investigate the difference in behavioral and biological risk factors for NCDs among those with different urban exposures;
2. To investigate the difference in changes in biological risk factors for NCDs among those with different urban exposures;
3. To investigate the association between occupational factors such as shift work with burnout and depression;
4. To investigate the patterns of substance use, such as sedative use and its association with alcohol consumption and smoking.

The objective of this paper is to describe the study methods and present the sociodemographic characteristics of the study population.

Methods

Design

This was an occupationally based cross-sectional survey.

Setting and participants

Between 2012 and 2013 a team of investigators from the Faculty of Medicine of CMU and the London School of Hygiene and Tropical Medicine developed an NCD screening protocol that would be accessible to all health care workers employed by the Faculty of Medicine of CMU, irrespective of age, health status, or type of medical insurance. The Faculty of Medicine of CMU and Maharaj Nakorn Chiang Mai Hospital employs over 5,000 health care workers. As part of hospital and government policy, health workers at CMU Hospital are offered periodic health checkups. Attendance of health workers at these checkups was used to deliver the health screening protocol between January 2013 and June 2013.

Recruitment strategy

The study used an online recruitment and enrollment program. A pilot study using online electronic enrollment and a questionnaire had been conducted in 2008.[9] The topics in the 2008 survey included known history of chronic diseases, lifestyles and behavior, and exposure to occupational hazards. The pilot study yielded a 77% response rate.

For this study, 1 month before enrollment, promotional videos and posters were created and distributed in the official faculty website, by email, and newsletter. The initial enrollment period was from the beginning of January 2013 to early February 2013. The short recruitment time used initially was so that the study team could coordinate and plan a realistic timetable for the physical examination and laboratory investigations that would follow from March 2013 to June 2013. A second enrollment started in the middle of March 2013 and ended in May 2013 to allow for additional participants who may have missed the initial enrollment period. During the second enrollment, in addition to the recruitment strategies previously employed, a new poster stating that the enrollment period had been extended was used as desktop wallpaper on all hospital-operated computers. For participants who did not have easy access to a computer at work, two computers were set aside to help with enrollment at the Health Promotion Unit in the hospital. In addition, a paper format of the enrollment form was also able to be requested, and entered online at a later convenience. A flowchart of the recruitment process is demonstrated in Figure 2.

Data collection

The data collection consisted of two parts. The first was the online registration with a subsequent online questionnaire. The second part was when the participants came in for their interview and received a physical examination, along with laboratory investigations (Figure 3).

Online registration, consent, and online questionnaire

For the online registration, health workers could log in online using their Thai national identification number. This was used to confirm their working status within the hospital. A study information sheet and consent form was presented on-screen. If consent was given, the participants were asked to fill in their basic demographic information and details of current shift work status and risk of burnout, using Maslach Burnout Inventory questionnaires.[10] They could then choose from an allocated time and date to come in for their interview and examination.

Face-to-face interview with examination and sample collection

Participants were asked to fast for at least 8 hours before the day of their examination. On the day of their examination they were assigned a study identification number and given a set of self-administered questionnaires. The questionnaires covered three topics:

1. Risk of harm from substance use using the WHO Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) questionnaire;[11]

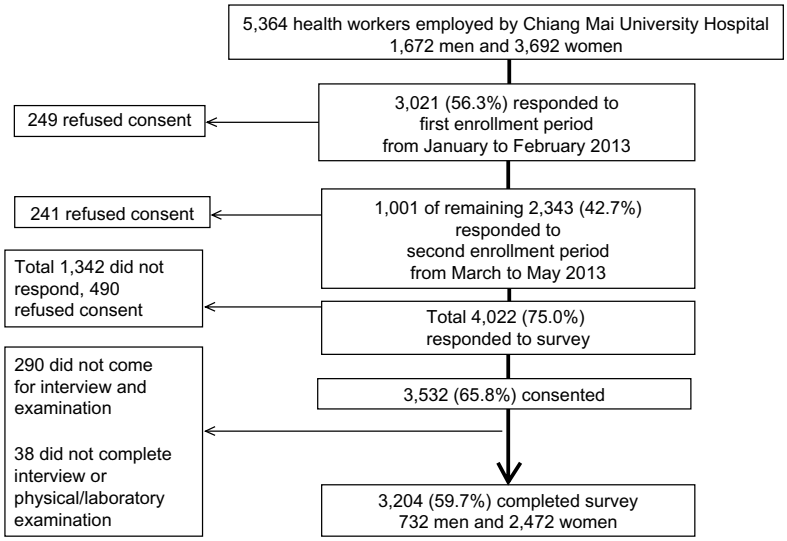

Figure 2 Enrollment process and response.

2. Depression screening using the Patient Health Questionnaire-9 (PHQ-9);[12]
3. Health-related quality of life using the 36-Item Short Form Health Survey (SF-36).[13]

The participants were later interviewed by members of the research team. All face-to-face interviews were carried out by members who were not working at CMU Hospital. Using an online computer system, the participant and researcher would together enter information about the participant's previous migration history and risk factors for NCDs, based on the WHO STEPwise approach to chronic disease risk factor surveillance (STEPS) instrument.[14]

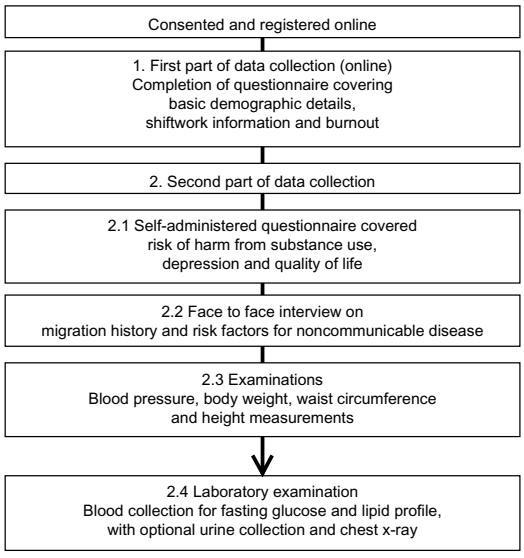

Figure 3 Flow chart of data collection process.

At the examination area, standing height (without shoes), weight, and leg length were measured using a portable stadiometer, an electronic scale, and a standard measuring tape. Waist circumference, hip circumference, and leg length were measured to the nearest 0.1 cm. Waist circumference was measured at the midway point between the lowest palpable rib and the anterior superior iliac crest. Hip circumference was measured around the widest part of the buttock. Leg length was measured from the anterior superior iliac crest to the medial malleolus. All measurements were carried out by trained investigators. Three blood pressure readings were taken 5 minutes apart using an ADC® digital e-sphyg™ 2 nonmercury sphygmomanometer (American Diagnostic Corporation, Hauppauge, NY, USA). Two different cuff sizes were available, and the machines were calibrated every 2 months. Venous blood samples were drawn and processed at the Central Diagnostic Laboratory in CMU Hospital. The complete list of laboratory examinations, which includes fasting blood glucose (FBG) and lipid profiles, along with the methods used, can be found in Table 1. Ten percent of blood samples, chosen at random, were aliquoted and stored in an ultralow temperature (−70°C) freezer for future use/validation studies.

Variables of interest

The factors that were assessed by this study were urban/occupational influences, individual risk factors for NCDs, and self-reported NCDs and other NCD-related health conditions

Table 1 List of laboratory examinations and methods used

Investigation	Sample	Methods used
Complete blood count	Ethylenediaminetetraacetic acid blood	Automated cell counter
Fasting blood glucose	Clotted blood	Glucose hexokinase
Total cholesterol	Clotted blood	Direct enzymatic method
Low-density lipoproteins	Clotted blood	Direct enzymatic method
High-density lipoproteins	Clotted blood	Direct enzymatic method
Triglycerides	Clotted blood	Direct enzymatic method
Blood urea nitrogen	Clotted blood	Urease enzymatic method
Creatinine	Clotted blood	Modified Jaffe's method
Aspartate aminotransferase	Clotted blood	Kinetic method
Alanine aminotransferase	Clotted blood	Kinetic method
Alkaline phosphatase	Clotted blood	Kinetic method
Uric acid	Clotted blood	Urease enzymatic method
Urinalysis	Mid-void urine sample	Automated
Chest X-ray		

Notes: The Ministry of Public Health, Thailand provides a list of accredited laboratory investigations and methods used to obtained ISO 15189. http://webdb.dmsc.moph.go.th/ifc_qa/DBQA/ifc_qa/userfiles/15189%204027_TH.pdf.

and outcomes. Population and occupational factors consisted of lifetime urban exposure and exposure to shift work. Risk factors for NCDs consisted of four behavioral (unhealthy diet, physical inactivity, and alcohol, and tobacco use) and four biological/physiological (increased blood pressure, obesity, hyperlipidemia, and hyperglycemia) risk factors. The absence or presence of an NCD (cardiovascular disease, diabetes, chronic respiratory disease, and cancer) was assessed using self-report. Other health-related conditions consisted of burnout, depression, substance use, and health-related quality of life

Key variable definitions

1. Urban exposure: The United Nations defines an urban agglomeration as "the built-up or densely populated area containing the city proper, suburbs and continuously settled commuter areas. It may be smaller or larger than a metropolitan area; it may also comprise the city proper and its suburban fringe or thickly settled adjoining territory."[15] For our study, districts in Bangkok and the ten districts in the Chiang Mai metropolitan area (Figure 4) were considered urban. The rest of the districts in Thailand were classified as rural. By tracking the area of residence during crucial development points, urban and rural exposure, total years of urban exposure, and proportion of lifetime exposure to the urban area could be calculated.
2. Behavioral risk factors for NCDs: All variables were derived through interviews using the WHO STEPS questionnaire. Alcohol consumption was defined as having consumed alcohol within the past 12 months. A heavy drinking pattern was defined as having more than five standard drinks per sitting for men and more than four standard drinks per sitting for women. Smoking status was classified according to whether participants currently used tobacco product daily. An unhealthy diet was classified using standard units of fruit and vegetables consumed per week. It is suggested that five units per day is the minimal requirement. Physical inactivity was classified using the WHO recommendation on physical activity for health.[16] Throughout the week, an adult should do at least 75 minutes of vigorous-intensity physical activity or 150 minutes of moderate-intensity physical activity or the equivalent of 600 metabolic equivalent minutes.
3. Biological/physiological risk factors for NCDs: The average of the second and third blood pressure reading was used as the blood pressure for each participant. Increased blood pressure was defined as systolic blood pressure (SBP) $\geq$140 mmHg or diastolic blood pressure (DBP) $\geq$90 mmHg. Body mass index (BMI), calculated from taking the weight (in kg) and dividing by height (in meters) squared, was used to define obesity. Using standard Asian criteria,[17] a BMI of $\geq$25 was considered the cutoff point for obesity. Hyperglycemia was measured using FBG. A participant was considered to have high blood glucose if their blood glucose was $\geq$126 mg/dL. Low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides were used as measures of dyslipidemia. A participant was considered to have high LDL cholesterol if their LDL level was $\geq$160 mg/dL. The HDL cutoff points for low HDL were $<$40 mg/dL in men and $<$50 mg/dL in women. The cutoff point for high triglyceride level was $\geq$150 mg/dL.

Data entry and quality control

Members of the research team were trained to perform interviews and examinations by the lead investigators. All materials/questionnaires used in the study were translated into Thai and were tested for validity in the Thai population

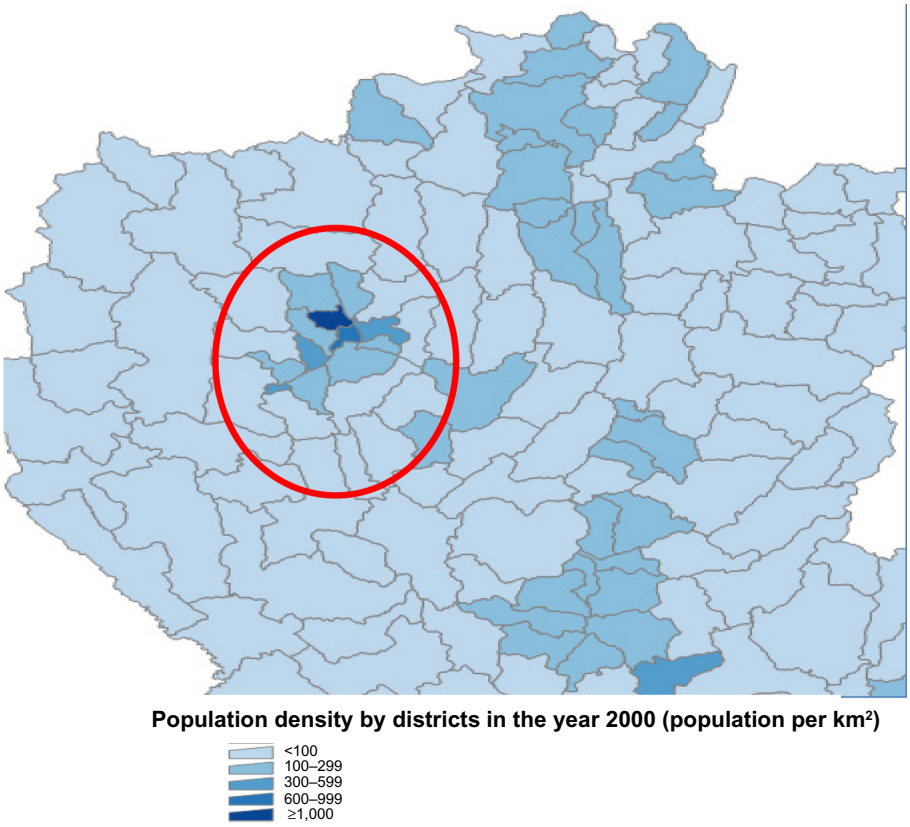

Figure 4 Ten districts in the Chiang Mai metropolitan area.

or have been published in past literature.[18–22] Source documents from questionnaires and the physical examination were scanned and entered into the research database using a double entry system. All laboratory investigations were processed by the Central Diagnostic Laboratory in CMU Hospital. The laboratory undergoes a routine internal and external quality control process and has been accredited with International Organization for Standardization (ISO) 15189:2007.

To obtain laboratory results from the hospital's network, the study identification numbers and hospital numbers were linked using an electronic barcode system. Once linked to laboratory results, the hospital number and Thai national identification number were stripped from the research database. The research database was stored within the CMU Faculty of Medicine's intranet system and accessible only to members of the research team.

Power calculations

Using the 2008 pilot data, a conservative estimate for the ratio between urban group (health care workers born in an urban area) and rural to urban migrant group (health care workers born in a rural area) was 4:1. Assuming a similar compliance rate of 80%, it was estimated that 3,200 participants would be classified as urban and 800 participants would be classified as rural to urban migrants. Given the assumed number of participants and results from the pilot study, it was estimated that the study would have 92% power to detect differences in BMI and 85% power to detect differences in SBP.

Ethics

The study was approved by the Faculty of Medicine of CMU (No 069/2012) and the London School of Hygiene and Tropical Medicine's ethical review boards (Ref: 6521).

Analysis plan

Different multivariable regression models will be built by carefully grouping sets of explanatory variables using the framework previously described in Figure 1. A life course approach and analysis[23] will also be taken to explore the possible mechanisms for association between urbanization and NCD risk factors. A detailed analysis plan for each of the objectives will be presented in individual publications. For this paper, sociodemographic characteristics were summarized using descriptive statistics.

Results

Response rates

As of July 2013 there were 5,364 people working for the Faculty of Medicine of CMU. A total of 4,022 (75.0%) responded to the survey and 3,532 (65.8%) consented to participate in the study. In the end, 3,204 (59.7%) completed the entire data collection process (Figure 2). The study sample represented 43.7% of all male and 66.9% of all females working for the Faculty of Medicine of CMU and Maharaj Nakorn Chiang Mai Hospital. Using records from the faculty's official personnel database, we found that our study population represented the entire source population well, in terms of age and education status, but men and certain occupational groups such as doctors and dentists may have been under-represented (Table 2).

Table 2 Comparison of characteristics between study population and source population using the Chiang Mai University Hospital's official personnel database

	Study population	Source population
Number	3,188[a]	5,364
% female	77.3	68.8
Mean age, years (standard deviation)	39.7 (10.7)	40.5 (11.0)
Age distribution (%)		
<25 years	10.7	8.8
25–30 years	13.6	14.3
30–35 years	13.5	12.7
35–40 years	14.0	12.6
40–45 years	11.7	10.9
45–50 years	16.2	15.4
50–55 years	12.0	13.9
55–60 years	8.3	10.5
>60 years	0.5	0.6
Job position (%)		
Special advisor	0.0	<0.1
Instructor (doctor of medicine)	1.8	6.4
Instructor (not a doctor of medicine)	1.2	1.9
Doctor/dentist	0.7	5.8
Pharmacist	2.1	2.2
Nurse	38.7	31.1
Nurse aide	13.2	12.2
Other health professionals	2.8	3.0
Nonhealth professionals	7.1	6.4
Administration officers	4.1	3.9
Workers	28.2	26.9
Highest education (%)		
Elementary school	4.0	4.3
Early secondary school	6.3	6.4
Late secondary school	13.6	12.9
Bachelor's degree	66.5	62.0
Master's degree	6.7	6.3
PhD/equivalent	2.8	8.0

Note: [a]16 participants were included in the research database but were not in the personnel database as of July 2013 when the analysis was conducted.

Characteristics of the study population

Of 3,204 participants who completed the entire survey, 732 participants were male (22.8%) and 2,472 (77.2%) were female. The mean age of the study population was 40.2 years. Nurses represented the largest occupation group in the survey (38.8%). The majority of the participants had at least a bachelor's degree (64.6%). A total of 41.8% of the workers were born outside Bangkok or Chiang Mai metropolitan area (Table 3). The majority of participants were not currently smoking at the time of the survey (93.8%), but more than half had consumed alcohol within 12 months. Only 14.3% had at least five servings of fruit and/or vegetables per day, and 52.1% had an appropriate physical activity level as recommended by the WHO. Men were more likely to smoke and drink. They were also less likely to meet the recommended portions of fruit/vegetable consumption but were more likely to meet the requirement for physical activity

Table 3 Demographic characteristics of participants in the Chiang Mai University Health Worker Study

Characteristics	Total N=3,204	Female N=2,472	Male N=732
Mean age, years (standard deviation)	40.2 (10.7)	40.1 (10.9)	40.6 (9.9)
Age group: N (%)			
<30 years	677 (21.1)	564 (22.8)	113 (15.4)
30–40 years	878 (27.4)	642 (26.0)	236 (32.2)
40–50 years	876 (27.3)	672 (27.2)	204 (27.9)
>50 years	773 (24.1)	594 (24.0)	179 (24.4)
Sex: female: N (%)	2,472 (77.1)	2,472 (100)	0 (0)
Job position: N (%)			
Instructors/doctors/ dentists	118 (3.7)	71 (2.9)	47 (6.4)
Nurses	1,236 (38.6)	1,166 (47.2)	70 (9.6)
Other health professionals	660 (20.6)	548 (22.2)	112 (15.3)
Administration officers and nonhealth professionals	356 (11.1)	259 (10.5)	97 (13.2)
Workers	834 (26.0)	428 (17.3)	406 (55.5)
Highest education: N (%)			
Below bachelor's degree	1,134 (35.4)	721 (29.2)	413 (56.4)
Bachelor's degree	1,690 (52.7)	1,432 (57.9)	258 (35.2)
Higher than bachelor's degree	380 (11.9)	319 (12.9)	61 (8.3)
Household income per month (Baht)[a] N (%)			
<20,000	1,196 (37.3)	777 (31.4)	419 (57.2)
20,000–40,000	927 (28.9)	766 (31.0)	161 (22.0)
40,000–60,000	522 (16.3)	460 (18.6)	62 (8.5)
>60,000	559 (17.5)	469 (19.0)	90 (12.3)
Urban exposure status based on location at birth N (%)			
Rural area (rural to urban migrant)	1,340 (41.8)	1,127 (45.6)	213 (29.1)
Urban area	1,964 (58.2)	1,345 (54.4)	519 (70.9)

Note: [a]31 Baht approximately equals US $1.

Table 4 Behavioral and biological/physiological risk factors for noncommunicable diseases in participants of the Chiang Mai University Health Worker Study

	Total N=3,204	Female N=2,472	Male N=732
Behavioral risk factors			
Currently smoking: N (%)	199 (6.2)	7 (0.3)	192 (26.3)
Alcohol consumption in past 12 months: N (%)	1,729 (54.0)	1,130 (45.7)	599 (81.8)
Heavy drinking in past 30 days:[a] N (%)	503 (15.7)	152 (6.1)	351 (48.0)
Eating >5 portions of fruit or vegetables per day: N (%)	457 (14.3)	370 (15.0)	87 (11.9)
Appropriate physical activity:[b] N (%)	1,668 (52.1)	1,202 (48.6)	466 (63.7)
Biological and physiological risk factors			
Mean SBP in mmHg (SD)	116.1 (15.5)	112.9 (14.2)	126.8 (14.9)
Mean DBP in mmHg (SD)	73.9 (11.4)	71.7 (10.6)	81.0 (11.2)
High blood pressure SBP ≥140 or DBP ≥90: N (%)	357 (11.1)	180 (7.3)	177 (24.2)
Mean (SD) BMI kg/m^2	23.4 (4.1)	23.0 (4.0)	24.9 (3.8)
Obesity: N (%)			
Normal: BMI <23	1,658 (51.7)	1,421 (57.5)	237 (32.4)
Overweight: BMI 23–25	602 (18.8)	424 (17.1)	178 (24.3)
Obese I: BMI 25–30	732 (22.9)	484 (19.6)	248 (33.9)
Obese II: BMI >30	212 (6.6)	143 (5.8)	69 (9.4)
Mean WC in centimeters (SD)	75.4 (10.8)	72.9 (9.7)	83.7 (10.0)
Truncal obesity N (%) (WC >90 cm in men and >80 cm in women)	659 (20.6)	500 (20.2)	159 (21.7)
Mean fasting blood glucose in mg/dL (SD)	91.0 (16.2)	89.3 (14.0)	96.6 (21.1)
High fasting blood glucose (≥126 mg/dL): N (%)	73 (2.3)	36 (1.5)	37 (5.1)
Mean LDL in mg/dL (SD)	131.0 (35.5)	129.6 (34.0)	136.0 (39.6)
High LDL ≥160 mg/dL: N (%)	614 (19.2)	413 (16.7)	201 (27.5)
Mean HDL in mg/dL (SD)	58.5 (13.3)	60.5 (12.8)	52.0 (12.8)
Low HDL <50 mg/dL in women and <40 mg/dL in men: N (%)	578 (18.1)	481 (19.5)	97 (13.3)
Mean triglycerides in mg/dL (SD)	102.2 (96.0)	87.1 (81.6)	153.2 (120.5)
High triglycerides ≥150 mg/dL: N (%)	504 (15.7)	228 (9.2)	276 (37.8)

Notes: [a]A heavy drinking pattern is defined as having more than five standard drinks per sitting for men and four standard drinks per sitting for women; [b]throughout the week, an adult should do at least 75 minutes of vigorous-intensity physical activity or 150 minutes of moderate-intensity physical activity or the equivalent of 600 metabolic equivalent minutes.

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure; WC, waist circumference; SD, standard deviation.

(Table 4). Mean SBP and DBP were 126.8 mmHg and 81.0 mmHg, respectively. About 11.1% of the participants had high blood pressure (SBP ≥140 mmHg or DBP ≥90 mmHg). Mean BMI was 23.4 kg/m^2 (standard deviation [SD] =4.1) in men and 23.0 kg/m^2 (SD =4.0) in women. Overall, almost 30% were considered to be obese (BMI ≥25 kg/m^2). Mean FBG was 96.6 mg/dL (SD =21.0) Only 2.3% had high FBG (≥126 mg/dL) and the most common abnormal lipid profile was high LDL (LDL ≥160 mg/dL), which was found in 19.2% of participants (Table 4).

Discussion

This paper describes the protocol, response rates, and characteristics of the study population in the CMU Health Worker Study. A study of health care workers offered three potential advantages toward understanding NCDs in Thailand. The first advantage was the potential for a migration study: ie, the study of health effects of people moving from a rural to an urban area to work. The mechanisms or pathways by which sociocultural/environmental exposures influence NCD risk factors could be explored using a migration study, as changes in environmental exposures can be documented.[24] Most health personnel have moved since birth and early life, whether for education or employment purposes.[25] Second, a study of health personnel allowed the investigators to control for access to care. Access to care is potentially a key confounder toward understanding the development of NCDs in Thailand.[3] Lastly, a study of health personnel allowed easy access to laboratory and clinical investigations and potential for long-term follow-up. This enables ascertainment of a number of clinical outcomes and provides potential for future studies focusing on therapeutic and prognostic issues related to NCDs.

Many factors contributed to the completion of the survey. The pilot data from 2008 provided a valuable starting point for the study. The planning of the study began 1 year prior to data collection. This helped ensure that the electronic systems and supports were in place. The second recruitment period, with more aggressive advertising, allowed us to enroll and recruit populations with an initially low response rate. The data collection process, especially during the second process (interview, examination, and laboratory investigation), was considered to be time consuming. Two pilot runs (of the second part of the data collection process) were conducted to ensure smooth running and help calculate the manpower needed to keep the entire process between 30 minutes and 45 minutes per participant, in order to fit the busy schedule of workers in a large teaching hospital. Participants were contacted up to three times if they had missed their original appointment for physical and laboratory examinations. Integrating a research component into a routinely offered service helped subsidize the cost of research and promoted mutual collaboration between researchers and hospital administrators.

The study has some limitations that could influence the validity and generalizability of our results. Differential response rates among different sexes and occupational groups may have caused selection bias, which would limit the generalization to the actual source population. However, depending on the mechanism of the bias, multiple techniques such as restriction, stratification, or inverse probability weighting can be used to deal with selection bias or nonresponse bias in future analysis.[26] An occupational study could limit generalization to the Thai population, and the "healthy worker" effect is likely to underestimate most associations seen if seriously ill patients are less likely to be employed. Nonetheless, the relative risks within the study population are still valid.[27]

To our knowledge, there have been only two large cohorts from Thailand examining the transition and trends associated with chronic NCDs. The first is a cohort of workers from the Electricity Generating Authority of Thailand,[28] who looked at the trends in known cardiovascular risk factors and their association with all cause mortality and cardiovascular mortality. The authors stated that the study's main strength was in the breadth of biological markers available and the detailed verification of mortality and causes of mortality. However, there were limited data on behavioral factors (only smoking and alcohol consumption) and population level influences, such as urbanization. The second cohort is a study of Sukhothai Thammathirat Open University students.[29] Its aim was to look at Thai health transition. The main aim was to study how the proximal and distal determinants of health influence health outcomes. Although both population determinants and detailed individual determinants were collected, no biological samples were taken. Our study could help provide linking evidence between the two large cohorts in Thailand and enhance the understanding of NCDs in Thailand.

If current patterns of economic development toward higher income, better education, and access to care in Thailand continue, our study could provide useful information on the development of NCDs as the rest of the country becomes more developed.

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Disclosure

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4.5.2 Issues encountered during fieldwork

The published manuscript presented in this chapter details the methods and results of the new data collection. Table 4.5 summarizes the issues I encountered during the first week of data collection and the measures I took to address these issues in order to minimize their impact on the overall integrity of the dataset.

Table 4.5 Issues encountered during the first week of data collection

Issues	Solutions
Approximately 50% of workers came early at 8.00 am instead of at their later time slots. We did not have enough research staff to meet high demands early in the morning.	I increased the number of research staff from 6 to 9 in order to help with data collection early in the morning.
We planned that the entire duration of the data collection process should be kept to a minimum so that it would not disrupt the participant's work schedule. However, the process initially took about 45-60 minutes, which was too slow for our participants.	From the pilot, I learned that there were two rate-limiting stations in our data collection process: the blood pressure measurement and interview. A ratio of 1:1 between these two stations worked well. By increasing my research staff to 9 per day, I also increased the number of blood pressure monitors to 9. After increasing the number of research staff and blood pressure monitors, the participants were able to complete all stations in 30-45 minutes.
The 30-45 minutes duration to complete all stations was too long for some groups of workers, specifically for doctors.	I developed a fast track system. One blood pressure machine was set aside and one senior researcher was assigned to give priority to doctors.
Some participants did not come to their appointments.	I decided on a triple reminder system. Researchers could make contact one week before participants' appointments. We would send a text message reminder to their mobile phones one day before appointments. If they missed their appointment, we would phone to reschedule an appointment.
Although researchers were trained to check whether the participants had answered all the questionnaires, there were still some issues with missing data.	I lead a meeting of researchers to identify trouble spots within the questionnaires which researchers should pay special attention to.

4.5.3 Additional results and discussion

The proposed framework of the thesis outlined that individual socioeconomic status (SES) could be considered as a mediator or confounder in the association between urbanization and NCDs (Figure 1.1). In addition to the results presented in the manuscript, I also explored whether current SES was associated with NCD risk factors in my occupational survey. I used three measures of socioeconomic status: 1) job position, 2) level of education and 3) average monthly household income.

Adjusted for age and sex, the results demonstrated that for most NCD risk factors, those with lower SES (in all three measures of SES) had higher levels of NCD risk factors than those with higher SES. This was consistent across most behavioural, physiological and biological risk factors (Table 4.6 and Table 4.7). There were some exceptions. For low-density lipoprotein (LDL) cholesterol, there was no evidence for associations with the three measures of SES.

For inadequate physical activity and inadequate diet (consuming less than 5 servings of fruits and/or vegetable per day), those with lower SES were less likely to have these two risk factors. Results from the World Health Survey, conducted in low and middle income countries, have also demonstrated that there were varying patterns and degrees of socioeconomic inequalities across different NCD risk factors (74).

The additional results from this chapter demonstrated that, even among a population of urban health care workers employed by the same hospital, socioeconomic status was still likely to be a key factor in NCD development. Hence, I decided that the analysis plan for the subsequent chapters in the thesis would need to take into consideration the potential impact of SES on the associations between urbanicity and NCD outcomes of interest.

Table 4.6 Association between socioeconomic status and behavioural risk factors for NCDs in the Chiang Mai University Health Worker Study

SES	OR currently smoking	OR heavy drinking in 30 days	OR inadequate diet*	OR inadequate activity**
Job position				
Worker	Reference	Reference	Reference	Reference
Administrators and non-health personnel	0.43 (0.24 to 74)	0.54 (0.38 to 0.76)	1.09 (0.77 to 1.55)	1.92(1.48 to 2.48)
Other health professionals	0.34 (0.20 to 0.58)	0.56 (0.41 to 0.76)	1.27 (0.94 to 1.72)	1.13 (0.91 to 1.41)
Nurses	0.16 (0.08 to 0.35)	0.23 (0.17 to 0.33)	1.33 (1.01 to 1.75)	1.17 (0.96 to 1.42)
Doctors/Dentists/Instructors	0.14 (0.05 to 0.41)	0.06 (0.02 to 0.16)	1.13 (0.65 to 1.97)	2.16 (1.45 to 3.22)
p (trend)	<0.001	<0.001	0.052	0.090
p (departure from linearity)	0.648	0.006	0.903	<0.001
Highest Education: N (%)				
Below bachelor's degree	Reference	Reference	Reference	Reference
Bachelor's degree	0.33 (0.22 to 0.49)	0.42 (0.33 to 0.54)	1.18 (0.94 to 1.48)	1.48 (1.25 to 1.74)
Higher than bachelor's degree	0.23 (0.10 to 0.53)	0.18 (0.10 to 0.31)	1.18 (0.85 to 1.63)	1.64 (1.29 to 2.07)
p (trend)	<0.001	<0.002	0.192	<0.001
p (departure from linearity)	0.172	0.906	0.483	0.080
Household income per month (Baht)*				
<20,000	Reference	Reference	Reference	Reference
20,000-40,000	0.52 (0.34 to 0.80)	0.61 (0.47 to 079)	1.05 (0.81 to 1.36)	0.92 (0.77 to 1.10)
40,000-60,000	0.32 (0.15 to 0.67)	0.46 (0.31 to 0.67)	0.93 (0.70 to 1.26)	1.16 (0.93 to 1.44)
>60,000	0.44 (0.24 to 0.81)	0.29 (0.20 to 0.44)	1.09 (0.81 to 1.48)	1.04 (0.84 to 1.28)
p (trend)	<0.001	<0.001	0.756	0.394
p (departure from linearity)	0.129	0.743	0.623	0.154

Total sample size of Chiang Mai University Health Worker study 3,204; * Inadequate diet: less than 5 standard servings of fruit or vegetables per day; ** Adequate physical activity: less than75 minutes of vigorous-intensity physical activity or 150 minutes of moderate-intensity physical activity or equivalent of 600 Metabolic equivalent (MET)-minutes. All results adjusted for age and sex.

Table 4.7 Association between socioeconomic status and physiological/biological risk factors for NCDs in the Chiang Mai University Health Worker Study

	Systolic blood pressure (mmHg)	Fasting glucose (mg/dL)	BMI (kg/m^2)	LDL (mg/dL)	HDL (mg/dL)	TG (mg/dL)
Job position						
Worker	Reference	Reference	Reference	Reference	Reference	Reference
Administrators and non-health personnel	-3.07 (-4.75 to 01.40)	-1.72 (-3.65 to 0.21)	-0.92 (-1.40 to -0.43)	4.63 (0.25 to 9.00)	0.80 (-0.79 to 2.40)	-10.15 (-21.57 to 1.27)
Other health professionals	-2.66 (-4.08 to -1.24)	-1.57 (03.21 to 0.07)	-0.73 (-1.14 to -0.32)	6.19 (2.48 to 9.89)	0.67 (-0.69 to 2.02)	-17.64 (-27.32 to -7.96)
Nurses	-4.88 (-6.17 to -3.59)	-3.39 (-4.89 to -1.91)	-1.92 (-2.29 to -1.55)	0.16 (-3.21 to 3.53)	3.29 (2.06 to 4.53)	-31.16 (-39.97 to -22.36)
Doctors/Dentists/Instructors	-7.61 (-10.18 to -5.04)	-3.87 (-6.84 to -0.90)	-2.16 (-2.90 to -1.42)	-4.27 (-10.98 to 2.44)	6.37 (3.92 to 8.82)	-32.37 (-49.91 to -14.83)
p (trend)	<0.001	<0.001	<0.001	0.481	<0.001	<0.001
p (departure from linearity)	0.105	0.624	0.004	0.002	0.015	0.713
Highest Education						
Below bachelor's degree	Reference	Reference	Reference	Reference	Reference	Reference
Bachelor's degree	-3.03 (-4.10 to -1.95)	-2.25 (-3.49 to -1.00)	-1.48 (-1.80 to -1.17)	0.27 (-2.55 to 3.10)	2.34 (1.31 to 3.37)	-19.77 (-27.15 to -12.38)
Higher than bachelor's degree	-5.56 (-7.12 to -3.99)	-3.31 (-5.12 to -1.50)	-1.40 (-1.85 to -0.94)	-2.08 (-6.19 to 2.02)	4.96 (3.46 to 6.46)	-20.23 (-30.97 to -9.50)
p (trend)	<0.001	<0.001	<0.001	0.476	<0.001	<0.001
p (departure from linearity)	0.649	0.348	<0.001	0.357	0.784	0.010
Household income per month (Baht)*						
<20,000	Reference	Reference	Reference	Reference	Reference	Reference
20,000-40,000	-2.00 (-3.17 to -0.84)	-1.25 (-2.60 to 0.09)	-0.85 (-1.19 to -0.51)	0.29 (-2.76 to 3.33)	1.42 (0.31 to 2.53)	-6.31 (-14.28 to 1.66)
40,000-60,000	-1.70 (-3.12 to -0.28)	-2.14 (-3.78 to -0.51)	-0.84 (-1.26 to -0.43)	0.00 (-3.71 to 3.71)	2.39 (1.04 to 3.74)	-14.85 (-24.56 to -5.15)
>60,000	-3.79 (-5.20 to -2.38)	-3.39 (-5.01 to -1.77)	-0.92 (-1.33 to -0.51)	-0.24 (-3.92 to 3.43)	3.41 (2.07 to 4.76)	-19.59 (-29.21 to -9.98)
p (trend)	<0.001	<0.001	<0.001	0.899	<0.001	<0.001
p (departure from linearity)	0.113	0.961	0.003	0.967	0.865	0.921

Total sample size of Chiang Mai University Health Worker study 3,204; All results are age and sex adjusted using linear regression; * 31 baht = approximately 1 US dollar; BMI - body mass index; LDL - low density lipoprotein cholesterol; HDL - high density lipoprotein cholesterol; TG – triglyceride.

4.6 Dealing with study limitations

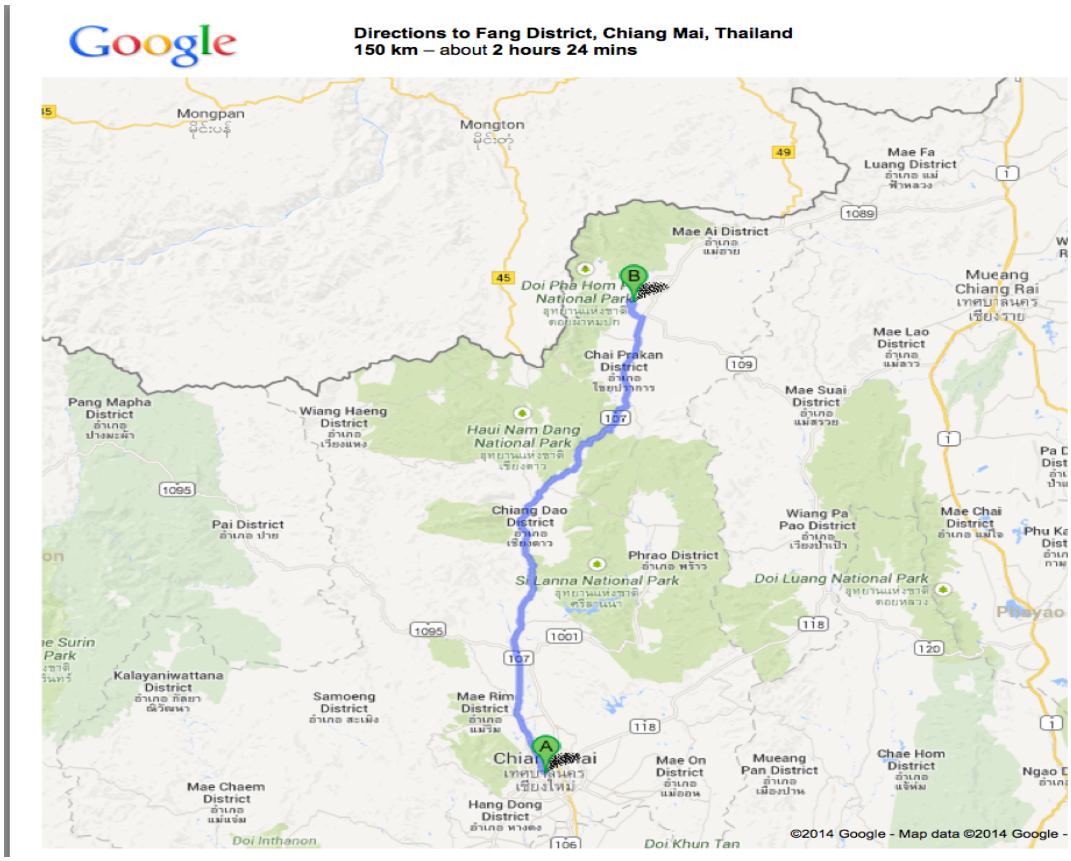
4.6.1 Limitations of cross-sectional dataset

Based on the power calculations in section 4.4, I could be underpowered to detect differences in some NCD risk factors such as changes in blood pressure between rural-urban migrants and urban dwellers. It was also expected that there would be limited variations in urban exposure status throughout the life course if data were only collected amongst workers already living in an urban area. Thus, during the period of data collection, I conducted a similar survey at Fang District Hospital (rural) to help increase the sample size and to include more rural study participants.

Fang Hospital is a district (rural) hospital, situated in Fang District in Chiang Mai province. It is about 150 kilometres from the city of Chiang Mai. This 120-bed hospital has approximately 400 health care workers providing services for over 140,000 people within the area. This location is separated from the Muang (city) district of Chiang Mai by mountains and highlands (Figure 4.3), a factor which helped to limit cross-contamination of exposure. Using a similar protocol as described in the publication, the Fang research team distributed and collected questionniares along with consent forms. Within 2 weeks of the questionnaires being collected, participants came for physical examinations and laboratory investigations in Fang Hospital.

The examination and laboratory investigations took place on the same day. All blood specimens were collected and analyzed at the laboratory in Fang hospital. However, a random sample of 100 blood specimens was also sent for analysis at CMU Hospital to assess agreement between the two sites.

Figure 4.3 Locations of Muang (city) District of Chiang Mai and Fang District



A - Muang (city) District of Chiang Mai; B - Fang District, Chiang Mai; Source: Google maps (75)

Out of 459 eligible health care workers at Fang Hospital, 312 (68.0%) completed the survey. The dataset from Fang Hospital represented its source population well in terms of age, gender and occupation (Table 4.8). Adding the dataset from Fang to the CMU Health worker study allowed me to address with more confidence the third objective of my PhD research, which was to explore the differences in behavioural, physiological and biological risk factors for NCD among those with different urban exposures (Table 4.9).

Table 4.8 Distribution of demographic factors in the study sample and total population of health workers at Fang Hospital

	Fang Hospital	
	Sample population	Total population
Number	312	459
% Female	75.3	74.5
Mean age (sd)	33.1 (10.7)	34.1 (10.8)
Age Distribution (%)		
< 25	23.1	21.1
25-30	21.8	20.9
30-35	16.9	18.6
35-40	12.7	13.4
40-45	6.5	5.7
45-50	5.4	6.4
50-55	9.4	9.0
55-60	3.3	4.4
> 60	0.6	1.0
Job Position		
Doctor/Dentist	5.8	7.4
Pharmacist	1.3	3.0
Nurse	22.4	24.8
Other health professional	10.9	9.4
Non-health professional	4.2	4.6
Administrative support staff	2.9	2.6
Non-skilled worker	15.7	14.2
Skilled worker	36.9	34.0

Table 4.9 Distribution of urban and migration status in the study sample according to hospital of employment

	Chiang Mai University Hospital	Fang Hospital
Total number of completed data	3,204	312
Mean age (sd) in years	40.2 (10.7)	33.1(10.7)
% Female	77.1	75.3
Median number of moves (inter-quartile range-IQR)	1 (0-1)	1 (0-2)
Mean number of moves (sd)	0.9 (1.1)	1.3 (1.4)
Migration (birth-current location in 2013): N (col %)		
Rural-Rural	--	265(84.9)
Urban-Rural	--	47 (15.1)
Rural-Urban	1,340 (41.8)	--
Urban-Urban	1,864 (58.2)	--
% of urban life years: N (col %)		
0-10	74 (2.3)	174 (55.8)
10-20	104 (3.3)	69 (22.1)
20-30	170 (5.3)	21 (6.7)
30-40	145 (4.5)	9 (2.9)
40-50	197 (6.2)	7 (2.2)
50-60	314 (9.8)	9 (2.9)
60-70	283 (8.8)	3 (1.0)
70-80	94 (2.9)	5 (1.6)
80-90	60 (1.9)	3 (1.0)
90-100	1,752 (54.7)	11 (3.5)
Missing	11 (0.3)	1 (0.3)

Locations outside Chiang Mai metropolitan area were classified as rural and locations within Chiang Mai metropolitan area as urban (see section 4.2.1)

One major limitation of the combined dataset was that, for practical reasons, there were some systematic differences in the assessment of risk factors. Information on behavioural risk factors (inadequate physical activity, inadequate fruit/vegetable consumption, smoking and alcohol consumption) was obtained through interviews at CMU Hospital and through self-completed questionnaires at Fang Hospital. Blood pressure readings were taken using digital sphygmomanometers in Chiang Mai University hospital and by manual mercury sphygmomanometers in Fang Hospital.

I considered cross-validation between different methods. However, as participants came for assessment during working hours, validation with two different types of instrument and different modes of administering questionnaires would have taken 30-40 additional minutes. This was not feasible for the study at the time. As only one method was used for each site, I planned to conduct a sensitivity analysis using restricted analysis from the CMU site as it provided a larger sample size.

All blood samples were handled at their respective hospitals' laboratory. Of laboratory analyses, standardization was less likely to be an issue as both sites are government hospitals and undergo the same external validation process by the Ministry of Public Health. Moreover, 100 random samples from Fang Hospital were processed at Chiang Mai University hospital to assess agreement.

The findings from the combined dataset from Fang and CMU hospitals, results of the sensitivity analysis and the agreement between laboratory results from Fang and CMU hospitals will be presented in more detail in Chapter 5.

4.6.2 Limitations of the cohort dataset

As with the cross-sectional dataset, the cohort dataset could be underpowered to detect changes in NCD risk factors over time. Moreover, as discussed in the published paper, it may be difficult to generalize my findings to the entire Thai population.

To address this limitation, I planned to collaborate with investigators from the Thai Cohort Study (TCS) (introduced in Chapter 1, section 1.5) to obtain their large dataset of over 80,000 participants. The investigators of the TCS have suggested that their cohort profile represents the Thai population well (Figure 1.2) (36). Presenting findings from both cohorts could be useful in helping to understand how associations between urban environments and body mass index can differ among different study populations in Thailand.

4.6.3 Other limitations

A methodological limitation, similar to most migration studies that seek to understand urbanization and health, is that the new dataset does not allow empirical distinction between migration and urbanization (47). The TCS also offers the unique opportunity to explore both recent migration and urbanicity of locations as separate exposures of interests. These additional datasets from the TCS will be introduced and presented in more detail in Chapters 6 and 7.

Chapter 5 : Urban Environments and Risk Factors for Non-communicable Diseases

Summary

Introduction: It is unclear whether the associations between urban environments and behavioural/physiological risk factors translate to corresponding associations with biological risk factors (biomarkers) in Thailand.

Objective (3): To investigate the differences in behavioural, physiological and biological risk factors for non-communicable disease (NCD) amongst those with different urban exposures in Thailand and to explore the possible life course models behind such associations.

Study population: Health care workers in Chiang Mai University and Fang Hospital

Exposures: i) Early life urban exposure to represent the early life critical/sensitive period model and ii) Proportion of urban life years to represent the accumulation of risk model

Outcomes: Four behavioural risk factors (alcohol, tobacco, inadequate physical activity, inadequate fruit/vegetable consumption), two physiological risk factors (blood pressure, BMI) and four biological risk factors (glucose, LDL, HDL, TG)

Key findings: Both measures of urbanicity were independently associated with increases in all behavioural and physiological risk factors. However, urbanicity did not always translate into higher levels of biological risk factors. For some biological risk factors (glucose, LDL and HDL), there was evidence that the effect of proportion of urban life years may differ by early life exposure, such that people spending their early life in an urban area may be more susceptible to the effects of an increased proportion of urban life years compared to those growing up in rural areas.

5.1 Introduction

In Chapter 1, I summarized the current state of knowledge on urban exposure and its association with an increase in multiple behavioural (smoking, alcohol consumption, inadequate fruit and vegetable intake) and physiological risk factors (high blood pressure and body mass index).

However, it is unclear whether the directions and strength of associations are consistent across more proximal NCD risk factors such as high glucose and cholesterol. This inconsistency in direction and strength of associations was also supported by findings from previous chapters that there are varying associations between urban exposure with NCDs (Chapter 3) and NCD mortality (Chapter 2).

In this chapter, I present findings from the cross-sectional dataset as described in Chapter 4. A life course approach was taken in order to obtain evidence on the potential mechanisms behind the observed differences in behavioural, physiological and biological risk factors for NCD among those with different urban exposures.

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Living in an urban environment and non-communicable disease risk in Thailand: Does timing matter?

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Student	Chaisiri Angkurawaranon
Principal Supervisor	Dorothea Nitsch
Thesis Title	Urbanization and internal migration as risk factors for non-communicable disease in Thailand

If the Research Paper has previously been published please complete Section B, if not please move to Section C

SECTION B – Paper already published

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Living in an urban environment and non-communicable disease risk in Thailand: Does timing matter?

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ABSTRACT

Background: This paper uses a life-course approach to explore whether the timing and/or duration of urban (vs rural) exposure was associated with risk factors for NCDs.
Methods: A cross-sectional survey was conducted among health care workers in two hospitals in Thailand. Two measures of urbanicity were considered: early-life urban exposure and the proportion of urban life years. We explored four behavioral NCD risk factors, two physiological risk factors and four biological risk factors.
Results: Both measures of urbanicity were each independently associated with increases in all behavioral and physiological risk factors. For some biological risk factors, people spending their early life in an urban area may be more susceptible to the effect of increasing proportion of urban life years than those growing up in rural areas.
Conclusion: Urbanicity was associated with increases in behavioral and physiological risk factors. However, these associations may not translate directly into increases in biological risk factors. It is likely that these biological risk factors were results of a complex interaction between both long term accumulation of exposure and early life exposures.

1. Introduction

Thailand, like many countries in Southeast Asia and developing regions, faces a growing burden of non-communicable diseases (NCDs) (Dans et al., 2011; Abegunde et al., 2007). One of the main drivers of non-communicable disease is urbanization. Urbanization is thought to be associated with a range of socio-economic, cultural and environmental changes which may contribute to the development of NCDs (World Health Organization, 2005b).

Most research on the link between urbanization and risk factor for NCDs unfortunately does not offer insight into the mechanisms driving the associations (Harpham, 2009). In recent decades, a life course approach to chronic disease epidemiology (Lynch and Smith, 2005) has been suggested as a way forward in the understanding of urbanization and health (Kinra, 2004). A life course approach considers the effect of an exposure (such as urbanization) during different periods of life (from gestation to adult life) on later health-related risks and outcomes. Two main conceptual life-course models exist (Ben-Shlomo and Kuh, 2002). The first is the critical period or sensitive period model. This model emphasizes the importance of the timing of the exposure. It is based on theories that there may be a limited period in which an exposure may affect structural or functional development (the critical period model) or that there is a time period when an effect of an exposure may be stronger than other time periods (the sensitive period model). An example of a critical/sensitive period model is the association between intrauterine growth retardation (IUGR) and low birth weight with many chronic diseases such as coronary heart disease and diabetes (Darnton-Hill et al., 2004). Urbanization is associated with IUGR and low birth weight through many mediating factors such as maternal nutritional

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status and smoking (Ohmi et al., 2001; Kramer, 1987). The second main conceptual life course model is the accumulation of risks model. This model emphasizes the importance of cumulative exposure over time. An example of an accumulation model is where the risk of obesity and diabetes rises with the time spent in urban environments (Sobngwi et al., 2004).

Evidence from life course models can help identify targets for, and timing of, public health interventions. Evidence for critical/sensitive period models would favor interventions during these critical time frames; interventions at others times would be less effective. Evidence for accumulative models would suggest that interventions across the lifespan would be effective (Liu et al., 2010).

In Thailand, recent studies have explored the associations between urbanization and risk factors for NCDs. These studies suggest that urban residence was associated with obesity and high blood pressure, but they did not use a life course approach (Lim et al., 2009; Banwell et al., 2009). Two life-course studies were conducted in a cohort of Thai university students (Sleigh et al., 2008). Using urban residence at two or three different points in time, the studies found that people who had spent more time in an urban area had higher prevalences of smoking, alcohol consumption, obesity (BMI $\geq$ 25) and a higher incidence of self-reported medical diagnosis of hypertension and dyslipidemia than those spending more time in a rural area (Yiengprugsawan et al., 2011; Zhao et al., 2014). However, the authors did not explicitly differentiate between life-course models and did not have actual measurements for blood pressure and laboratory investigations.

This paper utilized survey data from the Chiang Mai University (CMU) Health Worker Study (Angkurawaranon et al., 2014). The overall aim of the CMU Health Worker Study was to generate evidence on the links, and potential life course mechanisms, between urban environments, NCD risk factors, and development of NCDs. The aim of this paper is to explore the association of urban (vs. rural) residence with risk factors for NCDs in Thailand using two different life course models, the early life critical/sensitive period model and the accumulation of risk model. The study will also explore whether the associations between growing up in urban areas and NCD risk factors are modified by later accumulation of urban exposure.

Table 1
Demographic characteristics and urban exposure in study population.

	Chiang Mai University (CMU) Hospital	Fang Hospital	Total
Number of participants	3204	312	3516
Mean age in years (sd)	40.2 (10.7)	33.1(10.7)	39.6 (10.9)
Female: *N* (%)	2472 (77.1)	235 (75.3)	2707 (77.0)
Highest education: *N* (col%)			
Below Bachelor's degree	1134 (35.5)	143 (46.0)	1277 (36.3)
Bachelor's degree/ equivalent	1690 (52.6)	152 (48.9)	1842 (52.4)
Higher than Bachelor's degree	380 (11.9)	15 (5.1)	396 (11.3)
Monthly household income in baht*: *N* (col%)			
< 20,000	1196 (37.4)	133 (42.8)	1329 (37.8)
20,000–40,000	927 (28.9)	106 (34.1)	1033 (29.4)
40,000–60,000	522 (16.3)	40 (12.9)	562 (16.0)
> 60,000	559 (17.4)	32 (10.2)	591 (16.8)
Early life exposure (Age 0–5)** *N*(col%)			
Rural	1397 (43.7)	272 (87.5)	1669 (47.6)
Urban	1797 (56.3)	39 (12.5)	1836 (52.4)
Proportion of urban life years in percent #: *N* (col%)			
< 25%	245 (7.7)	260 (83.6)	505 (14.4)
25–50%	445 (13.9)	20 (6.4)	465 (13.3)
50–75%	656 (20.5)	15 (4.8)	671 (19.1)
> 75%	1847 (57.9)	16 (5.1)	1863 (53.2)

* 1 US dollar = approximately 32 baht; one missing value from Fang Hospital.
** 11 missing value, 10 from CMU hospital.
# 12 missing value, 11 from CMU hospital.

2. Methods

2.1. Study population

A cross sectional survey of health care workers in two government hospitals in Northern Thailand was conducted between January and June 2013. The first hospital was Chiang Mai University (CMU) Hospital, employing over 5000 workers. The details of the study population, methods, strengths and limitations of the survey conducted in CMU Hospital have been published (Angkurawaranon et al., 2014). The survey utilized a periodic health check up program offered to health care workers. Questionnaires, interviews, physical and laboratory examinations were used to collect data on detailed migration history from birth to current age and information on behavioral, physiological and biological risk factors for NCDs. Using a similar protocol, the survey was extended to a rural hospital in Fang District. The leading investigators of the study trained researchers at both sites to use standard measurement protocols.

2.2. Measurements and variable definitions

2.2.1. Urban exposure

The classification of urban areas in Thailand is defined using government administrative criteria largely driven by population density. In 1970, only three areas were considered 'cities': Bangkok, Thonburi (a suburb of Bangkok) and Chiang Mai (Goldstein and Goldstein, 1978). For our study, all districts in Bangkok and the

Table 2
Relationship between early life urban exposure and proportion of urban life years.

Proportion of urban life years*	Early life Urban exposure (*n*, column%)	Early Life Rural Exposure (*n*, column%)	Total (*n*, column%)
< 25%	6, 0.33	499, 29.9	505, 14.4
25–50%	16, 0.87	449, 26.9	465, 13.3
50–75%	41, 2.23	630, 37.8	671, 19.1
> 75%	1773, 96.6	90, 5.4	1863, 53.2
Total	1836	1668	3504

* 12 missing values in proportion of urban life years.

Table 3
Association between early life urban exposure (age 0–5) and proportion of urban life years with behavioral and physiological risk factors for NCDs.

	Behavioral Risk Factors								Physiological Risk factors			
	Current smoking		Heavy alcohol drinking		Inadequate physical activity		Inadequate fruit and vegetable intake		BMI (kg/m^2)		Systolic blood pressure[##] (mmHg)	
	Odds ratio (95% CI) and p-value		Odds ratio (95% CI) and p-value		Odds ratio (95% CI) and p-value		Odds ratio (95% CI) and p-value		Regression coefficient β (95% CI) and p-value		Regression coefficient β (95% CI) and p-value	
Early Childhood (0–5) urban exposure	1.87 (1.32–2.64)	< 0.001	2.35 (1.92–2.87)	< 0.001	1.16 (1.01–1.33)	0.034	1.29 (1.06–1.56)	0.010	0.69 (0.43–0.95)	< 0.001	2.54 (1.56–3.49)	< 0.001
Proportion of urban life years												
0–25%	Reference		Reference		Reference		Reference		Reference		Reference	
25–50%	0.94 (0.48–1.86)	0.865	0.82 (0.55–1.21)	0.316	1.12 (0.87–1.45)	0.362	1.71 (1.19–2.45)	0.004	0.20 (−0.28 to 0.68)	0.421	0.23 (−1.86 to 2.32)	0.827
50–75%	0.61 (0.30–1.24)	0.171	1.02 (0.69–1.51)	0.919	1.10 (0.86–1.42)	0.449	1.65 (1.17–2.32)	0.004	0.38 (−0.09 to 0.86)	0.116	−1.61 (−3.74 to 0.51)	0.136
75–100%	1.58 (0.97–2.57)	0.069	2.12 (1.56–2.88)	< 0.001	1.34 (1.08–1.67)	0.007	1.92 (1.42–2.59)	< 0.001	0.90 (0.49–1.30)	< 0.001	1.52 (−0.38 to 3.44)	0.117
Overall p-value	0.003*		< 0.001*		< 0.003#		< 0.001#		< 0.001#		< 0.001*	

Reference group for early childhood urban exposure is early childhood rural exposure; each exposure is modeled separately adjusting for age and sex; analysis performed separately for each NCD risk factors using logistic regression for behavioral risk factors and linear regression for physiological risk factors; more than five standard drinks per sitting in men and more than four standard drinks per sitting in women were cutoff points for heavy alcohol consumption; less than 35 units standard units of fruits and/or vegetable consumption per week were the cutoff point for inadequate fruits and vegetable intake. Less than 75 min of vigorous-intensity physical activity or 150 min of moderate-intensity physical or an equivalent of 600 metabolic equivalent (MET) minutes per week was the cutoff point for inadequate physical activity.

* p-overall association.
# p-trend.
Data only from Chiang Mai University Hospital (n=3194).

Table 4
Association between Early life urban exposure (age 0–5) and proportion of urban life years with biological risk factors for NCDs.

	Blood glucose (mg/dL)		Low density lipoprotein (LDL) cholesterol (mg/dL)		Triglyceride (mg/dL)		High density lipoprotein (HDL) cholesterol (mg/dL)	
	Regression coefficient β (95% CI) and p-value		Regression coefficient β (95% CI) and p-value		Regression coefficient β (95% CI) and p-value		Regression coefficient β (95% CI) and p-value	
Early childhood (0–5) urban exposure	1.51 (0.41–2.61)	0.007	2.17 (−0.25 to 4.59)	0.079	−4.33 (−10.6 to 1.95)	0.176	0.31 (−0.58 to 1.20)	0.493
Proportion of urban life years in percent								
0–25%	Reference		Reference		Reference		Reference	
25–50%	4.12 (2.10–6.14)	< 0.001	6.12 (1.66–10.5)	0.007	−4.75 (−16.3 to 6.83)	0.421	−0.07 (−1.70 to 1.57)	0.936
50–75%	3.56 (1.56–5.57)	< 0.001	7.10 (2.68–11.5)	0.002	-19.2 (−30.7 to −7.71)	0.001	0.48 (−1.13 to 2.11)	0.557
75–100%	4.50 (2.81–6.20)	< 0.001	6.81 (3.07–10.5)	< 0.001	−15.5 (−25.2 to −5.77)	0.002	0.63 (−0.74 to 2.00)	0.367
Overall p-value	< 0.001*		0.003#		0.002#		0.279#	

Reference group for early childhood urban exposure is early childhood rural exposure; analysis performed separately for each NCD risk factor using linear regression. Each exposure is modeled separately adjusting for age and sex.

* p-overall association.
# p-trend.

ten districts in Chiang Mai Metropolitan Area, consisting of Muang (Chiang Mai Province), Sarapi, Sanpatong, Hang Dong, Mae Rim, Sansai, Doi Saket, Mae On, Sang Kampang, Muang (Lumphun Province), were considered urban. The remaining districts in Thailand, such as Fang, were classified as rural. By tracking the location (district) of residence during each participant's life, two exposures related to living in an urban environment were defined:

(i) Early life urban exposure was defined by using the main location (district) of residence while participants were aged between 0 and 5 years. This variable was used to represent the early life critical/sensitive period model (Kuh et al., 2003)[#]:
(ii) The proportion of urban life years was calculated as total years of urban exposure divided by current age, expressed as a percentage. This was used to represent the accumulation of risk model (Kuh et al., 2003). Small differences in the proportion of urban life years were unlikely to produce notable differences in levels of risk factors for NCDs, thus the variable 'proportion of urban life years' was classified into four categories: < 25%, 25–50%, 50–75%, > 75%.

2.2.2. Risk factors for NCDs

Using the World Health Organization's framework (World Health Organization, 2005a) the risk factors for NCDs were classified into three categories: behavioral, physiological and biological. This classification reflects assumed causal pathways between urbanization and development of NCDs. Behavioral risk factors were considered as more distal, physiological risk factors as

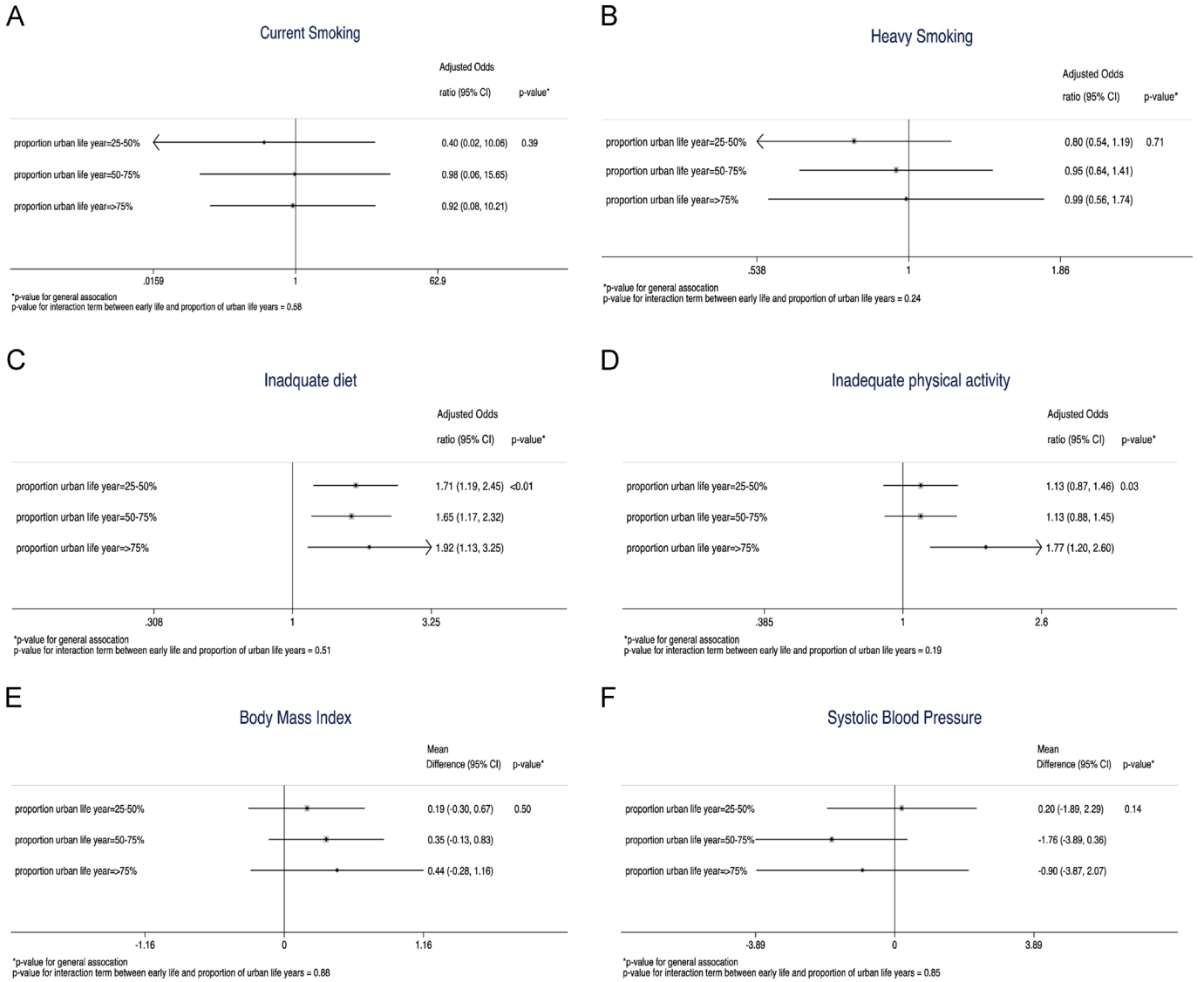

Fig. 1. Associations between proportion of urban life years with behavioral and physiological risk factors for NCDs adjusted for age, sex and early life exposure. The reference group for all analysis was 'proportion of urban life year $<25\%$'; more than five standard drinks per sitting in men and more than four standard drinks per sitting in women were cutoff points for heavy alcohol consumption; less than 35 units standard units of fruits and/or vegetable consumption per week were the cutoff point for inadequate fruits and vegetable intake. Less than 75 min of vigorous-intensity physical activity or 150 min of moderate-intensity physical or an equivalent of 600 metabolic equivalent (MET) minutes per week was the cutoff point for inadequate physical activity.

intermediate and biological risk factors as more proximal towards the development of NCDs (World Health Organization, 2005b).

Behavioral Risk factors for NCDs were obtained using questionnaires derived from the WHO STEPS instrument (World Health Organization, 2005a). The four behavioral risk factors consisted of current smoking, heavy alcohol consumption, inadequate fruit and vegetable intake, and inadequate physical activity. Information on behavioral risk factors was obtained through interviews at CMU Hospital and through self-answered questionnaires at Fang Hospital. Literature has suggested that for behavioral factors such as alcohol and physical activity, the two methods of administration can provide similar results (Bongers and Van Oers, 1998; Craig et al., 2003). Both smoking and tobacco chewing were considered as 'current smoking'. More than five standard drinks per sitting in men and more than four standard drinks per sitting in women were cutoff points for heavy alcohol consumption. Less than 35 units standard units of fruit and/or vegetable consumption per week was the cutoff point for inadequate fruit and vegetable intake. Less than 75 min of vigorous-intensity physical activity, 150 min of moderate-intensity physical activity, or an equivalent of 600 metabolic equivalent (MET) minutes per week were the cutoff points for inadequate physical activity.

Physiological risk factors for NCDs consisted of raised blood pressure and raised body mass index.

Three blood pressure readings were taken 5 min apart. The average of the second and third blood pressure reading was used as the blood pressure for each participant. Blood pressure readings were taken using digital sphygmomanometers in Chiang Mai University hospital and by manual mercury sphygmomanometers in Fang Hospital. A portable stadiometer and an electronic scale were used to measure standing height and body weight. Body mass index was calculated using weight (in kg) divided by height (in meters) squared.

Biological risk factors for NCDs were derived from participants' blood samples. They consisted of blood glucose level, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL)

Table 5
Mutually adjusted associations for early life urban exposure (age 0–5) and proportion of urban life years with behavioral and physiological risk factors for NCDs.

Exposure	Behavioral risk factors								Biological risk factors			
	Current smoking		Heavy alcohol drinking		Inadequate physical activity		Inadequate fruit and vegetable intake		BMI (kg/m^2)		Systolic blood pressure[##] (mmHg)	
	Odds ratio and *p*-value		Odds ratio and *p*-value		Odds ratio and *p*-value		Odds ratio and *p*-value		Difference (urban–rural) and *p*-value		Difference (urban–rural) and *p*-value	
Early life (0–5) urban exposure	1.37 (0.59–1.20)	0.468	2.20 (1.34–3.59)	0.002	0.75 (0.54–1.05)	0.094	1.00 (0.63–1.59)	0.985	0.48 (−0.15 to 1.10)	0.135	2.53 (0.16–4.90)	0.036
Proportion of urban life years												
0 – 25%	Reference		Reference		Reference		Reference		Reference		Reference	
25 – 50%	0.93 (0.47–1.83)	0.829	0.80 (0.53–1.19)	0.270	1.14 (0.88–1.46)	0.335	1.71 (1.19–2.46)	0.004	0.19 (−0.30 to 0.67)	0.450	0.20 (−1.89 to 2.29)	0.852
50 – 75%	0.59 (0.29–1.21)	0.153	0.95 (0.64–1.41)	0.795	1.13 (0.87–1.45)	0.362	1.65 (1.17–2.32)	0.004	0.35 (−0.13 to 0.83)	0.154	−1.76 (−3.89 to 0.36)	0.104
75 – 100%	1.17 (0.45–3.00)	0.747	0.99 (0.56–1.74)	0.976	1.77 (1.20–2.60)	0.004	1.92 (1.13–3.25)	0.016	0.44 (−0.28 to 1.16)	0.232	−0.90 (−3.87 to 2.07)	0.552
Overall *p*-value	0.580[#]		0.932[#]		0.028[#]		0.004[#]		0.127[#]		0.126[#]	
p-interaction	0.58		0.24		0.19		0.51		0.88		0.85	

Each exposure is modeled together adjusting for age and sex; analysis performed separately for each NCD risk factors using logistic regression for behavioral risk factors and linear regression for physiological risk factors; [*]*p*-overall association.

[#] *p*-trend.

[##] Data only from Chiang Mai University Hospital (n=3194).

cholesterol and triglyceride (TG) levels. All participants were asked to fast at least eight hours before examination. All blood samples were handled at their respective hospitals' laboratory. Since both sites are government hospitals, they undergo the same external validation process from the Ministry of Public Health. Furthermore, 100 random samples from Fang Hospital were processed at Chiang Mai University hospital to assess agreement.

2.3. Analysis plan

Descriptive statistics were used to describe the socio-demographic patterns and urban exposure status for the study participants. Early life urban exposure and the proportion of urban life years, representing the two different life course models, were considered the main exposures of interest. Each exposure was modeled separately using logistic regression or linear regression depending on the outcome of interest. The proportion of urban life years was tested for general association, linear trend and departure from linearity.

Current age and sex were considered *a priori* confounders. We did not adjust for other variables such as income and education because we considered this might lead to over adjustment for mediating factors in the pathways between urbanization and risk factors for NCDs.

To account for the temporal ordering between the two exposure variables, the data were stratified by early life urban exposure and analyses conducted separately on each group. To formally test whether the associations differed by early life urban exposure, multivariable regression was used by modeling both exposure variables together along with their interaction term.

2.3.1. Sensitivity analyses

We tested for interactions by sex as there was evidence that gender may modify associations between urbanicity and NCD risk factors, such as BMI and blood pressure (Kinra et al., 2011; Sovio et al., 2013). To explore potential non-differential information bias due to different methods of data collection and different blood pressure instruments used between the two sites, a sensitivity analysis was done using data from only the CMU hospital (larger sample size). Results from this restricted analysis were reported only if they yielded materially different conclusions from the original results. Bland-Altman plots (Bland and Altman, 1986) were used to assess agreement between laboratory measurements on one hundred blood samples chosen at random from Fang Hospital, which were also processed at Chiang Mai University Hospital.

2.4. Ethics

Informed consent was obtained from all participants. The study was approved by a institutional review board from Fang Hospital and Chiang Mai University (No. 069/2012) and London School of Hygiene and Tropical Medicine (Ref. 6521).

3. Results

3204 healthcare workers from CMU Hospital (58.3% of all eligible workers) and 312 healthcare workers in Fang Hospital (67.8% of all eligible workers) participated in the study. The sample from CMU hospital represented the source population well in terms of age and education level, although females were slightly over-represented. The sample from Fang hospital represented the population well in terms of age, gender and job distribution. Characteristics of responders and non-responders by study site can be found in Appendix A.

In total, 3516 participants were included in the study (59.0% of all eligible workers). The mean age of the study population was 39.6 years (sd=10.9), although the sample from CMU Hospital (mean 40.2, sd=10.7) was older than Fang Hospital (mean 33.1 years, sd=10.7). In both sites, the majority (63.7%) had at least a bachelor's degree or equivalent. Almost half (47.6%) spent their early life (between age 0 and 5) in a rural area. The majority from Fang Hospital (83.6%) had spent less than 25% of their lifetime in an urban area while more than half (57.9%) from Chiang Mai University Hospital had spent more than 75% of their life time in an urban area (Table 1). Early life urban exposure was positively correlated with proportion of urban life years. Those spending their early life in an urban area were more likely to have spent higher proportions of their lives in an urban area than those spending their early life in a rural area (Table 2).

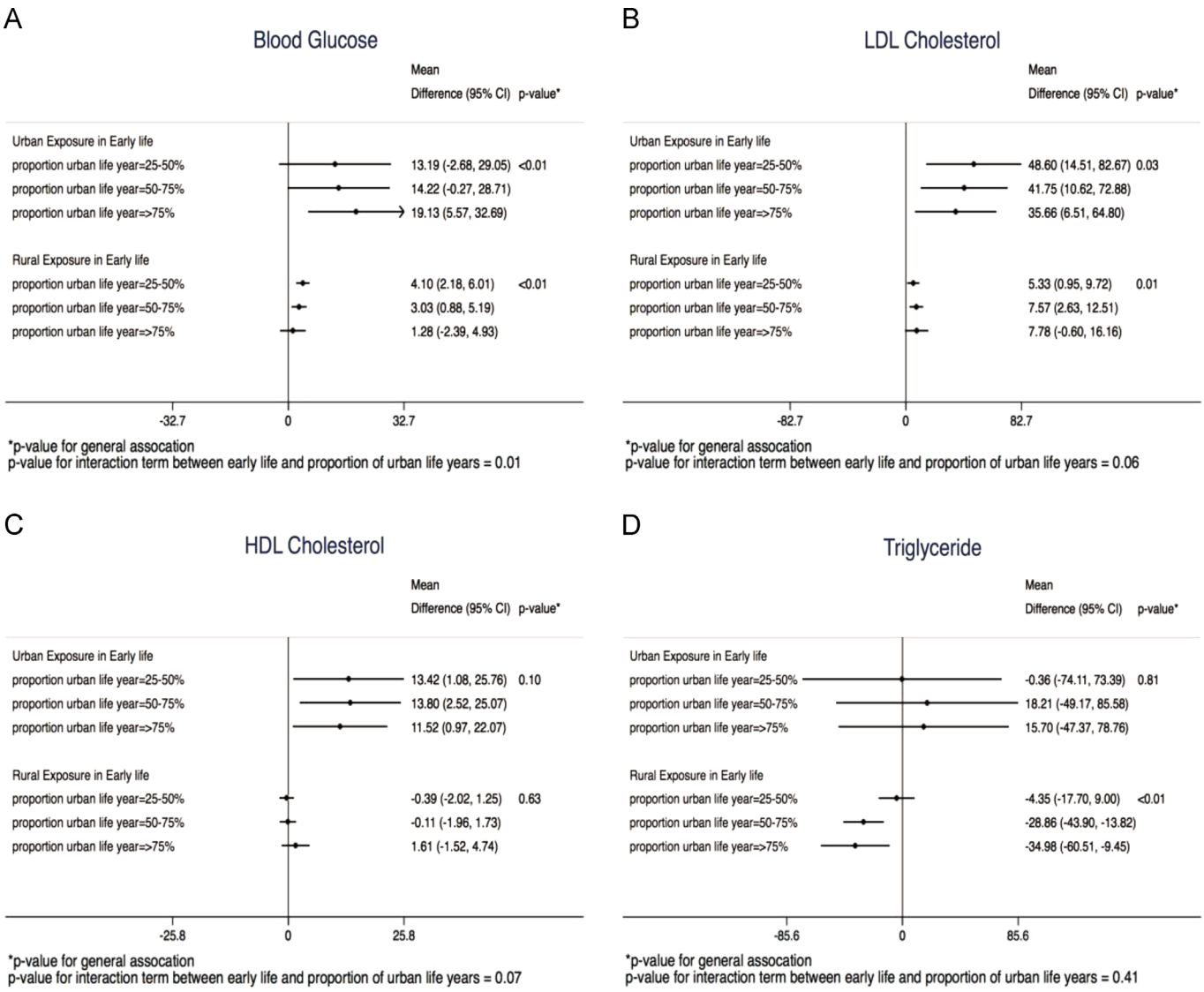

Fig. 2. Associations between proportion of urban life year and biological risk factors for NCDs stratified by early life urban exposure. All results adjusted for age and sex. For each risk factor, the first group of results was restricted to those spending early life in urban area, the second group of results was restricted to those spending early life in rural area. The reference group for all analysis was 'proportion of urban life year $<25\%$'. LDL-low density lipoprotein; HDL-high density lipoprotein; Units for all risk factors are in mg/dL.

When modeling each exposure separately and adjusting for age and sex, both exposures of interest were associated with increases in all four behavioral and both physiological NCD risk factors (Table 3). For biological risk factors, both exposures were associated with increased glucose and LDL cholesterol but there was no evidence for association with HDL. For triglyceride levels, unlike other risk factors for NCDs, an increasing proportion of urban life years was associated with a lower triglyceride level (Table 4).

From modeling both exposures simultaneously, there was no evidence that the associations between proportion of urban life years with behavioral and physiological risk factors were modified by urban early life exposure. For inadequate physical activity and inadequate fruit and vegetable intake, early life urban exposure lost its statistical significance when adjusted for proportion of urban life years. Those having spent more than 75% of their lifetime in an urban area were more likely to have inadequate physical activity (OR 1.77, 95% CI 1.20–2.60) and inadequate fruit/vegetable intake (OR 1.92, 95% CI 1.13–3.25) compared to those who have spent less than 25% of their life time in an urban area. (Fig. 1, Table 5). However, those spending their early life in an urban area were 2.2 times more likely to be heavy alcohol drinkers (OR 2.20; 95% CI 1.34–3.59) and the mean systolic blood pressure was 2.5 mmHg higher (95% CI 0.16–4.90) compared to those spending early their early life in a rural area, even when adjusting for their later proportion of urban life years (Table 5).

For three of the four biological risk factors (glucose, LDL, and HDL), there was some evidence for interactions between early life exposure and the proportion of urban life years (Fig. 2). For those spending their early life in an urban area, there was a strong positive relationship between increasing proportions of urban life years and blood glucose, and for those who had a rural childhood there was evidence of an inverse trend. For those who had an urban exposure in early life, there was a more pronounced association with LDL levels than seen for those with a rural upbringing. There was some weak evidence that increasing proportion of urban life years was associated with higher HDL only among those who spent their early life in an urban area. Although the point estimates for the people with urban upbringing were more extreme for proportion of urban life years spent, the confidence intervals were wide.

3.1. Sensitivity analysis

For all analyses, there was no evidence for interaction by sex. Some power was lost in the restricted analysis (Appendix B and C), however the findings from the full and restricted analysis did not materially differ for all four behavioral risk factors and BMI. The only exception was for blood pressure, thus only observations from CMU hospital were used for analysis. There was good agreement between the biological risk factor laboratory results between Fang and CMU hospital (Appendix D).

4. Discussion

There was consistent evidence to support that both measures of urbanicity were independently associated with increases in all behavioral and physiological risk factors for NCDs. However, urban residence may not be associated with increases in all types of biological risk factors. For some biological risk factors, there was evidence that the association between proportion of urban life years and risk factors for NCDS may differ, depending on whether there was early life urban exposure.

Increases in distal behavioral and physiological risk factors may not translate directly to higher proximal biological risk factors such as high triglycerides and low HDL in Thailand. Dietary patterns may help explain such findings. Consumption of calories from dietary carbohydrates, such as sticky rice, may be higher in rural or less developed areas in Thailand (Kosulwat, 2002; Kedjarune et al., 1997). These dietary carbohydrates are be associated with high triglyceride and low HDL blood levels (McKeown et al., 2009). Urbanization may also be associated with lower biological risk factors through better awareness, availability of laboratory testing, and medical control (Porapakkham et al., 2008; Aekplakorn et al., 2011a). Data from the 2009 Thai National Health Examination Survey also demonstrated that not all biological risk factors were higher in urban areas (Aekplakorn et al., 2011b).

By modeling both exposures together, our study attempted to disentangle the life course mechanisms driving such associations. Our results suggest that for the all four behavioral risk factors, BMI and blood pressure, both the early life critical/sensitive period model and the cumulative risk model were possible. Heavy drinking and blood pressure may be predominantly driven by an early life critical/sensitive period model, while inadequate physical activity and inadequate fruit and vegetable intake may be predominantly driven by a cumulative risk model. Life course socioeconomic status (SES), a key mediator between urbanization and health, may help to explain such findings. Childhood SES, which is often measured through parental SES, has been linked to adult behavioral risk factors such as smoking and drinking (Van De Mheen et al., 1998; Bowes et al., 2013). However, for other behavioral risk factors such as physical activity, early life SES is less important than later life influences on the risk of NCDs (Tammelin et al., 2003; Kuh and Cooper, 1992).

Distal behavioral and physiological risk factors are likely to be mediated through proximal biological risk factors. For these biological risk factors, our evidence suggests that living in an urban environment early in life interacts with urban life years. For example, people spending their early lives in urban areas may be more susceptible to developing diabetes as a result of additional cumulative years of urban exposure than people who spent their early lives in a rural environment. It may be possible that some early life exposures have prolonged influences in health behavior and physiological factors as previously mentioned. It may also be possible that the rate of urbanization or changes in environmental influences are greater in areas already considered more urban (World Health Organization, 2011). It is however unlikely that these NCD risk factors in Thailand were predetermined outcomes of influences in early life but rather a complex interaction between both long term accumulation of exposure and early life exposures.

The study had several limitations. Due to the cross sectional study design we could only assume temporal relationships between increasing proportions of urban life years and increases in NCD risk factors. Data suggested that men could be underrepresented in the study population but the study population represented the source population well in terms of age and education level. The differences in methods of data collection between the two hospitals represented potential for information bias. However, restricted analysis did not materially change the conclusions for most of the outcomes. The results for biological outcomes were less likely to be affected by information bias as there was good agreement between the two hospitals. Our method of classifying urban versus rural exposure based solely on location may be prone to misclassification. We could not take into consideration the fact that some locations may have become urbanized over time. However, since few locations were considered as urban in our study, rural exposure is more likely to be misclassified. If recent changes in the degree of urbanicity have accelerated in recent years, especially for areas already considered urban, the associations seen, particularly for early life urban exposure, are likely underestimates. Due to the relationship between the two exposures and shared mediating factors, it may not be possible to empirically provide proof of one life course mechanism over the other (Hallqvist et al., 2004). Not all life course models, such as the social mobility model (in essence urban migration or rapid urbanization) could be assessed. Due to limited heterogeneity of exposure in this occupational cohort we were unable to explore the role of other critical periods, such as adolescence.

Our early life exposure also cannot distinguish between the critical period effect and the sensitive period effect. Our study did not focus on potential mediators between life course urban exposure and NCD risk factors (such social capital, parental and individual SES), which should be explored in future studies. The study of health care workers in the Northern region means that the results seen may not be generalizable to the Thai population. Nonetheless, the results should provide meaningful evidence as the rest on the county becomes more developed.

5. Policy implications

Despite its limitations, our study offers evidence towards understanding how urbanization may drive NCDs in a developing country such as Thailand. Our findings are in line with other finding from developing countries (Miranda et al., 2008). Urban life years was associated with many risk factors for NCDs such as obesity and higher blood pressure in India (Kinra et al., 2011). Both life time urban exposure and percentage of life time urban exposure was associated with obesity and diabetes in Cameroon (Sobngwi et al., 2004). These findings support evidence for targeting public health interventions during early life and throughout adulthood. For Thailand, targeting children in urban areas may be useful for behavioral and physiological risk factors as early life urban exposure (compared to early life rural exposure) was associated with increase odds of heavy alcohol drinking (OR 2.20, 95% CI 1.34–3.59) and higher systolic blood pressure (2.53 mmHg, 95% CI 0.16–4.90) in adulthood despite adjusting for proportion of urban life years. Trials have shown that childhood interventions can be effective measures to prevent and combat substance use, obesity and elevated blood pressure (Van Lier et al., 2009; Cai et al., 2014; Flynn et al., 2006).

To effectively decrease biological risk factors, it may be important to integrate public health interventions in adulthood. Those who spent their early childhoods in an urban area and more than 75% of their life in an urban residence had a much higher LDL cholesterol level than those who also spent their childhoods in urban areas but have spent less than 25% of their lives in an urban residence, an effect size of similar magnitude to the effect of statins in lowering LDL cholesterol (Law et al., 2003). Incorporating individual and population level interventions focusing on population shifts in distributions of risk factors (Rose, 2001), such as the one conducted in Sweden that focused on adults from age 30 (Weinehall et al., 1999, Long et al., 2014), could be a cost-effective public health policy to prevent NCDs in developing countries such as Thailand (Tables A1–A3).

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Appendix A

See Table A1.

Table A1
Distribution of demographic factors in sample and total population by hospitals.

	Fang Hospital		Maharaj Nakorn Chiang Mai Hospital (Chiang Mai University Hospital)	
	Sample population	Total population	Sample population	Total population
Number	312	459	3188*	5364
% Female	75.0	74.5	77.3	68.8
Mean age (sd)	33.4 (10.6)	34.1 (10.8)	39.7 (10.7)	40.5 (11.0)
Age distribution (%)				
< 25	23.1	21.1	10.7	8.8
25–30	21.8	20.9	13.6	14.3
30–35	16.9	18.6	13.5	12.7
35–40	12.7	13.4	14.0	12.6
40–45	6.5	5.7	11.7	10.9
45–50	5.4	6.4	16.2	15.4
50–55	9.4	9.0	12.0	13.9
55–60	3.3	4.4	8.3	10.5
> 60	0.6	1.0	0.5	0.6
Job position#				
Special advisor	–	–	0.0	< 0.1
Instructor (MD)	–	–	1.8	6.4
Instructor (non-MD)	–	–	1.2	1.9
Doctor/dentist	5.8	7.4	0.7	5.8
Pharmacist	1.3	3.0	2.1	2.2
Nurse	22.4	24.8	38.7	31.1
Nurse aide	–	–	13.2	12.2
Other health professionals	10.9	9.4	2.8	3.0
Non-health professionals	4.2	4.6	7.1	6.4
Administrative staff	2.9	2.6	4.1	3.9
Non-skill worker	15.7	14.2	12.5	12.1
Skill worker	36.9	34.0	15.7	14.8
Highest education				
Elementary school	3.2	Not available	4.0	4.3
Early secondary school	5.8		6.3	6.4
Late secondary school	37.0		13.6	12.9
Bachelor's degree	48.9		66.5	62.0
Higher than Bachelor's degree	5.1		9.5	14.3

* 16 additional participants are in the study population but were no longer in the hospital database by July 2014 when demographic characteristics of the source population were obtain from official hospital personnel records.

Due to difference in how job positions are classified between the two hospitals, the job positions are broadly grouped by similar potential for earnings and educational requirements or training. Other health professionals included pharmacists, physiotherapist, laboratory technicians. Non-health professionals include positions such as accountants, lawyers, social workers.

Appendix B

See Table B1.

Table B1
Sensitivity analysis of associations between early life urban exposure (age 0–5) and proportion of urban life years with behavioral and physiological risk factors for NCDs using only results from Chiang Mai University.

Exposure	Behavioral risk factors								Physiological risk factors			
	Current Smoking		Heavy alcohol drinking		Inadequate physical activity		Inadequate fruit and vegetable intake		BMI (kg/m^2)		Systolic blood pressure[##] (mmHg)	
	Odds ratio and *p*-value		Odds ratio and *p*-value		Odds ratio and *p*-value		Odds ratio and *p*-value		Difference (urban–rural) and *p*-value		Difference (urban–rural) and *p*-value	
Early childhood (0–5) urban exposure	1.92 (1.31–2.82)	0.01	2.27 (1.84–2.80)	< 0.001	1.14 (0.99–1.32)	0.067	1.14 (0.93–1.40)	0.213	0.58 (0.40–0.96)	< 0.001	1.41 (0.49–2.33)	0.003
Proportion of urban life years		0.005[*]		< 0.001[*]		0.009[#]		0.377[#]		< 0.001[#]		< 0.001[*]
0–25%	Reference		Reference		Reference		Reference		Reference		Reference	
25–50%	0.88 (0.38–2.02)	0.761	0.58 (0.37–0.92)	0.021	1.17 (0.85–1.60)	0.331	0.99 (0.61–1.60)	0.978	0.17 (−0.43 to 0.78)	0.575	−2.87 (−4.55 to -1.17)	0.001
50–75%	0.54 (0.22–1.30)	0.169	0.77 (0.49–1.20)	0.249	1.12 (0.82–1.55)	0.472	0.93 (0.58–1.50)	0.782	0.45 (−0.16 to 1.07)	0.150	−5.07 (−6.75 to −3.39)	< 0.001
75–100%	1.45 (0.73–2.88)	0.288	1.60 (1.10–2.33)	0.014	1.37 (1.02–1.82)	0.035	1.09 (0.70–1.69)	0.696	0.95 (0.40–1.51)	0.001	−1.91 (−3.33 to −0.49)	0.008

Each exposure is modeled separately adjusting for age and sex; analysis performed separately for each NCD risk factors using logistic regression for behavioral risk factors and linear regression for physiological risk factors.

[*] *p*-overall association.
[#] *p*-trend.
[##] Data only from both hospital ($n=3504$).

Appendix C

See Table C1.

Table C1
Sensitivity analysis of associations between early life urban exposure (age 0–5) and proportion of urban life years with behavioral and physiological risk factors for NCDs using only Chiang Mai University data.

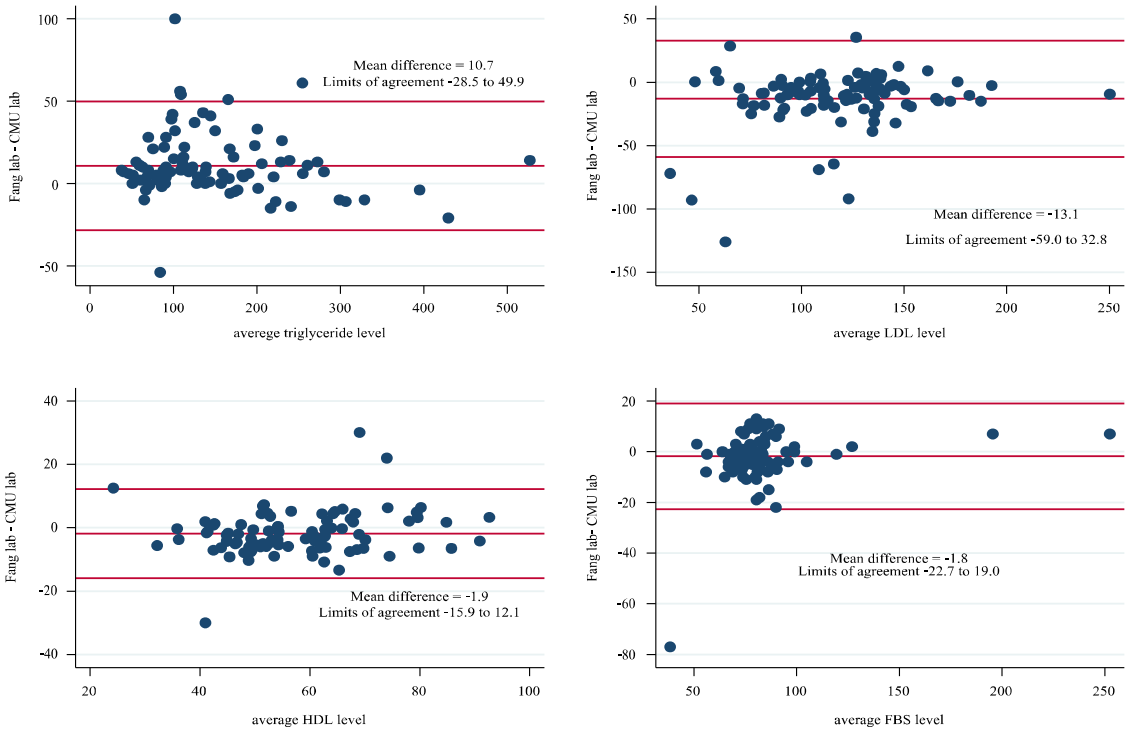
Exposure	Behavioral risk factors								Physiological risk factors			
	Current smoking		Heavy alcohol drinking		Inadequate physical activity		Inadequate fruit and vegetable intake		BMI (kg/m^2)		Systolic blood pressure[##] (mmHg)	
	Odds ratio and p-value		Odds ratio and p-value		Odds ratio and p-value		Odds ratio and p-value		Difference (urban–rural) and *p*-value		Difference (urban–rural) and *p*-value	
Early childhood (0–5) urban exposure	1.33 (0.53–3.33)	0.537	2.22 (1.29–3.83)	0.004	0.75 (0.52–1.07)	0.115	1.06 (0.64–1.73)	0.828	0.52 (−0.17 to 1.21)	0.141	2.28 (0.09–4.47)	0.041
Proportion of urban life years		0.583[#]		0.364[#]		0.055[#]		0.919[#]		0.163[#]		< 0.001[#]
0–25%	Reference		Reference		Reference		Reference		Reference		Reference	
25–50%	0.88 (0.38–2.03)	0.765	0.58 (0.37–0.91)	0.018	1.17 (0.86–1.61)	0.318	0.99 (0.61–1.60)	0.976	0.17 (−0.44 to 0.78)	0.591	−2.92 (−4.61 to −1.22)	0.001
50–75%	0.54 (0.22–1.29)	0.164	0.72 (0.46–1.14)	0.162	1.14 (0.93–1.58)	0.409	0.93 (0.58–1.50)	0.772	0.42 (−0.20 to 1.04)	0.180	−5.23 (−6.92 to 3.55)	< 0.001
75–100%	1.11 (0.37–3.29)	0.849	0.74 (0.39–1.42)	0.364	1.81 (0.15–2.85)	0.010	1.04 (0.54–1.97)	0.914	0.46 (−0.41 to 1.32)	0.301	−4.09 (−6.62 to −1.57)	0.001
p-interaction		0.81		0.33		0.49		0.60				0.20

Each exposure is modeled together adjusting for age and sex; analysis performed separately for each NCD risk factors using logistic regression for behavioral risk factors and linear regression for physiological risk factors; [*]*p*-overall association.

[#] *p*-trend.
[##] Data only from both hospitals ($n=3504$).

Appendix D. Bland–Altman Plots and 95% limits of agreement for biological risk factors between the two hospitals

Y-axis represents differences in laboratory results in the same individual (Fang Hospital – Chiang Mai University Hospital).



X-axis represents the mean values of the laboratory result in the same individual (Fang Hospital+Chiang Mai University Hospital/2).

All units are in mg/dL.

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5.3 Summary and conclusion

This research explored associations between urbanicity and ten NCD risk factors using a life course approach. It produced two key results. Firstly, urbanicity was found to be associated with increases in behavioral and physiological risk factors. However, these associations may not translate directly into increases in biological risk factors (Figure 5.1).

Secondly, evidence from life course models suggested that early life urban exposure could play an important role for some NCD risk factors such as high body mass index and high fasting glucose (Table 5.1 and Table 5.2).

However, the positive association between early life urban exposure and NCD risk factors did not initially support the developmental origins of disease theory, such that we would expect those with early life rural exposure to be more susceptible to NCDs in adulthood, as discussed in Chapter 4. The potential role of early life urban exposure on changes in BMI and fasting glucose will be further explored using the cohort dataset in the next chapter.

Figure 5.1 Conceptual framework of this thesis with adaptations to incorporate findings from Chapter 5

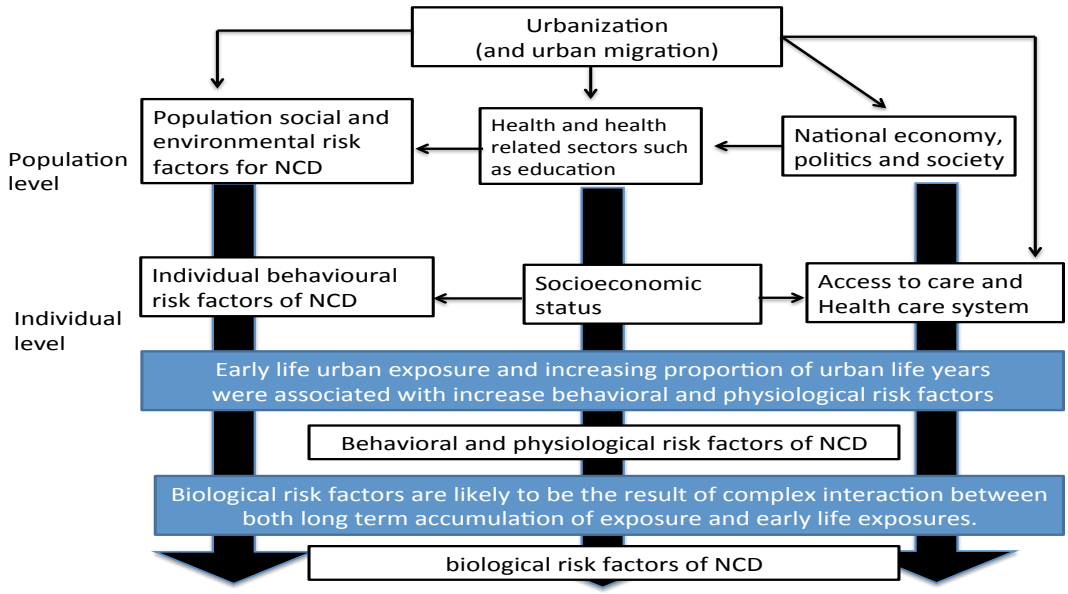

Table 5.1 Summary (statistical evidence, direction of association) of the published manuscript for Chapter 5 between early life urban exposure, proportion of urban life years and behavioral/physiological risk factors by modeling both early life urban exposure, proportion of urban life years separately and together in regression models

	Modeling each exposure separately		Modeling both exposures together		Overall Summary
	Evidence for early life model and accumulation of risk model*	Direction of association for urban exposures	Does additional proportion of urban life years matter after controlling for early life exposure?	Does early life urban exposure matter after controlling for proportion of urban life years?	
Behavioural risk factors					
Current smoking	Both models	Increase	No evidence	No evidence	Evidence for both models
Heavy drinking	Both models	Increase	No evidence	Yes, effect size reduced but remained significant	Evidence for both models, predominantly early life model
Inadequate physical activity	Both models	Increase	Yes, increased risk	Potentially associated with increased risk (p=0.09)	Evidence for both models, predominantly accumulation of risk model
Inadequate fruit and vegetable intake	Both models	Increase	Yes, increased risk	No evidence	Evidence for both models, predominantly accumulation of risk model
Physiological risk factors					
BMI	Both models	Increase	No evidence	No evidence	Evidence for both early life and accumulative model
SBP	Both models	Increase	No evidence	Yes, effect size not materially altered	Evidence for both models, predominantly early life model

Early life urban exposure at age 0-5 represents an early life critical/sensitive period model; proportion of urban life years represents accumulation of risk model; all results were adjusted for age and sex; more than five standard drinks per sitting in men and more than four standard drinks per sitting in women were cut off points for heavy alcohol consumption; less than 35 standard units of fruit and/or vegetable consumption per week was the cut off point for inadequate fruit and vegetable intake; less than 75 minutes of vigorous-intensity physical activity or 150 minutes of moderate-intensity physical activity or an equivalent of 600 metabolic equivalent (MET) minutes per week was the cut off point for inadequate physical activity; BMI - body mass index; SBP - systolic blood pressure.

Table 5.2 Summary (statistical evidence, direction of association) of the published manuscript for Chapter 5 between early life urban exposure, proportion of urban life years and biological risk factors by modeling both early life urban exposure, proportion of urban life years separately and together in regression models

	Modeling each exposure separately		Modeling both exposures together		Overall Summary
	Evidence for early life model and accumulation of risk model*	Direction of association for urban exposures	Does additional proportion of urban life years matter after controlling for early life exposure?	Does early life urban exposure matter after controlling for proportion of urban life years?	
Biological risk factors					
Glucose	Both models	Increase	Potential dependency of associations on early life exposure (p-value for interactions = 0.01)		Proportion of urban life years may have different effect depending on early life exposure
LDL	Both models; weak evidence for early life (p=0.08)	Increase	Potential dependency of associations on early life exposure (p-value for interactions =0.06)		Proportion of urban life years may have different effect depending on early life exposure
TG	Only accumulation of risk model	Decrease	Yes, decreased risk	No evidence	Suggestive of cumulative model
HDL	No evidence	No evidence	Potential dependency of associations on early life exposure (p-value for interactions =0.07)		Proportion of urban life years may have different effect depending on early life exposure

Early life urban exposure at age 0-5 represents an early life critical/sensitive period model; proportion of urban life years represent accumulation of risk model; all results were adjusted for age and sex; LDL - low density lipoprotein; HDL - high density lipoprotein; TG – triglyceride.

Chapter 6 : Early life urban environment as a risk factor for later development of obesity and impaired fasting glucose in adulthood

Summary

Introduction: Obesity and obesity-related conditions are contributing to pronounced non-communicable disease (NCD) morbidity and mortality. There has been limited cohort data examining the role of early life urban environments on obesity and related conditions in developing countries such as Thailand.

Objective (4): To investigate changes in body mass index and fasting glucose among those with different levels of early life urban exposure in Thailand.

Study population: Thai Cohort Study (TCS) and Chiang Mai University (CMU) cohort members who had BMI within the normal range at baseline, and who were later followed up (baseline 2005 - followed up in 2009 for TCS; baseline 2008 - followed up in 2013 for CMU).

Exposure: Early life urban exposure (vs. rural exposure)

Outcomes: Development of obesity and impaired fasting glucose

Key findings: Adjusting for age and sex, those who spent their early life in urban environments were 1.21 times more likely to develop obesity in the TCS (OR 1.21, 95% CI 1.12 to 1.31) and 1.65 times more likely in the CMU Health Worker Study (OR 1.65, 95%CI 1.12 to 1.31), than those who did not. These associations remained significant despite adjusting for later life urban exposure and current household income. The study was underpowered to detect an association between early life urban exposure and development of impaired fasting glucose.

6.1 Introduction

Chapter 5 demonstrated results that early life urban environments were associated with increases in body mass index (BMI) and that people spending their early lives in urban areas could be at higher risk of developing impaired fasting glucose and diabetes. I wanted to explore this in more detail, using a separate cohort and focusing on changes in BMI and fasting glucose level over time.

This chapter used the CMU Health Worker cohort dataset described in Chapter 4 along with additional data from the TCS to examine whether early life exposure was associated with increased risk of developing obesity and impaired fasting glucose in adulthood. The details of the dataset and results are presented as a manuscript for publication.

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RESEARCH PAPER COVER SHEET

Early life urban exposure as a risk factor for developing obesity and impaired fasting glucose in later adulthood: Results from two cohorts in Thailand

PLEASE NOTE THAT A COVER SHEET MUST BE COMPLETED FOR EACH RESEARCH PAPER INCLUDED IN A THESIS.

SECTION A – Student Details

Student	Chaisiri Angkurawaranon
Principal Supervisor	Dorothea Nitsch
Thesis Title	Urbanization and internal migration as risk factors for non-communicable disease in Thailand

If the Research Paper has previously been published please complete Section B, if not please move to Section C

SECTION B – Paper already published

Where was the work published?			
When was the work published?			
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion			
Have you retained the copyright for the work?*		Was the work subject to academic peer review?	

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SECTION C – Prepared for publication, but not yet published

Where is the work intended to be published?	BMC Public Health
Please list the paper's authors in the intended authorship order:	Chaisiri Angkurawaranon, Anawat Wisetborisut, Kittipan Rerkasem, Sam-ang Seubsman, Adrian Sleigh, Pat Doyle and Dorothea Nitsch
Stage of publication	Under review

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	In consultation with my supervisor, I conceived the design and collected data in the CMU Health Worker Study. I signed the data access agreement form in order to obtained the TCS dataset. I wrote the manuscript and coordinated all co-authors' feedback and comments. I am first and corresponding author for the article.

Student Signature: _____ **Date:** 13 April 2015

Supervisor Signature: _____ **Date:** 9/7/15

Early life urban exposure as a risk factor for developing obesity and impaired fasting glucose in later adulthood: Results from two cohorts in Thailand

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Early life urban exposure as a risk factor for developing obesity and impaired fasting glucose in later adulthood: Results from two cohorts in Thailand

Background: Obesity and obesity related conditions, driven by processes such as urbanization and globalization, are contributing to pronounced cardiovascular morbidity and mortality in developing countries. There is limited evidence on the influence of living in an urban environment in early life on obesity and obesity related conditions later in life in developing countries such as Thailand.

Methods: We used data from two cohort studies conducted in Thailand, the Thai Cohort Study (TCS) and the Chiang Mai University (CMU) Health Worker Study, to investigate the association between early life urban (vs rural) exposure and the later development of obesity. We additionally explored the association between early life urban exposure and impaired fasting glucose in adulthood using data from the CMU Health Worker Study.

Results: Among 48,491 adults from the TCS, 9.1% developed obesity within 4 years of follow-up. Among 1,804 initially non-obese adults from CMU Health worker study, 13.6% developed obesity within 5 years of follow-up. Early life urban exposure was associated with increased risk of developing obesity in adulthood in both cohorts. Adjusting for age and sex, those who spent their early lives in urban areas were 1.21 times more likely to develop obesity in the TCS (OR 1.21, 95% CI 1.12 to 1.31) and 1.65 times more likely in the CMU Health Worker study (OR 1.65, 95% CI 1.23 to 2.20). These associations remained significant despite adjustment for later life urban exposure and current household income. No evidence for an association was found for impaired fasting glucose.

Conclusions: Early life urban exposure was associated with increased risk of developing obesity in adulthood. These findings support public health intervention programs to prevent obesity starting from early ages.

Early life urban exposure as a risk factor for developing obesity and impaired fasting glucose in later adulthood: Results from two cohorts in Thailand

Introduction

The rapidly increasing prevalence of obesity and obesity related conditions such as impaired fasting glucose and diabetes, have been considered a worldwide phenomenon [1]. This is becoming a major issue in developing countries, where obesity and diabetes are now contributing to a pronounced cardiovascular morbidity and mortality [2-4].

Obesity and diabetes are considered to have early life origins [5]. Early life risk factors for childhood and adult obesity include maternal malnutrition, maternal obesity, low birth weight, high birth weight, rapid weight gain in the first year of life, and rapid linear growth in childhood [6-8]. In India, there is evidence that accelerated growth during childhood is linked with obesity, insulin resistance and diabetes later in life [9]. These early life risk factors may also be enhanced or modified by later life environmental influences [10].

Urbanization is linked with many of these early life risk factors [11, 12] and is considered one of the key environmental factors driving obesity and diabetes trends [13]. In developing countries, there is evidence that urbanization may increase the risk of obesity and diabetes through lower physical activity and unhealthy dietary habits such as high glucose consumption [14]. However, urbanization may also be associated with many factors that could decrease the later risk of obesity and diabetes, such as improved socioeconomic status leading to a healthier life style, and better access to care [15]. Compared to developed countries, the rate of urbanization has occurred more rapidly in developing countries[16].

Thailand is a country considered at a tipping point of transition towards becoming a developed country [17]. Obesity has doubled within previous decades [18]. A nationally representative survey in 2009 estimated that around 63.8% of Thai women and 49.7% of Thai men aged over 20 were obese (BMI≥25). The prevalence of diabetes in Thailand was around 8.1% and 6.4%, amongst women and men respectively in 2009. There is also evidence that the prevalence of obesity and diabetes is higher in urban areas [19]. At an ecological level we can thus link urban residence and obesity. A recent cross sectional study among adult healthcare workers in Thailand has also suggested that exposure to urban environments in early life (compared to rural environments) was associated with higher levels of body mass index and fasting glucose in adulthood [20] . However, to properly investigate the influence of early life urban environments on the development of obesity and obesity related conditions, a cohort study is required [21]. Such cohort studies are rare in Thailand. An understanding of the relationship between early life environments with later development of obesity could help identify appropriate targets and timing of interventions to help combat the burden of obesity in Thailand.

We aimed to investigate the association between early life urban exposure with later development of obesity in adulthood using two cohort studies conducted in Thailand between 2005 and 2013. This analysis will also explore whether early life urban exposure remained independently associated with obesity despite later accumulation of adulthood urban exposure. Using data from one of the cohort studies, we will further investigate the association between early life urban exposure with impaired fasting glucose in adulthood.

Methods

The study utilized data from two cohort studies conducted in Thailand, the Thai Cohort Study (TCS) and the Chiang Mai University (CMU) Health Worker Study.

The cohort studies

The Thai Cohort Study (TCS) is a cohort of students at the Sukhothai Thammathirat Open University in 2005. TCS enrolled 87,142 students residing all over Thailand. The study represented the Thai population well in terms of age structure, gender, geographic and income distribution [22]. This cohort was followed up in 2009 [23].Using a 20-page questionnaire, data was collected in seven major areas that include socio-demographic details, income and work, food and physical activity, tobacco and alcohol use. This included self-reported body weight and height at baseline and follow up. (Figure 1)

The Chiang Mai University (CMU) Health Worker Study surveyed health care workers at the Faculty of Medicine, Chiang Mai University and CMU hospital in 2008. CMU hospital, situated in an urban area of Chiang Mai province, is the largest teaching hospital in Northern Thailand. The study enrolled over 3,500 participants [24]. Self-reported demographic status, monthly income, risk behaviors and common chronic diseases such as hypertension and diabetes were collected using an online questionnaire. Subsequently, all workers were offered a physical examination as well as a complete blood count (CBC) and urine examination according to the Thai National guideline [25] . Other laboratory investigations (fasting glucose and lipid profiles) were only offered to those ages 35 or above. During examinations, standing height and weight were measured using a portable stadiometer and electronic scale. Blood samples were sent to the Central Laboratory Unit in the hospital for processing. The participants were followed up in 2013 [26]. On the day of examinations and laboratory

investigations, face-to-face interviews were conducted to obtain a complete migration history from birth to current age. (Figure 2)

Migration history and urban exposure definition

The TCS used self-classification of urban-rural residence at three life course periods: early life at age 10-12; in 2005 (base line survey); and in 2009 (follow up survey). Participants were asked whether their permanent home during these three periods were considered 'countryside or city/town' [27].

The CMU health worker study used an urban classification derived from the Thai urban hierarchy based on population density and the size of municipalities [28]. Urban residence was defined as living in any districts making up Bangkok and Chiang Mai Metropolitan Area. These districts consisted of Muang (Chiang Mai Province), Sarapi, Sanpatong, Hang Dong, Mae Rim, Sansai, Doi Saket, Mae On, Sang Kampang, Muang (Lumphun Province). All other districts in Chiang Mai and Lamphun province were classified as rural. Participants were asked about their entire migration history during their lifetime. District of residence at two life course periods, early life at age 5 and early adulthood at age 20, were determined through interviews.

Outcome definitions

For obesity, body mass index (BMI) was calculated using body weight (in kilograms) divided by height (in meters) squared. As suggested for Asian populations, obesity was defined as having a body mass index of 25 kg/m^2 and above [29]. The development of obesity in both

cohorts were defined as those who were not obese in the baseline survey and having a BMI of at least 25 kg/m^2 in the follow up survey.

For impaired glucose and diabetes, data were only available from the CMU Health Worker study. Preliminary analysis showed that the 5-year incidence for diabetes (fasting blood glucose of at least 126 mg/dL) was small (<1%). A fasting glucose of at least 100 mg/dl, which is the criteria for impaired fasting glucose [30], was used as the outcome of interest. The development of impaired fasting glucose was defined as having a fasting glucose of less than 100 mg/dL in 2008 and a fasting glucose level of at least 100 mg/dl in 2013 or taking medication for diabetes in 2013.

Other variable of interests:

Socioeconomic status, which is considered a key mediator and/or confounder between urbanization and health outcomes [31], was measured through self reported household monthly income. This information was collected during the baseline survey and follow-up survey for both cohorts.

Analysis strategy

Data from each cohort were analyzed and presented separately. Demographic data were stratified by gender for descriptive purposes. Demographic factors associated with early life urban residence were tested using chi-square or t-tests. Logistic regression was used to determine the association between early life urban residence and risk of developing obesity and impaired fasting glucose/diabetes. To determine whether early life urban exposure predicts the development of obesity independently of later adulthood urban exposure, further analysis were done adjusting for later urban exposures.

For the TCS, the association between early life urban exposure (at age 10-12) with obesity was further adjusted for urban exposure in 2005 (baseline) and in 2009 (follow up). Additional adjustments were done for current socioeconomic at follow up (in 2009).

For the CMU cohort study, the association between early life urban residence (at age 5) with obesity and impaired fasting glucose/diabetes was further adjusted for early adulthood urban exposure (at age 20). As all health care workers were already working and living in an urban area of Chiang Mai in 2008 (baseline survey), any further adjustments for later life exposure (after 20) would not provide additional information. Additional adjustments were also done for current socioeconomic at follow up (in 2013).

We considered interactions between early life urban exposure and age and sex. In both cohorts, we did not find evidence for interactions between age or sex and early life urban exposure on incident obesity. Thus age and sex were considered as confounders in all final analyses.

Ethical approval

Informed consent was obtained from all participants in both cohorts. The TCS was approved by the Sukhothai Thammathirat Open University Research and Development Institute (protocol 0522/10) and the Australian National University Human Research Ethics Committee (protocol 2004344). The CMU Health Worker study was approved by Ethical committees from the Faculty of Medicine, CMU (no. 069/2012) and London School of Hygiene and Tropical Medicine (ref. 6521).

Results

Follow up rates in TCS

In 2005, 87,134 students agreed to participate (44.0% response). Using self-reported weight and height, 72,442 were not considered obese. In 2009, 68.3% (49,490) of non-obese participants were followed up with completed data for analysis (Figure 1). The participants who were lost to follow up were younger compared to those followed up. However, for gender, baseline BMI, urbanicity of locations in early life and in 2005, there were no obvious differences (appendix table 1).

Follow up rates in CMU Health Worker Study

In 2008, 3,527 health care workers agreed to participate (66.0% response). Of these participants, 2,946 were not considered obese. In 2013, 61.2% (1,804) of non-obese participants were followed up (Figure 2). The participants who were lost to follow up were more likely to be male and slightly older compared to those who were followed up. However, the baseline BMI and fasting glucose level in 2008 did not differ between those followed up and loss to follow up (appendix table 2).

Participant Characteristics

Demographic characteristics of participants in the TCS are displayed in Table 1, and those of the CMU Health Worker Study in table 2. The average age of the TCS participants at baseline was 30.7 years (sd=7.9), which was younger than CMU health worker study participants at baseline (average age 38.3, sd=8.6).Women represented the majority of both cohorts at 59.0% and 79.9% for TCS study and the CMU study respectively. For early life urban exposure, 25% of the TCS participants and over 50% of the CMU study participants spent their early life living in urban areas. For TCS, the proportion living in urban areas rose

from 50.3% in 2005 to 54.8% in 2009. By early adulthood (age 20), over 90% of the participants from the CMU study were living in urban areas.

Among the initially non-obese participants in the TCS, the baseline mean body mass index (BMI) in 2005 was 20.2 kg/m^2 for women and 21.6 kg/m^2 for men. By 2009, the average increase in BMI for women was 0.84 kg/m^2 and 0.75 kg/m^2 for men. The risk of developing obesity was 7.3% in women and 11.8% in men (Table 1). As participants from the CMU study were older, the baseline BMI and risks of developing obesity were higher than those of the TCS study. Among the initially non-obese participants in the CMU study, the baseline mean body mass index (BMI) in 2008 was 21.3 kg/m^2 for women and 22.8 kg/m^2 for men. By 2013, the average increase in BMI for women was 1.38 kg/m^2 and 1.10 kg/m^2 for men. The risk of developing obesity over the follow-up period was 12.8% in women and 16.6% in men. (Table 2)

Distribution of potential confounders

In the TCS, those who lived in an urban areas at age 10-12 were more likely to be older, female and have higher income at follow up in 2009 compared to those who lived in a rural areas at age 10-12. For CMU Health Worker study, those who lived in an urban area at age 5 were more likely to be older, male and have lower income at follow up in 2013 compared to those who spent their early life in rural residences (Table 3).

Early life urban exposure as a risk factor for developing obesity

There was consistent evidence from both cohorts that among initially non-obese participants, exposure to urban environments in early life was associated with the later development of

obesity in adulthood. Adjusting for age and sex, those who spent their early life in an urban area were 1.21 times more likely to develop obesity in the TCS (OR 1.21, 95% CI 1.12 to 1.31) and 1.65 times more likely in the CMU Health Worker study (OR 1.65, 95% CI 1.23 to 2.20). Adjustment for later adulthood urban residence and current socioeconomic status attenuated these effects, but the associations remained statistically significant. After adjustment for age, sex, later adulthood urban exposure and current socioeconomic status, those spending their early life in an urban area were 1.18 times more likely to develop obesity in the TCS (OR 1.18, 95% CI 1.09 to 1.28) and 1.46 times more likely in the CMU Health Worker Study (OR 1.46, 95% CI 1.06 to 2.03) (Table 4).

Early life urban exposure as a risk factor for developing impaired fasting glucose

After adjustment for age and sex, we did not find evidence that exposure to urban environments in early life was associated with development of impaired fasting glucose in the CMU study population (OR 0.91, 0.61 to 1.36). The association between early life urban exposure and development of impaired fasting glucose did not materially alter with additional adjustments for later adulthood urban exposure at age 20 and current socioeconomic status (OR 0.82, 95% CI 0.51 to 1.31). (Table 5)

Discussion

We found consistent evidence from two cohorts that among initially non-obese Thai adults, exposure to an urban environment in early life was associated with increased risk of obesity in adulthood. No evidence was found for an association between early life urban exposure and the development of impaired fasting glucose.

It is important to acknowledge the strengths and limitations of the study before further discussion and interpretations can be made. This study utilized data from two cohort studies which were set up to investigate the role of urbanization and the development of NCDs in Thailand [32]. Some systematic differences between responders and non-responders were observed but these groups did not differ by baseline BMI and fasting glucose level in the CMU Health worker study, or by baseline BMI and early life urban exposure in the TCS. The definition of urban exposure in both cohorts may be prone to misclassification bias. However, since only limited districts could be considered urban in the CMU Health worker study, urban exposure was unlikely to be misclassified. For TCS, self reported urban classification of residence has been shown to be associated with many aspects of urban living such as higher income, possession of cars and modern household appliances [33]. TCS used self-reported body weight and height to obtain the participant's BMI, which may also be prone to information bias. However, TCS has conducted a small validation study on these self-reported body weight and height measurements and found that the small discrepancies did not alter any of the associations between health behavior and body mass index [34]. Moreover, using self reported weight and height, the specificity for diagnosis of obesity (BMI≥25) was over 97% with a positive predictive value of 94% amongst TCS participants [35]. Although not considered major issues, these imprecise measurements of urban exposures and BMI would be likely to underestimate the associations seen, rather than overestimate them.

The two cohorts offered different strengths. The cohort composition of TCS suggests that the results are likely to be generalizable to the Thai population [22]. While results from the CMU health worker study may not be generalizable to the Thai population, it offers a unique opportunity to control for some elements of urbanization that may be difficult to disentangle in TCS [26]. The CMU health worker study was restricted to a population with similar access to health services, employment, and similar living and working conditions.

Obesity and diabetes have early life origins that track into adulthood [5]. Urbanization is one of the key drivers linked with childhood obesity [36]. Studies have suggested that BMI in early life is associated with persistently higher BMI in adulthood [37] , which in turn is associated with diabetes [38]. The socio-cultural environment associated with urbanization differs between countries, making direct comparison with other settings or populations difficult [39]. However, the results seen in this study are consistent with other studies from developing countries using a life course approach. Lifetime urban exposure was associated obesity and diabetes in Cameroon [13] and increasing BMI and fasting glucose in India [31]. Similar to our study, the associations seen were independent of age, current level of physical activity, and current socioeconomic status and residence.

This study provides evidence that non-obese young adults who had lived in an urban environment in their early life were at increased risk of developing obesity later on in adulthood compared to young adults who had not lived in an urban environment in early life. Although not considered obese at baseline, those with early life urban residence had slightly higher baseline BMI than those without, indicating that the progression to later obesity had already begun. Since most sociocultural and environmental influences associated with urbanization were controlled for in the CMU Health Worker Study, the main mediator for the association is thus likely to be lifestyle influences. Evidence from other another study using TCS data suggested that those spending their early lives (at age 10-12) in urban areas were less likely to engaged in regular activity, and more likely to have unhealthy diets in adulthood, than those spending their early life in rural areas [33].

We found no evidence for an association between early life urban exposure and development of impaired fasting glucose in the CMU Health worker study. As the risk of developing impaired fasting glucose was low, our study was underpowered to detect association and a longer duration of follow up is required. However, there are also a number of other plausible reasons why we could not detect an association between early life urban exposure and development of impaired fasting glucose. Since 90% of participants had been living in an urban area since age 20, there was likely to be a convergence of risks due to similar exposures to social and environmental factors, as seen in India [40]. Any differences due to early life urban exposure could be diluted if these biological risks (such as glucose level) were associated with more current or recent exposures rather than exposure in early life. Unlike BMI, fasting glucose has large biological variability and is more likely to reflect the current glucose homoeostasis[41]. It is also considered to be more susceptible to recent or current lifestyle habits and interventions [42, 43]. In a US study, a three- year history of weight gain among pre-obese adults was found not to result in higher levels of glucose compared to those who had maintain their weight [44]. Another possible explanation why our study could not detect an association between early life urban exposure and development of impaired fasting glucose was that the effect of urban environments may not be consistent across all health outcomes [31]. In some developing countries, including Thailand, while urbanization was associated with higher BMI and blood pressure, it was not always concurrently associated with higher lipid and glucose level [45, 46].

Recommendations and Public health implications

Consistent evidence from two cohorts found that early life urban exposure was associated with increase risk of developing obesity in adulthood. There are multiple underlying factors driving the association between urbanization and obesity, including genetic factors, maternal

conditions, socio-environmental factors, and individual lifestyles [47, 48]. In this study, lifestyle or behavioural factors are likely to be the key drivers, but further research is needed to understand the factors and mediators underlying the link between early life urban exposure and risk of obesity in Thailand [49].

As already supported by previous research [50], there are benefits to delaying the onset of obesity in order to prevent diabetes and other conditions. Public health intervention programs should be implemented to halt the development of obesity in children and young adults in Thailand

Authors' contribution

CA, PD, DN were responsible for the conception of the study. SS and AS were responsible for the design and acquisition of data for the TCS study. CA, AW, PD, DN were responsible for the design and acquisition of data for the CMU health worker study. CA analyzed the data and wrote the first draft of the manuscript. All authors contributed to interpretation of the data, revised the manuscript and approved the final manuscript.

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Conflicts of interest: None declared

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Table1 Distribution of demographic characteristics and risk of developing obesity among initially non-obese participants of the Thai Cohort Study

Thai Cohort Study	Female (N=28,635)	Male (N=19,855)	Total (48,490)
Mean age in 2005 (sd)	29.6 (7.4)	32.2 (8.4)	30.7 (7.9)
Monthly household income in 2009: (%:n)			
<10,000 baht	22.1 (6,333)	22.5 (4,461)	22.3 (10.794)
10,000-20,000 baht	24.6 (7,046)	24.7 (4,902)	24.6 (11,948)
20,000-50,000 baht	38.4 (10,985)	39.2 (7,792)	38.7 (18,777)
>50,000 baht	13.4 (3,842)	11.4 (2,255)	12.6 (6,097)
Missing	1.5 (429)	2,2 (445)	1.8 (874)
Early life location at age 10-12: (%,n)			
Rural	74.6 (21,373)	79.2 (15,731)	76.5 (37,104)
Urban	25.4 (7,262)	20.8 (4,124)	23.5 (11,386)
Residence in 2005 (%,n)			
Rural	48.0 (13,753)	51.6 (10,235)	49.5 (23,988)
Urban	51.8 (14,8219)	48.2 (9,575)	50.3 (24,394)
Missing	0.2 (63)	0.2 (45)	0.2 (108)
Residence in 2009 (%,n)			
Rural	42.1 (12,059)	46.8 (9,2823)	44.0 (21,341)
Urban	56.6 (16,209)	52.2 (10,371)	54.8 (26,580)
Missing	1.3 (367)	1.0 (202)	1.2 (569)
BMI in 2005 (mean, sd)	20.2 (2.1)	21.6 (2.0)	20.8 (2.2)
BMI in 2009 (mean,sd)	21.0 (2.6)	22.4 (2.3)	21.6 (2.6)
Increase in BMI (mean, sd)	0.84 (1.6)	0.75 (1.5)	0.80 (1.6)
Developed obesity (BMI ≥25) by 2009 (%,n)	7.3 (2077)	11.8 (2,346)	9.1 (4,423)

BMI= body mass index in kg/m2

Table 2 Distribution of demographic characteristics and risk of developing obesity and impaired fasting glucose/diabetes among initially non-obese participants of Chiang Mai University Health Worker Study

CMU Health Worker Study	Female (N=1443)	Male (N=361)	Total (1,804)
Mean age in 2008 (sd)	38.4 (8.6)	38.1 (8.3)	38.3 (8.6)
Monthly household income in 2013: (%:n)			
<10,000 baht	7.7 (111)	19.9 (72)	10.2 (183)
10,000-20,000 baht	20.0 (288)	36.3 (131)	23.2 (419)
20,000-50,000 baht	41.4 (598)	27.4 (99)	38.6 (697)
>50,000 baht	30.9 (446)	16.3 (59)	28.0 (505)
Early life location at age 5: (%,n)			
Rural	44.0 (635)	29.1 (105)	41.0 (740)
Urban	56.0 (808)	70.9 (256)	59.0 (1,064)
Early adulthood location at age 20 (%,n)			
Rural	9.8 (141)	7.8 (28)	9.4(169)
Urban	90.0 (1,302)	92.2 (333)	90.6 (1,635)
BMI in 2008 (mean, sd)	21.3 (2.2)	22.8 (2.0)	21.6 (2.2)
BMI in 2013 (mean,sd)	22.7 (2.9)	23.9 (2.5)	22.9 (2.9)
Increase in BMI (mean, sd)	1.38 (1.9)	1.10 (1.8)	1.32 (1.9)
Developed obesity (BMI ≥25) by 2009 (%,n)	12.8 (185)	16.6 (60)	13.6 (245)
Fasting glucose in 2008* (mean, sd)	84.5 (8.9)	87.2 (9.2)	85.0 (9.0)
Fasting glucose in 2013* (mean, sd)	90.1 (8.4)	94.7 (12.6)	91.1 (9.6)
Increase in fasting glucose* (mean,sd)	5.63 (9.9)	7.53 (12.4)	6.03 (10.5)
Developed impaired fasting glucose/diabetes*, (%,n)	8.6 (76)	20.2 (45)	10.9 (121)

BMI= body mass index in kg/m2; Fasting glucose in mg/dL ; Impaired fasting glucose/diabetes defined as having fasting glucose ≥ 100 mg/dL; *A sample of 885 women and 223 men with fasting glucose measurement

Table 3 Demographic factors, BMI and fasting glucose by early life urban residence

	CMU Health Worker Study			Thai Cohort Study (TCS)		
	Early Life Residence at age 5			Early Life Residence at age 10-12		
	Rural n=740	Urban n=1,064	p-value	Rural n=37,105	Urban n=11,385	p-value
Mean age at baseline (sd)	37.2 (8.5)	39.1 (8.5)	<0.01	30.3 (7.7)	31.8 (8.6)	<0.01
Sex: (col %,n)			<0.01			<0.01
Female	85.8	75.9		57.6	63.8.	
Male	14.2	24.1		42.4	36.2	
household income at follow up (col %,n)			<0.01			<0.01
<10,000 baht	6.9	12.4		25.7	11.1	
10,000-20,000 baht	15.1	28.9		26.3	19.4	
20,000-50,000 baht	45.0	34.2		37.3	43.2	
>50,000 baht	33.0	24.5		8,9	24.6	
Missing	0.0	0.0		1.8	1.7	
Mean BMI at baseline (sd)	21.3 (2.2)	21.8 (2.2)	<0.01	20.8 (2.2)	20.8 (2.2)	0.14
Mean BMI at follow up (sd)	22.6 (2.8)	23.2 (2.9)	<0.01	21.5 (2.5)	21.6 (2.6)	<0.01
Mean increase in BMI (sd)	1.34 (1.8)	1.31 (1.9)	0.73	0.80 (1.6)	0.84 (1.6)	0.01
Mean fasting glucose in 2008 (sd)	83.7 (8.5)	84.0 (7.7)	0.53	Not available		
Mean fasting glucose in 2013 (sd)	89.7 (8.8)	90.7 (9.1)	0.07	Not available		
Increase in fasting glucose (sd)	6.0 (9.9)	6.7 (10.0)	0.26	Not available		

BMI at baseline was in 2008 for CMU Health worker study and 2005 for TCS; BMI at follow up was in 2013 for CMU Health Worker study and 2009 for TCS. 32 baht is approximately 1 US dollar; For fasting glucose N for early rural =429, early urban= 679. Unit for BMI in kg/m^2, Unit for fasting glucose in mg/dL

Table 4 Early life urban exposure and risk of developing obesity in adulthood

		Model 1	Model 2	Model 3
	% (n) Obese by follow-up	Adjusted OR for obesity (95% CI) and p-value	Adjusted OR for obesity (95% CI) and p-value	Adjusted OR for obesity (95% CI) and p-value
CMU Health Worker study: Early Life Residence at age 5				
Rural (n=740)	10.3 (76)	Reference	Reference	Reference
Urban (n=1,065)	15.9 (169)	1.65 (1.23 to 2.21) p<0.01	1.71 (1.24 to 2.32) p<0.01	1.46 (1.06 to 2.03) p=0.02
Thai Cohort Study (TCS): Early Life Residence at age 10-12				
Rural (n=37,105)	8.8 (3,251)	Reference	Reference	Reference
Urban (n=11,386)	10.3(1,172)	1.21 (1.13 to 1.30) p<0.01	1.21 (1.12 to 1.31) p<0.01	1.18 (1.09 to 1.28) p<0.01

BMI at baseline was in 2008 for CMU Health worker study and 2005 for TCS; BMI at follow up was in 2013 for CMU Health Worker study and 2009 for TCS. Obesity defined as BMI ≥ 25 kg/m^2

Model 1: adjusted odds ratio (OR) for age and sex

Model 2: adjusted odds ratio for age and sex, and later urban exposure in adulthood; Results from CMU Health worker study was adjusted for urban residence at age 20, Results from TCS adjusted for urban residence in 2005 and 2009

Model 3: Adjusted odds ration for age, sex, later urban exposure (same as model 2) and current household income at follow up

No evidence for interactions between early life urban residence and sex in both cohorts

Table 5 Early life urban exposure and risk of developing impaired fasting glucose/diabetes in adulthood (Fasting Blood glucose ≥ 100 gm/dL)

		Model 1	Model 2	Model 3
CMU Health Worker study:	% (n) with impaired glucose by follow-up	Adjusted OR for impaired glucose (95% CI) and p-value	Adjusted OR for impaired glucose (95% CI) and p-value	Adjusted OR for impaired glucose (95% CI) and p-value
Early Life Residence at age 5				
Rural (n=429)	10.6% (45)	Reference	Reference	Reference
Urban (n=679)	11.2% (76)	0.91 (0.61 to 1.36) 0.66	1.00 (0.64 to 1.54) 0.99	0.82 (0.51 to 1.31) 0.41

Fasting glucose at baseline measured in 2008 and followed up was in 2013 in Chiang Mai University (CMU) Health Worker Study

Model 1: adjusted odds ratio (OR) for age and sex

Model 2: adjusted odds ratio for age and sex, and later urban exposure in adulthood at age 20,

Model 3: Adjusted odds ration for age, sex, later urban exposure in adulthood at age 20 and current household income at follow up in 2013

No evidence for interactions between early life urban residence and sex

Figure 1 Flow chart of recruitment and follow up in the Thai Cohort Study

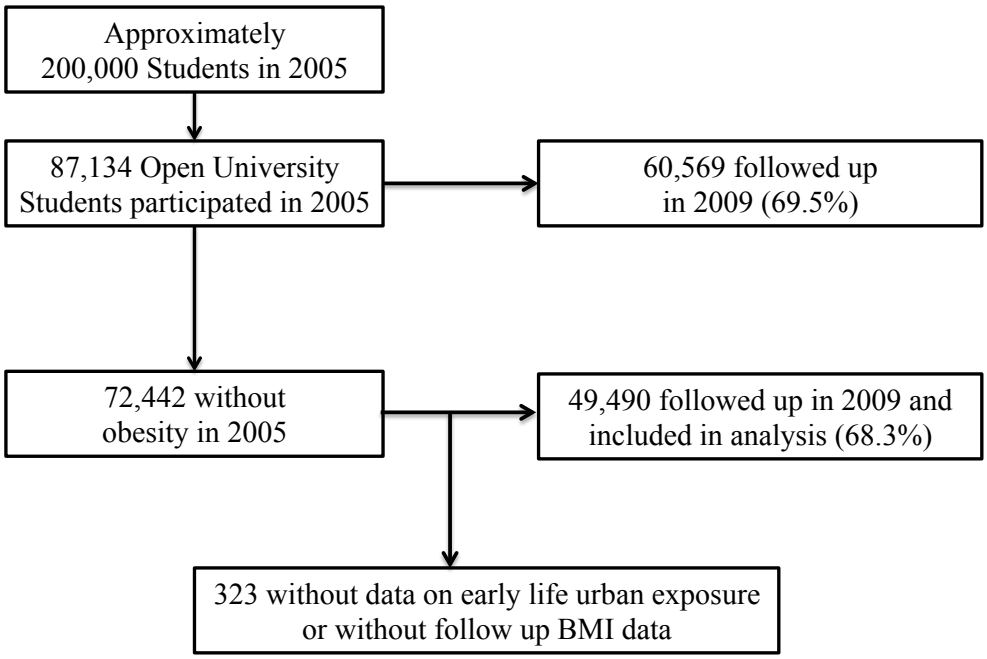
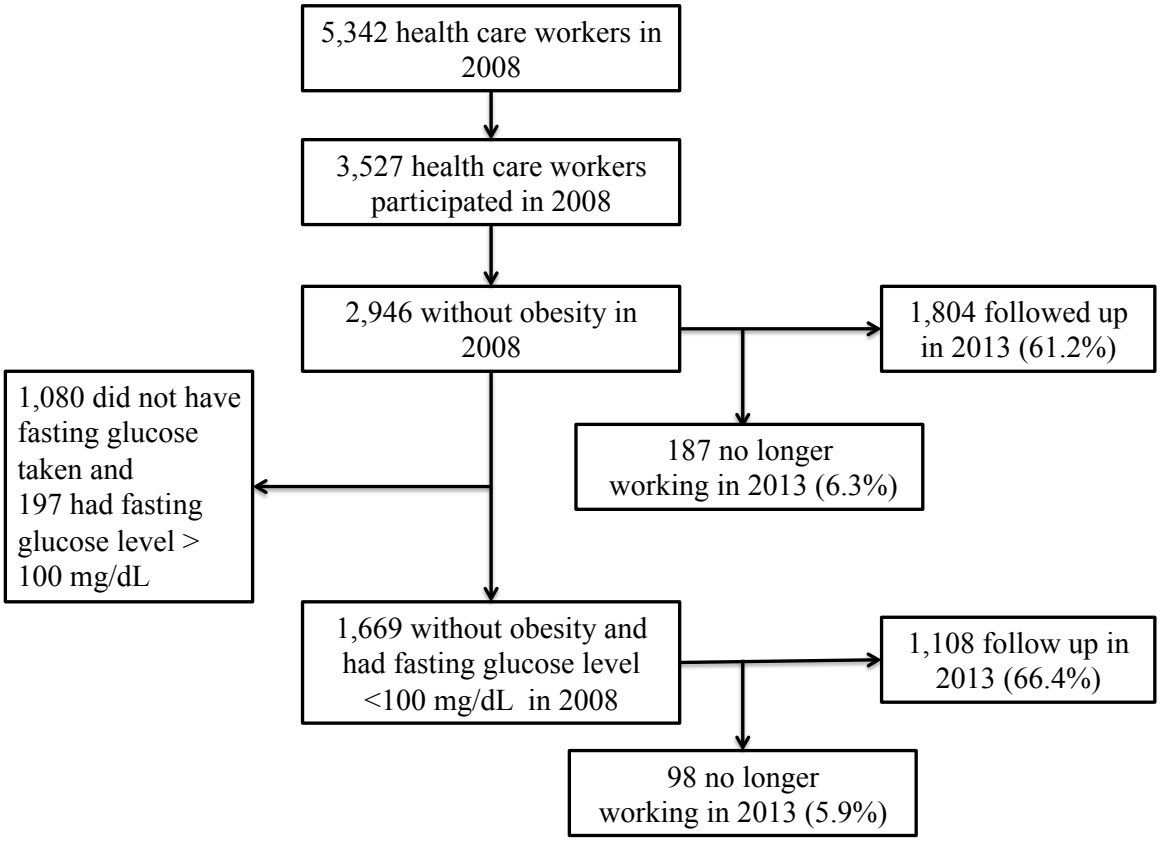


Figure 2 Flow chart of recruitment and follow up in the Chiang Mai University Health Worker Study



6.3 Summary and conclusion

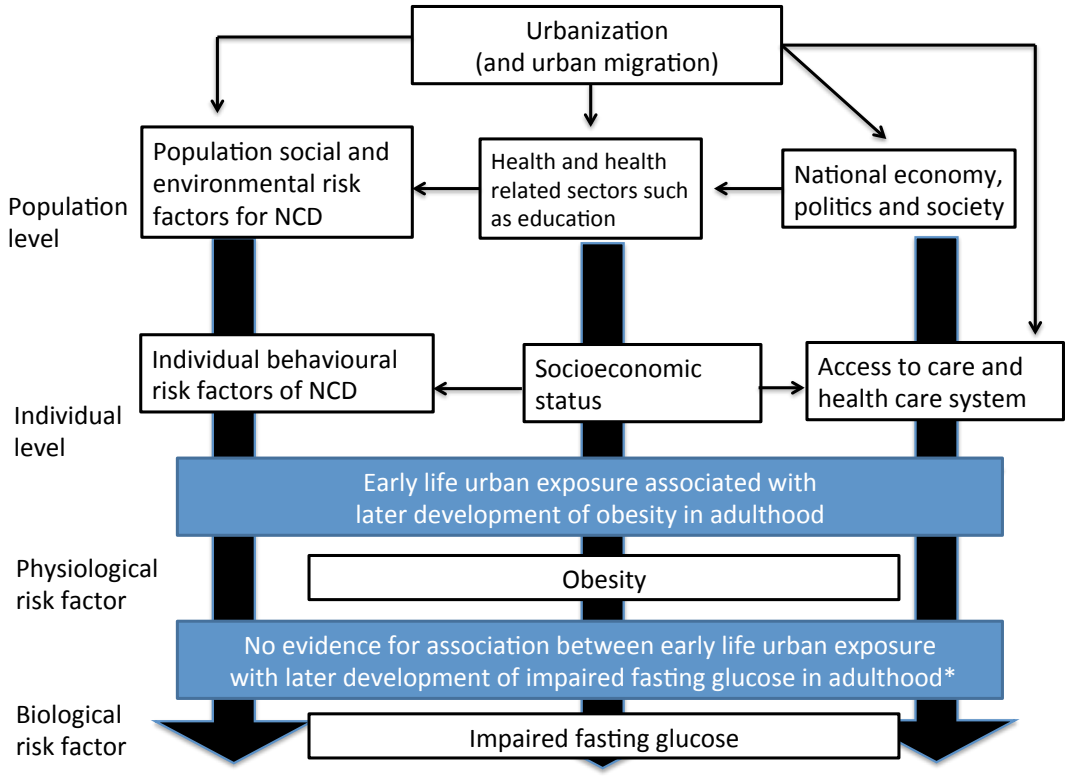
The 'developmental origins of chronic diseases' hypothesis highlights the importance of early life under-nutrition (from in utero to early childhood) as an important factor influencing the development of NCDs (76). I, therefore, initially hypothesized in Chapter 4 that people growing up in rural areas in Thailand could be more susceptible to NCDs.

My findings from both cohort studies in Thailand did not support this notion. Thailand, although considered a developing country, has been relatively successfully in combating under-nutrition. The prevalence of children who are underweight amongst the preschool population decreased from 51% in 1980 to below 10% by 2006 (77). Thus, those with early life rural exposure were not necessarily more likely to experience under-nutrition in early life.

While my study was underpowered to detect an association between an early life urban environment and development of impaired fasting glucose, the study provided evidence that living in an urban environment early in life was associated with an increased risk of developing obesity in adulthood (Figure 6.1).

Having consistent evidence generated from two different cohorts, each with different strengths, as discussed in the published manuscript, provides evidence to support the role of living in an urban environment as an important driver of obesity in Thailand. The pattern of association between early urban exposure and socioeconomic status (SES) and gender was opposite in the cohorts, whilst still showing consistent associations for the association between early life urban exposure and obesity. Hence, it is very unlikely that these results are explained by residual confounding by gendered behaviors or SES.

Figure 6.1 Conceptual framework of this thesis with adaptations to incorporate findings from Chapter 6



* under-powered to detect association

Chapter 7 : Urban environments and recent migration: their association with psychosocial health, well-being and body mass index

Summary

Introduction: There are limited data exploring changes in urbanicity and migration and psychosocial outcomes, and whether these psychosocial outcomes translate into NCD risk factors in Thailand.

Objectives (5): (i) To investigate the influence of rapid changes in urbanicity (urban/rural location) and recent internal migration on psychosocial health and well-being.

(ii) To investigate whether lower levels of psychosocial health and well-being translate to an increase in body mass index (BMI).

Study population: the Thai Cohort Study (TCS) of university students attending Sukhothai Thammathirat Open University.

Exposures: urbanicity (urban versus rural location) and recent migration.

Outcomes: social trust, emotional problems, personal well-being, quality of life and BMI.

Key findings: Rapid changes in ubanicity and the process of recent migration had very small immediate associations with psychosocial health and well-being. Both exposures were independently associated with higher emotional problems and lower social trust. Low social trust and emotional problems may potentially translate into increases in BMI but the effect size for both psychosocial factors with BMI were, likewise, very small. It is unclear whether these associations have clinical relevance.

7.1 Introduction

The associations between living in urban environments and behavioural/ physiological risk factors for NCDs have been documented in Chapter 5 and Chapter 6. One key issue towards a better understanding of the link between urbanization and NCDs that has not yet been addressed in the thesis is internal urban migration. As outlined in the introduction of the thesis (Chapter 1), urban migration is considered one of the key factors driving urbanization in developing countries including Thailand (59).

Literature has suggested that migrants may experience some health benefits by moving from poorer to more affluent environments (20). However, internal migrants face a number of factors that may also put them at risk of poor health. These factors include sociocultural factors such as being separated from family and familiar surroundings, as well as having a comparatively lower socioeconomic status (SES) than others in the new community (78). Migrants may also be excluded from some public health services as some schemes in Thailand are provided by local primary care units based on household registration (79).

Evidence from low and middle income countries (LMICs) is limited regarding the link between internal migration and psychosocial health, well-being and risk factors for NCDs (80). This is possibly due to a number of methodological challenges. The first methodological challenge is in finding a proper comparison group.

Earlier studies have compared the health of migrants to the health of those in the receiving population (after migration). However, the most appropriate comparison group for migrants is those in the sending population (before migration). This is considered a more appropriate 'counter factual' population as comparisons are made between a migrant population and a 'similar' population if these individuals had not migrated (81).

The second challenge relates to the fact that migration is a selective process. Migrants tend be healthier than those who do not migrate due to the physical,

emotional and economic demands of migration. This is known as the 'healthy migrant' hypothesis (82). Failure to account for this selectivity before migration may result in bias in research studies on migration and health outcomes.

Lastly, psychosocial health, well-being and NCD risk factors are likely to be influenced by the experiences before migration and by the environmental conditions and cultures of the new environment (83). This notion is supported by a study from China, which found that the mental health status of rural-to-urban migrants differed from urban-to-urban migrants (84).

This chapter aims to explore associations between internal migration and psychosocial health, well-being and BMI using data from a large cohort study from Thailand. Specifically, the study in this chapter had four main objectives, which were to explore:

1. associations between internal migration and psychosocial health and well-being by adjusting for a potential 'selective migration effect' and by using the sending population as a comparison group;
2. whether the associations with migration were independent of urbanicity of environments, before and after migration;
3. whether the associations between migration and psychosocial health and well-being were modified by urbanicity of environments;
4. whether lower levels of psychosocial health and well-being (found to be associated with migration and/or urban environments) translate into an increase in body mass index.

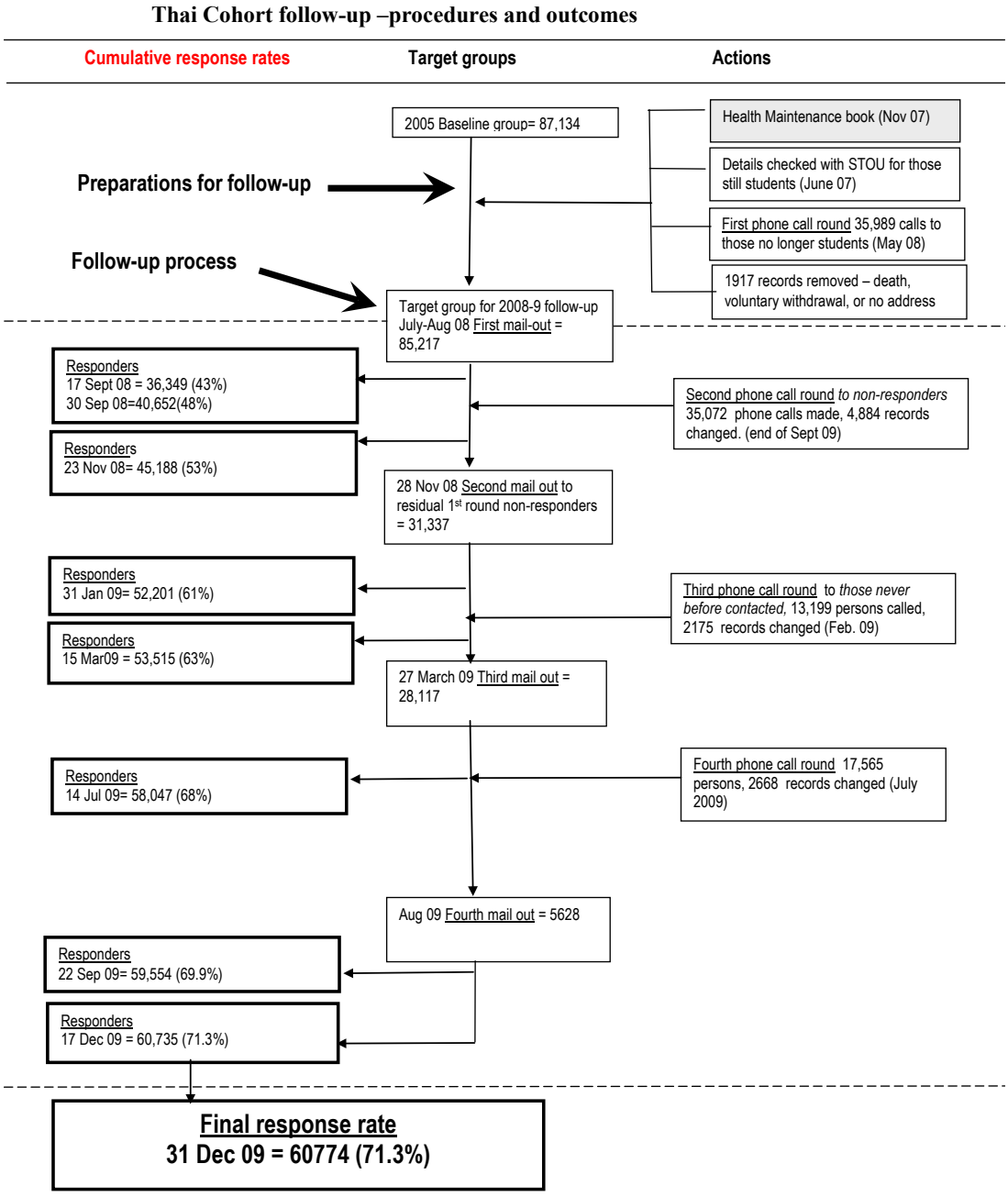
7.2 Methods

7.2.1 Study population

The study utilized data from the TCS, which is a large cohort of distance learning students who enrolled at Sukhothai Thammathirat Open University (STOU) in Thailand (36). In the baseline survey, conducted in 2005, 44% of the student population (N=87,134) completed a 20-page questionnaire. The questionnaire collected data on sociodemographic characteristics and health risks including smoking and alcohol use, underlying health conditions and injuries, social networks and well-being.

As earlier stated in Chapter 1, the cohort represented the Thai population well in terms of geographic (regional) and income distributions, median age and sex ratio (36, 38) (Figure 1.2). In the follow up survey, conducted in 2009, 71% of the participants responded with 60,774 completed questionnaires (37) (Figure 7.1).

Figure 7.1 Thai Cohort Study follow up outcomes between 2005 and 2009



Source: Seubsman S-a, Kelly M, Sleigh A, Peungson J, Chokkanapitak J, Vilainerun D, Methods used for successful follow-up in a large scale national cohort study in Thailand. *BMC Research Notes* 2011, 4:166 (37)

7.2.2 Measurement and definitions of key variables

Migration

As region of current location was asked in both questionnaires, internal migration was defined as a move to a different region since the 2005 baseline survey. Those who had stayed in the same region between 2005 and 2009 were considered non-migrants. Thus migration in the study captured recent interregional migration (within 4-5 years).

Evidence from Thailand suggests that interregional migration is more likely to be associated with long-term migration (85). Long-term migration patterns are more likely to have greater effects on population distributions and are considered to be drivers of urbanization in Thailand, rather than seasonal or short-term migration.

Urbanicity of locations

For urbanicity, participants were asked to rate whether their current location should be classified as 'countryside (rural)' or 'city/town (urban)'. A four-category variable was created based on urbanicity of locations in 2005 and 2009: rural-rural (RR), rural-urban (RU), urban-rural (UR) and urban-urban (UU).

Previous publications from the TCS have suggested that this self-classification of urbanicity correlated well with many aspects of living in urban environments such as higher personal income, ownership of a car and modern appliances (41). This four-category variable of urbanicity was also associated with lower physical activity, consumption of junk food and obesity (41, 44).

Psychosocial health, well-being and body mass index

For psychosocial health and well-being, the research focused on four outcomes: i) personal well-being, ii) quality of life, iii) social trust and iv) emotional problems. BMI was assessed using self-reported weight and height. Data on these five main outcomes were collected in both the 2005 and 2009 surveys. The outcomes in 2009 were considered to be the main outcomes of interest.

1. Personal well-being: personal well-being was measured in four domains: i) personal safety, ii) community connection, iii) standard of living and iv) general life satisfaction using the Personal Wellbeing Index (86). Participants were asked to rate their satisfaction in each of the four domains over an 11-point scale from '0 - no satisfaction at all' to '10 - completely satisfied'. As suggested by the manual, each domain could be considered as a separate variable and scores were transformed into the standard 0-100 point scale by multiplying each item score by ten. The normative range was between 50 and 100.
2. Quality of life: quality of life was assessed using the SF-8 questionnaire (87). The scores for each item were transformed and weighted to create a physical component summary (PCS) and a mental component summary (MCS) with scores from 0 to 100. Higher scores indicated better health related quality of life (88).
3. Social trust: participants were asked 'Generally speaking, would you say that most people can be trusted?' The possible responses were 'you cannot be too careful' or 'most people can be trusted'. Participants who answered the latter were considered to have social trust. A previous publication using TCS data has shown that this definition of social trust was positively correlated with overall health and psychological health (40).
4. Emotional problems: participants were asked 'During the past four weeks, how much have you been bothered by emotional problems (such as feeling anxious, depressed, or irritable)?' The six possible responses were 'not at all', 'slightly', 'moderately', 'quite a lot' and 'extremely'. For analysis, a binary variable was created. Participants answering with the last two categories were considered to have emotional problems.

5. BMI in 2005 and 2009 was derived from self-reported weight and height by dividing the reported weight (in kilograms) by weight squared (in metres).

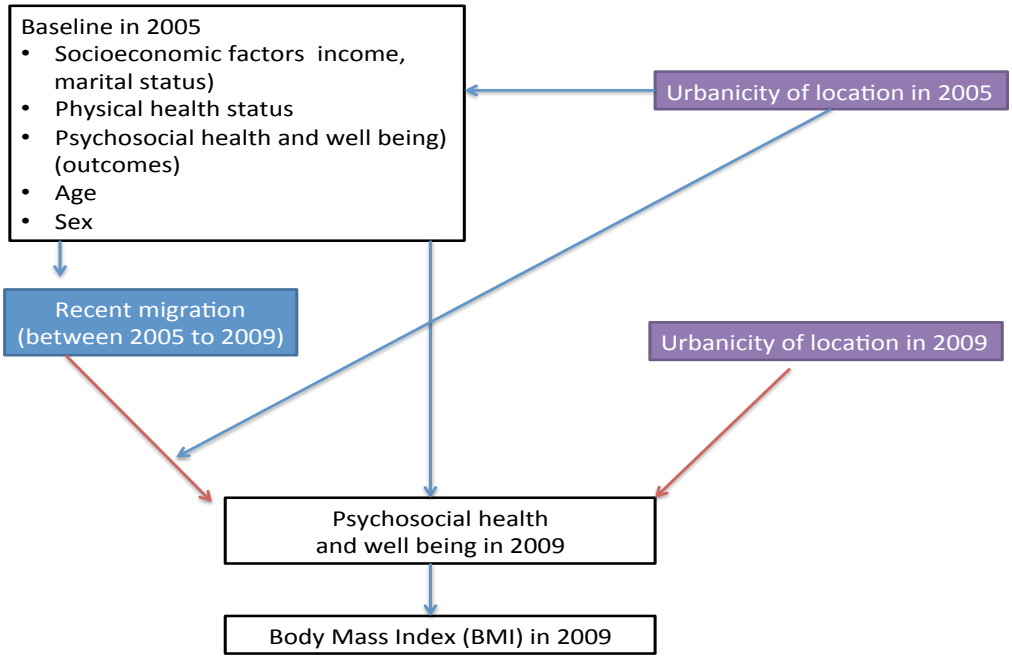
Other factors of interest

Other variables of interest included age, sex, marital status and personal income. Self-rated health status was considered as a proxy for overall physical health. Participants were asked to rate their overall health in the previous four weeks as 'excellent', 'very good', 'good', 'fair', 'poor' or 'very poor'. A recent publication has demonstrated that in the TCS, low self-rated health was associated with mortality from cardiovascular disease and cancer (89).

7.2.3 Conceptual framework, statistical methods and analysis strategy

A conceptual framework, taking into account all three methodological issues outlined in the introduction section, and mediating pathways between internal (urban) migration and health, is presented in Figure 7.2. In my framework, psychosocial health and well-being are considered the key mediating factors between migration and other health outcomes such as high BMI (90).

Figure 7.2 Chapter 7 conceptual framework between migration, psychosocial health/well-being and BMI



Psychosocial health and well-being consists factors relating to social trust, emotional problems, perceived personal well-being and quality of life.

The analysis strategy was based on this conceptual framework. Stratified by sex, baseline socio-demographic and economic characteristics in 2005 were compared between migrants and non-migrants. A comparison was carried out between migration with psychosocial health and well-being in 2009 and changes in psychosocial health and well-being (between 2005 and 2009). Crude associations were tested using t-test or chi-square tests.

To adjust for the potential 'selective migrant' effect, these associations were further explored using multivariable linear and logistic regression to adjust for age, sex, baseline socio-demographics and economic characteristics in 2005 along with the corresponding baseline value for each outcome of interests. To explore whether the associations between migration and psychosocial health and well-being in 2009 were independent or modified by urban location, urbanicity was added to the model. The interaction terms between

migration and urbanicity of locations were tested using the likelihood ratio test.

To explore whether significant psychosocial outcomes potentially translate into NCD risk factors as proposed in the framework, the associations between baseline psychosocial characteristics in 2005 and BMI in 2009 were explored using the same analysis strategy previously described. Relative risks and absolute risk differences were considered for all associations.

7.2.4 Sensitivity analyses

To investigate the robustness of the observed associations against attrition bias, multiple imputation was used to account for missing data (91). In total, seventy variables from the baseline 2005 data were used to impute the missing outcome variables. These included all the socioeconomic characteristics and psychosocial health outcomes previously described plus other variables for employment status, history of having children, social interactions and social support, alcohol and tobacco consumption, BMI, self-reported doctor-diagnosed history of underlying medical conditions and an interaction term between age and sex.

I used a large number of variables for imputation in order to try to satisfy the key assumption of multiple imputation that the pattern of missingness should be considered at random after accounting for all the observed variables included in model (92). Twenty-five imputed data sets were created and used for sensitivity analysis. All analysis was done using Stata version 13.

7.3 Result

Of the 60,774 participants followed up in the TCS, 58,459 had complete data on migration and urbanicity status (96.2%). Fifty-five percent of the participants were female. The average age for men in the study in 2005 was 33.4 years (sd=8.8 years). For women, the average age was 30.1 years (sd=7.7 years). From 2005 onwards, 7.4% of participants had moved to a different region by 2009.

People living in urban areas in 2005 were more likely to migrate, and the proportion of migrants did not significantly differ between men and women. Migrants tended to be younger, more likely to be single, and had a lower income in 2005 compared to non-migrants. Self-reported health status in 2005 was not associated with migration among men; however a slightly higher percentage of female migrants reported having a poor to very poor self-rated health status in 2005 compared to non-migrant women (5.1% vs. 6.0%, respectively, p-value = 0.02) (Table 7.1).

7.3.1 Associations between migration and psychosocial health, well-being and BMI

In 2005, migrants reported lower levels of well-being compared to non-migrants. They were more likely to have been bothered by severe emotional problems and less likely to feel that people could be trusted. However, there was little or no difference in reported quality of life between migrants and non-migrants in 2005. In both sexes, migrants had slightly lower BMI than non-migrants at baseline (Table 7.2 and Table 7.3).

By 2009, well-being (across all four domains) had improved for migrants and non-migrants. Migrants still reported lower levels of well-being in all four domains compared to non-migrants. However, the changes in well-being differed by domain. Although their scores were lower than non-migrants, both male and female migrants had a higher increase in satisfaction with standard of living. Migrant men had lower increases in satisfaction with

being part of the community compared to non-migrant men. Increases in other domains did not materially differ between the two groups. Quality of life, emotional problems and social trust remained stable for migrants and non-migrants with little or no apparent differences between the two groups.

There was evidence that the association between migration and changes in BMI were modified by sex (p-value for interactions 0.01). For BMI, migrant men had gained more weight than non-migrants. There was no evidence of an association between migration and BMI changes amongst women (Table 7.2 and Table 7.3).

Table 7.1 Characteristics of study population by sex and migration status in the Thai Cohort Study by 2009

	Men			Women		
	Non-migrants N=24,445	Migrants N=2,010	p-value	Non migrants N= 29,668	Migrants N= 2,336	p-value
Age (mean, sd)	33.7 (8.9)	30.3 (7.5)	<0.01	30.2(7.7)	27.8 (6.5)	<0.01
Age group			<0.01			<0.01
<20	1.3	1.6		2.5	2.4	
20-30	36.0	53.8		51.5	67.6	
30-40	37.8	32.3		32.5	23.5	
40-50	20.1	9.9		11.9	5.3	
>50	4.8	2.4		1.6	1.1	
Region of residence in 2005 (col %)			<0.01			<0.01
Bangkok	13.6	22.5		18.3	28.0	
Central (excluding Bangkok)	22.6	22.8		26.0	22.5	
North	21.0	15.8		28.3	15.7	
Northeast	24.2	26.0		17.6	21.4	
East	5.9	6.6		6.0	5.4	
South	12.7	6.2		13.8	7.0	
Marital status in 2005 (col %)			<0.01			<0.01
Single	38.7	55.0		53.3	67.4	
Married/living with partner	56.2	38.6		40.0	26.6	
Separated/divorced/widowed	3.3	4.2		5.1	4.4	
Missing value	1.8	2.2		1.6	1.6	
Personal income per month in 2005 (col %)			<0.01			<0.01
<3,000	9.7	9.8		9.0	9.3	
3,000-7,000	20.8	23.8		34.0	35.6	
7,000 to 10,000	22.0	27.4		22.9	28.9	
10,000 to 20,000	30.5	25.3		22.7	18.1	
>20,000	15.0	11.2		9.2	6.3	
Missing value	1.8	2.5		2.2	2.8	

Table 7.1 Characteristics of study population by sex and migration status in the Thai Cohort Study by 2009 (continued)

	Men			Women		
	Non-migrants N=24,445	Migrants N=2,010	p-value	Non migrants n= 29,668	Migrants N= 2,336	p-value
Self-reported health status (past 4 weeks) in 2005 (col %)			0.10			0.02
Poor to very poor	3.6	4.2		5.1	6.0	
Fair to good	72.2	70.0		76.2	77.4	
Very good/excellent	23.9	25.4		18.4	16.3	
Missing value	0.3	0.4		0.3	0.3	
Urbanity of residence 2005 (col %)			<0.01			<0.01
Rural	51.0	40.9		48.7	35.3	
Urban	49.0	59.1		51.3	64.7	
Urbanity of residence 2009 (col %)			<0.01			<0.01
Rural	47.2	32.7		43.4	30.6	
Urban	52.8	67.3		56.6	69.4	

Non-migrants defined as those who resided in the same region between 2005 and 2009; migrants defined as those who had moved location to a different region by 2009

Table 7.2 Personal well-being, quality of life, emotional problems, social trust and BMI in 2005 and 2009 by migration status among men in the Thai Cohort Study

	Observed data				Multiple imputation (M=25)			
	n	Men			n	Men		
	Total/ migrant	Non-migrants	Migrants	p-value	Total	Non migrants	Migrants	p-value
Satisfaction with personal safety (mean,sd)								
Score in 2005	27015/2040	72.8 (19.6)	69.6 (20.2)	<0.01*		--	--	--
Score in 2009	26913/2037	75.5 (19.4)	72.2 (20.2)	<0.01*	35812	75.1	73.1	<0.01
Changes in score (2009-2005)	26725/2019	2.73 (20.9)	2.63 (22.3)	0.84#	35624	2.61	2.35	0.52
Satisfaction with being part of community (mean,sd)								
Score in 2005	27001/2039	68.4 (21.7)	63.7 (20.8)	<0.01*		--	--	--
Score in 2009	26908/2038	71.9 (21.0)	65.9 (22.7)	<0.01*	35807	71.2	67.2	<0.01
Changes in score (2009-2005)	26707/2019	3.57 (22.4)	2.17 (26.0)	<0.01#	35604	3.57	2.60	0.03
Satisfaction with standard of living (mean,sd)								
Score in 2005	26968/2034	68.3 (20.0)	62.7 (20.8)	<0.01*		---	---	---
Score in 2009	26922/2038	71.9 (18.7)	68.4 (19.4)	<0.01*	35818	71.4	68.9	<0.01
Changes in score (2009-2005)	26687/2014	3.66 (20.5)	5.66 (21.6)	<0.01#	35583	3.82	5.16	<0.01
Satisfaction with life as a whole (mean,sd)								
Score in 2005	26997/2036	75.8 (17.1)	72.5 (18.0)	<0.01*		--	--	--
Score in 2009	26901/2038	77.9 (16.7)	74.7 (17.5)	<0.01*	35789	77.4	75.2	<0.01
Changes in score (2009-2005)	26695/2016	2.07 (17.5)	2.27 (18.8)	0.63#	35592	2.03	2.13	0.81

Non-migrants defined as those who resided in the same region between 2005 and 2009; migrants defined as those who had moved location to a different region by 2009; all satisfaction scores have been transformed by multiplying responses ranging from 0 “completely dissatisfied” to 10 “completely satisfied” by 10. * Wilcoxon rank sum test; # t-test, ** chi-square test;

Table 7.2 Personal well-being, quality of life, emotional problems, social trust and BMI in 2005 and 2009 by migration status among men in the Thai Cohort Study (continued)

	Observed data				Multiple imputation (M=25)			
	n	Men			n	Men		
	Total/ migrant	Non-migrants	Migrants	p-value	Total	Non migrants	Migrants	p-value
Physical quality of life (mean,sd)								
Score in 2005	26760/2030	59.4 (6.7)	59.6 (6.7)	0.12		--	--	--
Score in 2009	26865/2038	58.8 (6.8)	59.0 (6.9)	0.09	35966	58.8	59.0	0.07
Change in score (2009-2005)	26427/2010	-0.64 (7.8)	-0.59 (7.8)	0.78	35528	-0.60	-0.47	0.39
Mental quality of life (mean,sd)								
Score in 2005	26760/2030	57.2 (8.2)	56.1 (8.8)	<0.01		---	---	---
Score in 2009	26865/2038	57.3 (8.2)	56.1 (8.4)	<0.01	35966	57.1	56.2	<0.01
Change in score (2009-2005)	26427/2010	0.10 (8.9)	0.01 (9.5)	0.59	35528	0.09	0.04	0.79
Emotional problems in previous 4 weeks								
Emotional problems in 2005 (%)	27113/2047	10.7	15.2	<0.01**		---	---	---
Emotional problems in 2009 (%)	27097/2049	11.9	15.5	<0.01**	36052	12.5	15.3	<0.01
Social trust								
Feel that most people can be trusted in 2005 (%)	26609/2007	63.8	60.2	<0.01**		---	---	---
Feel that most people can be trusted in 2009 (%)	26672/2017	66.9	63.2	<0.01**	35578	66.4	64.1	0.02
BMI in kg/m2 (mean, sd)								
BMI in 2005	26005/1983	23.1 (3.3)	22.5 (3.1)	<0.01#		--	--	--
BMI in 2009	26143/1996	23.7 (3.4)	23.3 (3.3)	<0.01#	35897	23.6	23.3	<0.01
Change in BMI (2009-2005)	25740/1970	0.61 (1.6)	0.77 (1.7)	<0.01#	35501	0.64	0.74	<0.01

Non-migrants defined as those who resided in the same region between 2005 and 2009; migrants defined as those who had moved location to a different region by 2009; physical and mental quality of life assessed using physical component summary and mental component summary; * Wilcoxon rank sum test; # t-test, ** chi-square test

Table 7.3 Personal well-being, quality of life, emotional problems, social trust and BMI in 2005 and 2009 by migration status among women in the Thai Cohort Study

	Observed data				Multiple imputation (M=25)			
	n	Women			n	Women		
	Total/ migrant	Non-migrants	Migrants	p-value	Total	Non migrants	Migrants	p-value
Satisfaction with personal safety (mean,sd)								
Score in 2005	32749/2398	72.1 (18.9)	69.0 (19.4)	<0.01*		--	--	--
Score in 2009	32689/2387	74.3 (18.8)	71.7 (19.9)	<0.01*	43652	73.8	71.9	<0.01
Changes in score (2009-2005)	32452/2373	2.17 (20.7)	2.69 (22.7)	0.24#	43415	2.06	2.32	0.49
Satisfaction with being part of community (mean,sd)								
Score in 2005	32739/2401	65.5 (21.5)	61.0 (22.0)	<0.01*		--	--	--
Score in 2009	32660/2386	69.7 (20.7)	65.1 (22.0)	<0.01*	43626	69.1	66.0	<0.01
Changes in score (2009-2005)	32415/2375	4.19 (22.7)	4.19 (25.4)	0.99	43381	4.19	4.19	0.99
Satisfaction with standard of living (mean,sd)								
Score in 2005	32696/2398	69.3 (18.9)	65.1 (19.3)	<0.01*		---	---	---
Score in 2009	32702/2387	72.4 (17.9)	69.2 (18.8)	<0.01*	43666	71.9	69.4	<0.01
Changes in score (2009-2005)	32411/2373	3.12 (19.9)	4.16 (20.8)	0.02#	43375	3.27	4.08	0.03
Satisfaction with life as a whole (mean,sd)								
Score in 2005	32731/2396	77.1 (16.5)	73.9 (16.9)	<0.01*		--	--	--
Score in 2009	32666/2385	78.6 (16.3)	75.7 (17.4)	<0.01*	43629	78.1	75.9	<0.01
Changes in score (2009-2005)	32413/2370	1.46 (17.5)	1.76 (18.9)	0.45#	43376	1.51	1.76	0.48

Non-migrants defined as those who resided in the same region between 2005 and 2009; migrants defined as those who had moved location to a different region by 2009; all satisfaction score were transformed by multiplying responses ranging from 0 “completely dissatisfied” to 10 “completely satisfied” by 10.

* Wilcoxon rank sum test; # t-test, ** chi-square test

Table 7.3 Personal well-being, quality of life, emotional problems, social trust and BMI in 2005 and 2009 by migration status among women in the Thai Cohort Study (continued)

	Observed data				Multiple imputation (M=25)			
	n	Women			n	Women		
	Total/ migrant	Non-migrants	Migrants	p-value	Total	Non migrants	Migrants	p-value
Physical quality of life								
Score in 2005	32428/2369	58.8 (7.0)	58.5 (7.1)	0.02		--	--	--
Score in 2009	32594/2386	58.0 (7.1)	58.0 (7.2)	0.69	43797	57.9	58.0	0.76
Change in score (2009-2005)	32040/2342	-0.86 (8.1)	-0.47 (8.4)	0.03	43243	-0.80	-0.52	0.05
Mental quality of life (mean,sd)								
Score in 2005	32428/2369	56.1 (8.7)	55.1 (9.2)	<0.01		---	---	---
Score in 2009	32594/2386	56.6 (8.7)	55.7 (9.1)	<0.01	43797	56.4	55.6	<0.01
Change in score (2009-2005)	32040/2342	0.46 (9.7)	0.57 (10.1)	0.61	43243	0.50	0.56	0.70
Emotional problems in previous 4 weeks								
Emotional problems in 2005 (%)	32,856/2393	16.4	20.6	<0.01**		---	---	---
Emotional problems in 2009 (%)	32865/2406	16.2	19.8	<0.01**	43892	16.9	19.9	<0.01
Social trust								
Feel that most people can be trusted in 2005 (%)	32208/2354	62.3	56.9	<0.01*		---	---	---
Feel that most people can be trusted in 2009 (%)	32332/2359	68.5	63.6	<0.01**	43306	67.8	64.7	<0.01
BMI in kg/m2 (mean, sd)								
BMI in 2005	31639/2312	21.1 (3.3)	20.5 (2.9)	<0.01		---	---	---
BMI in 2009	31767/2321	21.9 (3.6)	21.3 (3.4)	<0.01	43768	21.8	21.4	<0.01
Change in BMI (2009-2005)	31414/2298	0.82 (1.7)	0.83 (1.8)	0.71	43433	0.83	0.84	0.75

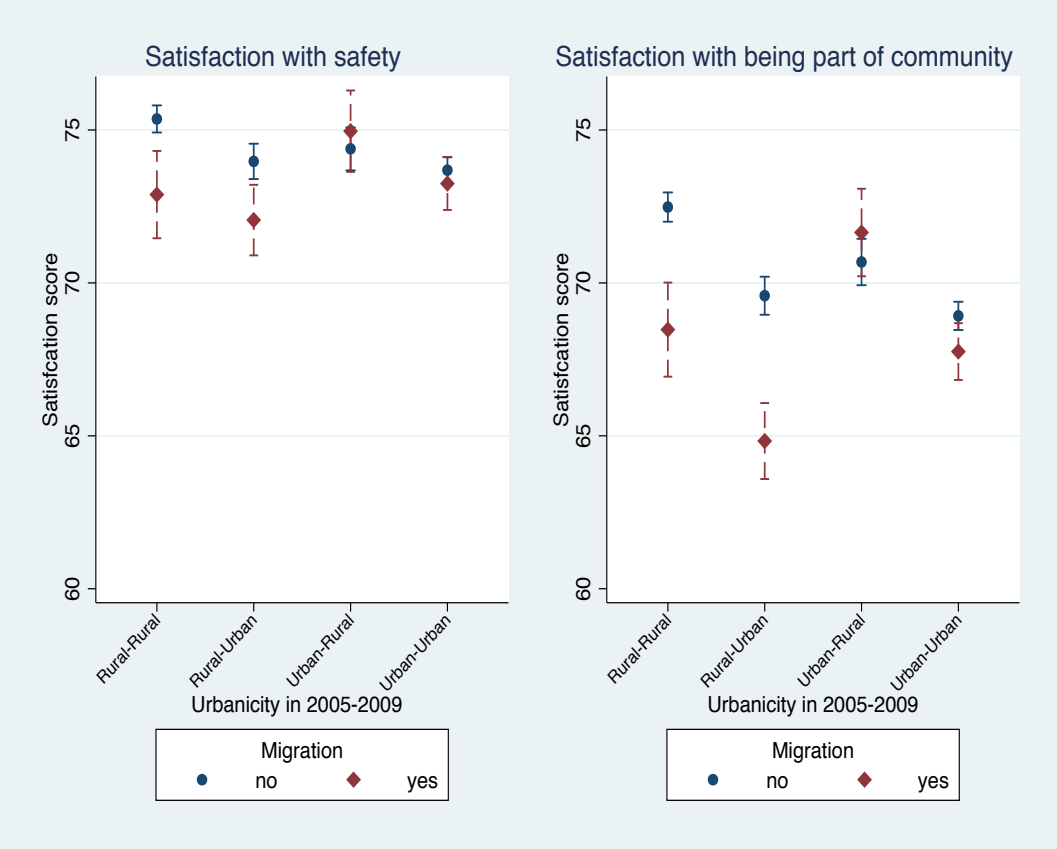
Non-migrants defined as those who resided in the same region between 2005 and 2009; migrants defined as those who had moved location to a different region by 2009; all satisfaction scores were transformed by multiplying responses ranging from 0 “completely dissatisfied” to 10 “completely satisfied” by 10. Physical and mental quality of life assessed using physical component summary and mental component summary; * Wilcoxon rank sum test; # t-test, ** chi-square test

7.3.2 Associations between migration and psychosocial health and well-being: Does urbanicity matter?

In multi-variable analyses adjusting for baseline socioeconomic status, self-reported health and baseline values for each of the outcomes of interests in 2005 (to adjust for the selective migration effect), there was potential evidence that the association between migration and all four domains of well-being were modified by the urbanicity of locations (all p-values for interactions <0.10).

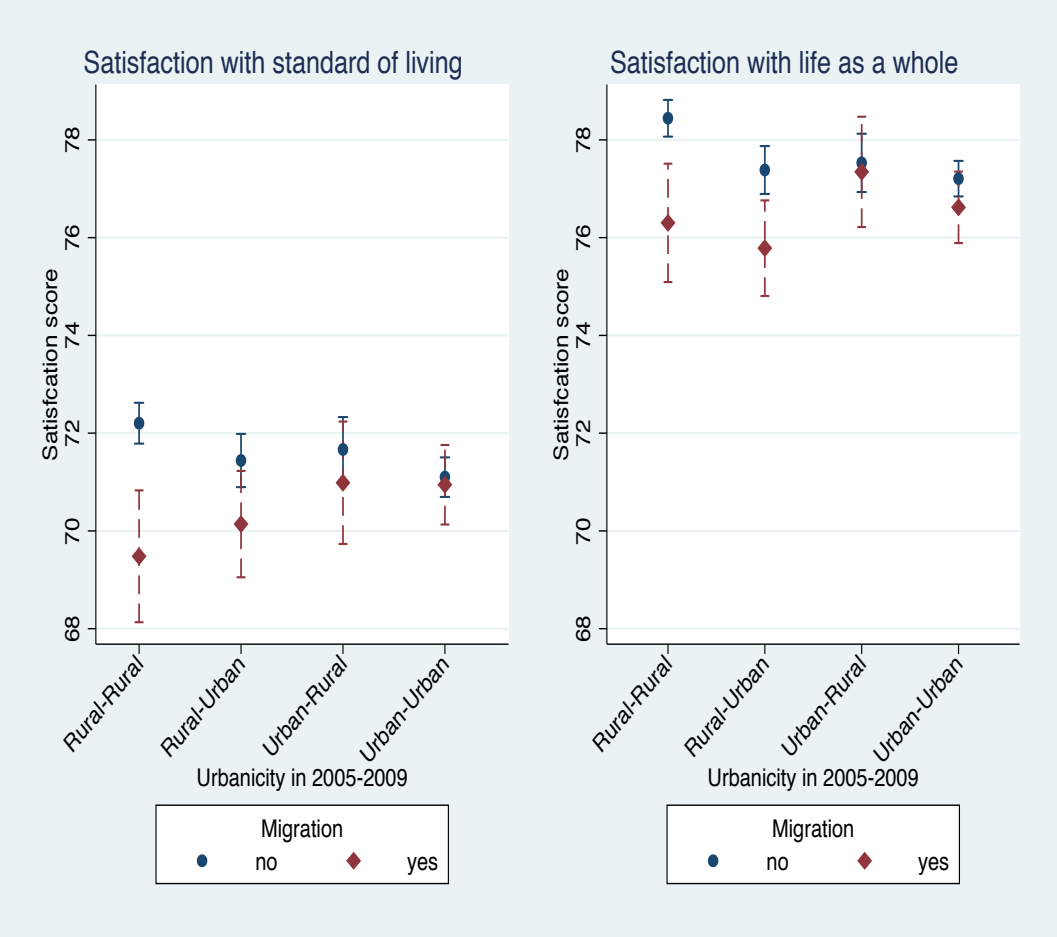
For three of the four domains of well-being (satisfaction with safety, feeling part of the community and general life satisfaction), migration was only associated with lower satisfaction if participants originally came from rural areas (Figure 7.3 and Figure 7.4). For these three domains, rural to urban migrants had the lowest satisfaction scores. For standard of living, migration was associated with lower standards of living only if the individual concerned had moved to a rural destination.

Figure 7.3 Associations between migration and well-being (satisfaction with safty and being part of community) by urbanicity of locations in 2005 and 2009



Results adjusted for age, sex, income in 2005, marital status in 2005, self-reported health status in 2005 and satisfaction scores in 2005 for each corresponding domain; Non-migrants defined as those who resided in the same region between 2005 and 2009; migrants defined as those who had moved location to a different region by 2009.

Figure 7.4 Associations between migration and well-being (satisfaction with standard of living and life as a whole) by urbanicity of locations in 2005 and 2009



Results adjusted for age, sex, income in 2005, marital status in 2005, self-reported health status in 2005 and satisfaction scores in 2005 for each corresponding domain. Non-migrants defined as those who resided in the same region between 2005 and 2009; migrants defined as those who had moved location to a different region by 2009

These differences in satisfaction scores due to migration translated into only small shifts in the percentage of people within the normative satisfaction range (satisfaction score ≥50). The largest proportional shift was found in the satisfaction with community domain, where 80.9% of rural-urban migrants and 88.9% of rural-urban non-migrants were satisfied with being part of the community in 2009 (adjusted mean difference 6.1%, 95% CI 3.92 to 8.28) (Table 7.4).

Table 7.4 Association between migration and well-being by urbanicity of locations in 2005 and 2009

		Urbanicity of locations in 2005-2009			
Well-being in 2009		RR	RU	UR	UU
Proportion (%) with normal satisfaction with safety	Migration				
	No	94.1	92.6	93.1	93.1
	Yes	90.9	89.7	92.2	91.1
	Differences (NM-M)	3.17	2.90	0.94	2.01
	Adjusted differences (NM-M)	2.08 (0.20 to 3.95)	2.26 (0.45 to 4.07)	0.51 (-1.56 to 2.59)	1.05 (-0.13 to 2.23)
Proportion (%) with normal satisfaction with community	Migration				
	No	93.0	88.9	90.0	88.3
	Yes	87.6	80.9	90.1	84.7
	Differences (NM-M)	5.39	8.02	0.15	3.58
	Adjusted differences (NM-M)	3.87 (1.85 t0 5.89)	6.10 (3.92 to 8.28)	-1.45 (-3.87 to 0.97)	1.52 (0.04 to 3.0)
Proportion (%) with normal satisfaction with standard of living	Migration				
	No	93.9	93.3	93.4	93.9
	Yes	89.3	90.8	91.2	91.7
	Differences (NM-M)	4.54	2.51	2.17	2.15
	Adjusted differences (NM-M)	3.33 (1.45 to 5.22)	0.82 (-0.89 to 2.53)	1.49 (-0.54 to 3.53)	0.51 (-0.60 to 1.62)
Proportion (%) with normal satisfaction with life as a whole	Migration				
	No	97.4	96.7	96.8	97.1
	Yes	94.7	96.1	95.6	95.7
	Differences (NM-M)	2.69	0.60	1.23	1.36
	Adjusted differences (NM-M)	1.70 (0.43 to 2.96)	-0.24 (-1.47 to 0.97)	0.99 (-0.46 to 2.43)	0.67 (-0.12 to 1.46)

Non-migrants defined as those who resided in the same region between 2005 and 2009; migrants defined as those who had moved location to a different region by 2009; normative range for satisfaction score is 50 to100 in Asian population; NM - non-migrants; M - migrant; RR -rural-rural; RU - rural-urban; UR - urban-rural; UU - urban-urban; adjusted differences adjusted for age, sex, income in 2005, marital status in 2005, self-reported health status in 2005 and satisfaction scores in 2005 for each corresponding domain.

After adjusting for the 'selective migrant effect' and baseline quality of life scores in 2005, there was no evidence of an association between the process of migration and physical quality of life in 2009. Physical quality of life was, however, influenced by the urbanicity of the living environment. The process of migration was associated with lower mental quality of life, independent of urbanicity of location. However, the differences in quality of life scores due to migration and urbanicity were all very small (Table 7.5).

Table 7.5 Associations between migration and urbanicity on quality of life

	Physical quality of life		Mental quality of life	
	β (95% CI)	p-value	β (95% CI)	p-value
Migration				
No	Reference		Reference	
Yes	0.13 (-0.08 to 0.34)	0.23	-0.30 (-0.56 to -0.05)	0.02
Urbanicity of location in 2005 and 2009		<0.01*		0.99#
Rural – Rural	Reference		Reference	
Rural – Urban	-0.19 (-0.38 to -0.01)	0.04	-0.15 (-0.37 to 0.07)	0.19
Urban – Rural	-0.12 (-0.35 to 0.11)	0.30	-0.20 (-0.47 to 0.07)	0.15
Urban - Urban	0.16 (0.04 to 0.29)	0.01	-0.01 (-0.16 to 0.14)	0.90

Non-migrants defined as those who resided in the same region between 2005 and 2009; migrants defined as those who had moved location to a different region by 2009; analysis using linear regression for physical and mental quality of life; higher scores indicate higher quality of life. Results mutually adjusted for each exposure, age, sex, income in 2005, marital status in 2005, self-reported health status in 2005, and each individual outcome of interest in 2005; *p-value for general association; #p-value for trend; p-value for interactions between migration and urbanicity of location all >0.10.

For emotional problems, there was evidence that migration was associated with a 14% increase in the odds of being bothered by severe emotional problems (adjusted OR 1.14, 95% CI 1.04 to 1.25). Urbanicity was also independently associated with emotional problems (Table 7.6). For social trust, there was some weak evidence that migration had an independent effect. Migrants were less likely to feel that people can be trusted (adjusted OR 0.94, 95% CI 0.87 to 1.01).

Urbanicity was also negatively associated with social trust (Table 7.7). Similarly to its associations with well-being, the proportional shifts in social trust and emotional problems due to migration and urbanicity were small. Compared to areas that were considered rural at both points in time, the negative effects of urbanicity (on emotional problems and social trust) had more impact on individuals living in areas that had only recently become urban (Table 7.6 and Table 7.7).

Table 7.6 Associations between migration and urbanicity with experiencing emotional problems in 2009

	Emotional problem in 2009 (%)	Crude difference (%)	Adjusted odds ratio (95% CI)	Adjusted differences in proportions (%) (95% CI)
Migration				
No	14.2	References	Reference	References
Yes	17.8	3.58	1.14 (1.04 to 1.25)	1.16 (0.41 to 1.91, p<0.01)
Urbanicity of location in 2005 and 2009				
Rural-Rural	14.1	Reference	Reference	References
Rural-Urban	16.4	2.37	1.12 (1.03 to 1.21)	0.79 (0.01 to 1.57, p=0.05)
Urban-Rural	15.9	1.81	1.08 (0.97 to 1.19)	0.46 (-0.48 to 1.40, p=0.34)
Urban-Urban	14.1	0.00	1.04 (0.98 to 1.10)	0.11 (-0.38 to 0.61, p=0.65)

Non-migrants defined as those who resided in the same region between 2005 and 2009; migrants defined as those who had moved location to a different region by 2009; emotional problems defined as having quite a lot of or extreme emotional problems during past 4 weeks=1. Results mutually adjusted for each exposure, age, sex, income in 2005, marital status in 2005, self-reported health status in 2005 and emotional problems in 2005; p-value for interactions between migration and urbanicity of location >0.10.

Table 7.7 Associations between migration and urbanicity with social trust in 2009

	Social trust in 2009 (%)	Crude difference (%)	Adjusted odds ratio (95% CI)	Adjusted differences in proportions (%) (95% CI, p-value)
Migration				
No	67.8	References	Reference	References
Yes	63.4	4.32	0.94 (0.87 to 1.01)	1.63 (0.00 to 3.36, p=0.07)
Urbanicity of location in 2005 and 2009				
Rural-Rural	70.3	Reference	Reference	References
Rural-Urban	65.0	5.43	0.83 (0.77 to 0.88)	4.51 (2.82 to 6.20, p<0.01)
Urban-Rural	65.5	4.90	0.88 (0.81 to 0.95)	3.05 (1.06 to 5.05, p<0.01)
Urban-Urban	65.9	4.47	0.85 (0.81 to 0.89)	3.71 (2.57 to 4.85, p<0.01)

Social trust defined as feeling you can trust others=1; Results mutually adjusted for each exposure, age, sex, income in 2005, marital status in 2005, self-reported health status in 2005 and social trust in 2005; p-value for interactions between migration and urbanicity of location >0.10.

7.3.3 Does poor psychosocial health and well-being translate into high BMI?

Previous results from sections 7.3.1 and 7.3.2 suggested that migration and urbanicity were associated with small negative changes in the sense of well-being, higher levels of emotional problems and lower levels of social trust.

Results from Table 7.8 provide evidence that increasing well-being in terms of satisfaction scores around safety and being part of the community were associated with lower BMI. However, the effect sizes were very small with very little clinical significance (Table 7.8).

Table 7.8 Associations between well-being in 2005 and BMI in 2009

Well-being scores in 2005	BMI in 2009			
	Completed data (n=54,588)		Multiple imputation (n=75,610)	
	β (95% CI)	p-value	β (95% CI)	p-value
Satisfaction score (per 10 unit increase)				
Life as a whole	0.00 (-0.01 to 0.01)	0.96	0.00 (-0.01 to 0.01)	0.74
Standard of living	0.00 (-0.01 to 0.00)	0.17	0.00 (-0.01 to 0.00)	0.33
Safety	-0.01 (-0.02 to 0.00)	<0.01	-0.01 (-0.02 to 0.00)	0.02
Part of community	-0.01 (-0.02 to 0.00)	<0.01	-0.01 (-0.02 to 0.00)	0.02

Analysis using linear regression; results for each domain adjusted for age, sex, BMI in 2005, migration, location status in 2005 and 2009, self-rated health in 2005, marital status in 2005 and income in 2005. Higher satisfaction scores indicate higher sense of well-being.

Emotional problems and social trust had larger effect sizes on BMI than well-being. When adjusted for age, sex, baseline BMI, socioeconomic status and overall health, emotional problems experienced in 2005 were associated with higher increases in BMI by 2009 (Table 7.9). The increase in BMI for those who had experienced emotional problems in 2005 was 0.09 kg/m^2 higher than those who had not experienced emotional problems (95% CI 0.05 to 0.15). Using the average height of the cohort, this translates into approximately 0.25 kilograms of additional weight gain amongst men and 0.22 kilograms of additional weight gain amongst women.

For social trust, having a higher level of social trust in 2005 was associated with smaller increases in BMI by 2009 (Table 7.10). Those who felt that they could trust people in 2005 had smaller increases in BMI compared to those who felt that people could not be trusted (β = -0.04, 95% CI -0.07 to -0.01). This translates into approximately 0.11 kilograms of lower weight gain amongst men and 0.10 kilograms of lower weight gain amongst women.

Table 7.9 Association between experiencing emotional problems in 2005 and BMI in 2009

	BMI in 2009			
	Completed data (n=54,768)		Multiple imputation (n=75,431)	
	β (95% CI)	p-value	β (95% CI)	p-value
Emotional problems in 2005				
No	Reference		Reference	
Yes	0.09 (0.05 to 0.14)	<0.01	0.08 (0.04 to 0.13)	<0.01

Emotional problems defined as having quite a lot of or extreme emotional problems during past 4 weeks=1; analysis using linear regression; results adjusted for age, sex, BMI in 2005, migration status, location in 2005 and 2009, self-rated health in 2005, marital status in 2005 and income in 2005.

Table 7.10 Association between having social trust in 2005 and BMI in 2009

	BMI in 2009			
	Completed data (n=53,813)		Multiple imputation (n=74,476)	
	β (95% CI)	p-value	β (95% CI)	p-value
Social Trust in 2005				
No	Reference		Reference	
Yes	-0.04 (-0.07 to -0.01)	<0.01	-0.04 (-0.07 to -0.01)	<0.01

Social trust defined as feeling you can trust others=1; analysis using linear regression; results adjusted for age, sex, BMI in 2005, migration status, location in 2005 and 2009, self-rated health in 2005, marital status in 2005 and income in 2005.

7.3.4 Sensitivity analyses

Using multiple imputation, the results suggest that the complete-case analysis may have underestimated the number of migrants. About 10.6% of participants could be considered migrants. Results using multiple imputation did not materially alter any crude estimates for the outcomes of interest (Table 7.2 and Table 7.3). However, the effect modification between recent migration and the urban environment was lost and the adjusted effect of migration on well-being was attenuated (Appendix J).

Analyses investigating the associations between migration and urbanicity with quality of life (Appendix K), social trust and emotional problems (Appendix L) were relatively robust. The associations between psychosocial health/well-being with BMI were also relatively robust (Tables 7.8-7.10).

7.4 Discussion

The study found that migrants had lower psychosocial health and well-being, both before and after migration, when compared to non-migrants in Thailand. After adjusting for the 'selective migration effect' and urbanicity, the process of migration itself was found to be associated with slightly lower levels of mental quality of life, higher levels of emotional problems and lower levels of social trust. Urbanicity itself also had independent negative effects on many aspects of psychosocial health and well-being, particularly on emotional problems and social trust.

Experiencing emotional problems was associated with greater increases in BMI over the period of follow up compared to who did not experienced emotional problems. Having a sense of social trust was associated with lower increases in BMI compared to those who felt that most people could not be trusted. However, whilst I found statistically 'significant' associations, the effect sizes were small, and it is unclear whether these associations have clinical relevance.

The study found evidence for a selective migrant effect; however, the selectivity of our population was not all in line with the classic 'healthy migrant effect'(93). Although migrants were younger, their self-rated health status did not materially differ from that of non-migrants. Migrants were more likely to report lower personal income in 2005. As this was a migration study among a relatively young and healthy group of university students, some of whom would have graduated between 2005 and 2009, those with lower baseline income might be more likely to migrate for better employment opportunities (94). A study from Indonesia found that, among the working age population (age 18-45), lower income was associated with internal migration (95).

This study provides some insight into the complex relationships between the process of migration, the influence of living environments and health (96). In terms of psychosocial health and well-being, a consistent pattern emerged suggesting that the process of migration may have negative impacts. Comparison of results with previous literature is challenging due to different definitions of migration and psychosocial outcomes. Other factors make direct comparison of results and effect sizes difficult as associations are likely to vary due to different environments and sociocultural norms along with duration of exposure within any given environment (6).

Nonetheless, my findings were in line with previous literature that migrants reported higher levels of well-being after migration (97). However, my study further demonstrates that the increases in well-being were less than the increases experienced by non-migrants. The difficulties that internal migrants in other Asian countries face in terms of integration with the new community, a lower sense of security and social exclusion, have been documented (98).

Studies from many European countries and some developing countries have shown that migration is associated with many issues relating to aspects of mental health (99, 100). Evidence from Indonesia by Lu et al. reported a similar effect size for urban migration and emotional problems as shown in my study. Using longitudinal survey data between 2000 and 2007 Lu et al.

found that, when compared to rural non-migrants, the odds of 'experiencing sadness in the past 4 weeks' was 1.73 time higher in rural to urban migrants (p-value 0.04) (81).

The study described in this chapter provides evidence that, in Thailand, the associations between migration and lower psychosocial health and well-being are not entirely to do with the process of migration. These associations are also influenced by urbanicity of locations before and after migration. Urbanicity relates to both the environmental and cultural impacts of living in urban areas.

Urbanicity has been linked to poorer health, potentially due to environmental exposures (such as pollution, traffic, fewer green spaces) and a promotion of unhealthy risk factors (such as alcohol or substance abuse) (101, 102). The evidence for potential effect modification due to migration may suggest that those starting off in rural areas may have difficulties coping with the demands of the new urban environment and the process of migration (90).

Psychosocial factors such as stress, anxiety, low self-esteem and social isolation, are key social determinants of health (103). These psychosocial factors, at the individual and community level, are also associated with NCD risk factors such as smoking, alcohol drinking and obesity, and with cardiovascular diseases (104-107). My findings of a link between low social trust and emotional problems and marginally higher BMI is supported by an abundance of existing literature (108). However, due to the heterogeneity of measures, direct comparison of results and effect sizes with previous literature is difficult.

In my study, the small effect sizes may be due to the short duration of participants' residence in the new environment. The study period for my study was between 2005 and 2009; thus, the duration of time spent in the new environment would be, at maximum, 4 to 5 years. A review of literature on duration of residence in the USA and body weight among international

immigrants has suggested that weight gain peaked at 21 years of duration for men and 15 years for women (109).

This study has a number of limitations that may limit the interpretation, implication and generalizability of findings. The effect size for each area of association presented was small, which limited the interpretation and implications of findings. No definitive conclusions could be drawn on the potential long-term impact of internal migration and urbanicity on psychosocial health, well-being and BMI. The main exposure, migration, did not differentiate between different types and characteristics of migration. The term could have referred to return migration (migration back to the place of origin) or out migration.

The reasons for migration in participants could also have been diverse, such as for work or family reasons. Evidence from Southeast Asian countries, including Thailand, has suggested that the characteristics of the different types of migration differ and may potentially lead to different health outcomes (95, 110). The exact time of migration and duration in the new environment was not measured; thus, it was not possible to determine whether the effects seen were increasing or decreasing with time spent in the new environments. The measurement of urbanicity, sense of social trust and severity of emotional problems was also subjective. These sources of imprecision in the measurement of key exposures and outcomes may contribute to dilution effects.

Other issues may also limit the generalizability of findings. The study population, although it had many similar characteristics to the national Thai population, consisted of university students. The associations seen may, thus, not be generalizable to other populations such as manual labour migrants.

The strengths of the study included the size of the cohort dataset, which enabled a proper comparison group for migrants. In particular, it enabled full exploration of the relationships between both migration and urban

environments and psychosocial health and well-being. The study also used multiple imputation, which, under a set of certain assumptions (to be discussed in the next section), allowed the investigation of possible attrition bias.

7.5 Analytical consideration

Although utilization of multiple imputation to investigate the role of potential attrition bias was one of the strengths of this study, there were analytical issues that should be taken into consideration. As stated in the methods, analyses using multiple imputation are valid if the systemic differences between the observed value and missing values have been accounted for by using observed variables included in the prediction model. This pattern of missingness is commonly known as “missing at random (MAR)”(111).

Although the dataset used in this chapter used seventy variables in the prediction model to help fulfill such criteria, there are no statistical tests or methods to ensure that such assumptions are met (112). More importantly, if the patterns of missingness in the data were attributed to the unobserved psychosocial outcomes in 2009, then it is not possible to account for such systematic differences even if I had included a large number of observed variables in the prediction model. Further simulations under different ranges of assumption could help explore the potential impact when data are not missing at random (NMAR) (113). However, in view of the small effect sizes found in this analysis, no further simulation was carried out.

The study used relative and absolute measures of association along with proportional shifts to explore associations between urbanicity, internal migration, and psychosocial outcomes. While studies on blood pressure and cardiovascular diseases have demonstrated that even small reductions in blood pressure could result in large benefits for the population in terms of development of cardiovascular diseases (CVDs) and CVD mortality (114, 115), my study was not able to demonstrate such large population benefits on body mass index and in terms of reducing potential harmful psychosocial

effects of urbanicity and migration.

7.6 Potential implications

Despite its limitations, the study identified areas for future research. Studies examining mediating pathways between psychosocial determinants of health and NCDs in developing countries are few. The large dataset from the TCS used is this research was unable to provide strong evidence linking psychosocial factors with BMI, but perhaps the period of follow up was too short. Furthermore, with no biological (blood) measurements and currently no validated data on the development of NCDs, the TCS is not well-placed to examine mediating pathways.

A more comprehensive example of a study examining the mediating pathways between the psychosocial determinants of health and NCDs is the Health, Alcohol and Psychosocial factors in Eastern Europe (HAPIEE) study (116-118). This cohort study, conducted in four Eastern and Central European countries, aimed to investigate the social, economic, psychosocial, behavioural and biological determinants of health with a particular interest in CVDs.

The HAPIEE study utilized survey data, biological (blood) measurements including DNA extraction, and validated CVD incidence and mortality. The study also plans to use a life-course approach to explore the associations between childhood socioeconomic status and risk of CVDs in adulthood (116), but results of the life-course study on CVDs have yet to be published.

As for potential implications from the results found in this research, community level interventions aimed at tackling cultural, economical and psychological determinants of health have already been suggested for NCD prevention (119). These measures should be sustainable and adaptable as psychosocial determinants are likely to play a key role in NCDs throughout the life-course of individuals (120, 121).

It has been suggested that, in Thailand, strengthening family ties and work place interactions, especially for those in urban areas, may be useful in improving social trust and well-being (40). Enhancing coping and problem-solving skills may also be useful (122). Interestingly, as the study presented in this chapter draws attention to the impact of culture and living environments on psychosocial health (123), a previous publication from the TCS suggested that 'spirituality and religion' may play a role in improvement of well-being in Thailand (124).

The Thai universal coverage health care system can be relatively robust in providing effective health care for Thai migrants if migrants re-register using their new household address or take part in employment-related schemes (125). However, as it has been suggested that around 42% of the TCS participants had forgone health service use in 2005, whether migrants utilize these services and how other non-financial barriers could effect their health should also be considered in Thailand (126).

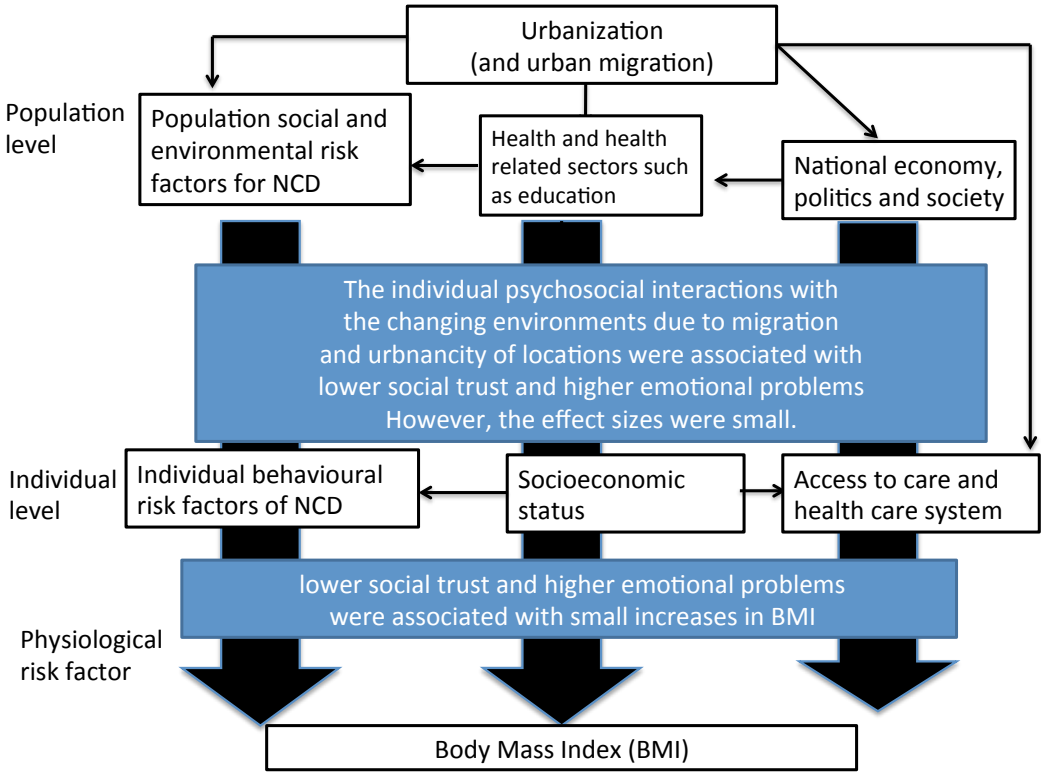
As for other areas of potential research, a recent framework for international migration has called for focus on the influence of both the sending and receiving countries (127). The direction of future research, such as examining population level influences of sending and receiving regions (ie environmental hazards, health policies), using a life course approach to understand the adaptation process and how changes in social determinants of health through migration may affect the health of migrants and their children, can be applied to internal migration.

7.7 Conclusion

Results from previous chapters in the thesis have focused on the importance of timing and the total duration of living in urban environments as risk factors for NCDs. This chapter offers some insights into how urban environments and the process of migration itself are associated with changes in psychosocial health and well-being, albeit small, which may translate into subsequent increases in BMI (Figure 7.5).

With urban environments and internal migration each having an independent association with lower social trust and emotional problems, urban migrants could be more susceptible to the future development of NCDs in Thailand. However, a longer follow up period is needed to explore this hypothesis of increased susceptibility to NCDs among urban migrants adequately.

Figure 7.5 Conceptual framework of this thesis with adaptations to incorporate findings from Chapter 7



Chapter 8 : Closing remarks

Summary

This chapter is divided into four sections. The first section provides a brief summary of key research findings as set out by the overall aim and objectives of this PhD research. The second section discusses the general strengths and limitations of the research and outlines areas for future research. The third section outlines the implications of the findings in relation to current understanding of urbanization and NCDs in developing countries. The last section contains my final reflection, key learning points from conducting the research, and my future career development plans.

8.1 Urbanization and internal migration as risk factors for NCDs in Thailand

The main research aim, as stated in Chapter 1, was to investigate associations between urban exposures and non-communicable disease (NCD) risk factors, NCD morbidity, and NCD mortality in Thailand in order to better understand the mechanisms underlying the link between urbanization and NCDs in Thailand. Figure 8.1 presents the proposed conceptual framework of factors linking urbanization and non-communicable disease along with the key areas explored in each chapter of the thesis.

8.1.1 Is urbanization driving NCD risk factors?

This research has found that living in an urban environment and internal migration within Thailand were both associated with psychosocial changes which, in turn, were associated with increases in BMI (Chapter 7). Urban environments were also associated with other behavioural and physiological risk factors for NCDs such as smoking, low fruit/vegetable consumption and high body mass index (BMI) (Chapter 5 and Chapter 6).

In terms of potential life-course mechanisms, both early life urban exposure and cumulative proportion of lifetime urban exposure were found to be associated with these behavioural and physiological risk factors (Chapter 5). In particular, the research demonstrated that early life urban exposure was a risk factor for later development of obesity in adulthood, independent of later life exposures and current socioeconomic status (Chapter 6).

8.1.2 Is urbanization driving NCD morbidity and mortality?

Urbancitiy was associated with increases in behavioural risk factors (low fruit/vegetable consumption, inadequate physical activity, smoking and high alcohol consumption) and physiological risk factors (BMI and blood pressure) for NCDs. However, urbanicity may not directly translate into increases in biological risk factors for NCD or high risk of developing NCDs, and NCD mortality.

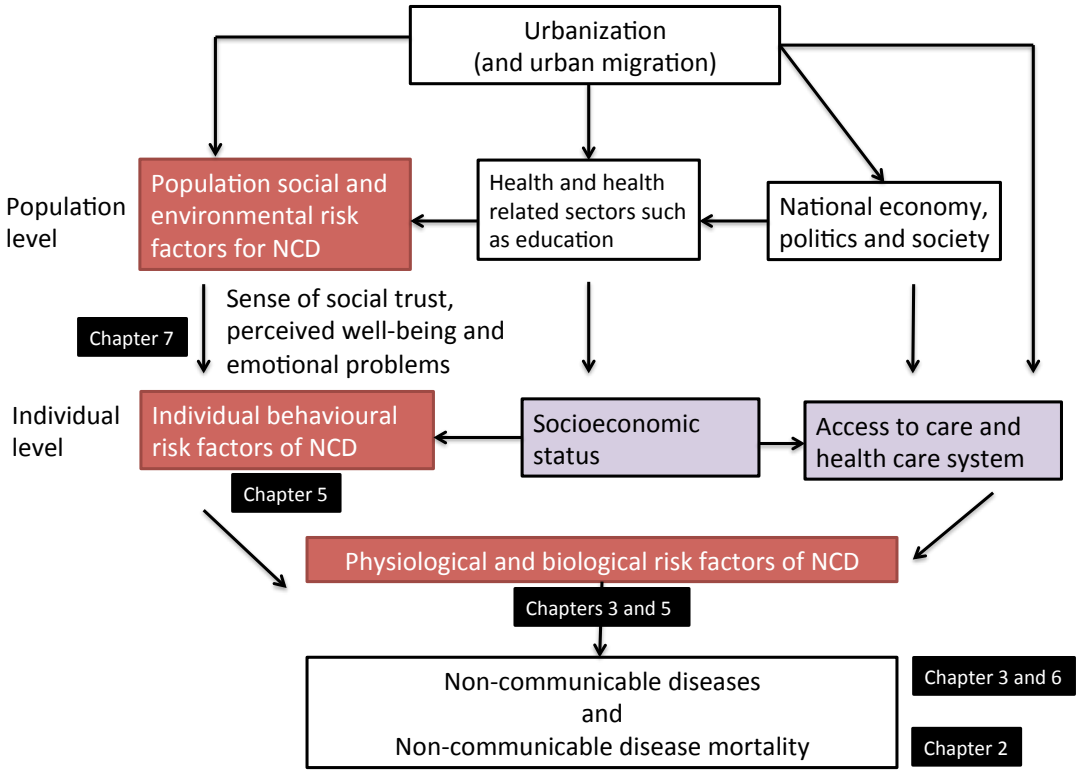
The results presented in Chapter 5 showed that, although urbanicity was associated with increases in some biological risk factors such as higher blood glucose and low density lipoprotein (LDL), it was negatively associated with triglyceride and there was no evidence for an association with high density lipoprotein (HDL) blood levels. The results in Chapter 6 found no evidence for association between living in an urban environment in early life and later development of impaired fasting glucose in adulthood, although power was limited to investigate this question.

These inconsistencies among the associations between urban environments with NCD outcomes, particularly NCD morbidity and NCD mortality, were also reflected in the systematic review and ecological study. The associations between urban environments with NCD morbidity (Chapter 3) and NCD mortality (Chapter 2) varied across major groups of NCDs. These variations were potentially due to different profiles for the underlying risk factors or causes of NCDs. It is likely that, in terms of biological risk factors, NCDs and NCD mortality could be more amendable to change from the positive influences of urbanization through higher socioeconomic status and potential access to better health care. Access to medication to control blood pressure and glucose, and access to advanced medical treatment such as revascularization in patients with acute ischemic stroke, have been documented to be more common and accessible in urban areas than in rural areas in Thailand (128-130).

This notion is supported by the ecological study, the systematic review and my own dataset. The ecological study found that increasing average household income was associated with lower NCD mortality. Although an increasing number of doctors per population was associated with higher NCD mortality, this was potentially due to confounding by urbanization (as discussed in the published manuscript in Chapter 2). In Chapter 3, the systematic review found that the country's economic development modified the association between urbanicity and diabetes

Compared to more economically developed countries in Southeast Asia, the effect sizes between urban environments and diabetes were larger in less developed countries in Southeast Asia. At an individual level, my own dataset suggested that, for some biological NCD risk factors (blood glucose, HDL and triglyceride), higher socioeconomic status (SES) was associated with lower levels of biological risk factors.

Figure 8.1 Conceptual framework of factors linking urbanization and NCD and the key areas explored in each chapter of the thesis



8.2 General strengths, limitations and recommendations for future research

8.2.1 Strengths

The strength of this research is that it attempted to provided evidence at different levels linking urbanization and NCDs in Thailand (Figure 8.1), beginning with potential psychosocial mediators and leading to NCD risk factors, NCD morbidity and ultimately NCD mortality. The research also explored the effect of the timing and duration of urban exposure in order to help identify key populations in whom public health interventions would be beneficial, and the points in their lives when interventions might be most effective.

8.2.2 Limitations

The limitations of my research studies have been given in detail within each chapter. One major limitation was that the inconsistent findings, in terms of direction and strength of associations, linking urbanization with biological risk factors for NCDs, NCD morbidity and NCD mortality could be attributed to the limitations of the study designs and available datasets.

My own cohort was underpowered to detect changes in blood glucose and the risk of developing impaired fasting glucose and diabetes by different urban exposures. There were limited data on NCD morbidity from Thailand, which resulted in the systematic review being extended to other countries in Southeast Asia. In the systematic review, most of the individual studies exploring urban environments in relation to NCD morbidity were cross-sectional in design, which limited causal interpretation. In the case of cancer, the evidence was sparse even across countries of Southeast Asian and few conclusions could be drawn. The results from my ecological study on NCD mortality may also be prone to ecological fallacy.

Another limitation of this work is that the main mediators and mechanistic pathways between early life urban exposure and life course urban exposure in relation to NCDs remain largely unexplored. Chapter 7 mentioned the HAPIEE study examining the relationships between psychosocial factors and cardiovascular diseases (116), which may be a useful example for future research.

Mediators that should be explored include under/over nutrition in pregnancy and childhood, changes in socioeconomic status and psychosocial factors, changes in lifestyles and changes in levels of risk factors throughout the life course. However, the undertaking of such a study would require a cohort with a large sample size along with detailed data collection and a long follow up duration, such as in the Andhra Pradesh Children and Parents Study (APCAPS) (131); this was not feasible for this PhD.

My own dataset of health care workers and, to some extent, the Thai Cohort Study (TCS) consisted of middle-aged adults. In essence, the associations found could represent the effects of urban environments approximately 20-30 years preceding this study. The current effects of urban environments, especially on behavioural risk factors (diet, physical activity, smoking and alcohol consumption) among children and early adolescents remain an important issue to be explored in Thailand.

A recent review of Thailand's nutritional transition, published in 2013, has also emphasized that early life nutrition and the risk of NCD in later life remains an emerging public health concern (132). Evidence generated from such studies could have implications for interventions. In other countries, school-based interventions have been shown as a promising strategy to help combat substance abuse and obesity, and to promote physical activity (133-135).

8.2.3 Recommendations for areas of future research

Although a unifying framework for NCD prevention exists (136), it remains to be seen whether, and which methods of, interventions targeting children and adults could be successful and cost-effective in the prevention of NCDs in the Thai setting. While Thailand has made great strides in alcohol and tobacco control policies, which have included increased taxation and warning labels on tobacco products (137, 138), the challenge of how to effectively reduce behavioural risk factors (which extends to inadequate diet and physical activity) remains one of the key public health research issues for Thailand (139).

Other NCD prevention and control strategies, which include an emphasis on NCD prevention and control in primary health care services and the strengthening of NCD advocacy and surveillance systems, are currently being implemented in Thailand (140, 141). It has been documented that implementation of such evidence-based health policies and practices in countries within the Southeast Asian region will require a critical mass of epidemiologists to generate continuous research evidence to inform policies (142).

The work described in this thesis has identified additional areas of research that could be useful. At the population level, separating features and components of urbanization (social environment, physical environment and provision of health and social services) (143) may provide a better understanding of the effect of urban environments on NCDs. This would help form community and environmental interventions and policies, which are considered to be helpful in combating NCDs (144).

Examples of these community and environmental interventions include i) working with local administrations, health providers and community leaders to improve the quality of living environments and the access to care, ii) providing integrated education programs for the entire community, iii) making healthy lifestyles choices more accessible (increasing green space and

fruit/vegetable outlets) and restricting outlets that may be detrimental to health (alcohol and tobacco). Examples of such community and environmental interventions for chronic obstructive pulmonary disease (COPD) (145), cardiovascular diseases (146) and promotion of adequate fruit/vegetable intake (147) can be seen in the literature. Furthermore, future studies should explore the extent to which recent improvements in patient treatment and care play a role in NCD morbidity and mortality in Thailand. An example of a positive change made through improvements in access to care has been documented in terms of reducing infant mortality in Thailand (148).

Another area of research that should be explored in Thailand is the intersection between NCDs and diseases of infectious origin. Thailand is a country facing a double burden of disease from both infectious and non-communicable diseases (149). Combating infectious diseases may lower resulting NCDs. For example, prevention of rheumatic heart disease and cancers of infectious origins (such as cervical cancer and liver cancer) could be achieved through better sanitation, treatment of infection agents and preventive vaccines (27). At the same time, through prevention and control of NCDs, the risk of developing infectious diseases could also be decreased. For example, controlling the diabetes epidemic has been suggested as one of the prevention strategies for tuberculosis (150).

Lastly, the main focus of the research described here has demonstrated that there are health inequalities between urban and rural areas. However, even within urban or rural areas themselves, there are inequalities in health (151, 152). My work has also demonstrated that some subpopulations in urban areas (such as migrants) or other disadvantaged groups, such as those with low SES (Chapter 4) could, potentially, be at greater risk of poor health in Thailand. Research on health inequality and policies to reduce such inequalities, especially in urban areas, will become even more relevant as the country continues to become more urbanized.

8.3 Overall implications of findings

Chapter 1 of this thesis highlighted that the three key components of urban living (or urbanicity) which can affect individual behaviours and health risks are 1) the social environment, 2) the physical environment and 3) provision of health and social services.

The research described in this thesis has painted an overall picture of how the social and physical environments of urban living, in a developing country like Thailand, are likely to result in higher psychosocial stresses and increases in behavioural and physiological risk factors for NCDs such as heavy alcohol consumption, low physical activity, high blood pressure and obesity. However, based on other findings presented here, an optimistic picture has emerged suggesting that improvement in socioeconomic position and provision of health and social services are likely to modify these negative effects in terms of reducing NCD morbidity and mortality.

This overall picture that NCD morbidity and mortality may be modifiable, was also reflected by recent findings published in the New England Journal of Medicine in 2014 (153). In this publication, Yusuf et al. demonstrated that the risk factors for NCDs, specifically for cardiovascular diseases, were higher in high-income countries. However, the rates of cardiovascular morbidity and mortality in high-income countries were substantially lower than in low-and-middle-income countries (LMICs).

My findings on the potential influence of urbanicity on NCDs were consistent with Yusuf's results. While the risk factor burden was higher in urban areas of LMICs, the risk of major cardiovascular morbidity and mortality were, instead, higher in rural areas. Yusef et al. attributed these patterns to better access to prevention and treatment measures such as medication and revascularization.

The results of my thesis as well as the findings from Yusuf et al (153) demonstrate a key concept in understanding the potential effect of urbanization on NCDs. At a give time point, different countries are at varying

stages of the nutritional transition, the epidemiological transition, and socioeconomic development. As the countries become urbanized, they go through different stages of the nutritional and epidemiological transition. With urbanization as of one the driving forces of socioeconomic development, NCDs with infectious origins such as rheumatic heart disease and gastric cancer are subsequently replace by NCDs associated with unhealthy diets, behavior and lifestyle such as coronary heart disease, diabetes and stroke. Finally in later stages of development, as seen in high income countries, greater efforts are made towards prevention, diagnosis and treatment of NCDs (154).

Different levels of urbanization within a country can represent the advancing stages of the nutritional and epidemiological transition in regions within a country. Thus the impact of urbanization on NCDs within a country will change as the country develops and will be modified by the overall stage of socioeconomic development of the country as demonstrated in my systematic review.

Urbanization is inevitable and not undesirable as it is considered a key factor driving economic growth, especially in developing countries (4). In 2014, the World Health Organization estimated that 54% of the world's populations was already living in urban areas. This proportion is expected to reach 66% by 2050. Over 90% of growth in urban populations is happening in developing countries (155). The work described in this thesis has identified three broad areas that developing countries undergoing rapid urbanization should consider as strategic priorities for health:

1. Countries should prepare and plan to minimize the potentially negative effects of urban living, particularly in terms of the psychosocial, behavioural and physiological risk factors.
2. Simultaneously, countries should maximize the potential benefits of urban living such as improving access to health care and social services.
3. Countries should identify and reduce the gaps in health inequalities between different subpopulations in urban areas.

Tools such as The Urban Health Equality Assessment and Response Tool (Urban HEART) (156), developed by the World Health Organization, could be useful in helping national and local organizations to achieve a better understanding of the effects of the social and built environment on health, to help organizations identify gaps and priorities and to help promote actions and interventions which are specific to the needs of different subpopulations within cities.

8.4 Final reflections and future career development

I am a family physician and currently hold a lecturer position at the Department of Family Medicine, Faculty of Medicine, Chiang Mai University. Before coming to the London School of Hygiene and Tropical Medicine (LSHTM), my main responsibilities at the Faculty of Medicine, aside from providing primary care for patients in the faculty's catchment area, involved the teaching of undergraduate and postgraduate medical students on topics such as the social determinants of health, primary health care and evidence-based medicine and epidemiology. I was also involved in a number of small local research projects and was a study physician in the HIV Prevention Trails Network (HPTN).

I received the Faculty of Medicine Development Scholarship to further my education in 2010. I attended the Master of Science course in Medical Statistics at LSHTM and continued to the PhD programme. During these four and a half years, I have learned many things. These learning points have been useful, not only in terms of my own personal growth and development, but also in their application to my future area of work. I can summarize my learning points through three key learning activities: 1) attending modules/lectures/seminars, 2) conducting my own research and 3) experiencing the supervision and mentoring process.

8.4.1 Learning points from attending modules/lectures/seminars

During my time at the LSHTM, I have attended a number of courses that have been useful for my PhD. These modules have included Causal Inference, Infectious Diseases Epidemiology, Social Epidemiology and Public Health. Aside from gaining knowledge through attending these modules, I have learned that the learning experience is better consolidated through practical sessions.

The interactions with staff and other students have helped to deepen my understanding and provide opportunities to clear up any unresolved issues. LSHTM also has summative evaluations to help monitor and provide individual feedback for students. I will apply these teaching and evaluation methods to my future courses when I am back in Thailand.

8.4.2 Learning points from conducting the PhD research

I had the unique opportunity to conduct my PhD research at my own institution (Faculty of Medicine, Chiang Mai University). With guidance from my supervisors and advisory committee, I planned the study, and with help from my local colleagues and support from my institution, I conducted my own fieldwork and data collection. I collaborated with colleagues from other universities in Thailand and Australia to obtain additional datasets. I subsequently analyzed and interpreted these data as evidenced by this thesis. I list below my own key learning points.

- I have learned that planning is one of the most important steps when conducting research. From my previous experience, I understood that setting up the proper research question and framework is vital to the success of any research project. I also understood that the research must be practical, i.e., realistic and achievable. This was demonstrated when I decided early in my PhD to switch my main study design from a population-based survey to an occupational survey as it was deemed more practical. However, I had underestimated the impact of other

issues such as sample size, variable definition, measurement error and the potential limitations and bias within different types of study designs. These issues were highlighted by the ethical approval process and in the PhD upgrading seminar. This has taught me that, although being practical with a clear aim can help get the research done, to obtain a higher quality of research I should be more critical in the finer details when planning my future work.

- Going back to my own hospital and university to conduct my own research has also taught me many lessons. Leading a team of approximately 20 researchers/staff members in collecting data from over 3,000 participants over a period of 6 months put my communication skills, negotiation skills and management skills to the test. I now have a deeper understanding and appreciation of the value of collaboration, teamwork and institutional support.
- I learned that the time gap between conception of a research project and the actual implementation of the project can be great. For my thesis, the planning of the data collection process and data entry system was ongoing for approximately a year prior to the start of the research. We piloted the appointment system so participants could choose an appropriate slot to attend during their working hours. We trained research staff and piloted the questionnaire and the data collection procedure. Once the actual data collection started, I encountered a number of problems in the first week that needed to be resolved in a swift manner to minimize the potential impact on the overall quality of the research (Chapter 4, section 4.5.2).
- Another gap between conception and implementation related to finance and staffing. I had planned to have other laboratory investigations such as Hemoglobin A1c and serum insulin carried out. This was not achievable, as I had underestimated the actual costs for additional staff and reagents required. I had also planned to extend the research sites to two rural hospitals. However, I could not be at all sites in person at the same time. Due to the quality of the actual data collected, I was only able to use data from one rural hospital site. Again, the key learning points for

me were the importance of proper planning, being more attentive to the finer details and having realistic expectations.

- I collaborated with other colleagues from Thailand and Australia, which took me out of my comfort zone of working with colleagues from my own institution. This taught me to work as part of a bigger collaborative project and broaden my research experience. Respect and clear communication of expected roles and outcomes were the keys to this successful collaboration.
- Having a chance to work with the large dataset of the TCS, I have a better understanding of how large datasets should be managed. This will be useful for my own future work.
- My PhD research used a number of different designs and analytical techniques ranging from basic statistical techniques to advanced statistical approaches such as multiple imputation. I have learned that, although advanced statistical techniques can help minimize the impact of certain limitations, for example missing data and attrition bias, they cannot replace the basic principle of conducting research that is designed to minimize these potential limitations from the outset.
- The process of writing manuscripts and the thesis has taught me to think carefully about the main point of my research and what message I want to get across to readers. The peer review process reiterates the value of being more critical of my own research and acknowledging limitations and their impact on findings.

8.4.3 Learning points through the supervision and mentoring process

Lastly — and I think this is the key process that ties the whole learning experience of the PhD together — I have had the pleasure of working with two very good supervisors who challenged me, supported me and guided me in the right direction. I have learned that, to be a good mentor, one should be approachable, considerate and have clear communication skills. Providing constructive feedback and being positive will help guide your students on the right track through difficult times.

Most importantly, a good supervisor will make you feel valued not just as a student but also as a person. I will take on these characteristics when it becomes my turn to mentor other students in Thailand. My supervisor had the foresight to see the importance of conducting research in my own setting so that I was able to build the foundations for future work when I return to Thailand. This has taught me not only to have the end of a project in mind but the future in mind as well.

8.4.4 Future work

For my future work, I am keen to follow up my own cohort of health care workers to explore the associations between urban environments and NCD morbidity and mortality. I also plan to examine areas with unanswered questions outlined in section 8.3. In particular, I plan to explore the intersections between NCDs and infectious diseases and the health inequities in access to care among different subpopulations in urban areas.

I plan to utilize routine electronic patient data to explore these research areas. Chiang Mai University Hospital is the first and largest tertiary hospital in Northern Thailand. The 1,400 bed hospital, with 28 operating theatres, provides care for over 800,000 patients in the out-patient department (OPD) and has over 45,000 admissions annually (157). The Suan Dok Medical Information system (SMI) is the hospital's electronic database, which is owned and developed by Maharaj Nakorn, Chiang Mai Hospital. The system collects data on basic demographic characteristics of patients such as age, gender, location and types of health care scheme held by patients. During each visit, electronic data are collected on many aspects of patient care including type of laboratory investigation, pathology and imaging results, medication and dosage, medical procedures and medical diagnosis.

The vast amount of information stored within the SMI provides a unique opportunity to explore the changing trends in referrals and intersections between NCDs and infectious diseases and to explore the inequalities in access to care. Electronic data linkage will help to identify future associations

in NCD morbidity and mortality in my own cohort of health care workers. It will also help to identify participants for future intervention studies.

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List of Appendices

Appendix A. Evidence of permission from copyright holder to include published article “Urbanization and Non-communicable Disease Mortality in Thailand”

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Appendix B. Supporting documents submitted for published article "Urban Environments and Obesity in Southeast Asia: A systematic Review, Meta-Analysis and Meta-Regression"

Appendix B1. Search strategy using EMBASE

	Searches
1	Southeast asia or SE Asia or SE-asia or South-east asia
2	brunei or myanmar or burma or cambodia or east timor or indonesia or laos or malaysia or philippines or singapore or thailand or vietnam
3	Southeast Asia/ OR Myanmar/ OR Cambodia/ OR Timor/ OR Indonesia/ OR Laos/ OR Malaysia/ OR Philippines/ OR Singapore/ OR Vietnam/ OR Thailand/ OR Brunei
4	1 or 2 or 3
5	Urbani#ation or urbanicity or urban or rural or rurality
6	Urban adj3 rural
7	(urban adj3 migra*) OR (rural adj3 migra*)
8	migration? or migrant?
9	urbanization/ or urban population/ or urban rural difference/ or rural population/
10	migration/
11	Or/5-10
12	Obesity or obese or overweight
13	BMI or body mass index or body-mass-index or waist circumference or (waist adj3 hip adj3 ratio)
14	exp abdominal obesity/ or exp obesity/
15	exp body mass/ or exp body height/ or exp body weight/
16	Or/12-15
17	16 and 11 and 4
18	17 and "human" [subjects]

Appendix B2. Lists of excluded articles by mains reasons for exclusion

1. **Risk of obesity not reported by urban exposure (N=102)**

Abdur R, Lutfun N, Hoang Van M, Ng N, Sanjay J, et al. (2009) Social factors and overweight: evidence from nine Asian INDEPTH Network sites. (Special Issue: Risk factors for chronic non-communicable disease: the burden in Asian INDEPTH health and demographic surveillance sites.). Global Health Action 2.

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Appendix B3. Study characteristics of studies conducted in children (<18) from Malaysia, Thailand and Indonesia

Author	Year of publication	Country	Year of conduct	Sample size	Urban definition	Comparison	Mean age / age range	% Female
Anuar Zaini[#]	2005	Malaysia	Not stated	1,045	Not clearly stated	Not clearly stated	Mean 9.68 9 to10	48.9
Sumarni[#]	2006	Malaysia	Not clearly stated	699	Urban according to classification by Department of Statistics, Malaysia	Rural according to classification by Department of Statistics, Malaysia	Mean 11.1 10.6 to 12.2	48.5
Zalilah[#]	2006	Malaysia	Not clearly stated	6,555	Urban based on secondary school categorization by Ministry of Education	Rural based on secondary school categorization by Ministry of Education	11 to 15.9	48.8
Naidu[#]	2013	Malaysia	2006	144	Urban according to National Health and Morbidity survey (NHMS III)	Rural according to National Health and Morbidity survey (NHMS III)	7 to 12	49.7
Poh[#]	2013	Malaysia	2011	3,542	Not clearly stated	Not clearly stated	0.5 to 12.9	50.2
Zainuddin[#]	2013	Malaysia	2008	18,078	Not clearly stated	Not clearly stated	8 to 10	Not clearly stated
Firestone[#]	2011	Thailand	2004	4,610	Urban classification to reflect economic and land use pattern in the province	Communities classified as rice growing, plantation, upland and mixed economy strata	2 to 10	48.7
Sakamoto[#]	2001	Thailand	1997	1,157	Districts in Saraburi municipality	13 districts outside Saraburi municipality	Mean 5.8 4 to 6	Not clearly stated
Rojroongwasinkul[#]	2013	Thailand	2011	3.119	Municipal areas	Non-municipal areas	0.5 to 12.9	Not clearly stated
Julia[#]	2004	Indonesia	1999	2,570	City of Yogyakarta. Urban subclassified into 2 groups: urban poor (from urban slum) and urban	City of Kidul, about 20 to 40 kms from Yogyakarta	Boys age 6-8.9 Girls age 6-7.9	42.3
Sandjaja[#]	2013	Indonesia	2011	7,211	Not clearly stated	Not clearly stated	0.5 to 12	48.5

[#] studies included in the meta analysis for children

Appendix B4. Study characteristics of studies conducted in children (<18) from Laos and Vietnam

Author	Year of publication	Country	Year of conduct	Sample size	Urban definition	Comparison	Mean age / age range	% Female
Jurgensen[#]	2009	Laos	2006	621	Schools in urban area of Vientiane	Schools in semi urban area of Vientiane	10 to 13	52.8
Tuyet	2003	Vietnam	1999	348	First district of Ho Chi Minh City (trading area and majority of people are merchants)	Binh Chanh District (most of people are farmers and fishermen)	7 to 9	100
Leirop[#]	2008	Vietnam	2004-2005	2,546	Six communities based on socioeconomic characteristics and ecological conditions in Binh Thuan Province	Ten communities based on socioeconomic characteristics and ecological conditions in Binh Thuan Province	Mean 7.5 6 to 10	Not clearly reported
Dang[#]	2010	Vietnam	1992	5,460	Urban according to General statistical office in both surveys. Status base on the classification at time of each survey	Rural according to General statistical office in both surveys. Status base on the classification at time of each survey	6 to 15	49.3 in 1992
			2000	9,870				48.7 in 2000
Tang[#]	2007	Vietnam	2002	1,504	Schools in wealthy urban distracts and less wealth urban district	Schools in semi rural and rural districts	Mean 13.1 11 to 16	49.9
Tuan**	2008	Vietnam	1992	24,068	Urban according to General statistical office in both surveys. Status base on the classification at time of each survey	Rural according to General statistical office in both surveys. Status base on the classification at time of each survey	2 to 65 with separate analysis for 2 to 18 and over 18	51.8 in 1992
			2002	158,019				51.5 in 2002
Le Nguyen[#]	2013	Vietnam	2011	2,872	Not clearly stated	Not clearly stated	0.5 to 11	49.8

[#] studies included in the meta analysis for children ** the only study conducted in both children and adults

Appendix B5. Study characteristics of studies conducted in adults from Malaysia and Philippines

Author	Year of publication	Country	Year of conduct	Sample size	Urban definition	Comparison	Mean age / age range	% Female
Rampal[#]	2007	Malaysia	2004	16,127	Urban according to Statistics Department of Malaysia	Rural according to Statistics Department of Malaysia	Mean 36.7 15 to 93	57.6
Amzi	2009	Malaysia	2002-2003	6,766	Urban according to Malaysian Adult Nutrition Survey (MANS)	Rural according to Malaysian Adult Nutrition Survey (MANS)	18 to 59	50.8
Jinam	2008	Malaysia	Not stated	266	Temuan and Bidayud communities	Kensiu and Jehai communities	20 to >70	60.1
Suzana[#]	2012	Malaysia	2006	4,676	Urban according to National Health and Morbidity survey (NHMS III)	Rural according to National Health and Morbidity survey (NHMS III)	60 to 80+	53.4
Mohamud	2012	Malaysia	2006	4,341	Urban according to National Health and Morbidity survey (NHMS III)	Rural according to National Health and Morbidity survey (NHMS III)	47.8 (SD 14.5)	64.9
Rasiah	2013	Malaysia	2007 to 2010	10,645	Ten communities from Western Peninsular Malaysia	Nine communities from Eastern Peninsular Malaysia and East Malaysia	30 and above	Not clearly stated
Shariff	2014	Malaysia	2005 to 2009	625	Households from Petaling, Selangor and cities of Kota Bharu and Kuala Lumpur	Households from palm plantations throughout Negeri Sembilan and Kalantan	19 to 49	100
Dahly[#]	2010	Philippines	2005	1,807	Urbanicity scale. Made up of 7 components: 1. Population size, 2. Population density, 3.Communications, 4 Transportation, 5. Markets, 6 Educational facilities and 7. Health services		Mean 21 .5 (SD 0.30)	45.3

[#] Studies included in meta-analysis

Appendix B6. Study characteristics of studies conducted in Adults from Thailand

Author	Year of publication	Country	Year of conduct	Sample size	Urban definition	Comparison	Mean age / age range	% Female
Aekplakorn[#]	2007	Thailand	1997	3,109	Urban according to Thai National Health Examination Survey (NHES II and III)	Rural according to Thai National Health Examination Survey (NHES II and III)	15 to 59	64.4
			2004	19,133				
Banwell[#]	2009	Thailand	2004	19,133	Self report urban location of residence at 10-12 and urban residence in 2005 (U-U)	Self report rural location of residence at 10-12 and in 2005 (R-R)	Median 29 15 to 87	52.5
Suriyawong-paisal	2003	Thailand	2000	5,305	Urban according to the Thai Ministry of Interior	Rural according to the Thai Ministry of Interior	Over 35	60.5
Jitarin[#]	2010	Thailand	2004-2005	3,163	Not clearly stated	Not clearly stated	Mean 40.7 (SD 17.2) 18 to 70	0
Aekplakorn (ref 54)	2011	Thailand	2000	5,305	Urban political district	Rural Political district	50.2 in men 50.6 in women	60.5
Aekplakorn[#] (ref 56)	2011	Thailand	2008	19,256	Urban according to Thai National Health Examination Survey (NHES IV)	Rural according to Thai National Health Examination Survey (NHES IV)	20 to 80+	52.5

[#] Studies included in meta-analysis

Appendix B7. Study characteristics of studies conducted in adults from Indonesia and Timor-Leste

Author	Year of publication	Country	Year of conduct	Sample size	Urban definition	Comparison	Mean age / age range	% female
Koyama	1988	Indonesia	1983	212	Sekeloa, Bandung City	Kampung Tanu, Bandung City	20 to 50+	60.0
Sartika	2011	Indonesia	Not clearly stated	180	Urban part of City of Depok (25% engaged in agricultural activities)	Rural part of city of Depok (the majority of household engaged in agricultural activity)	Mean 46.4 35.3 to 59.6	50.5
Ng[#]	2006	Indonesia	2001	2,927	Urban according to Purwejo Demographic Surveillance System	Rural area sub classified into quintiles according to an asset survey in 1999	15 to 74	49.7
Fuke	2007	Indonesia	Not clearly stated	177	Sangsit	Pedawan	20 to 60	100
Ramke[#]	2012	Timor Leste	2009-2010	2,003	Urban based on national census data	Rural based on national census data	≥ 40	48.1

[#] Studies included in meta-analysis

Appendix B8. Study characteristics of studies conducted in adults from Laos, Vietnam and Myanmar

Author	Year of publication	Country	Year of conduct	Sample size	Urban definition	Comparison	Mean age / age range	% Female
Nambooze	2014	Laos	2012	144	Vatluong village	Somsouk and Phouhome village	Over 65	61.8
Nguyen[#]	2007	Vietnam	1992-1993	11,981	All three survey use urban definition according to national census	All three survey use rural definition according to national census	15 to 51+	54.7
			1997-1998	15,971				54.3
			2001-2002	94,656				53.2
Hanh	2001	Vietnam	1999	300	Urban area was Ben Thanh ward (district 1) in Ho Chi Minh City	Sub urban area was Phuthuan village (Nha be District) and rural area was Tam Thon Hiep (Can Gio District) in Ho Chi Minh City	40 to 59	62.3
Hanh[#]	2001	Vietnam	2000	217	Nguyen Cu Trinh Ward, District 1	Tan Thanh Dong Village, Cu Chi District	60 to 69	69.2
Ly	2013	Vietnam	2010	1,621	Urban as determine by government official-the heads of each local commune Health Clinic	Rural and mixed urban/rural communes were defined as those that contain rural areas covering 30% to 50% of their geographic boundary	Mean 52 (SD12.5) 35 to 93	56.1
Ha[#]	2011	Vietnam	2000	14,542	Urban using National Population and Housing census in 1999	Rural using National Population and Housing census in 1999	25 to 64	51.2
			2005	17,213				50.7
Thu Hien	2013	Vietnam	2008	1,528	Not clearly stated	Not clearly stated	Mean 45.6	Not clearly stated
Myo Thet	1992	Myanmar	Not stated	2,611	Three urban township (Sanchaung, Latha and Pabedan) in Yangon City	Hmawbi Township	Over 15	63.4

[#] Studies included in meta-analysis

Appendix B9. Results of studies conducted in children from Malaysia

Author (year of publication)	Country (year of conduct)	Obesity definition	Prevalence (%) in urban exposure group (95% CI)	Prevalence (%) in comparison group (95% CI)	Crude odds ratio (95% CI)	Adjusted odds ratio (95% CI)	Adjusted factors
Anuar Zaini[#] (2005)	Malaysia	BMI >95th percentile for age and sex	6.5 (5.1 to 8.2)	5.4 (3.2 to 7.5)	Not clearly reported	1.22 (0.70 to 2.26)	Age and sex specific criteria for obesity
Sumarni[#] (2006)	Malaysia	Percentiles passing BMI of 25 by International Obesity Task force (IOTF)	20.8 (17.2 to 24.7)	23.7 (18.3 to 29.7)	Not clearly reported	0.85 (0.58 to 1.24)	Age and sex specific criteria for obesity
		Percentiles passing BMI of 30 by International Obesity Task force (IOTF)	7.2 (5.1 to 9.9)	7.0 (4.1 to 11.1)		1.03 (0.56 to 1.91)	
Zalilah[#] (2006)	Malaysia	BMI >85th percentile for age and sex base on WHO standard	19.4 (17.9 to 21.0)	17.3 (16.1 to 19.5)	Not clearly stated	1.15 (1.01 to 1.31)	Age and sex specific criteria for obesity
Naidu[#] (2006)	Malaysia	BMI >85th percentile for age and sex base on WHO standard	22.6 (21.2 to 24.1)	16.1 (14.7 to 17.5)	1.53 (1.33 to 1.74)	1.16 (1.01 to 1.36)	Age and sex specific definition of obesity, ethnicity, guardian BMI status, household income, guardian education
Poh[#] (2013)	Malaysia (2011)	Z-score based on WHO standard	12.7	8.2	Not clearly reported	1.63 (1.29 to 2.06)	Age and sex specific criteria for obesity
Zainuddin[#] (2013)	Malaysia (2008)	Weight for Age Z-score based on WHO standard	8.8 (8.0 to 9.8)	5.9 (5.2 to 6.8)	Not clearly reported	1.53 (1.10 to 1.77)	Age and sex specific criteria for obesity
		BMI for Age Z-score based on WHO standard	13.0 (11.9 to 14.3)	8.8 (7.9 to 9.8)		1.55 (1.24 to 1.94)	

[#] Studies included in meta-analysis

Appendix B10. Results of studies conducted in children from Thailand and Indonesia

Author (year of publication)	Country (year of conduct)	Obesity definition	Prevalence (%) in urban exposure group (95% CI)	Prevalence (%) in comparison group (95% CI)	Crude odds ratio (95% CI)	Adjusted odds ratio (95% CI)	Adjusted factors
Firestone[#] (2011)	Thailand (2004)	BMI >95th percentile for age and sex	Not clearly reported	Not clearly reported	2.66 (1.91 to 3.72)	1.73 (1.21 to 2.48)	Age and sex specific criteria for obesity, adjustments for household wealth, maternal education, household head occupation, maternal BMI, household size and ethnicity
Sakamoto[#] (2001)	Thailand (1997)	Weight for Height index >97 of the Thai national standard	22.7 (19.4 to 26.3)	7.4 (5.4 to 9.9)	Not clearly reported	3.68 (2.51 to 5.47)	Age and sex specific criteria for obesity
Rojroongwasinkul[#] (2013)	Thailand (2011)	Z-score based on WHO standard	11.8	5.9	Not clearly reported	2.13 (1.62 to 2.79)	Age and sex specific criteria for obesity
Julia[#] (2004)	Indonesia (1999)	Weight for Height Z-score > 2.0 based on WHO standard	4.1 in non poor urban	1.0	Not clearly reported	4.35 (2.32 to 8.33) for non poor urban	Age and sex specific criteria for obesity
			0.5 in poor urban			0.46 (0.51 to 2.09) for poor urban	
		Percentiles passing BMI of 25 by International Obesity Task force (IOTF)	4.9 in non-poor urban	1.0	Not clearly reported	5.26 (2.77 to 10.00) for non poor urban	
			0.7 in poor urban			0.69 (0.12 to 2.57) for poor urban	
		Percentiles passing BMI of 25 by International Obesity Task force (IOTF)	1.8 in non-poor urban	0.2	Not clearly reported	11.11 (2.56 to 50.0) for non-poor urban	
			0.0 in poor urban				
Sandjaja[#] (2013)	Indonesia (2011)	Z-score based on WHO standard	5.1	1.8	Not clearly reported	2.96 (2.21 to 3.99)	Age and sex specific criteria for obesity

[#] Studies included in meta-analysis

Appendix B11. Results of studies conducted in children from Laos and Vietnam

Author (year of publication)	Country (year of conduct)	Obesity definition	Prevalence (%) in urban exposure group (95% CI)	Prevalence (%) in comparison group (95% CI)	Crude odds ratio (95% CI)	Adjusted odds ratio (95% CI)	Adjusted factors
Jurgensen [#] (2009)	Laos (2006)	Percentiles passing BMI of 25 by International Obesity Task force (IOTF)	12.0 (8.9 to 16.9)	5.0 (2.8 to 7.9)	Not clearly reported	2.65 (1.40 to 5.24)	Age and sex specific criteria for obesity
Tuyet (2003)	Vietnam (1999)	Weight for Height Z-score > 2.0 based on WHO standard	5.2 (2.2 to 9.9)	0.0	Not clearly reported	Not clearly reported	
Leirop[#] (2008)	Vietnam (2004)	BMI >85th percentile for age and sex base on WHO standard	4.6 (3.3 to 5.9)	1.6 (1.0 to 2.2)	Not clearly reported	2.94 (1.66 to 5.56)	Age and sex specific criteria for obesity
Dang[#] (2010)	Vietnam (1992 and 2000)	Percentiles passing BMI of 25 by International Obesity Task force (IOTF)	0.7 (0.1 to 1.2) in 1992	0.4 (0.1 to 0.6) in 1992	Not clearly reported	1.83 (0.65 to 4.58) in 1992	Age and sex specific criteria for obesity
			6.2 (4.7 to 7.7) in 2000	1.2 (0.9 to 1.5) in 2000		5.46 (4.09 to 7.28) in 2000	
Tang[#] (2007)	Vietnam (2002)	Percentiles passing BMI of 25 by International Obesity Task force (IOTF	8.2 (4.0 to 12.5) in wealth urban	1.6 (0.8 to 2.4) in semi-rural and rural	Not clearly reported	5.53 (2.42 to 14.16) for wealthy urban	Age and sex specific criteria for obesity
			5.8 (4.0 to 7.7) in less wealthy urban			3.82 (1.73 to 9.56) in less wealthy urban	
		Percentiles passing BMI of 30 by International Obesity Task force (IOTF	0.6 (0.0 to 1.6) in wealthy urban	0.2 (0.0 to 0.6) in semi-rural and rural	Not clearly reported	2.86 (0.15 to 168.9) for wealthy urban	
			0.9 (0.2 to 1.7) in less wealthy urban			4.6 (0.56 to 214.3) in less wealthy urban	
Tuan (2008)	Vietnam (1992 and 2002)	BMI >85th percentile for age and sex base on WHO standard age 2-17	1.2 (0.5 to 1.9) in 1992	1.4 (0.9 to 1.9) in 1992	Not clearly reported	Not clearly reported	Age and sex specific criteria for obesity Prevalence weighted to be nationally representative
			4.7 (4.0 to 5.3) in 2002	1.1 (1.0 to 1.3) in 2002			
Le Nguyen[#] (2013)	Vietnam (2011)	Z-score based on WHO standard	14.3	1.4	Not clearly reported	11.8 (7.39 to 19.8)	Age and sex specific criteria for obesity

[#]Studies included in meta-analysis

Appendix B12. Results of studies conducted in adults from Malaysia and Philippines

Author (year of publication)	Country (year of conduct)	Obesity definition			Prevalence (%) in urban exposure group (95% CI)	Prevalence (%) in comparison group (95% CI)	Crude odds ratio (95% CI)	Adjusted odds ratio (95% CI)	Adjusted factors
Rampal[#] (2007)	Malaysia (2004)	BMI ≥ 30			12.0 (11.2 to 12.8)	11.3 (10.4 to 12.3)	1.07 (0.94 to 1.21)	1.16 (1.02 to 1.32)	Age, sex, ethnicity and current smoking
Amzi (2009)	Malaysia (2002)	BMI ≥ 30			12.0 (10.8 to 13.3)	12.3 (11.1 to 13.7)	Not clearly reported	Not clearly reported	None
Jinam (2008)	Malaysia	BMI 25-29 in men			25.5 in Bidayuh	7.1 in Jehai	Not clearly reported	Not clearly reported	Age corrected to 2000 indigenous Malaysian population
					42.2in Temuan	11.8 in Kensiu			
		BMI ≥ 30 in men			7.6 in Bidayuh	0 in Jehai	Not clearly reported	Not clearly reported	
					18.3 in Temuan	0 in Kensiu			
		BMI 25-29 in women			37.7 in Bidayuh	13.7 in Jehai	Not clearly reported	Not clearly reported	Age corrected to 2000 indigenous Malaysian population
					34.0 in Temuan	13.8 in Kensiu			
		BMI ≥ 30 in women			11.0 in Bidayuh	0 in Jehai	Not clearly reported	Not clearly reported	
					26.3 in Temuan	5.1 in Kensiu			
Suzana[#] (2012)	Malaysia (2006)	BMI ≥ 25			44.9 (42.8 to 47.0)	35.1 (33.0 to 37.2)	Not clearly reported	1.3 (1.2 to 1.6)	Age restricted population (60-80), adjustments for sex, ethnicity, education, household income and marital status
		BMI ≥ 30			11.5 (10.3 to 12.9)	9.9 (8.7 to 11.2)	Not clearly reported	1.1 (0.9 to 1.4)	
		WC ≥ 102 in men WC ≥ 88 in women			23.6 (21.9 to 25.4)	18.6 (17.0 to 20.3)	Not clearly reported	1.2 (1.0 to 1.4)	
Mohamud (2012)	Malaysia (2006)	WC ≥ 90 in men WC ≥ 80 in women			56.5 (54.4 to 58.6)	58.4 (56.2 to 60.5)	Not clearly reported	0.92 (0.82 to 1.04)	Sex specific criteria, not age adjusted
Rasiah (2013)	Malaysia (2007 to 2010)	BMI ≥ 25	Highest Education	University education	18	17	Not clearly reported	Not clearly reported	Analysis only in men Age standardized prevalence
				Technical education	22	23			
				Secondary education	15	14			
				Primary education	14	11			
				No education	9	3			

[#] Studies included in meta-analysis

Appendix B12. Results of studies conducted in adults from Malaysia and Philippines (con.)

Author (year of publication)	Country (year of conduct)	Obesity definition			Prevalence (%) in urban exposure group (95% CI)	Prevalence (%) in comparison group (95% CI)	Crude odds ratio (95% CI)	Adjusted odds ratio (95% CI)	Adjusted factors
Rasiah (2013)	Malaysia (2007 to 2010)	BMI ≥ 25	Highest Education	University education	17	14	Not clearly reported	Not clearly reported	Analysis only in women Age standardize prevalence
				Technical education	6	10			
				Secondary education	24	23			
				Primary education	24	21			
				No education	20	12			
Shariff (2014)	Malaysia (2005 to 2009)	BMI ≥ 25			Not clearly reported	Not clearly reported	0.98 (0.72 to 1.35)	Not clearly reported	None
Dahly[#] (2001) **	Philippines (2005)	BMI ≥ 30			Not clearly reported	Not clearly reported	1.22 (0.99 to 1.51) in men	1.08 (0.85 to 1.32) in men	Age restricted range, adjustments for assets, income education and marital status
							1.20 (0.85 to 1.52) in women	1.19 (0.93 to 1.51) in women	
		WC >85 in men			Not clearly reported	Not clearly reported	1.25 (0.99 to 1.57)	1.06 (0.82 to 1.35)	
		WC >80 in women					1.27 (0.95 to 1.69)	1.28 (0.95 to 1.71)	

[#] Studies included in meta-analysis; [**] Urban exposure in multivariable regression using urbanicity score (10 points): mean urbanicity score in male 40.6; range 8-61

Appendix B13. Results of studies conducted in adults from Thailand

Author (year of publication)	Country (year of conduct)	Obesity definition	Prevalence (%) in urban exposure group (95% CI)	Prevalence (%) in comparison group (95% CI)	Crude odds ratio (95% CI)	Adjusted odds ratio (95% CI)	Adjusted factors
Aekplakorn[#] (2007)	Thailand (1997 and 2004)	BMI 25-29 In men	20.4 17.2 to 24.1 in 1997	13.3 (11.4 to 15.5) in 1997	Not clearly reported	1.35 (0.84 to 1.58) in 1997	Male only analysis, adjusted for age, geographic region, smoking and marital status
			25.1 (23.6 to 26.6) in 2004	16.8 (15.4 to 18.2) in 2004		1.56 (1.40 to 1.78) in 2004	
		BMI ≥ 30 In men	7.1 (5.4 to 9.3) in 1997	2.8 (1.7 to 4.7) in 1997		1.30 (0.63 to 2.70) in 1997	
			7.1 (6.1 to 8.3) in 2004	4.5 (3.7 to 5.6) in 2004		1.47 (1.18 to 1.85) in 2004	
		WC > 90 in men	23.4 (18.2 to 29.5) in 1997	10.1 (7.7 to 13.1) in 1997		1.35 (0.83 to 2.22) in 1997	
			22.7 (21.1 to 24.3) in 2004	13.4 (12.0 to 14.9) in 2004		1.58 (1.40 to 1.82) in 2004	
		BMI 25-29 in women	23.9 (22.0 to 26.0) in 1997	22.1 (19.5 to 25.0) in 1997	Not clearly reported	1.36 (1.04 to 1.78) in 1997	Female only analysis, adjusted for age, geographic region, smoking and marital status
			25.4 (24.1 to 26.7) in 2004	26.9 (25.2 to 28.6) in 2004		1.12 (0.99 to 1.26) in 2004	
		BMI ≥ 30 in women	9.9 (8.7 to 11.1) in 1997	7.7 (6.5 to 9.2) in 1997		1.31 (0.95 to 1.78) in 1997	
			12.3 (11.1 to 13.) in 2004	8.8 (8.0 to 9.8) in 2004		1.35 (1.12 to 1.61) in 2004	
		WC > 80 in women	32.0 (29.5 to 34.6) in 1997	29.6 (27.2 to 32.2) in 1997		1.35 (1.14 to 1.64) in 1997	
			37.2 (34.8 to 39.7) in 2004	36.0 (33.7 to 38.3) in 2004		1.10 (0.98 to 1.12) in 2004	

[#] Studies included in meta-analysis

Appendix B13. Results of studies conducted in adults from Thailand (con.)

Author (year of publication)	Country (year of conduct)	Obesity definition	Prevalence (%) in urban exposure group (95% CI)	Prevalence (%) in comparison group (95% CI)	Crude odds ratio (95% CI)	Adjusted odds ratio (95% CI)	Adjusted factors
Banwell[#] (2009)	Thailand (2005)	BMI ≥ 25	Not clearly reported	Not clearly reported	1.61	1.47 (1.38 to 1.55)	Age, sex, income, education, marital status, ethnicity and region
Suriyawongpaisal (2003)	Thailand (2000)	BMI ≥ 25	43.0 (41.3 to 44.8)	28.0 (26.1 to 29.9)	1.94 (1.72 to 2.19)	Not clearly reported	None
Jitarin[#] (2010)	Thailand (2004)	BMI ≥ 23 in men	38.6 (36.3 to 40.9)	30.4 (28.0 to 32.9)	1.43 (1.23 to 1.67)	1.3 (1.1 to 1.6)	Male only analysis, adjusted for age and marital status
		BMI ≥ 23 in women	44.9 (42.6 to 47.2)	44.9 (42.3 to 47.5)	Not clearly stated	1.0 (0.87 to 1.15)	Female only analysis, did not adjust for age
Aekplakorn (2011, ref 54)	Thailand (2000)	BMI ≥ 30	6.6 (4.4 to 8.8) in men	3.1 (1.7 to 4.5) in men	Not clearly reported	Not clearly reported	Age standardized to Thai population in 2000
			12.6 (10.2 to 14.9) in women	9.7 (7.3 to 12.0) in women			
		WC > 90 in men	31.3 (25.4 to 37.2)	16.2 (9.9 to 22.5)			
		WC >80 in women	56.0 (53.1 to 58.9)	47.5 (40.4 to 54.5)			
Aekplakorn[#] (2011, ref 56)	Thailand (2008)	WC > 90 in men	28.6 (25.7 to 31.5)	15.2 (13.6 to 16.8)	Not clearly reported	2.23 (2.01 to 2.48)	Age standardized to Thai population in 2008, gender specific criteria
		WC > 80 in women	48.1 (47.4 to 50.4)	43.4 (40.6 to 46.1)	Not clearly reported	1.21 (1.12 to 1.31)	Age standardized to Thai population in 2008, gender specific criteria

[#] Studies included in meta-analysis

Appendix B14. Results of studies conducted in adults from Indonesia and Timor-Leste

Author (year of publication)	Country (year of conduct)	Obesity definition		Prevalence (%) in urban exposure group (95% CI)	Prevalence (%) in comparison group (95% CI)	Crude odds ratio (95% CI)	Adjusted odds ratio (95% CI)	Adjusted factors
Koyama (1988)	Indonesia (1983)	BMI ≥ 27		5.5 (1.1 to 15.1) in men	(1. 0 (0 to 9.0) in men	Not clearly reported	Not clearly reported	Male only analysis
				4.4 (1.2 to 11.0) in women	(1.0) (0 to 9.5) in women			Female only analysis
Sartika (2011)	Indonesia	BMI ≥ 25		57.7 (46.9 to 68.1)	32.9 (22.7 to 42.9)	2.88 (1.50 to 5.54)	Not clearly reported	None
Ng (2006)[#]	Indonesia (2000)	BMI ≥ 25		13.3 (9.6 to 18.1) men 23.7 (19.6 to 28.4) women	10.1 (6.2 to 16.1) men 19.6 (14.5 to 26.1) women in richest rural quintile	Not clearly stated	1.35(0.77 to 2.38) men 1.13 (0.84 to 1.88) women	Age and sex
					3.1 (2.2 to 4.2) men 10.2 (8.3 to 12.5) women in middle three quintile		4.35(2.65 to 7.14) men 2.44 (1.74 to 3.33) women	
					0.7 (0.2 to 2.9) men 2.6 (1.2 to 5.8) women in poorest quintile		16.67 (4.35 to 10.0) men 9.09 (4.17 to 20.0) women	
Fuke (2007)	Indonesia (not stated)	Visceral fat per body weight (cm^2/kg) as means (SD)	Age 20s	0.524 (0.186)	0.576 (0.235)	Not clearly reported	Not clearly reported	Age specific and male only analysis
			Age 30s	0.818 (0.278)	0.617 (0.148)			
			Age 40s	1.047 (0.299)	1.098 (0.307)			
			Age 20s	0.524 (0.186)	0.576 (0.235)			
Ramke [#] (2012)	Timor-Leste (2009)	BMI ≥ 25		Not clearly reported	Not clearly reported	4.3 (2.9 to 6.3)	2.9 (1.8 to 4.5)	Age, sex, literacy and household income
		BMI ≥ 30		Not clearly reported	Not clearly reported	9.5 (3.5 to 25.8)	5.0 (1.7 to 15.7)	

[#] Studies included in meta-analysis

Appendix B15. Results of studies conducted in adults from Laos, Vietnam and Myanmar

Author (year of publication)	Country (year of conduct)	Obesity definition	Prevalence (%) in urban exposure group (95% CI)	Prevalence (%) in comparison group (95% CI)	Crude odds ratio (95% CI)	Adjusted odds ratio (95% CI)	Adjusted factors
Nambooze (2014)	Laos (2012)	BMI ≥ 23	16.0	3.1	not clearly reported	5.78 (1.29 to 35.0)	Age restricted population (over 65)
Nguyen[#] (2007)	Vietnam (1992, 1997 and 2001)	BMI ≥ 25	4.8 (4.0 to 5.7) in 1992	1.2 (1.0 to 1.4) in 1992	4.13 (3.18 to 5.39) in 1992	1.79 (1.64 to 1.95) in 2001	Age, sex, education, occupation, food expenditure
			9.1 (8.3 to 9.9) in 1997	2.3 (2.0 to 2.6) in 1997	4.28 (3.64 to 5.02) in 1997		
			9.6 (9.3 to 9.9) in 2001	3.5 (3.4 to 3.6) in 2001	2.93 (2.77 to 3.11) in 2001)		
Hanh (2001)	Vietnam (1999)	BMI ≥ 25	17.8 (10.9 to 26.7)	13.0 (7.1 to 21.2) in suburban	1.45 (0.63 to 3.43) compared to suburban	Not clearly reported	None
				6.1 (2.2 to 12.7) in rural	3.36 (1.20 to 10.78) compared to rural		
Hanh[#] (2001)	Vietnam (200)	BMI ≥ 25	34.2 in men	5.6 in men	Not clearly reported	8.71 (2.73 to 36.0)	Age restricted population (60 to 69) and stratified by sex
			25.0 in women	5.4 in women		5.83 (1.01 to 59.6)	
Ly (2013)	Vietnam (2010)	BMI ≥ 23	Not clearly reported	Not clearly reported	Not clearly reported	1.28 (0.99 to 1.66) compared to mix urban-rural	Age, systolic blood pressure, diabetes (variable selected using backward stepwise approach)
						1.92 (1.0 to 3.70) compared to rural	
		BMI ≥ 25	Not clearly stated	Not clearly stated	Not clearly reported	1.41 (1.0 to 2.0) compared to mix urban-rural	Systolic blood pressure, diabetes, self reported heart attack (variable selected using backward stepwise approach)
						2.13 (0.57 to 7.69) compared to rural	

[#] Studies included in meta-analysis

Appendix B15. Results of studies conducted in adults from Laos, Vietnam and Myanmar (con.)

Author (year of publication)	Country (year of conduct)	Obesity definition	Prevalence (%) in urban exposure group (95% CI)	Prevalence (%) in comparison group (95% CI)	Crude odds ratio (95% CI)	Adjusted odds ratio (95% CI)	Adjusted factors
Ha[#] (2011)	Vietnam (2000 and 2005)	BMI ≥ 25	Not clearly reported	Not clearly reported	Not clearly reported	2.39 (1.70 to 3.19) in 2000 2.08 (1.60 to 2.72) in 2005	Age group, sex, education level and food expenditure
Tuan (2008)	Vietnam (1992 and 2002)	BMI ≥ 25	4.5 (3.4 to 5.6) in 1992 10.0 (9.5 to 10.6_ in 2002	1.1 (0.9 to 1.4) in 1992 3.5 (3.3 to 3.7) in 2002	Not clearly reported	Not clearly reported	Prevalence weighted to be nationally representative
Thu Hien (2013)	Vietnam (2008)	BMI ≥ 23	31.8	24.4	1.44 (1.14 to 1.82)	1.39 (1.02 to 1.67)	Education and smoking
Myo Thet (1992)	Myanmar	BMI > 25	10.7 (9.0 to 12.6)	5.9 (4.1 to 6.4)	2.2 (1.6 to 3.0)	Not clearly reported	None

[#] Studies included in meta-analysis

Appendix B16. PRISMA checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	n/a
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	3
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supporting document Table S1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	4-5

Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	6
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	5
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	6-7

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	7
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	6
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Page 7 and Supporting file Tables S3-S8
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Page 12 and Supporting file Tables S19-20
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Figures 2 and 3; supporting document Tables S9-

			S15
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Figures 2 and 3
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Page 12 and Supporting file Tables S19-20 and Figures S1-S2
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Page 9 Figure 4 Table 1
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	10-11
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	12
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	12-13
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	14

Appendix B17. Sensitivity Analysis: Results from random effect analysis meta-regression (Results from Table 1 of manuscript) and trim and fill analysis

Stratification	Randon effect meta-regression		Trim and fill analysis	
	OR for living in an urban environemnt	P-value	OR for living in an urban environemnt	P-value
None	1.99 (1.64 to 2.41)	<0.001	1.51 (1.34 to 1.71)	<0.001
Country/countries				
Philippines and Malaysia	1.29 (1.14 to 1.45)	0.001	1.29 (1.28 to 1.43)	<0.001
Thailand	1.66 (1.30 to 2.11)	0.001	1.47 (1.26 to 1.71)	<0.001
Vietnam and Laos	3.36 (2.14 to 5.27)	<0.001	1.95 (1.31 to 2.87)	<0.001
Indonesia and Timor-Leste	3.14 (2.22 to 4.46)	0.001	2.74 (2.10 to 3.59)	<0.001
Per capita GNI[#] (US dollars)				
<1,500	3.42 (2.42 to 4.84)	<0.001	2.03(1.46 to 2.83)	<0.001
1,500-2,500	1.62 (1.20 to 2.18)	<0.001	1.38 (1.13 to 1.69)	<0.001
> 2,500	1.50 (1.23 to 1.82)	0.01	1.50 (1.30 to 1.72)	<0.001
Year of field work				
2004 to 2013	1.85 (1.45 to 2.37)	<0.001	1.42 (1.26 to 1.73)	<0.001
Up to 2003	2.22 (1.60 to 3.09)	<0.001	1.52 (1.20 to 1.94)	<0.001
Sex of study population				
Men only	1.76 (1.14 to 2.73)	0.020	1.69 (1.32 to 2.18)	<0.001
Women only	1.47 (0.89 to 2.43)	0.106	1.21 (0.95 to 1.56)	<0.001
Both	2.19 (1.70 to 2.81)	<0.001	1.53 (1.30 to 1.80)	<0.001
Age of population				
Children	2.43 (1.72 to 3.43)	<0.001	1.52 (1.13 to 2.04)	<0.001
Adults	1.65 (1.36 to 1.99)	<0.001	1.50 (1.33 to 1.79)	<0.001
Obesity classifcation				
Non BMIclassifciation (using WC)	2.10 (0.53 to 8.28)	0.145	1.21 (0.71 to 2.06)	<0.001
Obesity defined BMI ≥ 23 or 25	2.13 (1.69 to 2.67)	<0.001	1.53 (1.33 to 1.78)	<0.001
Obesity defined as BMI ≥ 30	1.39 (0.90 to 2.16)	0.104	1.38 (1.07 to 1.88)	<.0.001

Reference groups is living in a rural environment; [#]GNI gross national income; WC waist circumference; * p-value for heterogeneity chi-square;** Likelihood ratio test for heterogeneity between subgroup by meta-regression, providing F-ratio and p-values

Appendix B18. Inter-rater agreement from abstract screening

Inter-rater agreement		Reviewer 2		
		Relevant/ Potentially relevant	Not relevant	Total
Reviewer 1	Relevant/ Potentially relevant	112	8	120
	Not relevant	23	558	581
	Total	135	566	701

588 articles were excluded from abstract reviews and 143 full text articles were assessed for eligibility.

Kappa = 0.85 (Results are shown for articles published up to April 2013)

Appendix B19. Summary of bias within studies among children

Study	Selection bias	Information bias in exposure measurement	Information bias in outcome measurement (BMI)	confounding
Anuar Zaini[#]	low risk	unclear risk, non differential	low risk	low risk
Sumarni[#]	low risk	low risk	low risk	low risk
Zalilah[#]	low risk	low risk	low risk	low risk
Naidu[#]	unclear risk	low risk	low risk	low risk
Poh[#]	low risk	unclear risk	low risk	low risk
Zainuddin[#]	unclear risk	low risk	low risk	low risk
Firestone[#]	low risk	low risk	low risk	low risk
Sakamoto[#]	low risk	low risk	low risk	low risk
Rojroongwasinkul[#]	low risk	low risk	low risk	low risk
Julia[#]	unclear risk	low risk	low risk	low risk
Sandjaja[#]	low risk	unclear risk	low risk	low risk
Jurgensen[#]	low risk	low risk	low risk	low risk
Tuyet	low risk	low risk	low risk	low risk
Leirop[#]	low risk	low risk	low risk	low risk
Dang[#]	low risk	low risk	low risk	low risk
Tang[#]	unclear risk	low risk	low risk	low risk
Tuan**	unclear risk	low risk	low risk	low risk
Le Nguyen[#]	low risk	unclear risk	low risk	low risk

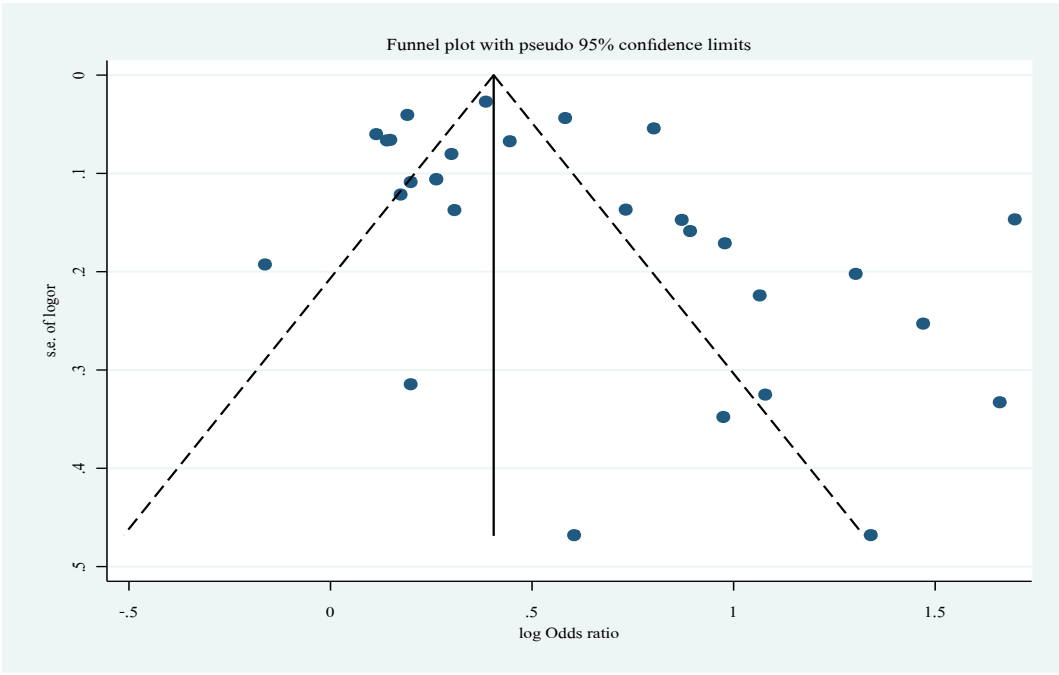
[#] Studies included in meta-analysis; ** Study conducted in both children and adults but reported estimates separately

Appendix B20. Summary of bias within studies among adults

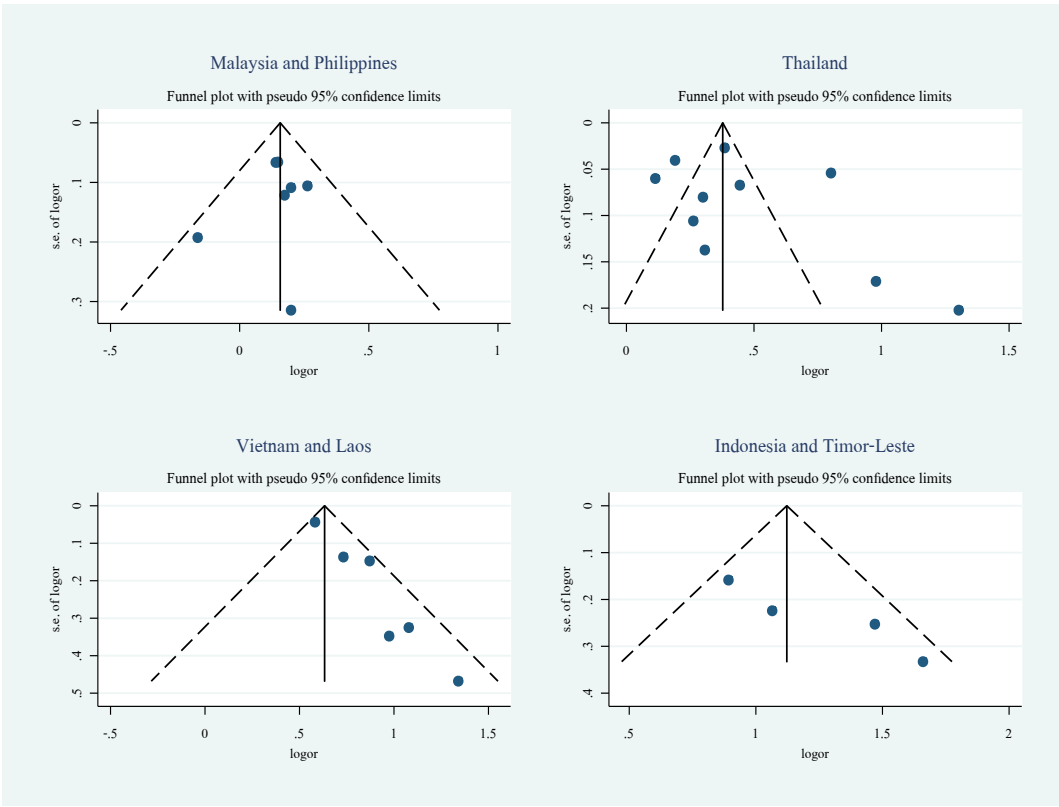
Study	Selection bias	Information bias in exposure measurement	Information bias in outcome measurement (BMI)	confounding
Rampal[#]	low risk	low risk	low risk	low risk
Azmi	unclear risk	unclear risk, non differential	low risk	unclear risk
Jinam	unclear risk	low risk	unclear risk	low risk
Suzana[#]	low risk	low risk	low risk	low risk
Mohamud	unclear risk	low risk	low risk	unclear risk
Rasiah	unclear risk	low risk	low risk	low risk
Shariff	low risk	low risk	low risk	unclear risk
Dahly[#]	low risk	low risk	low risk	low risk
Aekplakorn[#] (ref. 55)	low risk	low risk	low risk	low risk
Banwell[#]	unclear risk	unclear risk, non differential	low risk	low risk
Suriyawongpaisal	low risk	low risk	unclear risk	high risk
Jitarin[#]	unclear risk	unclear risk	unclear risk	low risk
Aekplakorn (ref. 54)	low risk	low risk	low risk	low risk
Aekplakorn[#] (ref. 56)	low risk	low risk	low risk	low risk
Koyama	unclear risk	low risk	unclear risk	unclear risk
Sartika	low risk	low risk	low risk	high risk
Ng[#]	low risk	low risk	low risk	low risk
Fuke	unclear risk	low risk	low risk for measurement of visceral fat	low risk
Ramke[#]	low risk	low risk	low risk	low risk
Nambooze	low risk	low risk	unclear risk	unclear risk
Nguyen[#]	unclear risk	low risk	unclear risk	low risk
Hanh (ref. 42)	unclear risk	low risk	low risk	high risk
Hanh[#] (ref. 45)	unclear risk	low risk	unclear risk	low risk
Ly	low risk	low risk	low risk	unclear risk
Ha[#]	low risk	low risk	low risk	low risk
Tuan**	unclear risk	low risk	low risk	low risk
Thu Hien	low risk	unclear risk	low risk	unclear risk
Myo Thet	low risk	low risk	unclear risk	high risk

[#] studies included in meta-analysis; ** Study conducted in both children and adults but reported estimates separately

Appendix B21. Funnel plots of results included in meta-analysis



Appendix B22. Funnel plots of results included in meta-analysis by country/countries



Appendix C. Supporting documents submitted for published article "Urbanization and non-communicable disease in Southeast Asia: a review of current evidence"

Appendix C1 Search Strategy (for EMBASE)

All terms are multipurpose (mp) search unless stated other wise [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword], (/) indicates subject heading search, (exp) indicates explosion search of subject headings, (*) indicates unlimited truncation, (#) indicates mandatory wildcard, (?) indicates optional wild card, (adj) indicates proximity searching

For setting (S)*

	Searches
1	Southeast asia or SE Asia or SE-asia or South-east asia
2	brunei or myanmar or burma or cambodia or east timor or indonesia or laos or malaysia or philippines or singapore or thailand or vietnam
3	Southeast Asia/ OR Myanmar/ OR Cambodia/ OR Timor/ OR Indonesia/ OR Laos/ OR Malaysia/ OR Philippines/ OR Singapore/ OR Vietnam/ OR Thailand/ OR Brunei
4	1 or 2 or 3 **(S)**

* S refers to final results from "setting" search

For exposure (E)**

	Searches
1	Urbani#ation or urbanicity or urban or rural or rurality
2	Urban adj3 rural
3	(urban adj3 migra*) OR (rural adj3 migra*)
4	migration? or migrant?
5	urbanization/ or urban population/ or urban rural difference/ or rural population/
6	migration/
7	Or/1-6 **(E)**

** E refers to final search result for "exposure" search

For outcomes

1. cardiovascular disease

	Searches
1	cardiovascular disease or heart disease or isch?emic heart disease or heart attack or coronary heart disease or single vessel disease or double vessel disease or triple vessel disease or cerebrovascular disease cerebrovascular accident or stroke or vascular disease or peripheral arterial disease
2	myocardial infarction or heart failure or cardiac failure or TIA or transient isch?eic attack or atrial fibrillation or angina or STEMI or non-STEMI or non STEMI or hypertensive heart disease or cadiomyopath*
3	cardiovascular disease/ or ischemic heart disease/ or cerebrovascular disease/ or exp heart disease/ or exp stroke/
4	1 or 2 or 3
5	4 and S and E
6	5 and "human" [subjects]

2. Cancer

	Searches
1	cancer? or malignanc* or tumor? or tumo?r? or neoplasm?
2	Neoplasm/ or malignant neoplastic disease/
3	1 or 2
4	3 and S and E
5	4 and “human” [subjects]

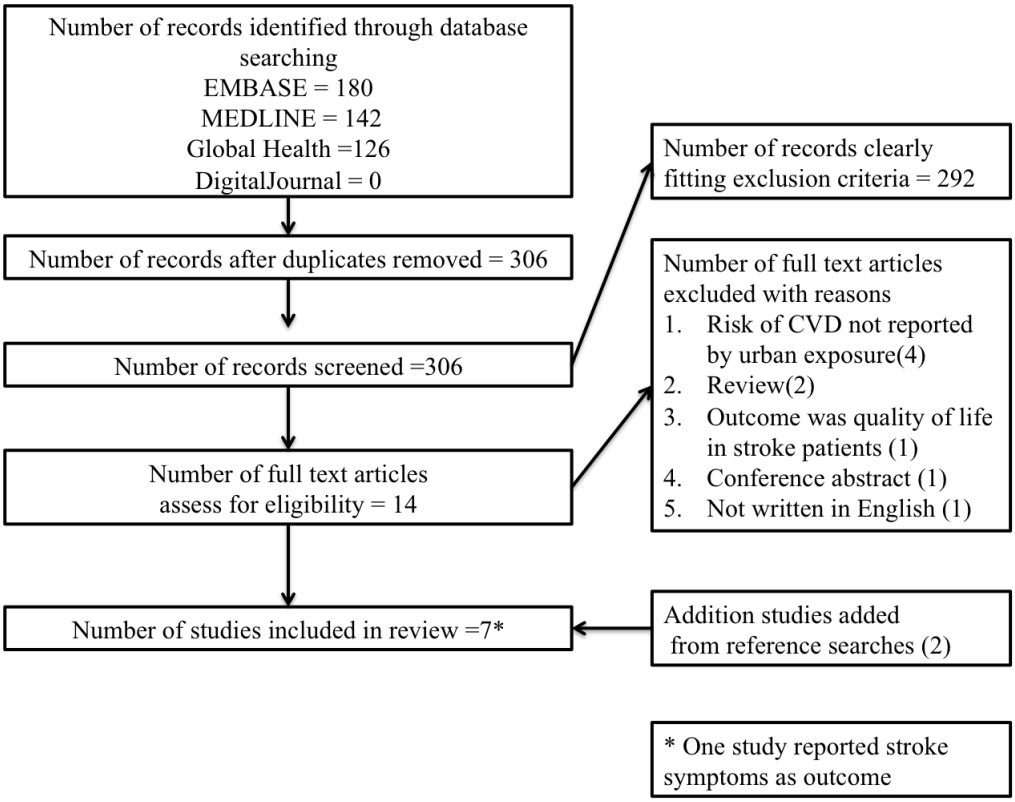
3. Chronic respiratory disease

	Searches
1	chronic respiratory disease or chronic lung disease or COPD or chronic obstruct* pulmonary disease or emphysema or chronic bronchitis or asthma or bronchiectasis
2	chronic obstructive lung disease/ or chronic respiratory tract disease/ or lung emphysema/ or chronic bronchitis/ or asthma/ or bronchiectasis/
3	1 or 2
4	3 and S and E
5	4 and “human” [subjects]

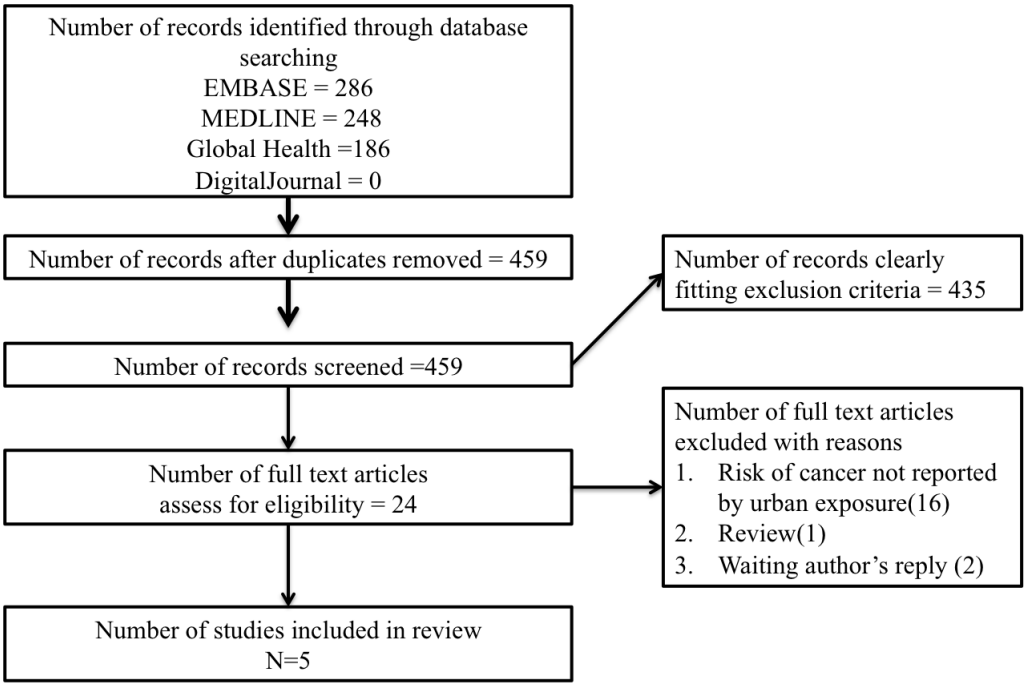
4. Diabetes

	Searches
1	diabet* or DM or impair* fasting glucose or IFG or impair* glucose tolerance or IGT
2	exp diabetes mellitus/ or impaired glucose tolerance/
3	1 or 2
4	3 and S and E
5	4 and “human” [subjects]

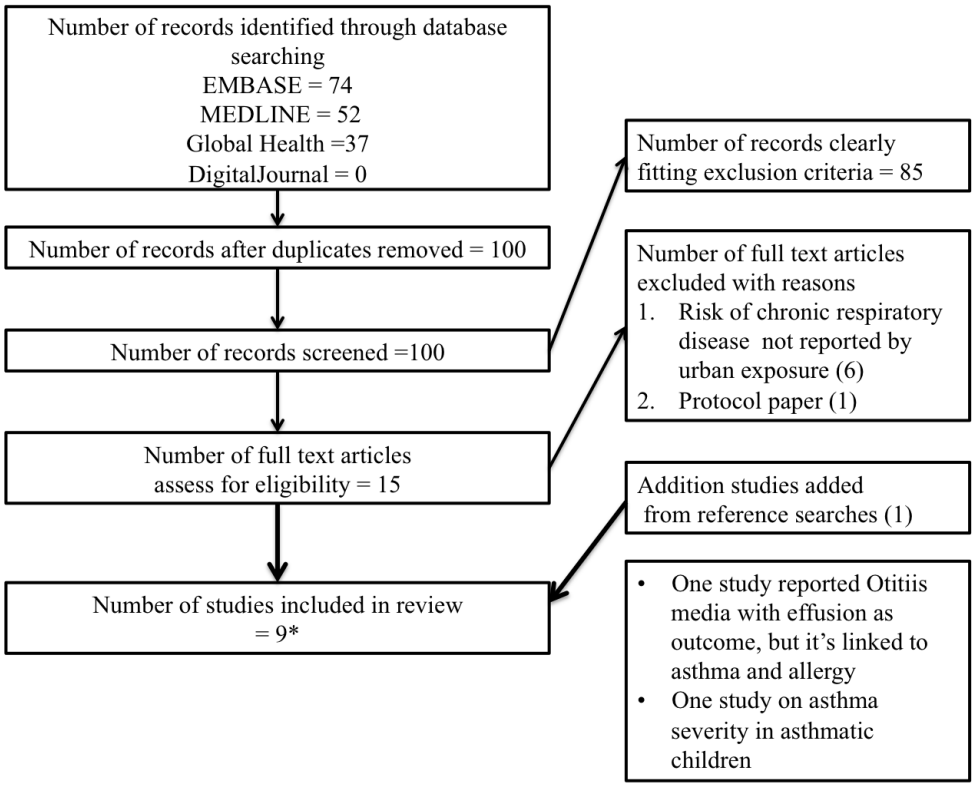
Appendix C2. Flow chart of articles included in the review for cardiovascular disease



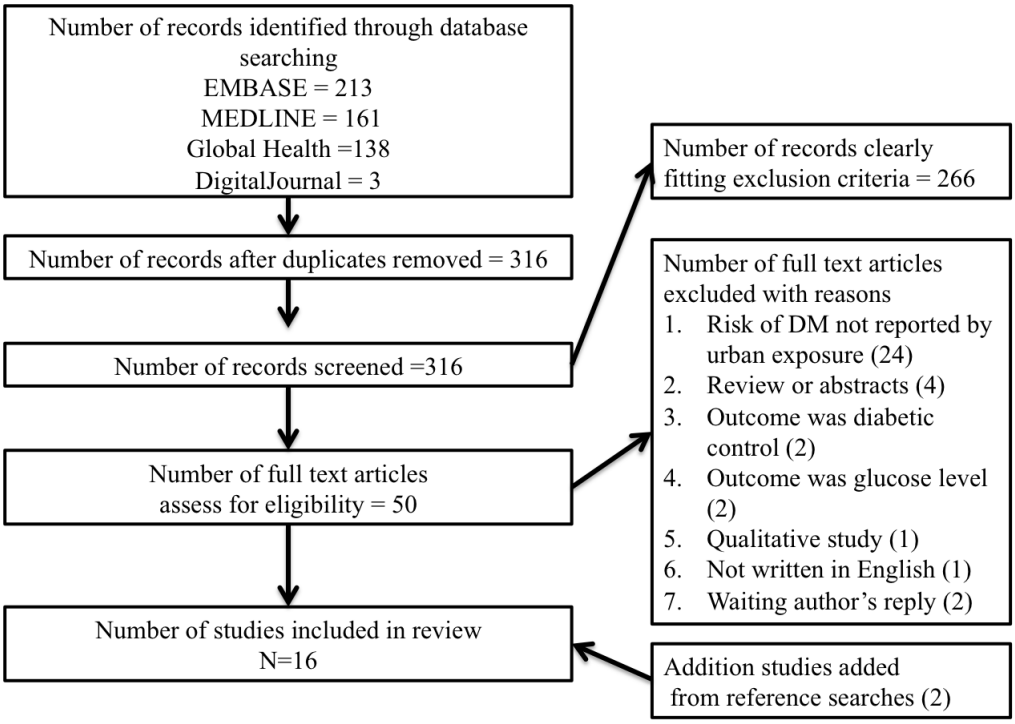
Appendix C3. Flow chart of articles included in the review for cancer



Appendix C4. Flow chart of articles included in the review for chronic respiratory disease



Appendix C5. Flow chart of articles included in the review for diabetes



Appendix C6. Characteristics of studies reporting association between urbanization and cardiovascular disease

Author	Year of publication	Country	Year of conduct	Sample size	**CVD outcome**	Urban definition	Comparison	Mean age / age range	% Female
Fitzpatrick	2012	Vietnam	2010	1,621	Symptoms for stroke	Urban according to classification by Vietnamese government	Considered mix if it had more than 30% agricultural land and respective farmer Rural according to classification by Vietnamese government	52.0 35 to 93	56.1
Myo Thet	1992	Myanmar	Not stated	2,611	Coronary Heart disease Rheumatic Heart Disease Rheumatic Heart disease	Adults in three urban township (Sanchaung, Latha and Pabedan) in Yangon City	Adults in Hmawbi Township	Over 15	63.4
Wada	2005	Myanmar	2004	336	Coronary Heart disease Stroke	Downtown Maubin	villages near Maubin	70.2 Over 60	47.9
Lim	1991	Malaysia	1987	2,139	Coronary heart disease Stroke	Address of patients, classified into hospital records	Address of patients, classified into hospital records	15 to 65	46.0
Ishine	2006	Thailand	2005	407	Coronary Heart disease Stroke	Elderly living in Khon Khan city	Elderly living in Thang Kwang villages in Waeng Noi district	68.5 Over 60	65.1
Ishine	2006	Vietnam	2003	387	Coronary Heart disease Stroke	Elderly in semi develop city, Viet-tri	Elderly living in underdeveloped rural village, Ngoc Quan	70.8 over 60	54.8
Wada	2005	Indonesia	2003	436	Coronary Heart disease Stroke	Elderly in Karawan town	elderly in Srirahayu	72.3 over 60	59.9

Appendix C7. Characteristics of studies reporting association between urbanization and cancer

Author	Year of publication	Country	Year of conduct	Sample size or number of cases	Urban definition	Comparison	Mean age / age range	% Female
Armstrong	1979	Malaysia	1968-1977	2,297 cases of Nasopharyngeal carcinoma	Using home address of patients residing in the 20 urban census districts of Kuala Lumpur, Petaling Java, and Kland and intermediate suburbs	All patients residing in the 11 rural census districts of Selangor	Not clearly stated	31.4 of cases
Jordan	2009	Thailand	2005	43 cases of self report breast cancer	Self urban classification using current residences Self urban classification using residence at age 10-12	Self rural classification using current residences Self rural classification using residence at age 10-12	Case control, matched by age	100
Phomphet	2011	Thailand	2008	338 samples size , 3 reported having cancer	Urban area of Srichan	Semi urban area at Daengnoi village and Remote area at Wangsaeng village	20-60	76.6
Simarak	1977	Thailand	1971	86 cases of oral and oropharyngeal cancer; 96 cases of larynx and hypopharynx cancer; 115 cases of lung cancer	Classification criteria not stated but obtained through interview and classified as urban or semi urban	Classification criteria not stated but obtained through interview and classified as rural	Case control, match by age	35.1 in cases 37.4 in controls
Bovill	1975	Malaysia	1969-1972	68 cases of osteogenic sarcoma	3 urban areas of west malyaisa (Slangor, Malacca and Penang)	7 least densely populated states of west malaysia (Pehang, Trengganu, Johore, Negri Sembilan, Perak, Kedah and Perlis	Not clearly stated	41.2 of cases

Appendix C8. Characteristics of studies reporting association between urbanization and chronic respiratory disease

Author	Year of publication	Country	Year of conduct	Sample size or number of cases	Urban definition	Comparison	Mean age / age range	% Female
Abong	2012	Philippines	2008	7,202	Definition based on population size, population density, street pattern or network, establishments and local occupations	All other location not fitting defined criteria for urban	20 to 70+	53.9
Chai	2004	Vietnam	1999 and 2001	3,610	Children attending public school in central Hanoi	Children attending public school in Dong Anh	5 to 11	52.0
Zakaria	2012	Malaysia	Not clearly reported	149	Asthmatic children attending school from Cheras and Petaling Jaya	Asthmatic children attending Schools from Hulu Langat (Beranang) and Kuala Langat (Morib and Banting)	8-11	Not clearly reported
Lam	2011	Vietnam	2007 to 2008	5,782	Adults in Hoankiem and inner city district of Hanoi	Adults in Bavi, a district of Hatay Province, 60 kg form Hanoi	21 to 70	50.6
Lim	1991	Malaysia	1987	2,139	Address of patients, classified into hospital records	Address of patients, classified into hospital records	15 to 65	46.0
Saim	1997	Malaysia	1993	1,097	Children attending kindergarten in Federal Territory of Kuala Lumpur	Children attending kindergarten in District of Kuala Selangor	5 to 6	47.9
Trakultivakorn	2007	Thailand	1995 and 2001	15,096 in 1995 and 14,749 in 2001	School children in Grade 1 and 8 in Bangkok	School children in grade 1 and 8 in Chiang Mai	6 to 7 and 13 to 14	Not clearly reported
Sriyaraj	2008	Thailand	2003	511	Four state school in urban district, likely to be exposed to high concentration of air pollutants	Two suburban schools, , not located in air polluted locations	6 to 12	48.7
Goh	1986	Singapore	1983	2,014	Schools near Queenstown	Schools near Sembawang	6 to 14	46.5

Appendix C9. Characteristics of studies reporting association between urbanization and for diabetes

Author	Year of publication	Country	Year of conduct	Sample size or number of cases	Urban definition	Comparison	Mean age / age range	% Female
Aekplakorn	2007	Thailand	2004	39290	Urban according to Third National Health Examination Survey (NHES III) using administrative area	Rural according to Third National Health Examination Survey (NHES III) using administrative area	15 to 75+	53.9
Aekplakorn	2011	Thailand	2000	5,305	Urban political district	Rural Political district	50.2 in men 50.6 in women	60.5
Aekplakorn	2011	Thailand	2009	18,629	Urban according to Third National Health Examination Survey (NHES IV) using administrative area	Rural according to Third National Health Examination Survey (NHES IV) using administrative area	Over 20	53.8
Ali	1993	Malaysia	2001	665	Two areas based on degree of development: Kamkong Kerinci Malays village and Lanjan near Kuala Lumpur	Rural area of Koyan and Betau Remote rural areas of Ulu sungai and Lanai	41.1	52.5
Baltazar	2004	Philippines	2002	7,044	National Capital Region (NCR) in Luzon	Outside NCR but classified as urban Luzon and Rural Luzon	20 to 65	Not clearly stated
Chailurkit	2012	Thailand	2008-2009	2,641	Urban according to Fourth National Health Examination Survey (NHES IV) using administrative area	Rural according to Fourth National Health Examination Survey (NHES IV) using administrative area	40.3 18 to 95	50.0
Ishine	2006	Thailand	2005	407	Elderly in Khon Khan city	Elderly in Thang Kwang villages, Waeng Noi district	68.5 over 60	65.1
Ishine	2005	Vietnam	2003	387	Elderly in semi develop city, Viet-tri	Elderly living in underdeveloped rural village, Ngoc Quan	70.8 over 60	54.8
King	2005	Cambodia	2004	2,246	Adults in two communities in Kampong Cham Province	Adults in two rural villages in Siemreap province	46.7 25 to over 65	63.6

Appendix C9. Characteristics of studies reporting association between urbanization and for diabetes (con.)

Author	Year of publication	Country	Year of conduct	Sample size or number of cases	Urban definition	Comparison	Mean age / age range	% Female
Lim	1991	Malaysia	1987	2,139	Address of patients, classified into hospital records	Address of patients, classified into hospital records	15 to 65	46.0
Mohamud	2011	Malaysia	2006	4341	According to National Health Morbidity Survey (NHMS III)	According to National Health Morbidity Survey (NHMS III)	47.8 sd 14.5	64.9
Porapakkham	2008	Thailand	2004	19374	Urban according to Third National Health Examination Survey (NHES III) using administrative area	Rural according to Third National Health Examination Survey (NHES III) using administrative area	≥60	51.2
Phomphet	2011	Thailand	2008	338	Urban area of Srichan	Semi urban area at Daengnoi village and remote area at Wangsaeng village	20 to 60	76.6
Surinyawongpaisal	2003	Thailand	2000	5,305	Criteria defined by the Department of community development of the Thai Ministry of the interior	Criteria defined by the Department of community development of the Thai Ministry of the interior	Over 35	60.5
Wada	2005	Myanmar	2004	336	Downtown Maubin	Villages near Maubin	70.2 Over 60	47.9
Wada	2005	Indonesia	2003	436	Elderly in Karawan town	Elderly in Srirahayu	72.3 Over 60	59.9

Appendix C10. Association between urbanization and cardiovascular disease

Author (year of publication)	Country (year of conduct)	CVD	Definition	Prevalence (%) in urban exposure group (95% CI)	Prevalence (%) in comparison group (95% CI)	Crude odds ratio (95% CI)	Adjusted odds ratio (95% CI)	Adjusted factors
Fitzpatrick (2012)	Vietnam (2010)	Symptoms of stroke	using Questionnaire for Verifying Stroke Free Status (QVSFS)	Not clearly reported	Not clearly reported	0.43 (0.27 to 0.70) compared to mixed urban-rural group	0.34 (0.20 to 0.58) compared to mixed urban-rural group	Age, sex, education , self report symptoms of diabetes, high cholesterol, hypertension, severe chest pain, smoking status, BMI, alcohol consumption, fruit/vegetables consumption and physical activity
						0.61 (0.40 to 0.92) compared to rural group	0.42 (0.25 to 0.71) compared to rural group	
Myo Thet (1992)	Myanmar	Coronary heart	Using trained physicians, diagnosis for coronary heart consisting of angina pectoris grade I and II, possible myocardial infarction (major Q wave), or history of myocardial infarction or severe chest pain for more than half an hour, and ischemic resting electrocardiographic abnormalities	1.3 (0.7 to 2.2)	0.8 (0.4 to 1.5)	1.59 (0.70 to 3.69)	1.34 (0.45 to 4.17) in men	Stratification by sex
							1.64 (0.41 to 6.83) in women	
		Rheumatic Heart	Based on modified Jones Criteria and the type of valvular lesion and characteristics clinical findings supported by other investigations including echocardiography	5.8 (2.3 to 12.1) per 1000	19.4 (12.8 to 28.1) per 1000	0.30 (0.11 to 0.71)	0.48 (0.04 to 3.34) in men	Stratification by sex
							0.28 (0.08 to 0.76) in women	
Wada (2005)	Myanmar (2004)	Stroke	Self report medical history	15.7 (11.1 to 21.4)	7.1 (3.3 to 13.0)	2.46 (1.10 to 6.05)	3.09 (0.97 to 13.0) in men	Age restricted population
							1.81 (0.56 to 6.90) in women	
		Heart disease	Self report medical history	11.4 (7.5 to 16.6)	2.4 (0.5 to 6,7)	5.36 (1.57 to 28.3)	Not clearly reported	

Appendix C10. Association between urbanization and cardiovascular disease (con.)

Author (year of publication)	Country (year of conduct)	CVD	Definition	Prevalence (%) in urban exposure group (95% CI)	Prevalence (%) in comparison group (95% CI)	Crude odds ratio (95% CI)	Adjusted odds ratio (95% CI)	Adjusted factors
Lim (1991)	Malaysia (1987)	Coronary heart	Hospital Discharge notes	16.6 (14.7 to 18.7)	5.1 (3.6 to 6. 8)	3.74 (2.63 to 5.42)	Not clearly reported	None
		Stroke	Hospital Discharge notes	7.7 (6.4 to 9.3)	5.4 (4.0 to 7.2)	1.42 (0.97 to 2.09)	Not clearly reported	
Ishine (2006)	Thailand (2005)	Heart disease	Self report medical history	9.1 (5.6 to 13.8)	3.0 (1.1 to 6.5)	3.20 (1.19 to 9.98)	Not clearly reported	Age restricted population
		Stroke	Self report medical history	3.3 (1.6 to 6.8)	1.0 (0.1 to 3.6)	3.40 (0.63 to 33.80)	Not clearly reported	
Ishine (2005)	Vietnam (2003)	Heart disease	Self report medical history	15.0 (10.1 to 20.8)	17.2 (12.1 to 23.0)	0.85 (0.47 to 1.52	Not clearly reported	Age restricted population
		Stroke	Self report medical history	3.2 (1.2 to 6.8)	7.6 (4.3 to 12.1	0.40 (0.13 to 1.14)	Not clearly reported	
Wada (2005)	Indonesia (2003)	Heart disease	Self report medical history	1.4 (0.3 to 4.1)	7.4 (4.4 to 11.8)	0.18 (0.03 to 0.63)	Not clearly reported	Age restricted population
		Stroke	Self report medical history	0.5 (0.01 to 2.6)	2.0 (0.5 to 4.5)	0.26 (0.01 to 2.72)	Not clearly reported	

Appendix C11. Association between urbanization and cancer

Author (year of publication)	Country (year of conduct)	Type of cancer	Definition	ES for urban exposure	ES for comparison	Crude ES ratio	Adjusted ES ratio	Adjusted factors
Armstrong (1977)	Malaysia (1968-1974)	Nasopharyngeal carcinoma	Histologically confirmed	10.2 Incidence rate per 100,000/year in men	8.9 Incidence rate per 100,000/year in men		1.15 in men	Sex specific
				5.4 Incidence rate per 100,000/year n women	3.5 Incidence rate per 100,000/year in women		1.54 in women	
Jordan 2009	Thailand 2005	Breast Cancer	Self confirmed reported of being diagnosed by doctor	Cant be calculated	Can't be calculated		0.84 (0.43 to 1.67) for current urban residence	Age matched, female only
							1.56 (0.80 to 3.04) for urban residence at age 10-12	
Phomphet 2011	Thailand 2009	Cancer	Self reported history of being diagnosed by doctor	0 (0.0 to 5.3)	1.4 (0.3 to 4.0) in semi-urban group	0 (0.0 to 4.0) compared to semi-urban group	Can't be calculated	None
					0 (0.0 to 6.4) in remote rural group			
Simarak 1979	Thailand 1971	Oral and oropharynx cancer	Presumptive diagnosis	Cant be calculated	Can't be calculated		0.38 (0.13 to 0.93) in men	Sex specific and age stratified selection of controls
							0.39 (0.13 to 0.99) in women	
		Larynx and hypo pharynx	Presumptive diagnosis	Cant be calculated	Can't be calculated		0.94 (0.53 to 1.61) in men	
		Lung	Presumptive diagnosis	Cant be calculated	Can't be calculated		1.40 (0.76 to 2.53) in men	
							2.03 (1.10 to 3.72) in women	

* ES= effect size which differs by study design

Appendix C11. Association between urbanization and cancer (con.)

Author (year of publication)	Country (year of conduct)	Type of cancer	Definition	ES for urban exposure	ES for comparison	Crude ES ratio	Adjusted ES ratio	Adjusted factors
Bovill (1975)	Malaysia (1969-1972)	Osteogenic sarcoma	63/68 patients had biopsy	0.294 (0.202 to 0.412) per 100,000 person year	0.116 (0.077 to 0.168) per 100,000 person year	2.53 (1.48 to 4.34)	1.72 (0.78 to 3.84) in Chinese racial groups 2.51 (0.95 to 6.36) in Malay racial group 4.27 (0.81 to 42.2) in Indian racial group	Ethnicity

- ES= effect size which differs by study design

Appendix C12. Association between urbanization and chronic respiratory disease

Author (year of publication)	Country (year of conduct)	Respiratory disease	Definition		Prevalence (%) in urban exposure group (95% CI)	Prevalence (%) in comparison group (95% CI)	Crude odds ratio (95% CI)	Adjusted odds ratio (95% CI)	Adjusted factors
Abong (2012)	Philippines (2010)	Allergic Rhinitis	Standardized 4-item questionnaire, validated locally, base on ISSAC instrument		18.0 (16.7 to 19.3) Overall	22.0 (20.8 to 23.4) overall	0.77 (0.69 to 0.87) overall	0.72 (0.61 to 0.86) in men	Separate analysis by sex
					17.2 (15.3 to 19.2) in men	22.3 (20.4 to 24.3) in men			
					18.5 (16.8 to 20.3) in women	22 (20.2 to 23.9) in women		0.80 (0.68 to 0.94) in women	
Chai (2004)	Vietnam (1999 and 2001)	Atopic symptoms	Nine ISSAC symptoms: 1) ever wheeze; 2) wheeze in last 12 months; 3) wheeze disturb sleep; 4)ever asthma; 5) doctor diagnosed asthma; 6) Ever AR; 7) AR-conjunctivitis in last 12 months; 8) ever hay fever 9) doctor diagnosed hay fever		Evidence that urban exposure in associated with lower prevalence of 3) wheeze disturb sleep (p=0.07); 4) ever asthma (<0.001); 5) doctor diagnosed asthma (<0.001) 6) ever AR (p=0.06); 7) AR conjunctivitis in last 12 months (p=0.008 and 8) ever hay fever (p<0.001)			Not clearly reported	None
Zakaria (2012)	Malaysia	Asthma Severity in asthmatic children	Asthma severity using classification by National Heart, Lung and Blood Institute under the Asthma Education Prevention Program Expert Panel Report 2 using peak expiratory flow reading and questionnaire completed by parent	Intermittent	22.9	17.0	Not clearly reported	Adjusted OR for urban exposure with severity of asthma 2.583 (1.163 to 5.736)	Age and gender
				Mild persistent	49.3	67.9			
				Moderate persistent	25.3	12.2			
				Severe persistent	2.3	1.9			

Appendix C12. Association between urbanization and chronic respiratory disease (con.)

Author (year of publication)	Country (year of conduct)	Respiratory disease	Definition		Prevalence (%) in urban exposure group (95% CI)	Prevalence (%) in comparison group (95% CI)	Crude odds ratio (95% CI)	Adjusted odds ratio (95% CI)	Adjusted factors
Lam (2011)	Vietnam (2007-8)	Asthma	Self report physician diagnosis		3.9	3.8	Not reported	1.02 (0.74 to 1.37)	Age, sex, family history of disease and smoking status
		Chronic bronchitis	Self report physician diagnosis		4.1	2.9		1.34 (0.98 to 1.83)	
Lim (1991)	Malaysia (1984)	Asthma	Hospital Discharge note		9.1 (7.6 to 10.8)	6.0 (4.5 to 7.9)	1.55 (1.09 to 2.43)	Not clearly reported	None
Saim (1997)	Malaysia (1993)	Otitis Media with Effusion (OME)	OME diagnosed if child had abnormal otoscopic findings, absence of ipsilateral acoustic reflex and type B tympanogram. History with questionnaire		17.9 (14.8 to 21.3)	9.5 (7.1 to 12.2)	Not clearly reported	2.08 (1.43 to 3.04)	Age restricted range
Trakultivakorn (2007)	Thailand (1995 and 2001)	Asthma	Using questionnaire and Criteria for diagnosis according to ISSAC steering group	Age 6-7	11.0 (10.0 to 12.1) in 1995	5.5 (4.8 to 6.2) in 1995		2.13 (1.78 to 2.54) in 1995;	Age restricted range
					15.0 (13.8 to 16.2) in 2001	7.8 (6.9 to 8.8)		2.09 (1.77 to 2.46) in 2001	
				Age 13-14	13.5 (12.4 to 14.6) in 1995;	12.6 (11.6 to 13.7) in 1995;		1.11 (0.97 to 1.27) in 1995;	
					13.9 (12.9 to 14.9) in 2001	8.7 (7.8 to 9.7)		1.69 (1.46 to 1.96)	
		Wheezing at rest	Using video questionnaire and Criteria for diagnosis according to ISSAC steering group	Age 6-7	n/a	n/a		n/a	
				Age 13-14	14.1 (13.0 to 15.2) in 1995;	6.0 (5.3 to 6.8) in 1995;		2.56 (2.18 to 3.02) in 1995	
					11.5 (10.6 to 12.4) in 2001	4.8 (4.1 to 5.6) in 2001		2.57 (2.14 to 3.09) in 2001	

Appendix C12. Association between urbanization and chronic respiratory disease (con.)

Author (year of publication)	Country (year of conduct)	Respiratory disease	Definition		Prevalence (%) in urban exposure group (95% CI)	Prevalence (%) in comparison group (95% CI)	Crude odds ratio (95% CI)	Adjusted odds ratio (95% CI)	Adjusted factors
Trakultivakorn (2007) con.	Thailand (1995 and 2001) Con.	Rhinitis	Using questionnaire and Criteria for diagnosis according to ISSAC steering group	Age 6-7	32.6 (31.1 to 34.2) in 1995	18.5 (17.3 to 19.8) in 1995; 23.5 (22.0 to 25.0)		2.13 (1.91 to 2.38) in 1995	Age restricted range
					43.2 (41.5 to 44.9) in 2001	18.5 (17.3 to 19.8) in 1995; 23.5 (22.0 to 25.0)		2.48 (2.22 to 2.76) in 2001	
				Age 13-14	43.4 (41.8 to 45.0) in 1995	38.3 (36.8 to 39.8) in 1995		1.23 (1.12 to 1.35) in 1995	
					57.4 (56.0 to 58.8) in 2001	46.6 (45.0 to 48.3) in 2001		1.54 (1.41 to 1.69 (in 2001	
		Rhinoconjunctivitis	Using questionnaire and Criteria for diagnosis according to ISSAC steering group	Age 6-7	10.0 (9.0 to 11.0) in 1995	4.8 (4.1 to 5.5) in 1995		2.20 (1.82 to 2.66) in 1995	
					13.4 (12.3 to 14.6) in 2001	6.2 (5.3 to 7.1) in 2001		2.35 (1.96 to 2.81)	
				Age 13-14	15.4 (14.2 to 16.6) in 1995	15.6 (14.5 to 16.8) in 1995		0.98 (0.87 to 1.12) in 1995	
					23.9 (22.6 to 25.1) in 2001	17.2 (16.0 to 18.5) in 2001		1.51 (1.35 to 1.69) in 2001	
		Eczema	Using questionnaire and Criteria for diagnosis according to ISSAC steering group	Age 6-7	12.5 (11.4 to 13.6) in 1995	11.4 (10.4 to 12.4) in 1995		1.04 (0.91 to 1.20) in 1995	
					13.3 (12.2 to 14.5) in 2001	16.3 (15.0 to 17.6) in 2001		0.79 (0.68 to 0.90) in 2001	
				Age 13-14	6.8 (6.0 to 7.6) in 1995	9.6 (8.7 to 10.6) in 1995		0.68 (0.58 to 0.81) in 1995	
					10.4 (9.5 to 11.3) in 2001	8.6 (7.7 to 9.6) in 2001		1.23 (1.06 to 1.44) in 2001	
Sriyaraj (2008)	Thailand (2003)	Asthma	Using questionnaire and Criteria for diagnosis according to ISSAC steering group		5.5 (3.3 to 8.5)	5.4 (2.5 to 10.0)		1.02 (0.43 to 2.61)	Age restricted to 6 to 12
		Atopic dermatitis			12.5 (9.2 to 16.4)	7.2 (3.8 to 12.3)		1.83 (0.91 to 3.92)	
		Rhinitis			24.3 (19.9 to 29.2)	15.7 (10.5 to 22.1)		1.73 (1.05 to 2.94)	

Appendix C12. Association between urbanization and chronic respiratory disease (con.)

Author (year of publication)	Country (year of conduct)	Respiratory disease	Definition	Prevalence (%) in urban exposure group (95% CI)	Prevalence (%) in comparison group (95% CI)	Crude odds ratio (95% CI)	Adjusted odds ratio (95% CI)	Adjusted factors
Goh (1986)	Singapore (1983)	Asthma	Parental/Guardian reported of diagnosed by doctor	8.8 (7.1 to 10.7)	6.7 (5.2 to 8.4)	1.34 (0.95 to 1.91)		Age restricted to 6 to 14
		Bronchitis/Pneumonia	Parental/Guardian reported of diagnosed by doctor	4.4 (3.2 to 5.9)	5.2 (3.9 to 6.7)	0.85 (0.55 to 1.30)		
		Blocked/running nose	Parental/Guardian reported	25.8 (23.1 to 28.6)	25.0 (22.3 to 27.7)	1.04 (0.85 to 1.28)		
		Eye irritation within 12 months	Parental/Guardian reported	6.0 (4.6 to 7.7)	6.8 (5.4 to 8.6)	0.87 (0.60 to 1.27)		

Appendix C13. Association between urbanization and diabetes

Author (year of publication)	Country (year of conduct)	DM Definition	Prevalence (%) in urban exposure group (95% CI)	Prevalence (%) in comparison group (95% CI)	Crude odds ratio (95% CI)	Adjusted odds ratio (95% CI)	Adjusted factors
Aekplakorn (2007)	Thailand (2004)	Fasting plasma glucose (FPG) ≥7 mmol/L, used of medication for treatment of diabetes during previous 2 weeks or report of previous diagnosis by doctor	Approx. 8 in male	Approx. 4 in male	Not clearly reported	Not clearly reported	Age and sex standardized to Thai population in 2004
			Approx. 8 in female	Approx. 7 in female			
Aekplakorn (2011)	Thailand (2000)	FPG ≥100 mg/dL (5.6 mmol/L) or previously diagnosed with type 2 diabetes	42.4 (37.2 to 47.7) in men	28.6 (20.6 to 36.6) in men	Not clearly reported	Not clearly reported	Age and sex standardized to Thai population in 2000
			38.5 (33.4 to 43.6) in women	21.1 (17.2 to 25.0) in women			
Aekplakorn (2011)	Thailand (2009)	FPG ≥7 mmol/L, used of medication for treatment of diabetes during previous 2 weeks or report of previous diagnosis by doctor	Approx. 7.5 in male	Approx. 5 in male	Not clearly reported	Not clearly reported	Age and sex standardized to Thai population in 2009
			Approx. 10 in women	Approx. 7.5 in women			
Ali* (1993)	Malaysia (1991)	A fasting venous whole blood glucose level of 6.7 mmol/L and a 2-h venous whole blood glucose level of > 10.0 mmol/L were diagnostic for diabetes.	7.7 (2.9-16.9) in Kamong (MAL)	7.4 (3.0-15.5) in koyan (MAL rural)	Not clearly reported	Not clearly reported	Age adjusted prevalence, stratified by ethnicity
				2.7 (0.6 to 8.1) in Ulu sungai (MAL remote rural)			
			0 in Lanjan (ABO)	1.7 (0.1 to 9.5) in betau (ABO rural)			
				and 0 in Lanai (ABO remote rural)			

* MAL = Malaysian population, ABO = aborigines (Oran Asli)

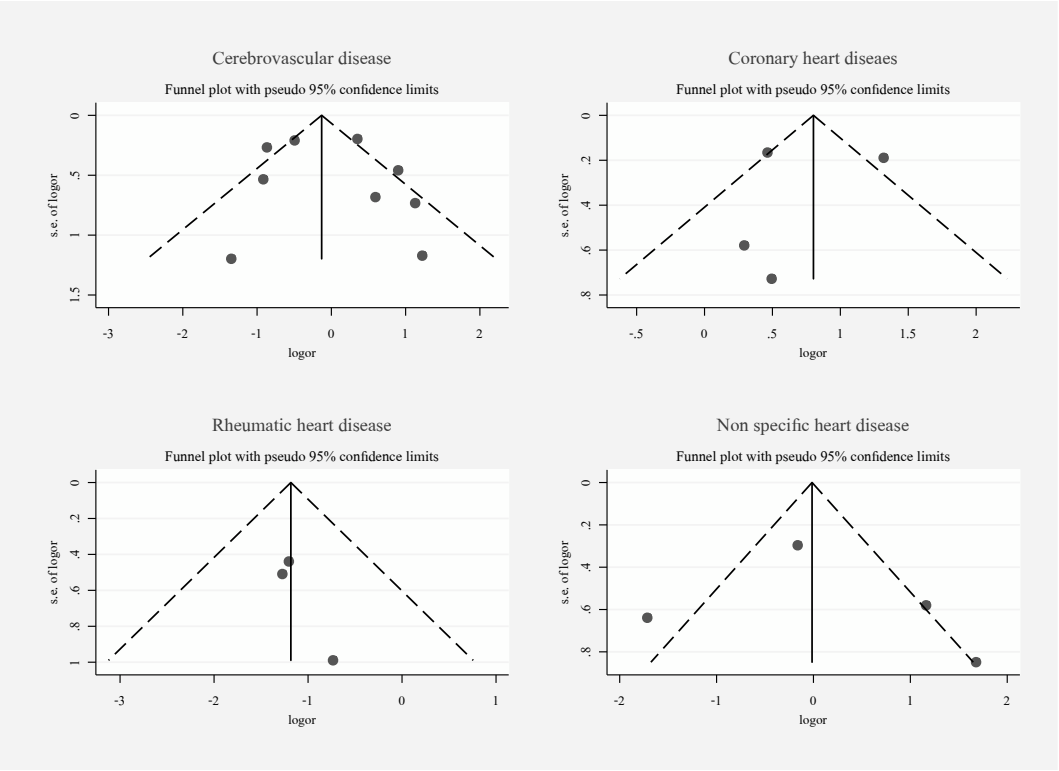
Appendix C13. Association between urbanization and diabetes (con.)

Author (year of publication)	Country (year of conduct)	DM Definition		Prevalence (%) in urban exposure group (95% CI)	Prevalence (%) in comparison group (95% CI)	Crude odds ratio (95% CI)	Adjusted odds ratio (95% CI)	Adjusted factors
Baltazar (2004)	Philippines (2000)	History of diabetes or 2-hour blood glucose value equivalent to ≥11.1 mmol/l	Men	5.8 (1.6 to 9.9) in National Capital Region (NCR);	3.6 (0.5 to 6.7) in urban Luzon 3.3 (0.5 to 6.1) in Rural Luzon	Not clearly reported	Not clearly reported	Age standardized to WHO World standard population
			Women	4.8 (1.9 to 7.6) in NCR	5.6(2.8-8.4) in urban Luzon 5.7 (3.0 to 8.5) rural Luzon			
Chailurkit (2012)	Thailand (2008)	A previous diagnosis of diabetes by physician and intake of hypoglycaemic drug during 2 weeks prior to the study or (ii) individuals who had a fasting plasma glucose concentration of 7·0 mM at the time of the present study		13.2 (11.5 to 15.1)	7.4 (6.0 to 9.1)	1.90 (1.45 to 2.50)	1.24 (0.35 to 4.44)*	Age, sex, BMI smoking, alcohol drinking, physical activity and vitamin D status *Significant interaction term between urban exposure and age(years) OR 1.0 1 (1.0 to 1.02)
Ishine (2006)	Thailand (2005)	Casual glucose (fasting and non fasting) ≥ 140 mg/dL		38.3 (31.6 to 45.2)	34.3 (27.8 to 41.4)	1.18 (0.77 to 1.81)	Not clearly reported	Age restricted population
Ishine (2005)	Vietnam (2003)	Casual glucose (fasting and non fasting) ≥ 140 mg/dL		4.3 (1.9 to 8.3)	5.5 (2.6 to 9.7)	0.79 (0.26 to 2.29)	Not clearly reported	Age restricted population
King (2005)	Cambodia (2004)	Currently taking diabetic medication or capillary blood glucose concentration of 11·1 mmol/L or greater, 2 h after a 75 g glucose load preceded by at least 8 h fasting		11.4 (9.6 to 13.3) all 11.5 (8.7 to 14.8) in men 11.3 (0.9 to 13.8) in women	4.8 (3.6 to 6.3) all 4.8 (2.9 to 7.5) in men 4.9 (3.3 to 6.8) in women	2.52 (1.79 to 3.59) all	2.57 (1.44 to 4.77) in men 2.49 (1.62 to 3.89) in women	Separate analysis by sex
Lim (1991)	Malaysia (1987)	Diagnosis on hospital discharge note		19.9 (17.8 to 22.2)	14.1 (11.7 to 16.7)	1.52 (1.19 to 1.95)	Not clearly reported	None
Mohamud 2011	Malaysia 2006	Fasting Plasma Glucose ≥ 5.6 or on medication for diabetes		34.9 (32.9 to 37.0)	38.6 (36.4 to 40.7)	0.85 (0.75 to 0.97)	Not clearly reported	None

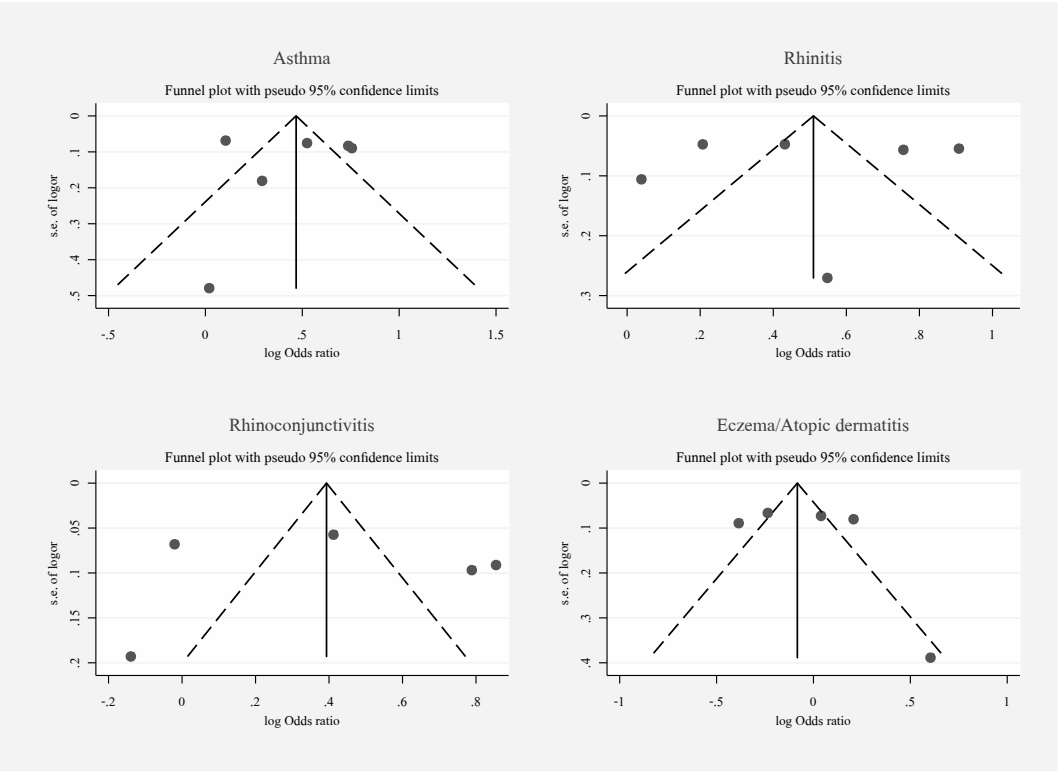
Appendix C13. Association between urbanization and diabetes (con.)

Author (year of publication)	Country (year of conduct)	DM Definition	Prevalence (%) in urban exposure group (95% CI)	Prevalence (%) in comparison group (95% CI)	Crude odds ratio (95% CI)	Adjusted odds ratio (95% CI)	Adjusted factors
Porapakkham (2008)	Thailand (2004)	FPG ≥7 mmol/l (126mg/dL), used of medication for treatment of diabetes during previous 2 weeks or report of previous diagnosis by doctor	16.9 (15.4 to 18.6) in men	11.3 (9.9 to 12.8) in men	Not clearly stated	Not clearly stated	Sex
			20.5 (19.1 to 22.0) in women	15.2 (13.8 to 16.7) in women			
Phomphet (2011)	Thailand (2008)	Self report previous diagnosis by doctor	7.3 (2.4 to 16.3)	10.8 (6.9 to 15.7) in semi urban	0.66 (0.19 to 1.88) to semi urban	Not clearly reported	None
				8.9 (3.0 to 19.6) in remote rural	0.81 (0.18 to 3.3) to remote rural		
Surinyawongpaisal (2003)	Thailand (2000)	FPG ≥7 mmol/l (126mg/dL), or report of previous diagnosis by doctor	11.9 (10.8 to 13.1) all	8.5 (7.4 to 9.8) all	1.45 (1.20 to 1.76) all	1.39 (1.02 to 1.89) in men	Sex
			11.1 (9.3 to 13.0) men;	8.2 (6.5 to 10.1) men			
			12.6 (11.1 to 14.1) women	8.8 (7.2 to 10.5) in women		1.50 (1.17 to 1.92) in women	
Wada (2005)	Myanmar (2004)	Casual glucose (fasting and non fasting) ≥ 140 mg/dL	18.2 (13.2 to 24.1)	15.1 (9.2 to 22.4)	1.26 (0.67 to 2.44)	None	Age restricted
Wada (2005)	Indonesia (2003)	Casual glucose (fasting and non fasting) ≥ 140 mg/dL	11.9 (7.8 to 17.1)	2.0 (0.7 to 5.1)	5.97 (2.18 to 20.30)	None	Age restricted

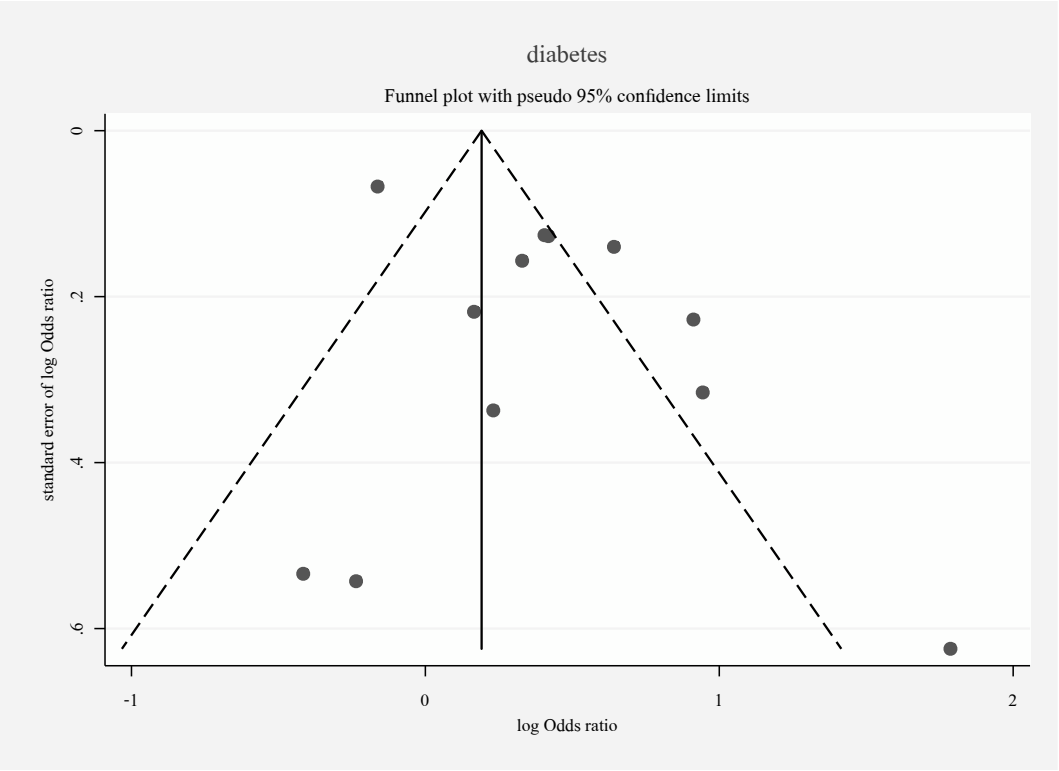
Appendix C14. Funnel plots of results included in review for cardiovascular disease



Appendix C15. Funnel plots of results included in review for respiratory disease in children



Appendix C16. Funnel plots of results included in review for diabetes



Appendix C17. Summary of bias of studies reporting association between urbanization and cardiovascular Disease

Study	Selection bias	Information bias in exposure measurement	Information bias in outcome (CVD)	Confounding
Fitzpatrick 2011	Low risk	Low risk	Unclear risk	Low risk
Myo Thet 1992	Low risk	Low risk	Low risk	Unclear risk, only sex adjusted
Wada 2005 (Myanmar)	Unclear risk	Low risk	Unclear risk	Low for IHD, unclear for stroke
Lim 1991	Unclear risk	Unclear risk	Low risk	Unclear, no adjustments
Ishine 2006	Unclear risk	Low risk	Unclear risk	Unclear, age restricted population
Ishine 2005	Unclear risk	Low risk	Unclear risk	Unclear, age restricted population
Wada 2005 (Indonesia)	Unclear risk	Low risk	Unclear risk	Unclear, age restricted population

Appendix C18. Summary of bias of studies reporting association between urbanization and cancer

Study	Selection bias	Information bias in exposure measurement	Information bias in outcome cancer	confounding
Armstrong 1978	Unclear risk	Low risk	Low risk	Unclear, only sex-specific analysis
Jordan 2009	Low risk, nested case control	Low risk, small validation study of self report urban/rural status	Unclear risk, Controls were not confirmed	Low risk
Phomphet 2011	Unclear risk	Low risk	Unclear risk, self report	Unclear, no adjustments
Simarak 1977	Unclear, hospital controls	Unclear	Unclear, uses presumptive diagnosis, only about 50% were histologically confirmed	Low risk
Bovill 1975	Low risk	Low risk	Low risk	Unclear risk

Appendix C19. Summary of bias of studies reporting association between urbanization and chronic respiratory disease

Study	Selection bias	Information bias in exposure measurement	Information bias in outcome respiratory disease	confounding
Abong 2012	Low risk	Low risk	Low risk	Unclear, only sex-specific analysis
Chai 2004	Low risk	Unclear risk, exposure defined by location of school, 20 kilometers apart	Low risk	Unclear, no adjustments
Zakaria 2012	Unclear, not stated	Unclear risk, exposure by school	Low risk	Low risk
Lam 2011	Low risk	Low risk	Unclear risk	Low risk
Lim 1991	Unclear risk	Unclear risk	Low risk	Unclear no adjustments
Saim 1997	Unclear risk	Low risk	Low risk	Unclear risk, only age adjusted
Trakultivakorn 2007	Low risk	Low risk, schools but far apart	Low risk	Unclear risk, only age adjusted
Sriyaraj 2008	Low risk	Low risk, schools based on pollution	Low risk	Unclear risk, only age adjusted
Goh 1986	Low risk	Low risk, schools based on pollution	Low risk	Unclear risk, only age adjusted

Appendix C20. Summary of bias of studies reporting association between urbanization and diabetes

Study	Selection bias	Information bias in exposure measurement	Information bias in outcome DM	confounding
Aekplakorn 2007	Low risk	Low risk	Low risk	Low risk
Aekplakorn 2011 (Ref. 37)	Low risk	Low risk	Low risk	Low risk
Aekplarkorn 2011 (Ref. 38)	Low risk	Low risk	Low risk	Low risk
Ali 1993	Low risk	Low risk	Low risk	Unclear, not adjusted for sex
Baltazar 2004	Low risk	Low risk	Low risk	Low risk
Chailurkit 2012	Unclear risk	Low risk	Low risk	Low risk
Ishine 2006	Unclear risk	Low risk	Unclear risk	Unclear risk, age restricted population
Ishine 2005	Unclear risk	Low risk	Unclear risk	Unclear risk, age restricted population
King 2005	Low risk	Low risk	Low risk	Low risk (standardization)
Lim 1991	Unclear risk	Unclear risk	Low risk	Unclear risk No adjustments
Mohamud 2011	Unclear risk	Low risk	Low risk	Unclear risk
Porapakkham 2008	Low risk	Low risk	Low risk	Unclear risk Age restricted
Phomphet 2011	Unclear risk	Low risk	Unclear risk, self report	Unclear No adjustments
Surinyawongpaisal 2003	Low risk	Low risk	Low risk	Unclear risk
Wada (2005)	Unclear risk	Low risk	Unclear risk	Unclear risk, age restricted population
Wada (2005)	Unclear risk	Low risk	Unclear risk	Unclear risk, age restricted population

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Appendix E. Ethical approval from Chiang Mai University for 2008 survey

No. **032/2008**

Certificate of Approval

Name of Ethics Committee : Research Ethics Committee **3** , Faculty of Medicine , Chiang Mai University
Address of Ethics Committee : 110 Intavaroros Rd., Amphoe Muang, Chiang Mai, Thailand 50200

Principal Investigator : Panida Tongtong,M.D.
Department of Family Medicine, Faculty of Medicine,
Chiang Mai University.

Protocol title: Health Survey of Personnel in Faculty of Medicine,Chiang Mai University

Study code : 08JAN041817

Documents filed	Document reference
Research protocol	- Version date 31 January 2008
Informed consent document /Patient information sheet	- Version 2 date 22 January 2008
Curriculum vitae of Principal Investigator	- Version date 31 January 2008
Questionnaire	- Version date 31 January 2008

Opinion of the Ethics Committee/Institutional Review Board
___√___ Approval
_____ Conditional approval (specify in space below)

DECISION: By expedited review process

Date of Review : January 31 , 2008 **Expiration Date:** March 31 , 2008

This Ethics Committee is organized and operates according to principles of good clinical practice and relevant international ethical guidelines, applicable laws, and regulations.

Signed: .....P. Kulapongs.....**Emeritus Professor Panja Kulapongs, M.D.**
(Chairperson, Faculty of Medicine)

Signed: .....N. Nantachit.....**Associate Professor Niwes Nantachit, M.D.**
(Dean, Faculty of Medicine)

GENERAL CONDITIONS OF APPROVAL:

Please refer to www.med.cmu.ac.th/research/ethics/inv_sop_announce.pdf, article 13. In particular, approval of this study must be renewed at least one month before the expiration date if work is to continue. Prior Research Ethics Committee approval is required before implementing any changes in the consent documents or protocol unless those changes are required urgently for the safely of subjects.

Appendix F. Additional analysis comparing those still working in CMU in 2011 and those lost to follow up by 2011

Appendix F1. Number of participants by age group (from 2008 Data)

	<25	25-29	30-34	35-39	40-44	45-49	50-54	55-59	>=60	Total
Without migration status	87	186	84	26	29	25	43	131	7	618
(%)	14.08	30.10	13.59	4.21	4.69	4.05	6.96	21.20	1.13	100.00
With migration status	150	425	525	471	694	626	487	146	1	3,525
(%)	4.26	12.06	14.89	13.36	19.69	17.76	13.82	4.14	0.03	100.00
Total 2008	237	611	609	497	723	651	530	277	8	4,143
	5.72	14.75	14.70	12.00	17.45	15.71	12.79	6.69	0.19	100.00

Mean (SD) Age for those without migration status	37.6 (13.53)
Mean (SD) Age for those who with migration status	40.0 (9.10)
Mean (SD) Age 2008 (overall)	38.7 (9.9)

Appendix F2. Assessing gender differences between participants with available migrant status data compared to those without migration status

	Female	Male	Total
Without migration status	427	191	618
(%)	69.09	30.91	100.00
With migration status	2,520	1,005	3,525
(%)	71.49	28.51	100.00
Total	2,947	1,196	4,143
	71.13	28.87	100.00

Appendix F3 Comparison between participants with available migrant status data compared to those without migration status by NCD outcomes

Outcome	Without migration status (N=618)	With migration status (N=3525)	p-value
SBP	116.0 (13.2)	116.1 (13.0)	0.94
DBP	73.3 (9.9)	74.2 (10.1)	0.04
BMI	22.1 (3.6)	22.9 (3.5)	<0.001
FBS[3]	89.9 (18.0)	89.0 (20.6)	0.55
TC[4]	220.5 (49.8)	219.6 (41.1)	0.79
LDL[2]	129.9 (44.7)	131.2 (36.7)	0.67
HDL[2]	56.9 (15.4)	56.4 (13.6)	0.66

Appendix F4. Comparison between participants with available migrant status data compared to those without migration status by NCD outcomes

Outcome	Without migration status (N=618)	With migration status (N=3525)	p-value
HT	67 (10.8%)	434 (12.3%)	0.30
Over weight	230 (37.2%)	1,531 (43.4%)	0.004
Obesity	120 (19.4%)	790 (22.4)	0.097
IFG[1]	20 (8.1%)	128 (5.5%)	0.088
DM[1]	8 (3.3%)	56 (2.4%)	0.435
High LDL[2]	76 (46.9%)	937 (49.3%)	0.556
Low HDL[2]	44 (27.2%)	419 (22.0%)	0.133
Current smoking	50 (8.1%)	209 (5.6%)	0.041

[3] number of observations in without migration status group = 246, number of observations in with migration status group = 2,299

[4] number of observations in without migration status group = 162, number of observations in with migration status group = 1,901

Appendix G. Ethical approval from Chiang Mai University for 2013 survey (translated)

(Translation)

[Official Emblem]

Document No. 069/2555

Certificate of Approval for Human Research Project

Ethical Review Committee: Ethical Review Committee Batch # 3

Faculty of Medicine, Chiang Mai University

Address: 110 Inthawarorot Rd. Sriphum, Muang, Chiang Mai 50200

Research Project Head: Chaisiri Angkurawaranon, M.D.

Affiliation: Department of Family Medicine, Faculty of Medicine, Chiang Mai University

Research Project Title: Epidemiological Change in the North of Thailand: Cohort Study of Health Care Workers

Study Code: FAM-12-888-EX / Research ID: 888

Research Scholarship Grantor: Faculty of Medicine Research Fund

Approved Document	Approved Volume
Research Project	Volume 10 Dated February 3, 2012
Information for Volunteers/ Letter of Consent	Volume 10 Dated February 3, 2012
Memorandum Form (Thai Version)	Volume 10 Dated February 3, 2012
Memorandum Form (English Version)	Volume 10 Dated February 3, 2012
Autobiography of the Project Head	Volume 10 Dated February 3, 2012

Research Project Consideration Process: Expedited Review

Consideration Results: The Ethical Review Committee has considered to:

[/] approve to conduct the research within the proposed scope of study.

[ ] approve to conduct the research under the following condition (s).

.....

.....

Approved on February 29, 2012 Effective until February 28, 2013

Certified Correct Translation
Assanee Nantachaipan
(Mr. Assanee Nantachaipan)
Translator
Language Institute Chiang Mai
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22 MAY 2012

Appendix H. Ethical approval from London School of Hygiene and Tropical Medicine for 2013 survey

London School of Hygiene & Tropical Medicine
Keppel Street, London WC1E 7HT
United Kingdom
Switchboard: +44 (0)20 7636 8636

www.lshtm.ac.uk

Observational / Interventions Research Ethics Committee

Chaisiri Angkurawaranon
Research Student
NCDE/EPH
LSHTM

30 October 2012

Dear Ms Angkurawaranon,

Study Title: **Association between Urbanization and Non-communicable Disease Risk Factor: An Internal Migration Study Among Health Personnel in Northern Thailand**
LSHTM ethics ref: **6251**

Thank you for your letter of 30 October 2012, responding to the Observational Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Conditions of the favourable opinion

Approval is dependent on local ethical approval having been received, where relevant.

Approved documents

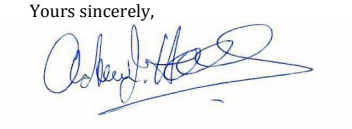
The final list of documents reviewed and approved by the Committee is as follows:

Document	Version	Date
LSHTM ethics application	n/a	09/08/2012
Protocol	V 1	03/02/2012
Information Sheet	V 1	03/02/2012
Consent form	V 1	03/02/2012

After ethical review

Any subsequent changes to the application must be submitted to the Committee via an E2 amendment form. All studies are also required to notify the ethics committee of any serious adverse events which occur during the project via form E4. At the end of the study, please notify the committee via form E5.

Yours sincerely,



Professor Andrew J Hall
Chair
ethics@lshtm.ac.uk
http://intra.lshtm.ac.uk/management/committees/ethics/

Appendix I. Materials for 2013 survey: questionnaires, record forms for physical examination and materials used during interview of non-communicable disease risk factors

Appendix I1. Questionnaire for 2013 online survey on demographics, occupational risk factors and family history of underlying diseases

โครงการ Healthy Suandokคัดกรองและติดตามโรคเรื้องรังในบุคลากรคณะแพทย์

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ส่วนที่ 2 เกี่ยวกับประวัติโรคเรื้อรัง ของท่าน รวมถึงประวัติโรคเรื้อรังในบิดา มารดาของท่าน

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7	เพศ	ชาย 0 หญิง 1	
8	สิทธิการรักษา	ข้าราชการ 0 ประกันสังคม 1 บัตรทอง 2 ประกันชีวิต 3 อื่นๆ 4	

Participant Id Number ☐☐☐ ☐☐☐ ☐☐☐

NO	Consent	Response	Code
9	ยินยอมเข้าโครงการ	ยินยอม 1 ไม่ยินยอม 0 If NO, END	
11	หมายเลขโทรศัพท์ติดต่อ		

ส่วนที่ 1 ประวัติทั่วไปและการทำงาน

Demographics and occupational Status			
NO	Question	Response	Code
12	ลักษณะงาน	อาจารย์แพทย์ 0 อาจารย์ 1 แพทย์ / ทันตแพทย์ 2 เภสัชการ 3 พยาบาล 4 ผู้ช่วยพยาบาล 5 นักวิชาการวิชาชีพ 6 นักวิชาการ 7 ผู้ปฏิบัติงาน (ธุรการ เลขานุการ) 8 ผู้ปฏิบัติงาน คนงาน 9	
13	การศึกษาสูงสุด	ไม่ได้รับ 0 ต่ำกว่าประถมศึกษา 1 จบระดับประถมศึกษา 2 จบระดับ ม.ต้น 3 จบประดับม.ปลาย 4 ระดับปริญญาตรี 5 สูงกว่าปริญญาตรี 6	
14	สถานะภาพ	โสด 0 แต่งงาน ยังอาศัยอยู่ด้วยกัน 1 แต่งงาน แยกกันอยู่ 2 หย่า 3 หม้าย 4 มีคู่ อาศัยอยู่ร่มกัน 5 ไม่ระบุ 88	
15	จำนวนสมาชิกในครอบครัวที่อายุน้อยกว่า 18 ปี	จำนวน ☐☐	
16	จำนวนสมาชิกในครอบครัวที่อายุมากกว่า 18 ปี รวมตัวท่าน	จำนวน ☐☐	

เลขที่โครงการ ☐☐☐ ☐☐☐ ☐☐☐

NO	Question	Response	Code
17	รายได้เฉลี่ยครัวเรือน ต่อ เดือน	<10,000 0 10,000 ≤ 20,000 1 20,000 ≤ 30,000 2 30,000 ≤ 40,000 3 40,000 ≤ 50,000 4 50,000 ≤ 60,000 5 60,000 ≤ 70,000 6 70,000 ≤ 80.000 7 80,000 ≤ 90.000 8 90,000 ≤ 100,000 9 > 100,000 10	
18	อายุเมื่อท่านเริ่มปฏิบัติงานในคณะแพทยศาสตร์	อายุ ☐☐	
19	ท่านเคยทำงานเป็น กะ หรือไม่ (การปฏิบัติงาน เป็นช่วงเวลา)	เคย 1 ไม่เคย 0 ถ้าไม่เคย ข้ามไป ข้อที่ 26	
20	ภายใน 12 เดือนที่ผ่านมาท่านทำงาน เป็นกะหรือไม่	ทำ 1 ไม่ทำ 0 ถ้าไม่เคย ข้ามไป ข้อที่ 23	
21	ใน 12 เดือนที่ผ่านมา โดยเฉลี่ยใน 1 เดือนท่านทำงานกะบ่าย (16.00 – 24.00) กี่เวร	จำนวน ☐☐	
22	ใน 12 เดือนที่ผ่านมา โดยเฉลี่ยใน เดือนท่าน 1ทำงานกะดึก (00.00 – 08.00) กี่เวร	จำนวน ☐☐	
23	ท่านเริ่มทำงานเป็น กะ ตั้งแต่อายุ	ปี ☐☐☐☐	
24	ปัจจุบัน ท่านทำงาน เป็นกะหรือไม่	ทำ 1 ถ้าทำ ข้ามไป ข้อที่ 23 ไม่ทำ 0	
25	ท่านเลิกทำงานเป็น กะ ตั้งแต่อายุ	ปี ☐☐☐☐	
26	ช่วงหนึ่งปีที่ผ่านมา โดยเฉลี่ยแล้วท่านมีวันพักที่ไม่ต้องมาทำงานกี่วัน ต่อ 1 เดือน	จำนวนวัน ☐☐	

เลขที่โครงการ ☐☐☐ ☐☐☐ ☐☐☐

NO	Question	Response	Code
27	ช่วงหนึ่งปีที่ผ่านมา โดยเฉลี่ยแล้วท่านนอนหลับ กี่ ชั่วโมงต่อ 1 วัน	ชั่วโมง ☐☐	

ส่วนที่ 1 แบบทดสอบการทำงานและภาวะเหนื่อยล้าจากการทำงาน ในคณะแพทยศาสตร์

NO	ข้อความเกี่ยวกับความรู้สึกของท่าน	ไม่เคยรู้สึกเช่นนั้น	ปีละ 2-3 ครั้ง	เดือนละ 1 ครั้ง	เดือนละ 2-3 ครั้ง	สัปดาห์ ละ 1 ครั้ง	สัปดาห์ละ 2-3 ครั้ง	ทุก ๆ วัน
28	ฉันรู้สึกจิตใจห่อเหี่ยวจากการทำงาน							
29	ฉันรู้สึกหมดเรี่ยวแรง เมื่อสิ้นสุดเวลาการทำงาน							
30	ฉันรู้สึกเพลียเมื่อตื่นนอนตอนเช้าและรู้ว่าต้องเผชิญกับการทำ งานอีกวัน							
31	ฉันสามารถเข้าใจถึงความรู้สึก ของ ผู้ป่วยที่มีต่อสิ่งต่างๆ ได้ง่าย							
32	ฉันรู้สึกว่าฉันได้ปฏิบัติต่อผู้ป่วย บางคนเสมือนเขาเป็นสิ่งที่ไร้ชีวิต จิตใจ							
33	การทำงานเกี่ยวกับการบริการ ผู้คนตลอดวันเป็นสิ่งที่ตึงเครียดสำหรับฉัน							
34	34. ฉันสามารถแก้ปัญหาของผู้ป่วย ได้อย่างมีประสิทธิภาพ							
35	ฉันรู้สึกเหนื่อยหน่ายในภาระงาน ของฉัน							
36	ฉันรู้สึกแน่ใจว่างานของฉันมีอิทธิพลต่อชีวิตของผู้อื่น							
37	ฉันเปลี่ยนเป็นคนหยาบกระด้าง และไร้ความเมตตาต่อผู้คนมากขึ้น ตั้งแต่เข้ามาทำงาน							

เลขที่โครงการ ☐☐☐ ☐☐☐ ☐☐☐

ส่วนที่ 1 แบบทดสอบการทำงานและภาวะเหนื่อยล้าจากการทำงาน ในคณะแพทยศาสตร์

NO	ข้อความเกี่ยวกับความรู้สึกของท่าน	ไม่เคยรู้สึกเช่นนั้น	ปีละ 2-3 ครั้ง	เดือนละ 1 ครั้ง	เดือนละ 2-3 ครั้ง	สัปดาห์ ละ 1 ครั้ง	สัปดาห์ละ 2-3 ครั้ง	ทุก ๆ วัน
38	ฉันวิตกกังวลว่างานที่ฉันทำกำลังทำให้จิตใจของฉันแข็งกระด้างขึ้น							
39	ฉันรู้สึกเปี่ยมพลัง							
40	ฉันรู้สึกคับข้องใจในการทำงาน							
41	ฉันรู้สึกว่าฉันกำลังทำงาน ที่หนักมากเกินไป							
42	ฉันไม่เคยไม่ใจว่าอะไรจะเกิดขึ้นกับผู้ป่วยบางคน							
43	การทำงานกับผู้ป่วยโดยตรงทำให้ฉันรู้สึกเครียดมากเกินไป							
44	ฉันสามารถสร้างบรรยากาศที่ ผ่อนคลายให้กับผู้ป่วยได้ง่าย							
45	ฉันรู้สึกเป็นสุขใจหลังจากการ ทำงานกับผู้ป่วยอย่างใกล้ชิด							
46	ฉันได้สร้างสรรค์สิ่งที่ มีคุณค่ามาก มายในการทำงานนี้							
47	ฉันรู้สึกสิ้นหวัง							
48	ในการทำงานฉันสามารถเผชิญ ปัญหาทางอารมณ์ได้อย่างสงบ							
49	ฉันรู้สึกว่าได้รับการตำหนิจากผู้ป่วยในปัญหาบางอย่างที่ เกิดขึ้น							

เลขที่โครงการ ☐☐☐ ☐☐☐ ☐☐☐

ความเชื่อและความตั้งใจในเรื่องของการดื่มแอลกอฮอล์

คุณมีความเชื่อและความตั้งใจอย่างไรในเรื่องของการดื่มแอลกอฮอล์
(1= ไม่เห็นด้วยอย่างมาก 2= ไม่เห็นด้วย 3= ไม่แน่ใจ 4= เห็นด้วย 5= เห็นด้วยอย่างมาก)

ข้อ	ความเชื่อและความตั้งใจในเรื่องของการดื่มแอลกอฮอล์	1	2	3	4	5
50	หลักฐานทางการแพทย์ที่แสดงถึงอันตรายของโรคต่างๆจากการ ดื่มแอลกอฮอล์ เป็นสิ่งที่เกินความจริง					
51	การดื่มแอลกอฮอล์ไม่ได้เสี่ยงอันตรายไปกว่าสิ่งอื่นๆที่ประชาชนทำกันอยู่หรอก					
52	อย่างไรก็ตามคุณก็จะต้องตายด้วยเหตุบางอย่าง ทำไมจะไม่ให้ความสนุกสนานแก่ชีวิตด้วยการดื่มแอลกอฮอล์”					
53	คุณคิดว่าคุณมียีนหรือบางอย่างที่ทำให้สุขภาพดี ซึ่งหมายความว่าคุณยังสามารถดื่มแอลกอฮอล์ได้ โดยไม่ได้รับอันตรายใดๆ					
54	คุณเพลิดเพลินในการดื่มแอลกอฮอล์มากกว่าที่จะหยุดดื่มมันได้					
55	การดื่มแอลกอฮอล์ทำให้คุณผ่อนคลาย เมื่อคุณเครียดหรือหงุดหงิด					
56	การดื่มแอลกอฮอล์ช่วยให้คุณมีสมาธิดีขึ้น					
57	การดื่มแอลกอฮอล์เป็นส่วนสำคัญของชีวิตคุณ					
58	การดื่มแอลกอฮอล์ช่วยให้คุณเข้าสังคมได้ง่ายขึ้น					

หากคุณไม่ได้ดื่มแอลกอฮอล์แล้วให้ข้ามข้อ 59 และ 60

59. คุณวางแผนในการหยุดดื่มแอลกอฮอล์หรือไม่

☐ วางแผนหยุดภายใน 1 เดือน
☐ วางแผนหยุดภายใน 6 เดือน
☐ วางแผนหยุดในอนาคตเกินกว่า 6 เดือน
☐ ไม่ได้วางแผนในการหยุดเลย

60. ถ้าคุณตัดสินใจที่จะเลิกดื่มแอลกอฮอล์อย่างเด็ดขาดภายในเวลา 6 เดือน คุณมีความมั่นใจมากแค่ไหนที่จะประสบความสำเร็จ?

☐ ไม่มั่นใจเล ☐ มั่นใจเล็กน้อย ☐ มั่นใจปานกลาง ☐ มั่นใจมาก ☐ มั่นใจมากที่สุด

เลขที่โครงการ ☐☐☐ ☐☐☐ ☐☐☐

ความเชื่อและความตั้งใจในเรื่องของการสูบบุหรี่

คุณมีความเชื่อและความตั้งใจอย่างไรในเรื่องของการสูบบุหรี่

(1= ไม่เห็นด้วยอย่างมาก 2= ไม่เห็นด้วย 3= ไม่แน่ใจ 4= เห็นด้วย 5= เห็นด้วยอย่างมาก)

ข้อ	ความเชื่อและความตั้งใจในเรื่องของการสูบบุหรี่	1	2	3	4	5
61	หลักฐานทางการแพทย์ที่แสดงถึงอันตรายของโรคต่างๆจากการสูบบุหรี่ เป็นสิ่งที่เกินความจริง					
62	การสูบบุหรี่ไม่ได้เสี่ยงอันตรายไปกว่าสิ่งอื่นๆที่ประชาชนทำกันอยู่หรอก					
63	อย่างไรก็ตามคุณก็จะต้องตายด้วยเหตุบางอย่าง ทำไมจะไม่ให้ความสนุกสนานแก่ชีวิตด้วยการสูบบุหรี่					
64	คุณคิดว่าคุณมียีนหรือบางอย่างที่ทำให้สุขภาพดี ซึ่งหมายความว่าคุณยังสามารถสูบบุหรี่ได้ โดยไม่ได้รับอันตรายใดๆ					
65	คุณเพลิดเพลินในการสูบบุหรี่มากกว่าที่จะหยุดสูบมันได้					
66	การสูบบุหรี่ทำให้คุณผ่อนคลาย เมื่อคุณเครียดหรือหงุดหงิด					
67	การสูบบุหรี่ช่วยให้คุณมีสมาธิดีขึ้น					
68	การสูบบุหรี่เป็นส่วนสำคัญของชีวิตคุณ					
69	การสูบบุหรี่ช่วยให้คุณเข้าสังคมได้ง่ายขึ้น					

หากคุณไม่ได้สูบบุหรี่แล้วให้ข้ามข้อ 70 และ ข้อ 71

70. “คุณวางแผนในการหยุดสูบบุหรี่หรือไม่”

☐ วางแผนหยุดภายใน 1 เดือน
☐ วางแผนหยุดภายใน 6 เดือน
☐ วางแผนหยุดในอนาคตเกินกว่า 6 เดือน
☐ ไม่ได้วางแผนในการหยุดเลย

71. “ถ้าคุณตัดสินใจที่จะเลิกสูบบุหรี่อย่างเด็ดขาดภายในเวลา 6 เดือน คุณมีความมั่นใจมากแค่ไหนที่จะประสบความสำเร็จ?”

☐ ไม่มั่นใจเลย ☐ มั่นใจเล็กน้อย ☐ มั่นใจปานกลาง ☐ มั่นใจมาก ☐ มั่นใจมากที่สุด

ส่วนที่ 2: ประวัติโรคเรื้อรัง

CORE: ประวัติความดันโลหิตสูง			
NO	Question	Response	Code
81	ท่านเคยได้รับการวัดความดันโลหิต โดยแพทย์ หรือ บุคลากรทางการแพทย์หรือไม่	เคย 1 ไม่เคย 0 *ถ้าไม่เคยข้ามไปข้อ 86*	
82	แพทย์ หรือ บุคลากรทางการแพทย์ เคยระบุว่าท่านเป็นโรคความดันโลหิตสูงหรือไม่	เคย 1 ไม่เคย 0 *ถ้าไม่เคยข้ามไปข้อ 86*	
83	ท่านเพิ่งได้รับการวินิจฉัยภายใน 12 เดือนที่ผ่านมา	ใช่ 1 ไม่ใช่ 0	
84	อายุเมื่อได้รับการวินิจฉัย (don't know 9999)	อายุ ☐☐☐☐	
85	ภายใน 2 สัปดาห์ ที่ผ่านมา ท่านได้ทานยา ควบคุมความดันโลหิตหรือไม่	ทานยา 1 ไม่ได้ทานยา 0	

CORE: ประวัติโรคเบาหวาน			
NO	Question	Response	Code
86	ท่านเคยได้รับ การตรวจระดับน้ำตาลในเลือด โดยแพทย์ หรือ บุคลากรทางการแพทย์หรือไม่	เคย 1 ไม่เคย 0 *ถ้าไม่เคยข้ามไปข้อ 92*	
87	แพทย์ หรือ บุคลากรทางการแพทย์ เคยระบุว่าท่านเป็นโรคเบาหวานหรือไม่	เคย 1 ไม่เคย 0 *ถ้าไม่เคยข้ามไปข้อ 92*	
88	ท่านเพิ่งได้รับการวินิจฉัยภายใน 12 เดือนที่ผ่านมา	ใช่ 1 ไม่ใช่ 2	
89	อายุ เมื่อได้รับการวินิจฉัย (don't know 9999)	อายุ ☐☐☐☐	
90	ภายใน 2 สัปดาห์ ที่ผ่านมา ท่านได้ฉีดยาอินซูลิน ควบตุมระดับน้ำตาลในเลือดหรือไม่	ฉีดยา 1 ไม่ได้ฉีดยา 0	
91	ภายใน 2 สัปดาห์ ที่ผ่านมา ท่านได้ทานยา ควบคุมระดับน้ำตาลในเลือดหรือไม่	ทานยา 1 ไม่ได้ทานยา 0	

CORE: ประวัติโรคไขมันโลหิตสูง			
NO	Question	Response	Code
92	ท่านเคยได้รับ การตรวจระดับไขมันในเลือดโดยแพทย์ หรือ บุคลากรทางการแพทย์หรือไม่	เคย 1 ไม่เคย 0 *ถ้าไม่เคยข้ามไปข้อ 97*	
93	แพทย์ หรือ บุคลากรทางการแพทย์ เคยระบุว่าท่านเป็นโรคไขมันในเลือดสูงหรือไม่	เคย 1 ไม่เคย 0 *ถ้าไม่เคยข้ามไปข้อ 97*	
94	ท่านเพิ่งได้รับการวินิจฉัยภายใน 12 เดือนที่ผ่านมา	ใช่ 1 ไม่ใช่ 0	
95	อายุ เมื่อได้รับการวินิจฉัย (don't know 9999)	อายุ ☐☐☐☐	
96	ภายใน 2 สัปดาห์ ที่ผ่านมา ท่านได้ทานยา ควบคุมระดับไขมันในเลือดหรือไม่	ทานยา 1 ไม่ได้ทานยา 0	

CORE: ประวัติโรค เส้นโลหิตในสมองแตกหรืออุดตัน (Cerebrovascular Disease, storke)			
NO	Question	Response	Code
97	แพทย์ หรือ บุคลากรทางการแพทย์ เคยระบุว่าท่านเป็นโรคเส้นโลหิตในสมองแตกหรือ อุดตันหรือไม่	เคย 1 ไม่เคย 0 *ถ้าไม่เคยข้ามไปข้อ 101*	
98	ท่านเพิ่งได้รับการวินิจฉัยภายใน 12 เดือนที่ผ่านมา	ใช่ 1 ไม่ใช่ 0	
99	อายุ เมื่อได้รับการวินิจฉัย (don't know 9999)	อายุ ☐☐☐☐	
100	ภายใน 2 สัปดาห์ ที่ผ่านมา ท่านได้ทานยา รักษาโรคเส้นโลหิตในสมองแตก หรืออุดตันหรือไม่	ทานยา 1 ไม่ได้ทานยา 0	

CORE: ประวัติโรคเส้นโลหิตในหัวใจตีบ หรือ อุดตัน (Cardiovascular Disease, heart attack)			
NO	Question	Response	Code
101	แพทย์ หรือ บุคลากรทางการแพทย์ เคยระบุว่าท่านเป็นโรคเส้นโลหิตในหัวใจ ตีบ หรือ อุดตันหรือไม่	เคย 1 ไม่เคย 0 *ถ้าไม่เคยข้ามไปข้อ 105*	
102	ท่านเพิ่งได้รับการวินิจฉัยภายใน 12 เดือนที่ผ่านมา	ใช่ 1 ไม่ใช่ 0	
103	อายุ เมื่อได้รับการวินิจฉัย (don't know 9999)	อายุ ☐☐☐☐	
104	ภายใน 2 สัปดาห์ ที่ผ่านมา ท่านได้ทานยา รักษาโรคเส้นโลหิตในหัวใจ ตีบ หรืออุดตันหรือไม่	ทานยา 1 ไม่ได้ทานยา 0	

CORE: ประวัติโรคถุมลมโป่งพอง (Chronic Obstructive Pulmonary disease: COPD)			
NO	Question	Response	Code
105	แพทย์ หรือ บุคลากรทางการแพทย์ เคยระบุว่าท่านเป็นโรค ถุงลมโป่งพอง หรือไม่	เคย 1 ไม่เคย 0 *ถ้าไม่เคยข้ามไปข้อ 109*	
106	ท่านเพิ่งได้รับการวินิจฉัยภายใน 12 เดือนที่ผ่านมา	ใช่ 1 ไม่ใช่ 0	
107	อายุ เมื่อได้รับการวินิจฉัย (don't know 9999)	อายุ ☐☐☐☐	
108	ภายใน 2 สัปดาห์ ที่ผ่านมา ท่านได้ทานยา รักษาโรคถุงลมโป่งพอง	ทานยา 1 ไม่ได้ทานยา 0	

CORE: ประวัติโรค มะเร็ง (Cancer)			
NO	Question	Response	Code
109	แพทย์ หรือ บุคลากรทางการแพทย์ เคยระบุว่าท่านเป็นโรค มะเร็ง หรือไม่	เคย 1 ไม่เคย 0 *ถ้าไม่เคยข้ามไปข้อ 113*	
110	ท่านเพิ่งได้รับการวินิจฉัยภายใน 12 เดือนที่ผ่านมา	ใช่ 1 ไม่ใช่ 0	
111	อายุ เมื่อได้รับการวินิจฉัย (don't know 9999)	อายุ ☐☐☐☐	
112	ภายใน 2 สัปดาห์ ที่ผ่านมา ท่านได้รับยารักษาโรคมะเร็ง	ทานยา 1 ไม่ได้ทานยา 0	

ส่วนที่ 2: ประวัติโรคเรื้อรังในมารดา

NO	Question	Response	Code
113	แพทย์ หรือ บุคลากรทางการแพทย์ เคยระบุว่า มารดา ท่านเป็นโรคความดันโลหิตสูงหรือไม่	เคย 1 ไม่เคย 0 ไม่ทราบ 9999	
114	แพทย์ หรือ บุคลากรทางการแพทย์ เคยระบุว่า มารดา ท่านเป็นโรคเบาหวานหรือไม่	เคย 1 ไม่เคย 0 ไม่ทราบ 9999	
115	แพทย์ หรือ บุคลากรทางการแพทย์ เคยระบุว่า มารดา ท่านเป็นโรคไขมันโลหิตสูงหรือไม่	เคย 1 ไม่เคย 0 ไม่ทราบ 9999	
116	แพทย์ หรือ บุคลากรทางการแพทย์ เคยระบุว่าท่าน มารดา เป็นโรคเส้นโลหิตในสมองแตก หรือ อุดตัน หรือไม่ (Cerebrovascular Disease, Stroke)	เคย 1 ไม่เคย 0 *ถ้าไม่เคยข้ามไปข้อ 118* ไม่ทราบ 9999 *ถ้าไม่ทราบข้ามไปข้อ 118*	
117	อายุ เมื่อได้รับการวินิจฉัย	<65 1 >65 0 ไม่ทราบ 9999	
118	แพทย์ หรือ บุคลากรทางการแพทย์ เคยระบุว่าท่าน มารดา เป็นโรคเส้นโลหิตในหัวใจ ตีบ หรือ อุดตันหรือไม่ (Cardiovascular Disease)	เคย 1 ไม่เคย 0 *ถ้าไม่เคยข้ามไปข้อ 120* ไม่ทราบ 9999 *ถ้าไม่ทราบข้ามไปข้อ 120*	
119	อายุ เมื่อได้รับการวินิจฉัย	<65 1 >65 0 ไม่ทราบ 9999	

ส่วนที่ 2: ประวัติโรคเรื้อรังในบิดา

NO	Question	Response	Code
120	แพทย์ หรือ บุคลากรทางการแพทย์ เคยระบุว่า บิดาท่านเป็นโรคความดันโลหิตสูงหรือไม่	เคย 1 ไม่เคย 0 ไม่ทราบ 9999	
121	แพทย์ หรือ บุคลากรทางการแพทย์ เคยระบุว่า บิดา ท่านเป็นโรคเบาหวานหรือไม่	เคย 1 ไม่เคย 0 ไม่ทราบ 9999	
122	แพทย์ หรือ บุคลากรทางการแพทย์ เคยระบุว่า บิดา ท่านเป็นโรคไขมันโลหิตสูงหรือไม่	เคย 1 ไม่เคย 0 ไม่ทราบ 9999	
123	แพทย์ หรือ บุคลากรทางการแพทย์ เคยระบุว่าท่าน บิดา เป็นโรคเส้นโลหิตในสมองแตก หรือ อุดตัน หรือไม่ (Cerebrovascular Disease, Stroke)	เคย 1 ไม่เคย 0 *ถ้าไม่เคยข้ามไปข้อ 125* ไม่ทราบ 9999 *ถ้าไม่ทราบข้ามไปข้อ 125*	
124	อายุ เมื่อได้รับการวินิจฉัย	<55 1 >55 0 ไม่ทราบ 9999	
125	แพทย์ หรือ บุคลากรทางการแพทย์ เคยระบุว่าท่าน บิดาเป็นโรคเส้นโลหิตในหัวใจตีบ หรือ อุดตันหรือไม่ (Cardiovascular Disease)	เคย 1 ไม่เคย 0 *ถ้าไม่เคย สิ้นสุดแบบสอบถาม* ไม่ทราบ 9999 *ถ้าไม่เคย สิ้นสุดแบบสอบถาม*	
126	อายุ เมื่อได้รับการวินิจฉัย	<55 1 >55 0 ไม่ทราบ 9999	

Appendix I2. Questionnaire used during interview for migration history and non-communicable disease risk factors

ส่วนที่ 2 การซักประวัติ

HN ☐☐☐☐☐☐

STUDY ID ☐☐☐☐

NO	Question	Response	Code
1.	ก่อนทำการตรวจนี้ ท่านได้งดอาหารและเครื่องดื่ม (ยกเว้นน้ำเปล่า) มา 8-12 ชั่วโมงหรือไม่	งด 1 ไม่ได้งด 2	
2.	**ภายใน 2 สัปดาห์** ที่ผ่านมา ท่านได้รับการรักษา หรือ ทานยาควบคุมความดันโลหิตหรือไม่	ได้รับ 1 ไม่ได้รับ 0	
3.	**วันนี้** ท่านได้**ฉีดยา** อินซูลิน หรือทานยา หรือได้รับการรักษา ที่ใช้ควบคุมระดับน้ำตาล ในเลือดหรือไม่	ได้รับ 1 ไม่ได้รับ 0	
4.	**ภายใน 2 สัปดาห์** ที่ผ่านมา ท่านได้ทานยา ควบคุมความดันโลหิตหรือไม่	ได้รับ 1 ไม่ได้รับ 0	

แบบสอบถามจะถามเกี่ยวกับสถานที่และสิ่งแวดล้อมของท่านขณะช่วงอายุต่างๆ และปัจจัยเสี่ยงต่อโรคเรื้อรัง ใช้เวลาประมาณ 10-15 นาที

Migration History

NO	Question	Response	Response	Question	Response	Question ลักษณะชุมชนที่อาศัย	Code
27.	สถานที่เกิด	อำเภอ	จังหวัด			ชนบท 0 เมือง 1	
28.	สถานที่ที่อาศัย	อำเภอ	จังหวัด	ช่วงอายุ (เริ่ม) ☐☐ ปี ช่วงอายุ (สิ้นสุด) ☐☐ ปี		ชนบท 0 เมือง 1	
29.	สถานที่ที่อาศัย	อำเภอ	จังหวัด	ช่วงอายุ (เริ่ม) ☐☐ ปี ช่วงอายุ (สิ้นสุด) ☐☐ ปี		ชนบท 0 เมือง 1	
30.	สถานที่ที่อาศัย	อำเภอ	จังหวัด	ช่วงอายุ (เริ่ม) ☐☐ ปี ช่วงอายุ (สิ้นสุด) ☐☐ ปี		ชนบท 0 เมือง 1	
31.	สถานที่ที่อาศัย	อำเภอ	จังหวัด	ช่วงอายุ (เริ่ม) ☐☐ ปี ช่วงอายุ (สิ้นสุด) ☐☐ ปี		ชนบท 0 เมือง 1	
32.	สถานที่ที่อาศัย	อำเภอ	จังหวัด	ช่วงอายุ (เริ่ม) ☐☐ ปี ช่วงอายุ (สิ้นสุด) ☐☐ ปี		ชนบท 0 เมือง 1	
33.	สถานที่ที่อาศัย	อำเภอ	จังหวัด	ช่วงอายุ (เริ่ม) ☐☐ ปี ช่วงอายุ (สิ้นสุด) ☐☐ ปี		ชนบท 0 เมือง 1	
34.	สถานที่ที่อาศัย	อำเภอ	จังหวัด	ช่วงอายุ (เริ่ม) ☐☐ ปี ช่วงอายุ (สิ้นสุด) ☐☐ ปี		ชนบท 0 เมือง 1	
35.	สถานที่ที่อาศัย	อำเภอ	จังหวัด	ช่วงอายุ (เริ่ม) ☐☐ ปี ช่วงอายุ (สิ้นสุด) ☐☐ ปี		ชนบท 0 เมือง 1	
36.	สถานที่ที่อาศัย	อำเภอ	จังหวัด	ช่วงอายุ (เริ่ม) ☐☐ ปี ช่วงอายุ (สิ้นสุด) ☐☐ ปี		ชนบท 0 เมือง 1	

พฤติกรรมเสี่ยงโรคเรื้อรัง

การใช้บุหรี่			
Now I am going to ask you some questions about various health behaviours. This includes things like smoking, drinking alcohol, eating fruits and vegetables and physical activity. Let's start with tobacco.			
NO	Question	Response	Code
37.	**ปัจจุบัน** ท่านใช้ผลิตภัณฑ์ ยาสูบมีควัน เช่น บุหรี่ ซิก้า หรือไม่	ใช่ 1 ไม่ใช่ 0 *(ถ้าไม่ใช้ข้ามไปข้อ 42)*	
38.	**ปัจจุบัน** ท่านใช้ผลิตภัณฑ์ ยาสูบ เช่น บุหรี่ ซิก้า **ทุกวัน** หรือไม่	ใช่ 1 ไม่ใช่ 0 *(ถ้าไม่ใช้ข้ามไปข้อ 42)*	
39.	**อายุที่**ท่านเริ่มใช้ผลิตภัณฑ์ ยาสูบ เช่น บุหรี่ ซิก้า **ทุกวัน**	อายุ (ปี) ☐☐ *(ถ้าตอบได้ข้ามไปข้อ, 41)* ไม่ทราบ 9999	
40.	จำได้ไหมว่าเริ่มสูบทุกวันมานานแค่ไหน *(บันทึก ตามหน่วย เพียง หน่วยเดียวตามที่อาสาสมัครใช้)*	จำนวนปี ☐☐ *(ถ้าตอบได้ข้ามไปข้อ, 41)* หรือ จำนวนเดือน ☐☐ *(ถ้าตอบได้ข้ามไปข้อ, 41)* หรือ จำนวนสัปดาห์ ☐☐ *(ถ้าตอบได้ข้ามไปข้อ, 41)* ไม่ทราบ 9999	
41.	โดยเฉลี่ยแล้ว ท่านใช้บุหรี่ชนิดต่างๆ ปริมาณเท่าใด *(RECORD FOR EACH TYPE, USE SHOWCARD)*	**บุหรี่โรงงาน** ☐☐ มวน บุหรี่มวนเอง ☐☐ มวน บุหรี่ขี้โย ☐☐ มวน **บุหรี่ซิการ์** ☐☐ มวน ไปป์ ☐☐ มวน อื่นๆ (ระบุ) ☐☐☐☐☐☐ *(ถ้าไม่ทราบข้ามไปข้อ, 45)* ไม่ทราบ 9999	
42.	**ในอดีต** ท่านเคยใช้ผลิตภัณฑ์ ยาสูบ เช่น บุหรี่ ซิก้า **ทุกวัน** หรือไม่?	เคย 1 ไม่เคย 0 *(ถ้าไม่เคยข้ามไปข้อ 45)*	
43.	**อายุที่**ท่านเลิกใช้ผลิตภัณฑ์ ยาสูบ เช่น บุหรี่ ซิก้า **ทุกวัน**	อายุ (ปี) ☐☐ *(ถ้าไม่เคยข้ามไปข้อ 45)* ไม่ทราบ 9999	
44.	ท่านเลิกสูบทุกวันมานานแค่ไหน? *(บันทึก ตามหน่วย เพียง หน่วยเดียว ตามที่อาสาสมัครใช้)*	จำนวนปี ☐☐ *(ถ้าไม่เคยข้ามไปข้อ 45)* หรือ จำนวนเดือน ☐☐ *(ถ้าตอบได้ข้ามไปข้อ 45)* หรือ จำนวนสัปดาห์ ☐☐ *(ถ้าตอบได้ข้ามไปข้อ 45)* *จำไม่ได้* 9999	
45.	**ปัจจุบัน** ท่านใช้ผลิตภัณฑ์ ยาสูบไม่มีควัน เช่น ยาเส้น ยานัตถุ์ หรือไม่	ใช้ 1 ไม่ใช้ 0 *(ถ้าไม่ใช้ ข้ามไปข้อ 48)*	
46.	**ปัจจุบัน** ท่านใช้ผลิตภัณฑ์ ยาสูบไม่มีควัน เช่น ยาเส้น ยานัตถุ์ **ทุกวัน** หรือไม่	ใช้ 1 ไม่ใช้ 0 *(ถ้าไม่ใช้ ข้ามไปข้อ 48)*	

การใช้บุหรี่			
NO	Question	Response	Code
47.	โดยเฉลี่ยแล้วท่านใช้ผลิตภัณฑ์ด้วยวิธีต่อไปนี้กี่ครั้งต่อวัน	อมหรือจุกยา ฉุนทางปาก ☐☐ สูดทางจมูก ☐☐ เคี้ยวทางปาก ☐☐ สูบ ☐☐ อื่นๆ ☐☐ อื่นๆ ระบุ ☐☐☐☐☐☐ *ข้ามไปข้อ 49* ไม่ทราบ 9999	
48.	**ในอดีต** ท่านใช้ผลิตภัณฑ์ ยาสูบไม่มีควัน เช่น ยาเส้น ยานัตถุ์ **ทุกวัน** หรือไม่	เคย 1 ไม่เคย 0	
49.	ใน 7 วันที่ผ่านมามีกี่วันที่มีคนสูบบุหรี่ ในบ้านของท่าน ขณะที่ท่านอยู่ด้วย	จำนวนวัน ☐☐ ไม่ทราบ 9999	
50.	ใน 7 วันที่ผ่านมา มีกี่วันที่มีคนสูบบุหรี่ ในที่ทำงานของท่าน ขณะที่ท่านอยู่ด้วย	จำนวนวัน ☐☐ ไม่ทราบ 9999	

การดื่มเครื่องดื่มที่มีแอลกอฮอล์			
The next questions ask about the consumption of alcohol.			
NO	Question	Response	Code
51.	ท่านเคยดื่มเครื่องดื่มที่มีแอลกอฮอล์ เช่น เบียร์, ไวน์, วิสกี้, หรือไม่	เคย 1 ไม่เคย 0 *(ถ้าไม่เคยข้ามไป ข้อ59)*	
52.	ใน 12 เดือนที่ผ่านมา ท่านเคยดื่มเครื่องดื่มที่มีแอลกอฮอล์ เช่น เบียร์, ไวน์, วิสกี้, หรือไม่	เคย 1 ไม่เคย 0 *(ถ้าไม่เคยข้ามไปข้อ 59)*	
53.	ใน 12 เดือนที่ผ่านมา บ่อยครั้งเพียงใดที่ท่านดื่มอย่างน้อย 1 ดื่มมาตรฐาน	ทุกวัน 4 5-6 วันต่อสัปดาห์ 3 1-4 วันต่อสัปดาห์ 2 1-3 วันต่อเดือน 1 น้อยกว่า 1 ครั้งต่อเดือน 0	
54.	ใน 30 วัน ที่ผ่านมา ท่านเคยดื่มเครื่องดื่มที่มีแอลกอฮอล์ หรือไม่	เคย 1 ไม่เคย 0 *(ถ้าไม่เคยข้ามไปข้อ 59)*	
55.	ใน 30 วันที่ผ่านมา มีกี่วันที่ท่านดื่มอย่างน้อย 1 ดื่มมาตรฐาน	วัน ☐☐ ไม่ทราบ 9999	
56.	ใน 30 วัน ที่ผ่านมา เมื่อ ท่านดื่มเครื่องดื่มที่มีแอลกอฮอล์ โดยเฉลี่ยท่านดื่มครั้งละ กี่ดื่มมาตรฐาน	ดื่มมาตรฐาน ☐☐ ไม่ทราบ 9999	
57.	ใน 30 วัน ที่ผ่านมาเมื่อท่านดื่มเครื่องดื่มที่มีแอลกอฮอล์ จำนวนดื่มมาตรฐาน สูงสุดในหนึ่งครั้งที่ดื่ม	จำนวนดื่มมาตรฐาน ☐☐ ไม่ทราบ 9999	
58.	ใน 30 วันที่ผ่านมา เมื่อท่านดื่มกี่ครั้งที่ท่านดื่มมากกว่า 5 ดื่มมาตรฐาน (สำหรับผู้ชาย) หรือ 4 ดื่มมาตรฐาน (สำหรับผู้หญิง)	จำนวนครั้ง ☐☐ ไม่ทราบ 9999	

การรับประทานอาหาร			
The next questions ask about the fruits and vegetables that you usually eat. I have a nutrition card here that shows you some examples of local fruits and vegetables. Each picture represents the size of a serving. As you answer these questions please think of a typical week in the last year			
NO	Question	Response	Code
59.	ในสัปดาห์ปกติ **ท่านทานผลไม้กี่วันต่อสัปดาห์** *(USE SHOWCARD)*	จำนวนวัน ☐☐ *(ถ้าไม่ทานเลยข้ามไปข้อ 61)* ไม่ทราบ 9999	
60.	ในหนึ่งวัน ท่านทานผลไม้ กี่หน่วยต่อครั้ง *(USE SHOWCARD)*	จำนวนหน่วย ☐☐ ไม่ทราบ 9999	
61.	ในสัปดาห์ ปกติ, **ท่านทานผัก กี่วันต่อสัปดาห์** *(USE SHOWCARD)*	จำนวนวัน ☐☐ *(ถ้าไม่ทานเลยข้ามไปข้อ 63)* ไม่ทราบ 9999	
62.	ในหนึ่งวัน ท่านทานผัก กี่หน่วยต่อครั้ง *(USE SHOWCARD)*	จำนวนหน่วย ☐☐ ไม่ทราบ 9999	

การรับประทานอาหาร			
63.	ที่บ้านของท่านใช้น้ำมันชนิดใดในการประกอบอาหาร *(USE SHOWCARD)* *(SELECT ONLY ONE)*	ไขมันพืช 0 ไขมันสัตว์ 1 เนย 2 มาการีน 3 อื่นๆ 4 *If Other, go to D5other* ไม่มีชนิดใดเป็นประจำ 5 ไม่ใช้ 6 ไม่ทราบ 9999 อื่นๆ ☐☐☐☐☐☐	
64.	โดยเฉลี่ย ในหนึ่งสัปดาห์ ท่านรับประทานอาหารที่ปรุงสำเร็จ (ไม่ได้ทำเอง หรือปรุงแต่งเอง) กี่มื้อต่อสัปดาห์ (1 วันมี 3 มื้อ)	จำนวนมื้อ ☐☐ *(สูงสุด 21 มื้อ/สัปดาห์)* ไม่ทราบ 9999	
65.	โดยเฉลี่ยในหนึ่งสัปดาห์ ท่านรับประทานอาหารที่ซื้อจากภายในบริเวณคณะแพทย์ที่ปรุงสำเร็จ กี่มื้อต่อสัปดาห์ (1 วันมี 3 มื้อ)	จำนวนมื้อ ☐☐ *(สูงสุด 21 มื้อ/สัปดาห์)* ไม่ทราบ 9999	

กิจกรรมทางกาย (Physical activity)			
คำถามเกี่ยวกับ ออกกำลังและกิจกรรม ใน 3 ช่วง คือ 1) ขณะทำงาน 2) เดินทาง 3) ขณะพักผ่อน			
NO	Question	Response	Code
66.	ในลักษณะงานของท่าน ท่านมีกิจกรรมที่ใช้ **พลังงานสูง** ซึ่งทำให้หายใจเร็วขึ้นหรือหัวใจเต้นเร็วขึ้นนานต่อเนื่องอย่างน้อย 10 นาที หรือไม่ เช่น ยกของหนัก ขนของ	มี 1 ไม่มี 0 *(ถ้าไม่มี ให้ข้ามไปข้อ 69)*	
67.	โดยปกติ ใน หนึ่งสัปดาห์ ท่านมี กิจกรรม ที่ใช้ **พลังงานสูง** ขณะทำงาน ที่วันต่อสัปดาห์	จำนวนวัน ☐☐	
68.	โดยปกติในหนึ่งวันท่านมีกิจกรรม ที่ใช้ **พลังงานสูง** ขณะทำงานนานเท่าใด	ชั่วโมง : นาที ☐☐:☐☐	
69.	ในลักษณะงานของท่าน ท่านมีกิจกรรมที่ใช้ **พลังงานปานกลาง** ซึ่งทำให้หายใจเร็วขึ้นเล็กน้อย หรือหัวใจเต้นเร็วขึ้นเล็กน้อย นานต่อเนื่องอย่างน้อย 10 นาที หรือไม่ เช่น เข็นผู้ป่วยอาบน้ำหรือไม่	มี 1 ไม่มี 0 *(ถ้าไม่มี ให้ข้ามไปข้อ 74)*	
70.	โดยปกติ ใน หนึ่งสัปดาห์ ท่านมี กิจกรรม ที่ใช้ **พลังงานปานกลาง** ขณะทำงานที่วันต่อสัปดาห์	จำนวนวัน ☐☐	
71.	โดยปกติในหนึ่งวันท่านมีกิจกรรมที่ใช้ **พลังงานปานกลาง** ขณะทำงานนานเท่าใด	ชั่วโมง : นาที ☐☐:☐☐ ชั่วโมง : นาที	

ในขณะการเดินทาง เช่น จะไปทำงาน ไปตลาด เป็นต้น			
The next questions exclude the physical activities at work that you have already mentioned. Now I would like to ask you about the usual way you travel to and from places. For example to work, for shopping, to market, to place of worship. *[Insert other examples if needed]*			
NO	Question	Response	Code
72.	ท่านเดิน หรือ ปั่นจักรยาน ต่อเนื่องอย่างน้อย 10 นาที	ใช่ 1 ไม่ใช่ 0 *(ถ้าไม่ใช่ ให้ข้ามไปข้อ 75)*	
73.	โดยปกติในหนึ่งสัปดาห์ท่านเดินหรือ ปั่นจักรยานต่อเนื่องอย่างน้อย 10 นาที กี่วันต่อสัปดาห์	จำนวนวัน ☐☐	
74.	โดยปกติในหนึ่งวันท่านเดิน หรือ ปั่นจักรยานนานเท่าใด	ชั่วโมง : นาที ☐☐:☐☐ ชั่วโมง : นาที	

CORE: Physical Activity, Continued			
The next questions exclude the work and transport activities that you have already mentioned. Now I would like to ask you about sports, fitness and recreational activities (leisure), *[Insert relevant terms]*.			
ในขณะพักผ่อน			
NO	Question	Response	Code
75.	ในช่วงเวลาพักผ่อน (ช่วงที่ไม่ได้ทำงาน) ท่านมีกิจกรรม ที่ใช้ **พลังงานสูง** ซึ่งทำให้หายใจเร็วขึ้น หรือหัวใจเต้นเร็วขึ้น นานต่อเนื่องอย่างน้อย 10 นาที หรือไม่ เช่น วิ่ง หรือ เล่นฟุตบอล	มี 1 ไม่มี 0 *(ถ้าไม่มี ให้ข้ามไปข้อ 78)*	
76.	โดยปกติ ในหนึ่งสัปดาห์ ท่านมีกิจกรรม ที่ใช้ **พลังงานสูง** ขณะช่วงเวลาพักผ่อนกี่วันต่อสัปดาห์	จำนวนวัน ☐☐	
77.	โดยปกติในหนึ่งวัน ท่านมีกิจกรรมที่ใช้ **พลังงานสูง** ขณะช่วงเวลาพักผ่อนนานเท่าใด	ชั่วโมง : นาที ☐☐:☐☐ ชั่วโมง : นาที	
78.	ในช่วงเวลาพักผ่อน (ช่วงที่ไม่ได้ทำงาน) ท่านมีกิจกรรม ที่ใช้ **พลังงานปานกลาง** ซึ่งทำให้หายใจเร็วขึ้นเล็กน้อย หรือหัวใจเต้นเร็วขึ้นเล็กน้อย นานต่อเนื่องอย่างน้อย 10 นาที หรือไม่ เช่น ว่ายน้ำ แอโรบิก	มี 1 ไม่มี 0 *(ถ้าไม่มี ให้ข้ามไปข้อ 81)*	
79.	โดยปกติในหนึ่งสัปดาห์ ท่านมีกิจกรรมที่ใช้**พลังงานปานกลาง** ในช่วงเวลาพักผ่อน กี่วันต่อสัปดาห์	จำนวนวัน ☐☐	
80.	โดยปกติในหนึ่งวัน ท่านมีกิจกรรมที่ใช้ **พลังงานปานกลาง** ขณะช่วงเวลาพักผ่อน นานเท่าใด	ชั่วโมง : นาที ☐☐:☐☐	

EXPANDED: Physical Activity			
พฤติกรรมอยู่กับที่ (Sedentary behavior) ซึ่งหมายถึง การนั่ง หรือ เอนตัวนอน ไม่ว่าจะเป็นช่วง ทำงาน ขณะเดินทาง (เช่น นั่งขับรถ) หรือพักผ่อนกับครอบครัวและเพื่อน โดยไม่นับช่วงการนอนหลับตอนกลางคืน			
NO	Question	Response	Code
81.	โดยปกติ ในหนึ่งวัน ท่านมี พฤติกรรมที่อยู่กับที่ นานเท่าใด	ชั่วโมง : นาที ☐☐:☐☐ ชั่วโมง : นาที	

Appendix I3. Questionnaire for 2013 survey on risk of depression, quality of life and risk of harm from substance use

ID

แบบสอบถาม

แบบสอบถามมี 3 ส่วน ใช้เวลาประมาณ 10 นาที

ส่วนที่ 1 ข้อมูลเกี่ยวกับศาสนา ความเครียดและคัดกรองภาวะซึมเศร้า
ส่วนที่ 2 ข้อมูลเกี่ยวกับคุณภาพชีวิต
ส่วนที่ 3 ข้อมูลการใช้บุหรี่ สุรา และสารเสพติด

ทั้งสองส่วนนี้เป็นการให้ข้อมูลโดยไม่มีการระบุชื่อ และผลของท่านจะถูกเก็บเป็นความลับ

ส่วนที่ 1 ข้อมูลเกี่ยวกับศาสนา ความเครียด และ คัดกรองภาวะซึมเศร้า

ข้อมูลด้านศาสนา

1. ท่านนับถือศาสนาใด

   ☐ พุทธ ☐ คริสต์ ☐ อิสลาม ☐ อื่นๆ ระบุ.....

2. ท่านประกอบศาสนากิจเองบ่อยเพียงใด (ศาสนาพุทธ เช่น ตักบาตร,รักษาศีล,นั่งสมาธิ ; ศาสนาคริสต์ เช่น อธิษฐานและขอบคุณพระเจ้า; ศาสนาอิสลาม เช่น การละหมาด, การถือศีลอด เป็นต้น)

   ☐ > 2 ครั้ง/สัปดาห์ ☐ 1-2 ครั้ง/สัปดาห์ ☐ 1-2 ครั้ง/เดือน

   ☐ 1-2 ครั้ง/ปี ☐ < 1 ครั้ง/ปี

3. ท่านได้เข้าร่วมกลุ่มประกอบศาสนากิจบ่อยเพียงใด (เช่น การเข้าวัด, เข้าโบสถ์ ,เข้ามัสยิด, การเข้าร่วมกลุ่มเช่น ชมรม, สมาคม เป็นต้น)

   ☐ > 2 ครั้ง/สัปดาห์ ☐ 1-2 ครั้ง/สัปดาห์ ☐ 1-2 ครั้ง/เดือน

   ☐ 1-2 ครั้ง/ปี ☐ < 1 ครั้ง/ปี

ID

ในช่วง **2 สัปดาห์** ที่ผ่านมา ท่านมีอาการดังต่อไปนี้บ่อยแค่ไหน

อาการ	ไม่เลย	มีบางวัน ไม่บ่อย	มีค่อนข้าง บ่อย	มีเกือบ ทุกวัน
1. เบื่อ ทำอะไรๆก็ไม่เพลิดเพลิน	☐	☐	☐	☐
2. ไม่สบายใจ ซึมเศร้า หรือท้อแท้	☐	☐	☐	☐
3. หลับยาก หรือ หลับๆตื่นๆ หรือหลับมากไป	☐	☐	☐	☐
4. เหนื่อยง่าย หรือ ไม่ค่อยมีแรง	☐	☐	☐	☐
5. เบื่ออาหาร หรือกินมากไป	☐	☐	☐	☐
6. รู้สึกไม่ดีกับตัวเอง คิดว่าตัวเองล้มเหลว หรือทำให้ตัวเองหรือครอบครัวผิดหวัง	☐	☐	☐	☐
7. สมาธิไม่ดี เวลาทำอะไร เช่นดูโทรทัศน์ ฟังวิทยุ หรือทำงานที่ต้องใช้ความตั้งใจ	☐	☐	☐	☐
8. พูดหรือทำอะไรช้าจนคนอื่นมองเห็น หรือกระสับกระส่าย จนท่านอยู่ไม่นิ่งเหมือนเคย	☐	☐	☐	☐
9. คิดทำร้ายตนเอง หรือคิดว่าถ้าตายๆไปเสียคงจะดี	☐	☐	☐	☐

ถ้าท่านตอบว่ามีอาการไม่ว่าในข้อใดก็ตาม อาการนั้นๆ ทำให้ท่านมีปัญหาในการทำงาน การดูแลสิ่งต่างๆในบ้าน หรือการเข้ากับผู้คน หรือไม่

☐ ไม่มีปัญหาเลย ☐ มีปัญหาบ้าง ☐ มีปัญหามาก ☐ มีปัญหามากที่สุด

ID

ส่วนที่ 2 ข้อมูลเกี่ยวกับคุณภาพชีวิต

1. โดยทั่วไป ที่ผ่านมา 1 เดือนสุขภาพของท่าน..... (เลือกเพียงหนึ่งช่อง)

☐ ดีเยี่ยม ☐ ดี ☐ พอใช้ ☐ ไม่ดีเลย

2. เปรียบเทียบช่วง 1 ปีที่ผ่านมา ปัจจุบันสุขภาพของท่าน..... (เลือกเพียงหนึ่งช่อง)

☐ ดีขึ้นมาก ☐ ดีขึ้นบ้าง ☐ เหมือนเดิม ☐ แย่ลงบ้าง ☐ แย่ลงมาก

ภาวะสุขภาพของท่านในปัจจุบัน <u>มีผลกระทบหรือเป็นข้อจำกัด</u> ในการประกอบกิจกรรมต่างๆ เหล่านี้หรือไม่มากน้อยเพียงใด (เลือกเพียงหนึ่งช่องในแต่ละข้อ)

การประกอบกิจกรรม	มีผลมาก	มีบ้างเล็กน้อย	ไม่มีผล
3. กิจกรรมที่ต้องออกแรงมาก เช่น วิ่ง ยกของหนักๆ เล่นกีฬาที่ใช้แรงมาก			
4. กิจกรรมที่ออกแรงปานกลาง เช่น ย้ายโต๊ะ ถูบ้าน			
5. ยกของ หรือหิ้วตะกร้าจ่ายตลาด			
6. เดินขึ้นบันไดหลายๆ ชั้น			
7. เดินขึ้นบันได 1 ชั้น			
8. ก้มตัว หรือคุกเข่า หรือโค้งตัว			
9. เดินระยะมากกว่า 1 กิโลเมตร			
10. เดินทางหลายช่วงเสาไฟฟ้า			
11. เดินทางมากกว่า 30 เมตร หรือประมาณครึ่งทางระหว่างเสาไฟฟ้า			
12. อาบน้ำและแต่งตัว			

ในช่วงหนึ่งเดือนที่ผ่านมา สุขภาพร่างกายของท่าน<u>มีผลต่อการทำงานหรือกิจวัตรประจำวัน</u>บ้างหรือไม่..... (เลือกเพียงหนึ่งช่องในแต่ละข้อ)

การทำงานหรือกิจวัตรประจำวัน	ใช่	ไม่ใช่
13. ทำให้ต้องลดเวลาในการทำงานหรือกิจกรรมลง		
14. ทำงานได้น้อยกว่าที่ตั้งใจไว้		
15. ทำงานหรือกิจกรรมบางอย่างไม่ได้อย่างที่เคย		
16. มีความยากลำบากในการทำงานหรือกิจกรรม ต้องใช้ความพยายามเพิ่มมากขึ้น		

ID

ในช่วงหนึ่งเดือนที่ผ่านมา ปัญหาทางอารมณ์ (เช่นซึมเศร้า หรือวิตกกังวล) มีผลต่อการทำงานหรือกิจวัตรประจำวันบ้างหรือไม่..... (เลือกเพียงหนึ่งช่องในแต่ละข้อ)

การทำงานหรือกิจวัตรประจำวัน	ใช่	ไม่ใช่
17. ลดเวลาในการทำงานหรือกิจกรรมลง		
18. ทำงานได้น้อยกว่าที่ตั้งใจไว้		
19. ขาดความรอบคอบในการทำงานหรือกิจกรรมเหมือนอย่างที่เคยทำ		

20. ในช่วง 1 เดือนที่ผ่านมาปัญหาสุขภาพกายหรือปัญหาทางอารมณ์รบกวนความสัมพันธ์ของท่านกับครอบครัว เพื่อนฝูง หรือเพื่อนบ้าน บ้างหรือไม่อย่างไร..... (เลือกเพียงหนึ่งช่อง)

☐ ไม่เลย ☐ เพียงเล็กน้อย ☐ ปานกลาง ☐ ค่อนข้างมาก ☐ มาก

21. ในช่วง 1 เดือนที่ผ่านมา ท่านมีอาการเจ็บปวดตามร่างกายหรือไม่..... (เลือกเพียงหนึ่งช่อง)

☐ ไม่มีเลย ☐ น้อยมาก ☐ เพียงเล็กน้อย

☐ ปานกลาง ☐ รุนแรง ☐ รุนแรงมาก

22. ในช่วง 1 เดือนที่ผ่านมา อาการปวดรบกวนการทำงานตามปกติของท่านหรือไม่.... (เลือกเพียงหนึ่งช่อง)

☐ ไม่เลย ☐ เพียงเล็กน้อย ☐ ปานกลาง ☐ ค่อนข้างมาก ☐ มาก

ID

คำถามต่อไปนี้ ถามเกี่ยวความรู้สึกและเรื่องราวที่ผ่านมาในช่วง 1 เดือน โปรดเลือกข้อใกล้เคียงกับความรู้สึกของท่านมากที่สุด ในแต่ละข้อ..... (เลือกเพียงหนึ่งช่องในแต่ละข้อ)

ความรู้สึก	ตลอดเวลา	เกือบตลอดเวลา	บ่อยๆ	บางเวลา	นานๆครั้ง	ไม่มีเลย
23. รู้สึกสดชื่นมีชีวิตชีวา						
24. ประสาทเครียด						
25. หดหู่จนไม่มีอะไรทำให้สดชื่นขึ้นได้						
26. สงบและเป็นสุข						
27. มีพลังมาก						
28. ท้อแท้ ห่อเหี่ยว						
29. รู้สึกว่าจะทนอะไรไม่ได้						
30. มีความสุข						
31. รู้สึกเหนื่อยล้า						

32. ในช่วง 1 เดือนที่ผ่านมา ปัญหาสุขภาพทางกายหรือจิตใจทำให้รบกวนต่อการเข้าสังคม การพบปะเพื่อนฝูง และญาติสนิทของท่านอย่างไรบ้าง.....(เลือกเพียงหนึ่งช่อง)

☐ ตลอดเวลา ☐ เกือบตลอดเวลา ☐ บางเวลา ☐ นานๆครั้ง ☐ ไม่รบกวน

เลือกคำตอบที่ตรงกับสุขภาพของท่านให้มากที่สุด.....(เลือกเพียงหนึ่งช่อง)

สุขภาพ	ถูกต้องที่สุด	ถูกต้องส่วนมาก	ไม่ทราบ	ไม่ถูกเป็นส่วนมาก	ไม่ถูกต้องเลย
33. ฉันดูเหมือนจะป่วยง่ายกว่าคนอื่นๆ					
34. ฉันมีสุขภาพดีเหมือนทุกคนที่ฉันรู้จัก					
35. ฉันคาดว่าสุขภาพของฉันจะแย่ลง					
36. สุขภาพของฉันดีเยี่ยม					

Study ID

ส่วนที่ 3 ข้อมูลเกี่ยวกับการใช้ สุรา บุหรี่ และสารเสพติดอื่น

ข้อ	ข้อคำถาม	คำตอบ (ความถี่ที่ใช้)	สุรา	บุหรี่	ยากล่อมประสาท/ยานอนหลับ (ซาแนกซ์/วาเลี่ยม/โดมิกุ้ม)	อื่นๆ.....
1.	ในชีวิตของคุณ คุณเคยใช้สารเหล่านี้หรือไม่		เคย /ไม่เคย	เคย /ไม่เคย	เคย /ไม่เคย	เคย /ไม่เคย
ถ้าเคยใช้สารเสพติดชนิดใด ให้ทำข้อ 2 ถึง 8 โดยวงกลมล้อมรอบตัวเลขตามหมวดสารเสพติดด้านขวานี้						
2.	**ใน 3 เดือนที่ผ่านมา** คุณใช้สารเหล่านี้บ่อยครั้งเพียงใด (วงกลมรอบตัวเลขคำตอบในช่องสารเสพติดที่เคยใช้) **ถ้าใน 3 เดือนที่ผ่านมาไม่เคยใช้สารใดๆเลยให้ข้ามไปถามข้อ 6**	0 = ไม่ใช้ 2 = ใช้ 1-2 ครั้ง 3 = ทุกเดือน 4 = ทุกสัปดาห์ 6 = ทุกวัน/เกือบทุกวัน	0 2 3 4 6	0 2 3 4 6	0 2 3 4 6	0 2 3 4 6
3.	**ใน 3 เดือนที่ผ่านมา** คุณมีความต้องการ หรือมีแรงผลักดันอย่างรุนแรงที่จะใช้สารเหล่านี้บ่อยครั้งเพียงใด	0 = ไม่มี 3 = มี 1-2 ครั้ง 4 = ทุกเดือน 5 = ทุกสัปดาห์ 6 = ทุกวัน/เกือบทุกวัน	0 3 4 5 6	0 3 4 5 6	0 3 4 5 6	0 3 4 5 6
4.	**ใน 3 เดือนที่ผ่านมา** การใช้สารเหล่านี้ ทำให้คุณมีปัญหาเกี่ยวกับสุขภาพ ครอบครัว สังคม กฎหมายหรือการเงินบ่อยครั้งเพียงใด	0 = ไม่มี 4 = มี 1-2 ครั้ง 5 = ทุกเดือน 6 = ทุกสัปดาห์ 7 = ทุกวัน/เกือบทุกวัน	0 4 5 6 7	0 4 5 6 7	0 4 5 6 7	0 4 5 6 7
5.	**ใน 3 เดือนที่ผ่านมา** การใช้สารเหล่านี้ ทำให้คุณไม่สามารถทำกิจกรรมที่คุณควรจะทำได้ตามปกติบ่อยครั้งเพียงใด	0 = ไม่ใช่ 5 = ใช่ 1-2 ครั้ง 6 = ทุกเดือน 7 = ทุกสัปดาห์ 8 = ทุกวัน/เกือบทุกวัน	0 5 6 7 8		0 5 6 7 8	0 5 6 7 8
6.	**ในชีวิตของคุณ** เพื่อนฝูง ญาติ หรือคนอื่นเคยแสดงความเป็นห่วงเกี่ยวกับการใช้สารเสพติดเหล่านี้ของคุณหรือไม่	0 = ไม่เคย 6 = เคย***ใน*** 3 เดือนที่ผ่านมา 3 = เคย***ก่อน*** 3 เดือนที่ผ่านมา	0 6 3	0 6 3	0 6 3	0 6 3
7.	**ในชีวิตของคุณ** คุณเคยพยายาม **ลด** หรือ**หยุดใช้**สารเสพติดเหล่านี้ แต่ไม่ประสบผลสำเร็จหรือไม่	0 = ไม่เคย 6 = เคย***ใน*** 3 เดือนที่ผ่านมา 3 = เคย***ก่อน*** 3 เดือนที่ผ่านมา	0 6 3	0 6 3	0 6 3	0 6 3

8.	ในชีวิตของคุณ **<u>เคยฉีด</u>**สารใดๆข้างบนนี้หรือไม่	( ) ไม่เคย ( ) เคยใน 3 เดือนที่ผ่านมา ( ) เคยก่อน 3 เดือนที่ผ่านมา
	ถ้าเคยฉีดท่านเคยฉีดสารชนิดใด	( ) ยากล่อมประสาท/ยานอนหลับ ( ) อื่นๆ (ระบุ).....

Appendix I4. Record forms for physical examination

Study ID

แบบบันทึกการตรวจร่างกาย

ส่วนที่ 1: Height and Weight		
Question	Measurement	Code
Height ส่วนสูง	in centimetres (cm) _____._____	
Weight น้ำหนัก	in kilograms (kg) _____._____	
คุณอยู่ระหว่างการตั้งครรภ์หรือไม่	1. ใช่ 0. ไม่ใช่	

ส่วนที่ 2 : Waist and Hip			
Question		Measurement	Code
Hip circumference (สะดือ)		in centimetres (cm) _____._____	
Hip circumference (ASIS)		in centimetres (cm) _____._____	
Waist circumference		in centimetres (cm) _____._____	
Hip circumference (buttock)		in centimetres (cm) _____._____	
Leg length	Right leg	in centimetres (cm) _____._____	
	Left leg	in centimetres (cm) _____._____	

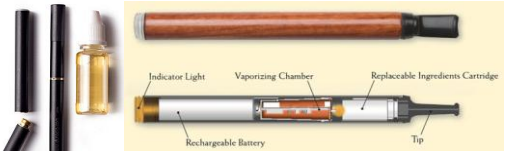
ส่วนที่ 3 : Blood pressure and Heart rate			
Question		Measurement	Code
Device ID _____	Blood pressure reading 1	Systolic (mmHg) _____	
		Diastolic (mmHg) _____	
	Heart rate reading 1	Beats per minute _____	
	Blood pressure reading 2	Systolic (mmHg) _____	
		Diastolic (mmHg) _____	
	Heart rate reading 2	Beats per minute _____	
	Blood pressure reading 3	Systolic (mmHg) _____	
		Diastolic (mmHg) _____	
	Heart rate reading 3	Beats per minute _____	

Appendix I5. Materials used during interview of non-communicable disease risk factors

Types of tobacco

ตัวอย่างผลิตภัณฑ์ยาสูบแบบมีควัน หรือใช้โดยวิธีการสูบบางชนิด	
บุหรี่โรงงาน	 
บุหรี่มวนเอง	  บุหรี่มวนเองแบบดั้งเดิม     เครื่องมวนบุหรี่มวนเองและกระดาษมวนแบบสมัยใหม่
ไปป์	
ซิการ์	
ผลิตภัณฑ์ยาสูบที่สูบผ่านน้ำ เช่น บารากู่ เป็นต้น	 
อื่นๆ	 บุหรี่ขี้โย

ตัวอย่างผลิตภัณฑ์ยาสูบแบบไม่มีควัน	
ยาเส้น/ ยาเส้นปรุง ใช้สำหรับอม/จุกทางปาก ใช้เคี้ยว หรือใช้เป็นส่วนผสมของหมากพลู	

ตัวอย่างผลิตภัณฑ์ยาสูบแบบไม่มีควัน (ต่อ)	
ยานัตถุ์ที่มีส่วนผสมของยาสูบ สำหรับใช้สูดทางจมูก	
บุหรี่อิเล็กทรอนิก/ บุหรี่ไฟฟ้า	 ในบุหรี่ธรรมดามีสารนิโคตินมวนละ 2 มิลลิกรัม แต่ในบุหรี่อิเล็กทรอนิกมีมากถึง 40 มิลลิกรัม

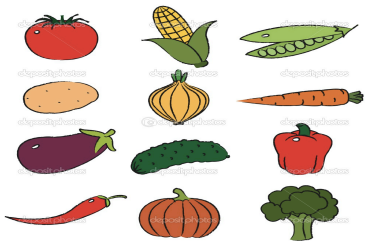
Standard drink

การเทียบปริมาณแอลกอฮอล์ในเครื่องดื่มเป็นดื่มมาตรฐาน (Standard Drink) **ในคำตอบข้อ 2 และ 3 ของ AUDIT**
หนึ่งดื่มมาตรฐานเท่ากับแอลกอฮอล์ 10 กรัม

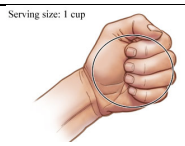
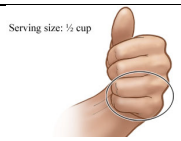
- **เหล้าแดง 35 ดีกรี** : 2 ฝาใหญ่ หรือ 30 cc = 1 ดื่มมาตรฐาน,
  หาก 1 แบนมี 350 cc : ¼ แบน = 3 ดื่มมาตรฐาน, ½ แบน = 6 ดื่มมาตรฐาน, 1 แบน = 12 ดื่มมาตรฐาน
  หาก 1 ขวดมี 700 cc : ¼ ขวด = 6 ดื่มมาตรฐาน, ½ ขวด= 12 ดื่มมาตรฐาน, 1 ขวด= 24 ดื่มมาตรฐาน
- **เหล้าขาว 40 ดีกรี** :1 เป๊ก หรือ 50 cc = 1.5 ดื่มมาตรฐาน
- **เบียร์ 5 %** เช่น สิงห์ ไฮเนเกน ลีโอ เชียร์ ไทเกอร์ ช้างดราฟ : ¾ กระป๋อง/ขวดเล็ก = 1 ดื่มมาตรฐาน,1 ขวดใหญ่ 660 cc = 2.5 ดื่มมาตรฐาน
- **เบียร์ 6.4 %** เช่น ช้าง : ½ กระป๋อง หรือ 1/3 ขวดใหญ่ = 1 ดื่มมาตรฐาน
- **ไวน์ 12 %** : 1 แก้ว 100 cc = 1 ดื่มมาตรฐาน, ไวน์คูเลอร์ 1 ขวด = 1 ดื่มมาตรฐาน
- **น้ำขาว อุ กระแช่ 10%** : 3 เป๊ก/ตอง/กึ๊ง หรือ 150 cc = 1 ดื่มมาตรฐาน
- **สาโท สุราแช่ สุราพื้นเมือง 6%** : 4 เป๊ก/ตอง/กึ๊ง หรือ 200 cc = 1 ดื่มมาตรฐาน

ที่สำคัญ อย่าลืมว่าผู้ดื่มส่วนใหญ่มักไม่ทราบปริมาณการดื่มของตนที่ชัดเจน และมัก**ประมาณการดื่มต่ำกว่าความเป็นจริง** และเครื่องดื่มแต่ละชนิด แต่ละยี่ห้อมีขนาดบรรจุที่แตกต่างกัน ข้อมูลที่ได้เป็นเพียงการประมาณการดื่มเท่านั้น

Unit of fruit and vegetable

vegetable	**1 หน่วย**	**ตัวอย่างชนิดผัก**
ผักสดใบเขียว	1 ถ้วย	ผักบุ้ง ผักคะน้า ผักกาด ผักกวางตุ้ง 
ผักชนิดอื่นๆ เช่น ผักชนิดที่หั่นเป็นชิ้น หรือที่ผ่นการปรุงอาหารแล้ว	½ ถ้วย	มะเขือ ฟักทอง แครอท แตงกวา กะหล่ำ ข้าวโพด เห็ด ถั่วสดชนิดต่างๆ หัวหอม 
น้ำผัก	½ ถ้วย	

fruit	**1 หน่วย**	**ตัวอย่างชนิดผลไม้**
ผลไม้เป็นลูกๆ	1 ผล ขนาดกลาง	กล้วย ส้ม แอปเปิ้ล
ผลไม้ที่หั่นเป็นชิ้น หรือผ่านการประกอบอาหาร หรือ ผลไม้กระป๋อง	½ ถ้วย	
น้ำผลไม้	½ ถ้วย	น้ำผลไม้สด

ตารางเปรียบเทียบหน่วย		
1 หน่วย = 1 ถ้วย = 80 กรัม		
½ ถ้วย		

หมายเหตุ: ไม่นับว่ามันฝรั่ง หรือมันสัมปะหลังว่าเป็นผัก ผลไม้

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Apr 07, 2015

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Appendix K. Sensitivity analysis for migration and urbanicity on well-being using multiple imputation

Appendix K1. Satisfaction with safety

		Completed cases (n=55,428)		Multiple imputation (n=75,600)	
		Regression coefficient (95% CI)	p-value	Regression coefficient (95% CI)	p-value
Migration	0 No	Reference		Reference	
	1 Yes	-2.47 (-3.88 to -1.07)	<0.01	-0.77 (-1.78 to 0.24)	0.14
Location in 2005 and 2009	0 R-R	Reference	<0.01*	Reference	<0.01*
	1 R-U	-1.38 (-1.96 8to -0.87)	<0.01	-1.20 (-1.72 to -0.68)	<0.01
	2 U-R	-0.98 (-1.63 to -0.32)	<0.01	-0.96 (-1.60 to -0.33)	<0.01
	3 U-U	-1.67 (-2.16 to -1.33)	<0.01	-1.54 (-1.89 to -1.19)	<0.01
Migration #location (interactions)			<0.01*		0.24*
	1 1	0.55 (-1.28 to 2.40)	0.56	-0.39 (-1.94 to 1.16)	0.62
	1 2	3.05 (1.05 to 5.05)	<0.01	1.39 (-0.26 to 3.04)	0.10
	1 3	2.03 (0.41 to 3.66)	0.01	0.51 (-0.77 to 1.80)	0.43

R-R rural-rural; R-U rural-urban; U-R urban –rural; U-U urban-urban; Results adjusted for age, sex, income in 2005, marital status in 2005, self-report health status in 2005 and satisfaction scores in 2005 for each corresponding domains; *overall p-value using likelihood ratio test

Appendix K2. Satisfaction with being part of the community

		Completed cases (n=55,379)		Multiple imputation (n=75,554)	
		Regression coefficient (95% CI)	p-value	Regression coefficient (95% CI)	p-value
Migration	0 No	Reference		Reference	
	1 Yes	-4.01 (-5.52 to-2.49)	<0.01	-1.99 (-3.00 to -0.98)	<0.01
Location in 2005 and 2009	0 R-R	Reference	<0.01*	Reference	<0.01*
	1 R-U	-2.90 (-3.46 to-2.34)	<0.01	-2.36 (-2.90 to -1.82)	<0.01
	2 U-R	-1.79 (-2.50 to -1.09)	<0.01	-1.77 (-2.45 to -1.09)	<0.01
	3 U-U	-3.56 (-3.92 to -3.18)	<0.01	-3.30 (-3.68 to -2.91)	<0.01
Migration #location (interactions)			<0.01*		<0.01*
	1 1	-0.74 (-2.72 to 1.24)	0.46	-1.11 (-2.71 to 0.49)	0.17
	1 2	4.97 (2.81 to 7.13)	<0.01	2.76 (1.05 to 4.48)	<0.01
	1 3	2.84 (1.09 to 4.59)	<0.01	1.37 (0.07 to 2.68)	0.04

R-R rural-rural; R-U rural-urban; U-R urban –rural; U-U urban-urban Results adjusted for age, sex, income in 2005, marital status in 2005, self-report health status in 2005 and satisfaction scores in 2005 for each corresponding domains; *overall p-value using likelihood ratio test

Appendix K3. Satisfaction with standards of living

		Completed cases (n=55,355)		Multiple imputation (n=75,528)	
		Regression coefficient (95% CI)	p-value	Regression coefficient (95% CI)	p-value
Migration	0 No	Reference		Reference	
	1 Yes	-2.72 (-4.05 to -1.39)	<0.01	-1.14 (-2.11 to -0.18)	0.02
Location in 2005 and 2009	0 R-R	Reference	<0.01*	Reference	<0.01*
	1 R-U	-0.76 (-1.24 to -0.27)	<0.01	-0.62 (-1.09 to -0.16)	<0.01
	2 U-R	-0.54 (-1.15 to 0.09)	0.09	-0.48 (-1.07 to 0.10)	0.11
	3 U-U	-1.10 (-1.43 to -0.78)	<0.01	-0.88 (-1.19 to -0.57)	<0.01
Migration #location (interactions)			0.01*		0.29*
	1 1	1.42 (-0.32 to 3.16)	0.11	0.19 (-1.22 to 1.61)	0.79
	1 2	2.04 (0.16 to 3.93)	0.03	0.80 (-0.86 to 2.45)	0.34
	1 3	2.56 (1.03 to 4.10)	<0.01	1.01 (-0.13 to 2.15)	0.08

R-R rural-rural; R-U rural-urban; U-R urban –rural; U-U urban-urban; Results adjusted for age, sex, income in 2005, marital status in 2005, self-report health status in 2005 and satisfaction scores in 2005 for each corresponding domains; *overall p-value using likelihood ratio test

Appendix K4. Satisfaction with life as a whole

		Completed cases (n=55,367)		Multiple imputation (n=75,538)	
		Regression coefficient (95% CI)	p-value	Regression coefficient (95% CI)	p-value
Migration	0 No	Reference		Reference	
	1 Yes	-2.13 (-3.33 to -0.94)	<0.01	-1.01 (-1.83 to -0.18)	0.02
Location in 2005 and 2009	0 R-R	Reference	<0.01*	Reference	<0.01*
	1 R-U	-1.06 (-1.49 to -0.62)	<0.01	-0.89 (1.32 to -0.45)	<0.01
	2 U-R	-0.91 (-1.47 to -0.35)	<0.01	-0.74 (-1.26 to -0.22)	<0.01
	3 U-U	-1.23 (-1.52 to -0.95)	<0.01	-1.06 (-1.34 to -0.78)	<0.01
Migration #location (interactions)			0.03*		0.30*
	1 1	0.54 (-1.02 to 2.10)	0.49	-0.05 (-1.31 to 1.22)	0.94
	1 2	1.96 (0.26 to 3.65)	0.02	1.02 (-0.34 to 2.38)	0.14
	1 3	1.55 (0.17 to 2.93)	0.03	0.65 (-0.34 to 1.64)	0.20

R-R rural-rural; R-U rural-urban; U-R urban –rural; U-U urban-urban; Results adjusted for age, sex, income in 2005, marital status in 2005, self-report health status in 2005 and satisfaction scores in 2005 for each corresponding domains; *overall p-value using likelihood ratio test

Appendix L. Sensitivity analysis for migration and urbanicity on quality of life using multiple imputation

	Physical quality of life				Mental quality of life			
	Completed data (n=54,413)		Multiple imputations (n=75,191)		Completed data (54,413)		Multiple imputations (n=75191)	
	β (95% CI)	p-value	β (95% CI)	p-value	β (95% CI)	p-value	Odds ratio (95% CI)	p-value
Migration								
No	Reference		Reference		Reference		Reference	
Yes	0.13 (-0.08 to 0.34)	0.23	0.09 (-0.08 to 0.26)	0.29	-0.30 (-0.56 to -0.05)	0.02	-0.21 (0.41 to -0.01)	0.04
Urbanicity of location in 2005 and 2009								
Rural – Rural	Reference		Reference		Reference		Reference	
Rural – Urban	-0.19 (-0.38 to -0.01)	0.04	-0.16 (-0.32 to 0.01)	0.06	-0.15 (-0.37 to 0.07)	0.19	-0.17 (-0.37 to 0.03)	0.09
Urban – Rural	-0.12 (-0.35 to 0.11)	0.30	-0.03 (-0.24 to 0.18)	0.80	-0.20 (-0.47 to 0.07)	0.15	-0.13 (-0.38 to 0.11)	0.29
Urban - Urban	0.16 (0.04 to 0.29)	0.01	0.14 (0.02 to 0.24)	0.02	-0.01 (-0.16 to 0.14)	0.90	-0.02 (-0.16 to 0.12)	0.75

Analyses using linear regression; Results mutually adjusted for each exposure, age, sex, income in 2005, marital status in 2005, self reported health status in 2005, and each individual outcomes of interest in 2005

Appendix M. Sensitivity analysis for migration and urbanicity on social trust and emotional problems

	Social trust				Emotional problems			
	Completed data (n=53,973)		Multiple imputations (n=74,312)		Completed data (55,720)		Multiple imputations (n=76,183)	
	Odds ratio (95% CI)	p-value	Odds ratio	p-value	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value
Migration								
No	Reference		Reference		Reference		Reference	
Yes	0.94 (0.87 to 1.01)	0.08	0.96 (0.91 to 1.02)	0.25	1.14 (1.04 to 1.25)	<0.01	1.09 (1.21 to 1.18)	0.02
Urbanicity of location in 2005 and 2009								
Rural – Rural	Reference		Reference		Reference		Reference	
Rural – Urban	0.83 (0.77 to 0.88)	<0.01	0.85 (0.80 to 0.90)	<0.01	1.12 (1.03 to 1.21)	<0.01	1.09 (1.01 to 1.17)	0.03
Urban – Rural	0.88 (0.81 to 0.95)	<0.01	0.89 (0.82 to 0.96)	<0.01	1.08 (0.97 to 1.19)	0.15	1.04 (0.94 to 1.16)	0.39
Urban - Urban	0.85 (0.81 to 0.89)	<0.01	0.86 (0.83 to 0.90)	<0.01	1.04 (0.98 to 1.10)	0.16	1.02 (0.97 to 1.08)	0.52

Emotional problems defined as having quite a lot or extreme emotional problems during past 4 weeks=1; Social trust defined as feeling you can trust others=1; analysis using logistic regression for emotional problem and social trust; Results mutually adjusted for each exposure, age, sex, income in 2005, marital status in 2005, self reported health status in 2005, and each individual outcomes of interest in 2005