Health, cardiovascular disease and their determinants in the Kazakh population

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Declaration

I, Adil Supiyev, 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 and properly referenced in the thesis.

Date: 26.11.2018

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Abstract

Background: The high and fluctuating mortality and rising health inequalities in post-Soviet countries have attracted considerable attention, but there are very few individual-level data on distribution of health outcomes in Central Asian countries of the former Soviet Union, including Kazakhstan. The main causes of death driving the low life expectancy (some 12 years shorter than in Western Europe) are chronic non-communicable diseases, particularly cardiovascular diseases (CVD).

Aim: The main aim of the thesis was to investigate the levels and distribution of risk factors of CVD and the associations between a range of risk factors and CVD in Kazakhstan.

Methods: This thesis describes a population-based cross-sectional survey and a case-control study of acute coronary syndrome (ACS) and stroke in the Astana (Kazakhstan capital city) region. The cross-sectional survey examined 977 men and women aged 50-74 years (493 in Astana city and 484 in a rural area) randomly selected from primary care registers. Subjects in the cross-sectional survey served as controls for 348 cases of acute coronary syndrome (ACS) and 235 cases of stroke hospitalised during the study period in two hospitals covering over 80% of acute admissions for these two conditions in the Astana region. The examination of both sets of cases followed identical protocol, including a structured questionnaire, objective examination and collection of blood samples.

Results: The cross-sectional survey found high prevalence of cardio-metabolic risk factors and differences in the prevalence of risk factors by socioeconomic and demographic characteristics, including less favourable pattern in urban vs. rural residents. The case-control study identified associations between ACS and stroke and cardio-metabolic risk factors, health behaviours and socioeconomic factors. A consistent finding was a less favourable risk profile in the Russian vs. Kazakh ethnicity.

Conclusions: The prevalence of cardio-metabolic risk factors in the Kazakh population is high compared to Western Europe. The associations of ACS and stroke with risk factors were as expected, and there were some specific associations with socio-demographic characteristics. The pronounced socio-demographic differences in prevalence of cardio-metabolic risk factors suggest that preventive strategies may target population groups at higher risk of CVD.

Impact Statement

The most important impact of this research is that it provides the first individual-level evidence on cardiovascular diseases (CVD) in Central Asia obtained using internationally comparable methodology. CVD are the main cause of persistently low life expectancy in the region and investigation of the rates and causes of CVD in the region is of a paramount importance, and this is the first step in the consideration of effective prevention strategy. So far, data on CVD and other non-communicable diseases available from international agencies were based on routine data, and information on risk factors was derived from uncertain sources or external extrapolation. The information presented in this thesis will be important for governmental officials and policy makers.

The second implication is on the general perception of CVD diseases within Central Asian countries. At present, CVD are deemed to be the domain of clinicians while public health professionals have not been involved in CVD control. The thesis presents convincing evidence that socio-demographic factors play a major role as determinants of CVD risk and need to be taken into account. With the emergence of evidence-based medicine and evidence-based public health, these locally specific data from Kazakhstan will provide a major impetus at the country and regional level to consider evidence in clinical and preventive deliberations.

The third implication is related to the fact that in the present study many participants were unaware of their CVD risk status. Therefore all types of screening programs, including opportunistic screening, are likely to be effective in identifying CVD risk factors, such as raised blood pressure, abnormal blood lipids and blood glucose. In such cases, timely and sustained lifestyle interventions are likely to reduce the risk of CVD events, such as ACS and stroke, and hence will significantly reduce premature morbidity, mortality and disability. The CVD risk (and risk factors) can also improve clinical decisions related to the preventive interventions, such as improving coverage of statin therapy among adults with high risk of future CVD event. Therefore, comprehensive strategies that consider a full range of CVD determinants both at population-level and high-risk individual levels would be the most effective.

Finally, this research will have an impact on academia and research. Epidemiology of non-communicable diseases has not been well developed in Kazakhstan and Central Asia. Traditionally, has epidemiology focused on communicable diseases and public health was concerned with industrial hygiene. As a result, non-communicable diseases in the region have been largely neglected. This population-based study provides an example that it is possible and affordable to conduct a high quality epidemiological study of a non-communicable disease in Central Asian settings. It is expected that this will provide a motivation to improve academic teaching and training in research methods, introduce modern methods in teaching and training curricula, and eventually lead to an expansion of academic research into non-communicable diseases in Kazakhstan and in the wider region.

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Thesis outputs

Published articles

1) **Supiyev A**, Kossumov A, Utepova L, Nurgozhin T, Zhumadilov Z, Bobak M: Prevalence, awareness, treatment and control of arterial hypertension in Astana, Kazakhstan. A cross-sectional study. *Public Health* 2015, 129(7):948-953.
2) **Supiyev A**, Kossumov A, Kassenova A, Nurgozhin T, Zhumadilov Z, Peasey A, Bobak M: Diabetes prevalence, awareness and treatment and their correlates in older persons in urban and rural population in the Astana region, Kazakhstan. *Diabetes Research and Clinical Practice* 2016, 112:6-12.
3) **Supiyev A,** Nurgozhin T, Zhumadilov Z, Peasey A, Hubacek JA, Bobak M: Prevalence, awareness, treatment and control of dyslipidemia in older persons in urban and rural population in the Astana region, Kazakhstan. *BMC Public Health* 2017, 17.

Supplementary articles

1) **Supiyev A**, Nurgozhin T, Zhumadilov Z, Sharman A, Marmot M, Bobak M: Levels and distribution of self-rated health in the Kazakh population: results from the Kazakhstan household health survey 2012. *BMC Public Health* 2014, 14.
2) Hubacek JA, Stanek V, Gebauerova M, Adamkova V, Lesauskaite V, Zaliaduonyte-Peksiene D, Tamosiunas A, **Supiyev A**, Kossumov A, Zhumadilova A et al: Traditional Risk Factors of Acute Coronary Syndrome in Four Different Male Populations - Total Cholesterol Value Does Not Seem To Be Relevant Risk Factor. *Physiological Research* 2017, 66:S121-S128.

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Acronyms and Abbreviations

ACS	Acute coronary syndrome
BMI	Body mass index
CA	Central Asia
CVD	Cardiovascular disease
CHD	Coronary heart disease
CIS	Commonwealth of Independent States
DBP	Diastolic blood pressure
EBM	Evidence-based medicine
FBS	Fasting blood sugar
FSU	Former Soviet Union
HDL	High density lipoprotein
HT	Hypertension
ICD 10	The 10th revision of the International Statistical Classification of Diseases and Related Health Problems
IHD	Ischaemic heart disease
IFG	Impaired fasting glucose
LDL	Low density lipoprotein
LMICs	Low- and middle-income countries
NCD	Non-communicable disease
OR	Odds ratio
SBP	Systolic blood pressure
SES	Socioeconomic status
SRH	Self-rated health
TG	Triglycerides
WHO	World Health Organization
95% CI	95% confidence interval

CHAPTER 1

INTRODUCTION

1.1. Health Challenges in Central Asia: globalization, urbanization and nutrition transition

The high mortality and morbidity rates and substantial changes in the Post-Soviet region since 1991 have attracted considerable attention [1-4]. These changes took place in a wider context of political and economic transitions and social and demographic upheavals [5]. Nevertheless, most of the data on health of the populations in the region so far derive from Russia and the Baltic States, while very little information is available from the Central Asian (CA) republics.

Since their independence, the CA countries began to diverge from each other in different ways, primarily regarding their socio-economic growth [6]. There are, however, still many similarities in their development including public health and wellbeing challenges that those countries face [7]. In this interesting region, we often observe an unequal distribution of wealth resources, scarce access and poor quality of healthcare [8]. It should be noted that Central Asia is a dynamically growing region [9] that faces universal challenges such as rapid rates of urbanization, nutrition transition and an overall shift towards globalisation processes that impact on local cultures, social norms, life style and health behaviours, and contribute to the composition of new global values in this region [10].

After the dissolution of USSR in 1991, the CA republics experienced uneven urbanization and modernization processes following the adoption of independent socio-economic development models and urbanization strategies, depending on their demographic characteristics, settlement patterns and socio-economic conditions [11]. However, common to all these countries was a similar history with primarily agro-industrial economies and predominantly rural population which, after the unexpected independence increasingly migrated to urban areas, a process which was mainly driven by the prospect of better employment opportunities and the hope for a prosperous life in the cities [12].

In general, the health of urban populations is usually better than that of rural populations, which may be associated with better education, access to healthcare and overall superior living conditions. However, when the process of urbanization is fast and unregulated, it may have adverse side effects on health, sometimes creating unfavourable conditions for both communicable and non-communicable diseases [13, 14]. It has been widely documented that urbanization is one of the key drivers of non-communicable disease progression, especially in developing and lower income countries [15, 16]. Several studies have shown that the urban-rural health gradient appears to be mainly driven by socioeconomic factors and individual lifestyle factors [17].

For example, there are reports on rapid changes in the pattern of life-styles and health behaviours, particularly diet, associated with urbanization in developing countries [18]. These nutrition transition processes, linked with the process of globalization. are associated with changes in the quantity and types of nutrients, as well as by price and attractiveness of foods available for consumption [19]. Diets and foods consumption in urban areas differ noticeably from their rural counterparts. The availability of inexpensive and energy-dense food in urban areas together with a sedentary life-style facilitates the development of obesity, metabolic syndrome and its unfavourable consequences [20].

1.2. Insight into the knowledge and gaps in evidence in Central Asia

There is a wide gap in mortality and morbidity indicators between Western countries and Central Asian and other post-soviet countries [21, 22]. Currently, Central Asia is undergoing rapid socio-economic changes, which carries many risks and challenges, including an epidemic of cardio-metabolic risk factors [23]. Similar to many western countries. the leading cause of death in the region is cardiovascular disease (CVD). Health-wise, the unique features of this region are the overall low life expectancy, as well as a dramatic gender gap in mortality [24] and in lifestyle patterns and health behaviours [25].

The high mortality and morbidity rates in Central Asia are difficult to explain only by economic factors, and national peculiarities in health behaviours should also be considered [26]. For example, Kazakhstan, although being the largest economy in Central Asia, has higher prevalence of negative health behaviours compared to less developed and less prosperous Kyrgyzstan [27]. In addition, in this region, there is a persistent misunderstanding of the negative health effects of such harmful behaviours as tobacco use [28]. Thereby, due to the increasing speed of socio-economic growth in the Central Asian region, particularly urbanization and nutrition transition processes, it is fundamental to study the health and its determinants in this population for the overall sustainable development of this region.

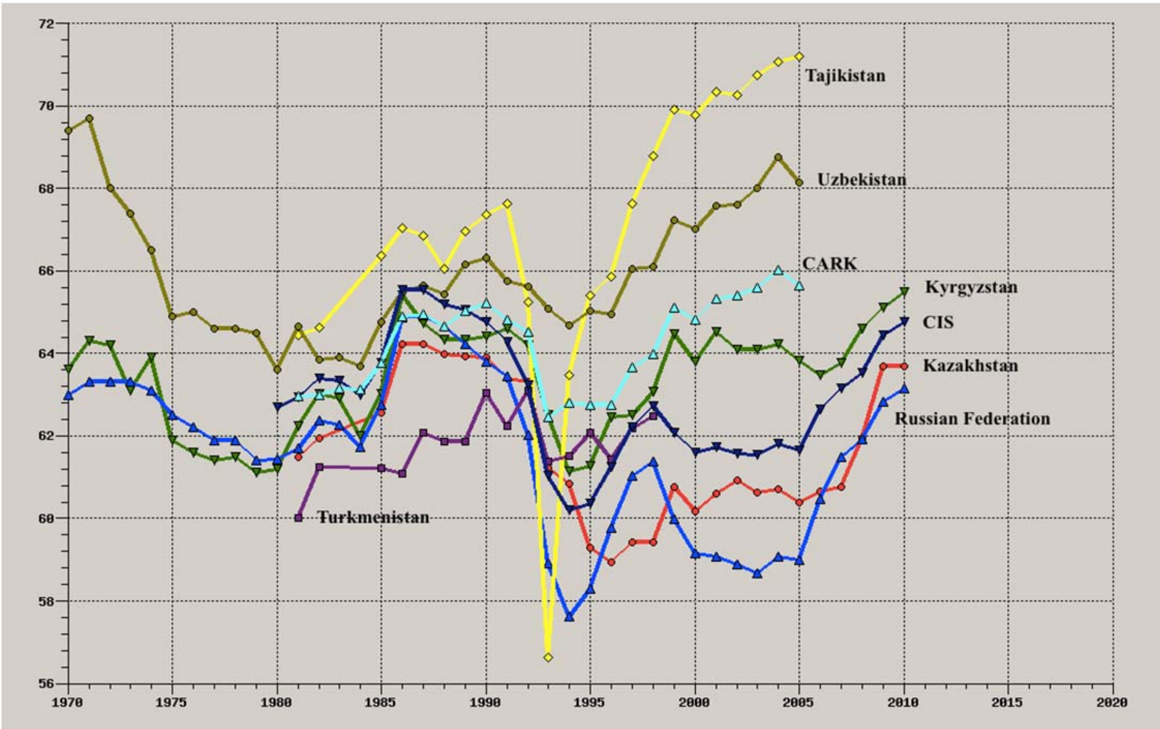
1.2.1. Mortality-based and other health indicators in the Central Asian region

In the present work under the term “Central Asia” we consider the following five republics of the former Soviet Union: Kazakhstan (pop. 17.9 million), Kyrgyzstan (5.8 million), Tajikistan (8.0 million), Turkmenistan (5.2 million), and Uzbekistan (30.2 million), with a combined total population of approximately 67 million as of 2013-2014 (Figure 1).

Figure 1 Political map of Central Asia

Among mortality-based indicators, life expectancy at birth is a useful and commonly used measure of the overall health of the populations, which is relatively reliable and comparable and is available for most countries. Before 1990, trends in life expectancy at birth in most CA republics followed more or less the same direction as in the Russian Federation, for both males and females (Figure 2 and Figure 3). After the dissolution of the USSR, the health patterns showed pronounced changes and fluctuations similarly to Russia, life expectancy at birth fell in all CA countries. This trend was more dramatic in Tajikistan, probably due to the civil war after May 1992 [6].

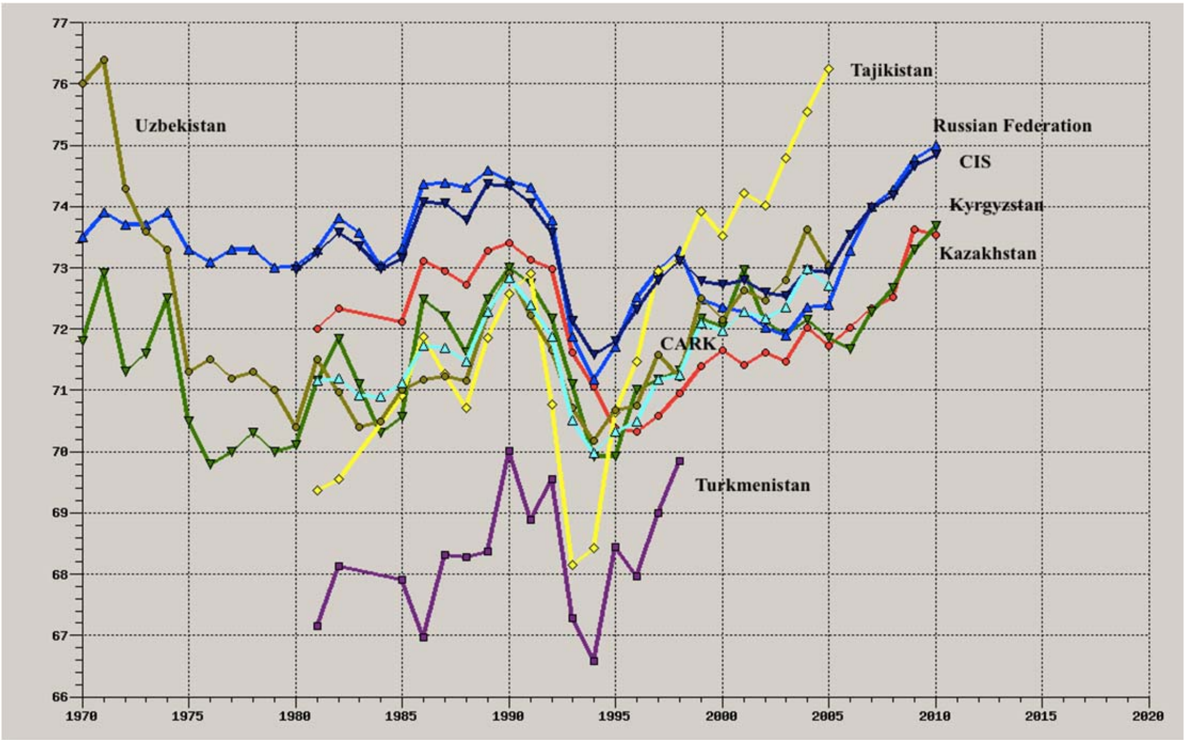
Figure 2 Trends in life expectancy at birth in Central Asia (years), males. Source: WHO Health for all database.



Y-axis: life expectancy at birth (years), x-axis: calendar year

After Tajikistan, the decline in life expectancy among men and women was the steepest in Kazakhstan and Kyrgyzstan (Figure 2 and Figure 3). After 1991 the decline in life expectancy among men in Kazakhstan broadly resembles the trend in the Russian Federation. Since 1996 life expectancy in Kazakhstan began to improve, but it remained the worst among the CA countries. Life expectancy figures among women are very similar. (Please note that more recent data are not available.)

Figure 3 Trends in life expectancy at birth in Central Asia (years), females. Source: WHO Health for all database.



Y-axis: life expectancy at birth (years), x-axis: calendar year

Kazakhstan has the highest (estimated) proportion of all-cause deaths attributable to non-communicable diseases (NCDs) among Central Asian countries – 84%, followed by Kyrgyzstan and Uzbekistan – 80% and 79% respectively - whereas the proportions were lower in Turkmenistan - 72% and in Tajikistan - 62% [29]. CVD is the largest contributor to the NCDs mortality, with death rates in Kazakhstan higher than in the WHO European region, where CVD accounts for 47% of all NCDs compared to 54% in Kazakhstan. Since the early 1990s, rates have increased steeply among men in each CA country, but this increase has been especially dramatic in Kazakhstan, where it has risen by more than 50 percent [30].

1.3. Overall structure of the thesis and main research interest

1.3.1. Main research interests

Understanding the factors underlying the cardiovascular disease epidemic in Central Asia is crucial to assess policy options due to a rapidly growing population in this region, socioeconomic transition and geopolitical situation in this region. The logical first step would be to investigate the determinants of CVDs in the region, taking into account the unique features of the Central Asian populations. This thesis seeks to contribute to such efforts. Therefore, the main aim of this project is to study the levels of distribution and determinants of CVD and their risk factors in Central Asia, and in Kazakhstan in particular, and to investigate the socioeconomic gradient of CVD and common risk factors in this region.

1.3.2. Structure of the thesis

To describe all major stages of my PhD project, the thesis is structured as follows. After this brief introduction and general information on the major health issues in the Central Asian region, the next chapter (Chapter 2) provides comprehensive background information on cardiovascular disease burden and its determinants in the Central Asian region. Chapter 3 describes the aims and objectives. The following sections, chapter 4 presents the methods section, including the design, fieldwork and data collection process. As the design of my PhD project included two components (a cross-sectional survey and a case-control study), the subsequent sections were split into two separate parts, dealing with cross-sectional data first and with the case-control study next. Therefore, Chapter 5 describes first the cross-sectional findings and then the case-control study results. Chapter 6 provides a discussion of the findings, again following the two components, in relation to existing research. Finally, chapter 7 provides brief conclusions and implications of the research described in the thesis.

CHAPTER 2

BACKGROUND

2.1. Cardiovascular disease in Central Asia: a region-specific literature review

The total population of the Central Asian countries is nearly 70 million people, and as a distinct region in the post-Soviet space, it is only behind Russia in terms of both population and territory size. This region is widely diverse in ethnic backgrounds, cultures and languages and it has unique economic and political characteristics. However, despite being geographically important and a considerably populated region, there has been very little domestic or international scientific interest in public health research and it remains the least studied region of the former Soviet Union (FSU) up to now.

To date, the best well studied areas of health and its determinants includes: (1) the assessment of Central Asia health systems analysis, taking into account the unique settings of economic and demographic transitions [6, 8]; and (2) work on communicable diseases, mainly due to health security reasons and to ensure that Central Asia communities are resilient to region specific health challenges, such as malaria, HIV/AIDS and tuberculosis [31-33]. Non-communicable diseases, and cardiovascular disease in particular, were the least investigated area of health research in Central Asia, despite their very high burden of these conditions in the region [34, 35].

Non-communicable diseases (NCD) are the major cause of the global burden of ill health. Of 57 million global deaths in 2008, 36 million, or 63%, were due to NCDs. Compared to communicable diseases, which are mainly predominant in the developing world; the proportions of death attributable to NCDs are similar in both developing and developed countries. As of 2008, nearly 80% of NCD deaths (29 million) occurred in low- and middle-income countries with about 29% of deaths occurring before the age of 60 [36]. In 2005, World Health Organization (WHO) re-evaluated the role of NCDs and denoted it as a neglected global health issue. However, still less than 3% of the global development assistance for health goes to NCD prevention and control [37]. The global burden of NCDs is very high but, so far, the control of these diseases globally has been largely unsuccessful because NCDs develop over a long-term, and risk factors are many and complex.

The leading causes of NCD deaths in 2000s were cardiovascular diseases (CVD), with 17 million deaths representing 29% of all NCD deaths, followed by cancers (14.5million deaths), and respiratory diseases, including asthma and chronic obstructive pulmonary disease (3 million). Diabetes caused another 1.3 million deaths but its role is underestimated, as it is an important cause of CVD [38]. CVDs were also responsible for the largest proportion of NCD deaths under age of 70 (39%). CVDs significantly contribute to the health costs in both developed and developing countries. Morbidity, mortality and disability of people suffering from CVDs, especially among the employed population have a high effect on economic development and represent a high burden to society [39]. With population ageing, annual NCD deaths are projected to rise substantially – up to 52 million in 2030: annual cardiovascular disease mortality is projected to increase by 6 million and annual cancer deaths by 4 million [40].

Despite the high importance of these conditions and the enormous burden of CVD, in the Central Asian region specific information on cardiovascular disease and its risk factors is of uncertain validity. There were only very few reports that attempted to generalize common trends and distribution of major health outcomes without a specific focus on cardiovascular disease [7]. Given the lack of information on this important topic in the region and the potential burden to society, it is important to investigate the levels of distribution of cardiovascular disease and its risk factors in all post-soviet Central Asian countries; and secondly, it is likely that there are differences or peculiarities not only between Central Asia and western countries, but also within the Central Asian region itself, possibly due to different stages of their economic and social development.

This chapter describes the available information on the levels of distribution of CVD and its risk factors in all post-soviet Central Asian countries. Given the evidence from high-income countries, the chapter focused on cardio-metabolic risk factors (such as blood pressure, obesity, diabetes and cholesterol), common behaviours (e.g. alcohol consumption and smoking) and socioeconomic risk factors. Despite similarity and general trends of CVD development both in developed and developing countries there are several region-specific characteristics that should be certainly noted, including, nutritional and epidemiological transition due to rapid socioeconomic and demographic changes, large-scale urbanization processes and increased migration activity, specifically for the Russian population after the dissolution of USSR.

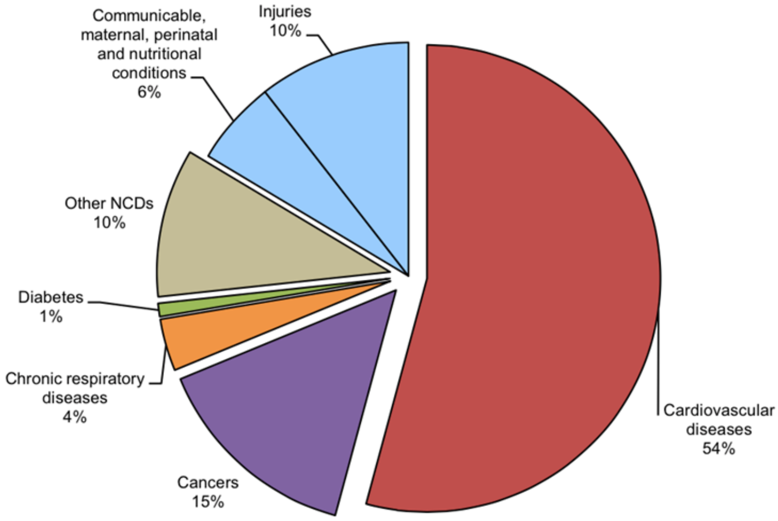
2.1.1. Background information about Kazakhstan

Kazakhstan has the largest and strongest performing economy in Central Asia. However, since independence Kazakhstan has faced a difficult period of economic recession after the collapse of the former Soviet Union in December 1991. The economy began to stabilize in 1996, but another period of stagnation was triggered by the Russian economic crisis in 1998. Economic recovery began in 1999 and accelerated in 2000, largely due to Kazakhstan's booming energy sector but more recently, the global economic crisis has negatively affected Kazakhstan. Education is universal and mandatory through to the secondary level. Adult literacy rate is 99.7% [41].

The size of Kazakhstan population is nearly 17 million people. Kazakhstan is populated by 131 ethnicities; the majority of the population is Kazakh (63%) and there is a high proportion of ethnical Russians (24%), in addition to many other minor ethnicities such as Uzbek, Ukrainian, German, Tatar, and Uyghur. Kazakhstan is officially a bilingual country: the Kazakh language is spoken natively by 64% of the population and has the status of the "state" language, while Russian, which is spoken by most Kazakhstan citizens, is declared the "official" language. Islam is the religion of about 70% of the population, while Christianity (mostly Orthodox) is practiced by 26%.

As mentioned above, trends in life expectancy in Kazakhstan are similar to those observed in other former Soviet countries, although the decline in life expectancy after 1991 was steeper and life expectancy in Kazakhstan has remained below the CIS average of post-Soviet countries (Figure 2 and Figure 3). Life expectancy at birth in Kazakhstan is among the lowest in the WHO European Region; it dropped from 68.8 in 1990 to 64.4 in 1996, and has since increased again to 68 in 2012. In 2012, healthy life expectancy in both sexes was 8years lower than overall life expectancy at birth. Cardiovascular disease, stroke and cancer are the main causes of death in the country (Figure 4).

Figure 4 Proportional mortality (% of total deaths, all ages and both sexes) in Kazakhstan.



Source: WHO global health observatory data repository. [29]

Kazakhstan has a large gender gap in life expectancy. Male life expectancy fell more steeply than female life expectancy in the first half of the 1990s, from 63.9 years in 1990 to 58.9 years in 1996, compared to 73.4 to 70.3 years in females. As of 2010, males have not yet regained life expectancy levels seen in 1990. In 2011, males were expected to live 62.3 years, while female life expectancy was 71.7 years [29].

Table 1 Population growth in Kazakhstan by age groups (in thousands) from 1950 to 2050.

	1950	1970	1980	1990	2000	2010	2020	2030	2040	2050
Total	6703	13110	14906	16530	14957	*16026*	17680	18873	20048	21210
<15	2303	4925	4820	5202	4135	*3925*	4867	4471	4465	4866
15-64	3962	7479	9176	10361	9802	*11015*	11410	12361	13156	13455
65+	438	706	910	967	1020	*1087*	1403	2041	2427	2889
80+	52	114	142	185	153	*193*	263	270	487	625

Source: World Population Prospects, 2017 [42]

The population size is relatively small for such a huge territory, although Kazakhstan's population is projected to grow up to 21 million by 2050 (Table 1). The dynamics of ageing population is slowly approaching the world's trends; in Kazakhstan, there is a steady growth of proportion of the population aged over 65 and over 80 years, which will subsequently increase NCDs prevalence in this population.

2.1.2. Healthcare in Kazakhstan

The process of healthcare system development in Kazakhstan should be viewed though the inherited Soviet model of healthcare organization that prioritised inpatient services and underrated primary health care, prevention (except of communicable diseases control) and health promotion. For example, in Kazakhstan the inpatient care consumed 53.4% of total public expenditure on health in 2008, while primary health care only received 16% [30].

Kazakhstan underwent large-scale health reforms after the dissolution of USSR. Since it achieved independence in 1991, Kazakhstan started rapid market-oriented health reforms with its first unsuccessful attempt to introduce compulsory health insurance system between 1996 and 1998. Afterwards in 2000, the country has introduced two major healthcare reform programmes that had to refocus the system from hospital sector to primary healthcare and simultaneously, with the support of international organization developed evidence-based medicine practices, as well as the allocation of huge investments into the healthcare facilities [30]. However, the overall healthcare expenditures in Kazakhstan (4.2% of GDP) remain low compared to other Eastern European, post-Soviet countries or the OECD average. This means that it is extremely challenging to achieve universal high quality healthcare services with this level of funding [43].

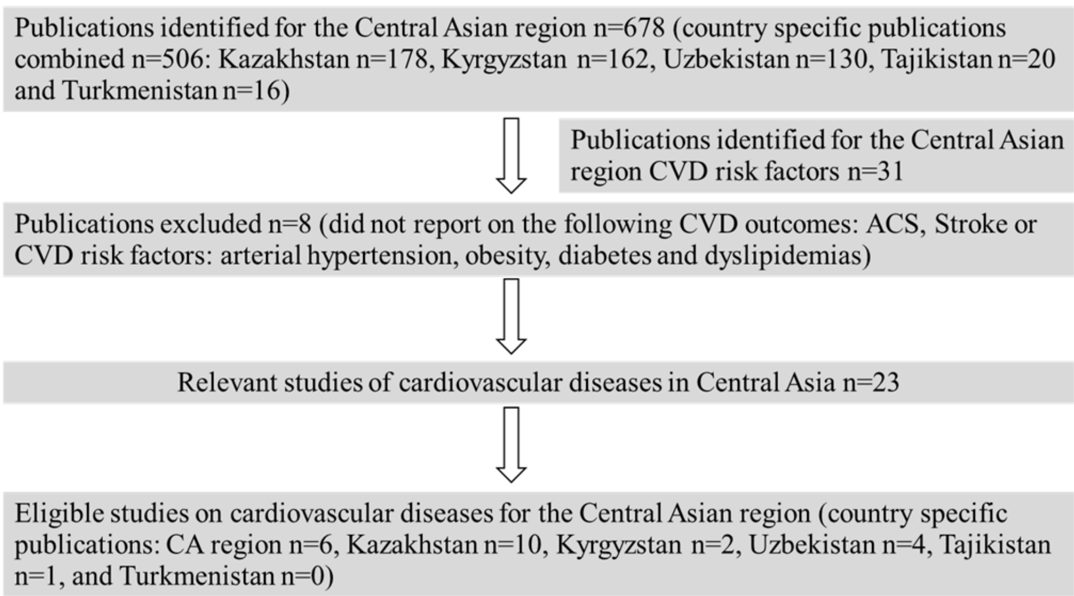
Despite the widely implemented healthcare reforms and the undertakings to introduce evidence-based medicine practices in Kazakhstan, there is still significant impact of the Soviet past that resulted in the dominant utilization of archaic diagnostic and treatment procedures and excessive hospitalizations [44]. Regarding the equitable access to healthcare, Kazakh rural households utilise significantly less ambulatory health care, and hospital admissions are lower compared to urban areas [45]. Interestingly, the unreformed healthcare system in another post-Soviet country, Belarus, appeared to provide more access than the Kazakh healthcare system that underwent the health reforms mentioned above [46].

2.1.3. Region-specific literature review search strategy

The literature review was conducted for the period between 1950 and 2018 using databases of PubMed, Web of Science and Scopus. Additional sources for grey literature included manual search and using general search engines such as Google Scholar for domestic journals and health reports both in

English and Russian languages. Articles were excluded only if they were letters, conference materials and studies and analyses not conducted on humans. All included works were assessed qualitatively. Due to literally very little information available on this topic pertinent abstracts without full-text articles both in Russian and English languages were also included in this review. Additionally, relevant citations from the obtained articles were also reviewed.

Figure 5 Strategy of study selection for the review



To identify all relevant studies on cardiovascular diseases, the search strategy included the following search terms: cardiovascular diseases in Central Asia, and similarly for every country in the region, e.g. Kazakhstan, Uzbekistan, Turkmenistan, Kyrgyzstan, and Tajikistan. Analogously, cardiovascular disease risk factors in all 5 republics were explored, including the following terms: arterial hypertension, obesity, diabetes and dyslipidaemia both in urban and rural regions. Stroke, acute coronary syndrome, coronary artery disease, ischemic heart disease were also used in search to extend and specify the disease outcomes. First, article titles and abstracts resulting from the search were reviewed for topic significance, and then potentially relevant articles or abstracts were read. The detailed strategy for the study selection for this review is presented in Figure 5; the descriptive details of journal articles from Central Asia are is shown in Appendix 10.

2.1.4. Cardiovascular disease and risk factors in Central Asia during socioeconomic transition

2.1.4.1. Mortality

The mortality, incidence, prevalence and burden of CVD have been abundantly reported for both developed and some developing countries, but there is only sparse individual-level information on CVD rates in Central Asia. Mainly, the data on CVD is limited to integrative ecological comparisons of WHO cross-countries statistics (i.e. based on routine data, mainly mortality) [47]. Although the general patterns of the CVD distribution in Central Asia is highlighted in the mentioned reports, it is necessary to explore some additional sources of information to grasp a more region-specific outlook for future public health implications in this region. Interestingly, after comprehensive examination of the extracted literature in all five Central Asian countries, only a few original research reports were found that dealt primarily with cardiovascular diseases and risk factors in the population.

According to WHO data, cardiovascular disease is common in low income countries [48], including Central Asia [49]. Although the Central Asian region, similar to developed countries, currently faces the emergence of a mortality pattern that is primarily driven by the rapid epidemiologic transition, where mortality due to cardiovascular and other non-communicable diseases overtakes mortality due to communicable diseases, the burden of communicable diseases remains high in the region [32]. This phenomenon, known as the double burden of non-communicable and communicable diseases, is a common pattern in a many developing countries [7]. Furthermore, analogously to Eastern Europe and other former Soviet Union countries, we might also expect the spatial inequality of CVD burden, particularly between rural-urban environments [50, 51].

Table 2 Top five causes of deaths in Central Asian countries in 2012

Rank	Kazakhstan	Kyrgyzstan	Uzbekistan	Turkmenistan	Tajikistan
1	IHD (32.5%)	IHD (31.7%)	IHD (34.2%)	IHD (33.0%)	IHD (21.4%)
2	Stroke (16.8%)	Stroke (13.8%)	Stroke (15.9%)	Stroke (12.3%)	Stroke (13.3%)
3	Cirrhosis of the liver (4.4%)	Cirrhosis of the liver (5.7%)	Cirrhosis of the liver (4.5%)	Cirrhosis of the liver (5.2%)	Lower respiratory infections (8.4%)
4	COPD (3.1%)	COPD (4.0%)	Lower respiratory infections (4.1%)	Lower respiratory infections (4.2%)	Preterm birth complicati ons (4.4%)
5	Self-harm (2.5%)	Road injury (3.1%)	Diabetes mellitus (2.2%)	COPD (2.9%)	Birth asphyxia and birth trauma (4.2%)

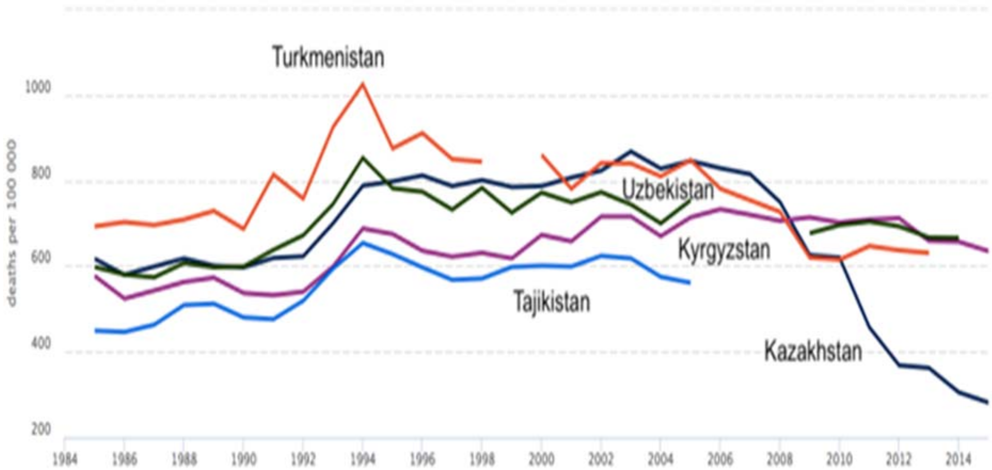
Source: WHO mortality database [52], IHD – ischemic heart disease; COPD – Chronic obstructive pulmonary disease

There were no detailed reports on CVD mortality in Central Asia. The best available data is the WHO mortality database [52], on which is based this overview of the general pattern of the CVD burden in the region.

Table 2 shows the top 5 causes of deaths in different CA populations. CVD was the largest cause of death in each of these countries. Ischaemic heart disease (IHD) was the leading cause of death in the region, followed by stroke. The percentages in the table indicate the proportion of the cause of death within each country and IHD and stroke together composed up to 50% of all deaths in CA countries, except Tajikistan where this percentage was slightly lower.

There are large variations in cardiovascular mortality worldwide. The highest age-adjusted mortality rates were reported in CA region and in Central and Eastern Europe, followed by several countries from the African region, while the lowest mortality rates were observed in west European and North American countries [40].

Figure 6 Diseases of the circulatory system per 100 000 (age-standardized death rate).

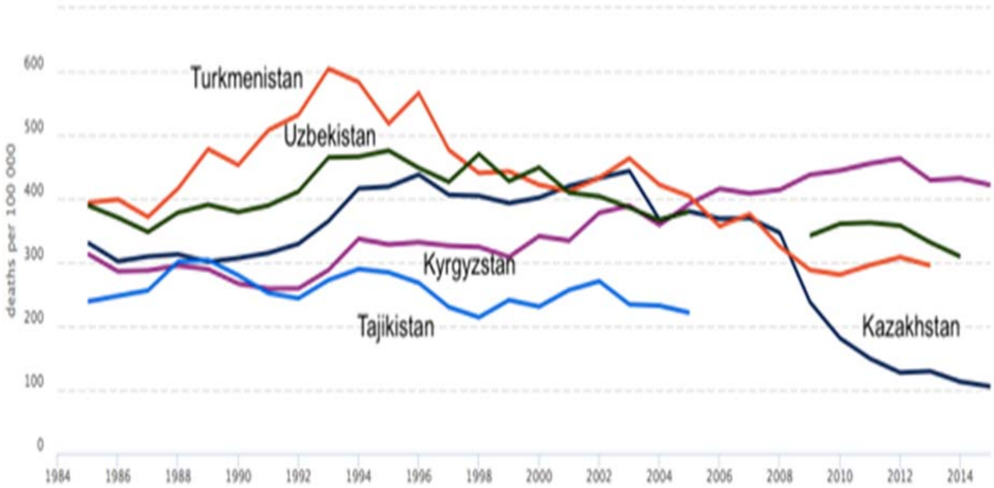


Source: WHO Health for all database

As stated previously, CVD is the leading cause of death in all CA countries. Mortality rates peaked in 1994, with the highest values in Turkmenistan, and have been gradually declining since then. After 2008, the steepest slope of declining mortality rates were observed in Kazakhstan, while the rest of CA countries continued to experience gradual decreasing rates in CVD mortality rates (Figure 6).

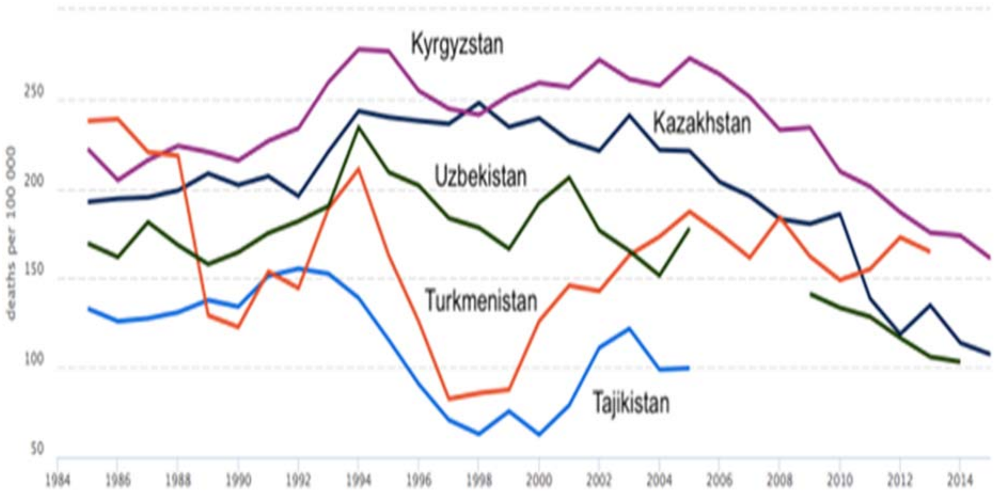
Similarly, ischaemic heart disease mortality rates resembled trends of overall CVD mortality, with a gradual decrease in values after 1994 and the steepest decline in Kazakhstan. However, the slight increase in IHD mortality was observed in Kyrgyzstan after 2000 (Figure 7).

Figure 7 Ischaemic heart disease per 100 000 both sexes (age-standardized death rate)



Source: WHO Health for all database

Figure 8 Cerebrovascular diseases per 100 000 both sexes (age-standardized death rate)



Source: WHO Health for all database

Stroke mortality dynamics in CA countries were less stable. Stroke mortality peaked in 1994 among all CA countries and started to decrease sharply up to 1999, since then the gradual increase was observed until 2005 and reached similar values as in 1994. After 2005, stroke mortality rates were steadily decreasing in most CA countries (Figure 8). However, cardiovascular mortality in CA populations is likely to grow in the near future, given the projection for most low and middle income countries, although there will be fluctuations and heterogeneity between the lower income countries, as well as within the Central Asian region [53].

2.1.4.2. Morbidity

Relatively little information is available regarding within country variations in CVD morbidity in Central Asia. Based on existing information from Central Asia, ischaemic heart disease (IHD) among the male population was slightly more prevalent in urban than rural areas. For example IHD prevalence in Uzbekistan was 10.8% vs. 8.8% respectively [54, 55]. There was an expected age gradient in the prevalence of CHD between 40-49 (5.8%) and 50-59 (13.1%). Cardio-metabolic risk factors increased the prevalence of IHD; e.g. the combination of arterial hypertension and obesity was associated with 3.5 fold increase in prevalence [54]. In a study in Kyrgyzstan, IHD prevalence was also high and differed by ethnic group, with a prevalence of 13.9% in Kyrgyzes, 12.8% in Russians and 8.3% in other Central Asian ethnicities. However, the methodology was not described, and there was no indication whether these differences were seen in both urban and rural areas [56].

2.1.4.3. Urban – rural differences

While the data on the levels and distribution of CVD in rural areas are inconsistent, one apparent common characteristic for rural areas in the CA region is a very low level of awareness, treatment and control of CVD risk factors [57, 58]. Given that the rural population is currently larger than urban population in most Central Asian countries except of Kazakhstan, which is highly urbanised and sets the urbanization trend which will impact the rest of Central Asia [59], and this may also affect future trends in IHD. However, due to incomplete and sometimes unreliable information on CVD in Central Asia, we may only speculate whether such CVD shifts will be greater in the urban regions.

According to studies from other low income countries, lifestyle changes and growing urbanization processes may play an important role [16, 60]. In a study of the Kazakh rural area, the diagnosis of ischaemic heart disease (IHD) was found in 4.1% of male participants aged 30 to 59 years and almost half of them (47.2%) were newly diagnosed cases. Interestingly, IHD among office clerks was found to be twice as common (7.2%) as in those engaged in physical job (3.3%) [61]. In younger urban first year students in Russia, Kazakhstan and Uzbekistan in the early 1980s, the prevalence of CVD risk factors (hypertension, smoking, overweight and low physical activity) was relatively high among both males and females [62]; however, no rural comparison group was available. It is expected that all Central Asian countries will gradually develop into highly urbanized populations and complex measures to combat the potential health risks will need to be considered.

2.1.4.4. Ethnicity

Historically, the Central Asian region was multi-ethnic, and the ethnic composition of certain parts of each CA country is also highly heterogeneous, which may in turn help explain regional and national variations in CVD mortality and morbidity [63].

There is substantial evidence that health and health-care experiences vary along ethnic lines and the need to understand ethnic health inequalities has repeatedly been highlighted [64]. A careful and specific approach is needed for a multicultural and multi-ethnic setting, such as Central Asia, and for Kazakhstan in particular. Although being repeatedly mentioned in documents discussing Central Asia and other CIS countries, very few studies have addressed ethnicity as independent determinant of health due to the sensitivities related to collecting data on ethnicity [65]. Two recent studies from Kazakhstan suggested a significant effect of ethnicity on health; with participants reporting Russian ethnicity having moderately increased risk of poor self-rated health compared to Kazakhs [23, 66].

Temporal CVD mortality variations in Central Asia may also be partly explained by different regional ethnic composition [67], however the major cause of these variations was hypothesised to be different alcohol consumption patterns in Slavic and Central Asian ethnicities [68]. This study results suggest that ethnic mortality gaps in Central Asia might be related to the degree of ‘russification’, which probably results in the patterns of alcohol consumption in non-Russian populations; the authors showed that adult mortality among Kazakhs was lower compared to Russians, but higher than in Kyrgyzstan. All-cause mortality rates for Russian men was 27% higher compared with Kazakh men, and alcohol-related mortality in Russian men were 2.5 times higher than in Kazakh men (15% and 4.1 times higher among females, respectively) [68].

2.1.4.5. Socioeconomic factors

Socioeconomic measures need also be considered when assessing distribution of health in the population [69, 70]. Since there are very few reports on CVD in relation to socioeconomic factors in CA, this section also included other health outcomes.
The association between education and health has been observed in many populations and time periods for a wide variety of health outcomes. The strength of the relationship between education and health varies by health outcome but, with very few exceptions, virtually all diseases are more common in persons with low education. For example, Cutler (2014) has shown that education was positively associated with healthier behaviours as regards to smoking, diet, obesity, health knowledge, the control of high blood pressure and diabetes in 31 countries in Europe [71]. Regarding all-cause mortality, Mackenbach found pronounced educational gradients in death rates in 22 European countries, include Central and Eastern Europe [72]. Educational gradients in CVD mortality has been found in many world regions, including Asia [73].

The evidence from CA is limited but existing reports confirm this pattern observed elsewhere [74-77]. For example, education was the most robust and consistent predictor of self-rated health in Kazakhstan [23, 66]; participants with less education than higher were 3 times more likely to report poor than good health [66]. Since education is unlikely to be affected by the reverse causation bias (because it is usually completed relatively early in life), it remains the most useful and readily available indicator of individual socioeconomic status in former communist countries.

In the Central Asian region, similar to other parts of the world, there are differences between urban and rural areas with regard to education level. For example in Kazakhstan the percentage of inhabitants having a higher education is greater in urban (62%) compared to rural areas (36%). [58] This is in turn could have a considerable effect on CVD trends and regional differences and to some extent might explain the urban/rural health disparities in CA region, especially low awareness levels in rural regions by various CVD risk factors.

Given the large variations in CVD rates by education levels, urban/rural and ethnic differences in Central Asian region, based on the scarce retrieved literature, it is of considerable interest to investigate alternative markers of socioeconomic status to capture the effect of economic transition in the region and its effect on health, CVD in particular. Indeed, there are many individual level socioeconomic indicators reported in the international literature to be associated with CVD mortality and morbidity [78-80]. Unfortunately, this important issue has not been addressed in the CA region; no such study was identified in the literature review.

The economic resources available to an individual or a household (e.g. income or wealth) have been hypothesized to affect health through the direct material effects of inadequate living conditions (absolute deprivation) and/or through social comparison with others (relative deprivation) [81] [82]. The effects of material conditions, wealth or income on health are to a large part interconnected, and the mediating mechanisms are likely to be similar. The associations of both household income and household wealth with less-than-good self-rated health were established in many studies [83, 84] but, as with other variables, there is little evidence from CA. In a national survey of

Kazakhstan, car ownership, used as marker of material conditions, was a powerful predictor of self-rated health [23]. However, there were literally no data available on the effect of material conditions on cardiovascular disease and/or its risk factors in CA region.

In the systematic search of CVD determinants in the CA region, no reports on unemployment and job insecurity in relation to CVD (or health more generally) have been found. This may reflect the issue of labour market measurements and their availability in official unemployment figures, which are generally low in CA region. This is an important problem, as both the under-reporting of unemployment and the misclassification of employment status in national registers might blur the health consequences, especially in rural areas. Although the number of insecure jobs has increased considerably over the recent decades, both in Eastern and Western Europe, relatively little is known about the health consequences of job insecurity in CA [85]. This question is particularly pertinent for the former socialist countries where unemployment was unknown until 1990, but has risen sharply after the collapse of the Soviet Union. It has been hypothesized that labour market factors played an important role in the mortality crisis in Russia [86-88]. Consistently with this hypothesis, unemployment and job insecurity was found to be significantly associated with an increased risk of mortality and poor health in Russia [87]. However, no studies so far have directly examined this issue in Central Asia.

2.1.4.6. Summary of findings

It can be concluded that CVD morbidity and mortality rates are high and mostly increasing in Central Asian countries. There are several factors potentially influencing the risk of CVD in these countries, including large urban/rural differences, ethnicity and socioeconomic factors. It is likely (although not well documented) that temporal trends were accelerated by the rapid societal and economic transition in the post-Soviet countries, but there is no direct evidence on any of such factors from CA. The limited evidence from CA countries highlights the necessity for further investigations, as it is likely that the pattern of the association between socioeconomic status, cardiovascular health and health behaviours in the region could be similar to that in Russia and other former soviet countries, although there may be some specific exceptions to the general rule [89]. Thus, significant efforts to address these issues should be undertaken in order to improve population health in the CA region.

2.1.5. Acute Coronary Syndrome: the magnitude and gender gap in mortality

Acute coronary syndrome (ACS), which includes myocardial infarction and unstable angina, is the major component of ischaemic heart disease (IHD), and in most population, ACS accounts for the majority of IHD deaths among younger persons (whereas heart failure is the most important cardiovascular cause of death among older persons). The treatment advances in recent years significantly improved coronary care and survival, and distinctly reduced mortality due to Acute Coronary Syndrome (ACS) in most western countries [90]. Nevertheless, ACS, specifically acute ST-segment elevation myocardial infarction (STEMI), remains one of the most fatal ACS conditions in the Central Asian region and Kazakhstan [91]. In contrast, in developed countries the rates of STEMI decrease while the incidence rates of non-STEMI (NSTEMI) increases [92]. The management of ACS is complex and comprises of several important components, including timely hospitalization and early treatment procedures, such as percutaneous coronary intervention (PCI) and appropriate in-hospital coronary care [93, 94].

One of the major components of both curative strategy and prevention is to maximize the patients' knowledge and awareness about ACS symptoms and risk factors. Awareness of symptoms may play the critical part in ACS management [95]. Supposing that in-hospital treatment is sufficiently developed in urban regions in CA countries and appropriate clinical guidelines are implemented, then there is still large proportion of rural population in Central Asian region that remain unaware [57]. Awareness of risk factors is essential for any preventive strategies. As it was discussed previously, low health awareness levels compared to urban areas may jeopardise the timely management of ACS from the onset of symptoms to hospitalization in CA region and may also affect effectiveness of any preventive programmes.

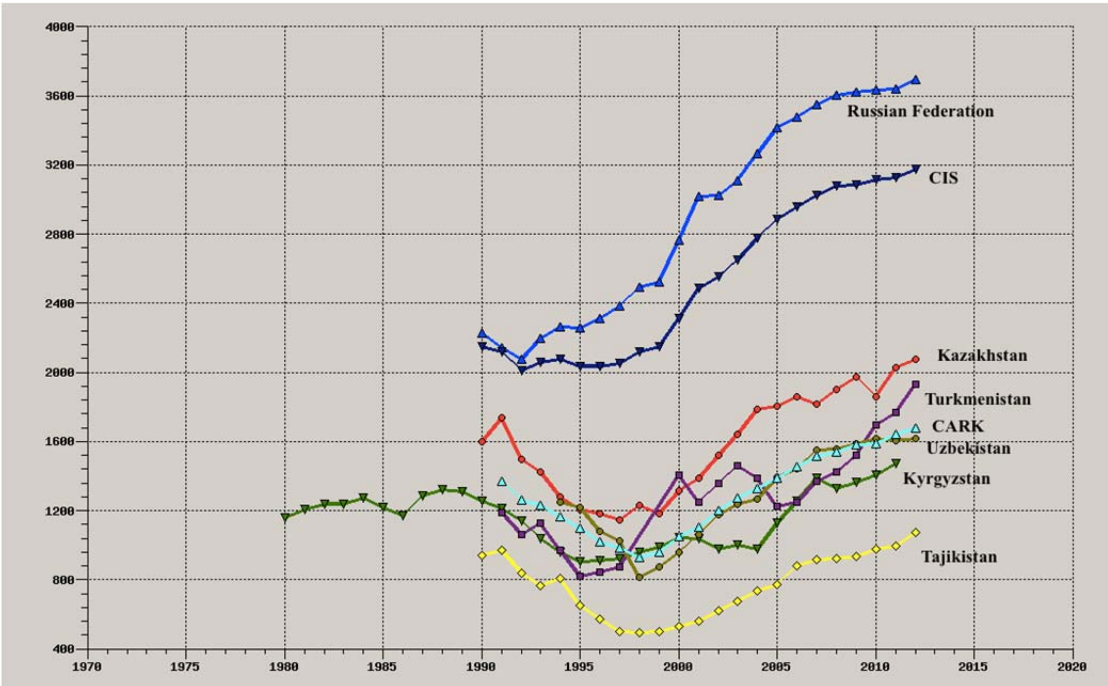
In Kazakhstan, the ACS in-hospital mortality between 2012 and 2015 was around 9.0% [91]. As expected, the mortality was significantly higher in females and in older patients, but surprisingly higher among the patients living in urban than rural areas which might suggest that either these patients had more complications and other chronic non-communicable diseases, as compared with the patients from rural regions, or that the patients from rural regions had not been delivered to hospital in time [91]. Unfortunately, more detailed information was unavailable to explain this observation.

An interesting and potentially important feature of CVD in post-Soviet countries is the large difference in the risk of mortality between men and women. For example, the gender gap in life expectancy in Russia is about twice as large as in Western Europe [96] and it has been suggested that the international differences in the gender gap in mortality are largely driven by differences in the prevalence of main risk factors, such as smoking and alcohol consumption. However, the available (and sparse) evidence from Central Asia is not entirely consistent with such a pattern. The Kazakh study mentioned above found a higher prevalence of ACS mortality in females [91] which is not consistent with previously published data from Eastern Europe where there was a rapid increase in IHD mortality among middle-aged men, [97]. Other factors such as older age, cardio-metabolic risk factors and history of coronary heart disease were all associated with increased hospital mortality in the expected direction [98].

In Uzbekistan, in-hospital outcomes in males and females did not differ significantly and were driven by the common tendency of late hospital admission, as women arrived to hospital on average in 4 hours later than men [99]. While the evidence base is inadequate, we might speculate that the causes of these differences in mortality between men and women in the CA region may be related to socio-economic factors (e.g. via low levels of treatment of dyslipidaemia and arterial hypertension) and to factors associated with health care delivery services.

It has been suggested that marital status is associated with various health determinants, morbidity and mortality and it may, to some extent, explain these gender differences, given the huge gender gap in life expectancy in CA region as was mentioned previously [100]. For example, in a Swedish population-based study of middle-aged men, the association between marital status and hypertension as well as CVD mortality risk remained statistically significant even after multiple adjustments for possible confounders, with single men having higher risk than married/cohabitating men [101]. However, the results on marital status and CVD risk in women were less consistent; the associations were weaker and only marginally statistically significant. Overall, the literature suggests that the marital status has a more consistent protective effect on mortality in men than in women. As with other factors, most studies come from Western countries, although there were several studies in Russia and other former Soviet countries which were consistent with the international literature [102] [23] [66].

Figure 9 Hospital discharges, circulatory system disease, per 100 000.
Source: WHO Health for all database

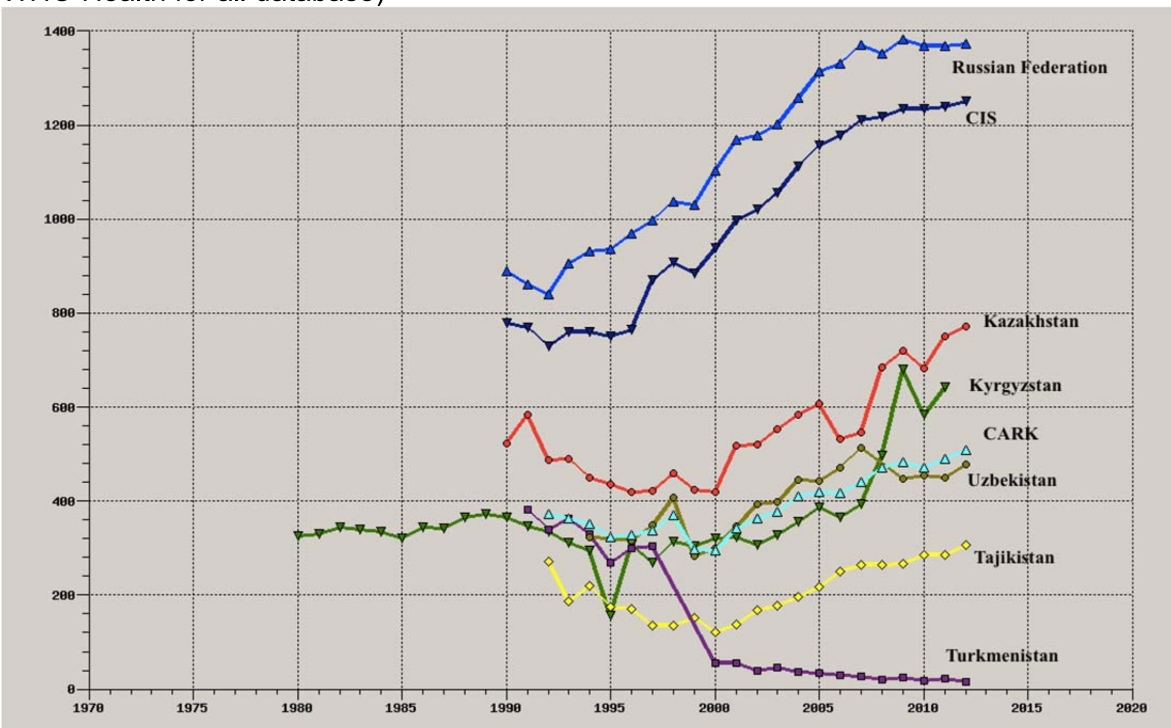


y- number of discharges per 100 000, x- time period (year)

While there are some limited data on CVD mortality in CA, albeit mainly from national statistics with questionable reliability, there is virtually no information on the incidence of CVD in the CA region. A very crude way to approximate the incidence rates might be to assess hospital discharges by each CA country. These data come from administrative sources and therefore reflect the specific organizations of the health system of each CA country, which makes it difficult to draw comparisons but this is the only available source

[103]. In all CA countries, the numbers of hospital discharges of circulatory system diseases after 2000 were steadily increasing (Figure 9). Kazakhstan is among the leaders among CA countries in the rates of hospital discharges for circulatory system disease patients and cerebrovascular disease (stroke) and ischemic heart diseases, in former Soviet Union, only Russia has higher rates (Figure 9, Figure 10 and Figure 11). Other CA countries show a similar growth in discharge rates after 2000 except Tajikistan with the lowest rate and smallest increase.

Figure 10 Hospital discharges, ischemic heart disease, per 100 000. (Source: WHO Health for all database)



y- number of discharges per 100 000, x- time period (year)

High levels of fatal and non-fatal CVD in all CA countries have major implications for the health in the region and present a challenge for the society and the health care system that needs to be addressed by public health and clinical care systems (Figure 10 and Figure 11).

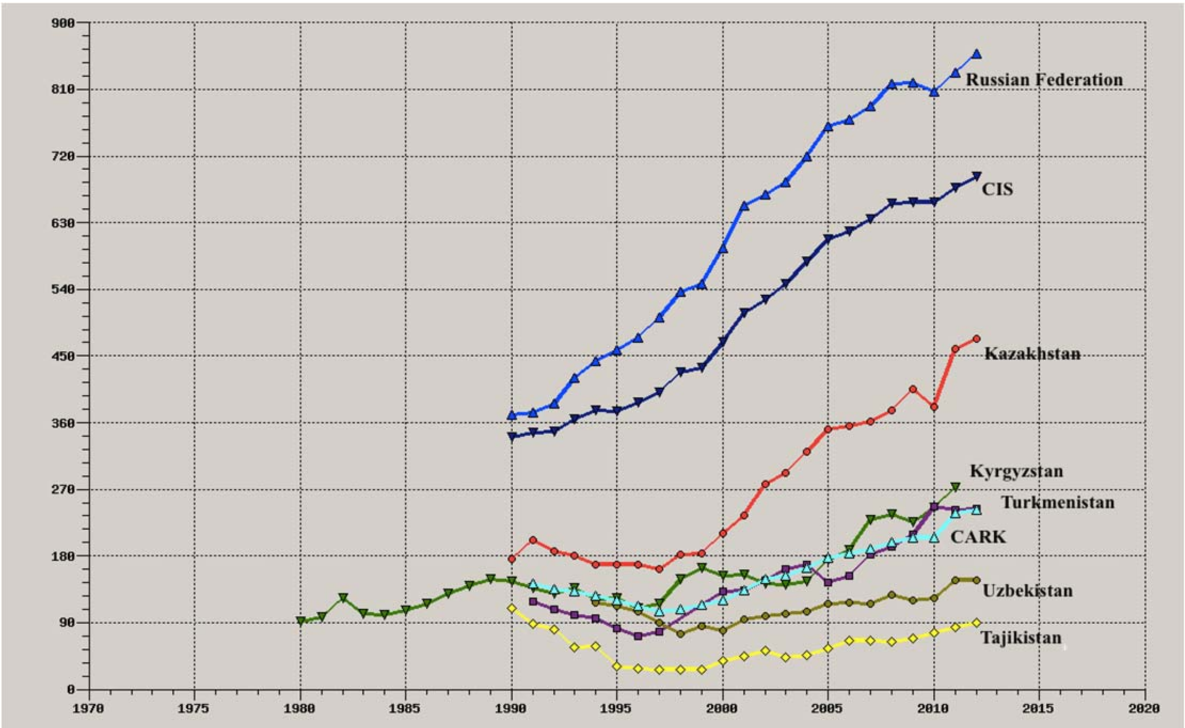
Unfortunately, the quality of individual level data on health status is poor (e.g. regarding self-reported health indicators) and difficult to compare, and there is a debate on the validity and consistency of data obtained from FSU countries [104]. As already mentioned, CA countries have very little empirical individual-level data on mortality and morbidity of NCDs, including CVD. The data on the rates of CVD outcomes were obtained from WHO Health for All database. This database, however, do not provide the source of the data and the methodology on how the data were collected. In some instances, there was a note that the original data provider was the local statistical agency. This may be somewhat problematic, as in our experience the national statistics agencies in Central Asian countries often under- or misreport major health outcomes due to the imperfect surveillance systems. In addition, many health outcomes prevalence rates were obtained by approximations from neighbouring countries. Overall, it is not clear how reliable these secondary data are.

Accurate data from this region are crucial to assess the trends to better understand the determinants of CVDs in the region, as they are likely to be, at least partly, prevented through life style changes as healthy diet, tobacco smoking cessation policies, regular exercise, and weight regulation. Such interventions alone could lead to a substantial reduction in heart diseases, stroke, diabetes, and cancer [105]. However CVD (and other NCDs) remain a neglected issue in the agendas of many governments, particularly in CA countries [37].

2.1.6. Stroke profile in Central Asia: unknown risks and implicit causes

For the last few decades, stroke has been recognized as a severe public health threat worldwide, not least because of its severe disability consequences [40]. The burden of stroke in developing countries has also increased; two thirds of global stroke occurs in low and middle-income countries [106]. Due to progressive ageing of the population in the world, and the increasing prevalence of major risk factors for stroke, such as hypertension, diabetes and obesity, the burden of stroke is expected to grow further in the future [40]. Similar trends may be happening as part of the epidemiological transitions processes reported in Central Asian region but the pattern of the risk of stroke in CA region is unclear, with only a few available sources from aggregated global studies of disease.

Figure 11 Hospital discharges, cerebrovascular diseases, per 100 000. Source: WHO Health for all database



y- number of discharges per 100 000, x- time period (year)

Surprisingly, the rates of stroke mortality seem higher in CA countries compared to the rest of the world [21]. Crude stroke mortality rate was higher in Kazakhstan (in 2003) than in any of the other country reporting mortality data to WHO. Interestingly, Kazakhstan, with such high stroke mortality rates had a considerably lower proportion of the population who are aged ≥65 years, less than 7%. Similarly, Kyrgyzstan, and Uzbekistan, with low proportions of older people, crude stroke mortality rates are similar to that in developed countries [107]. These data contradict with the conventional belief that the stroke is simply a consequence of aging processes. For instance, Japan with around 23% of the population aged ≥65 years has a relatively low levels of stroke mortality rates [107].

To reduce the burden of stroke in the CA region there should be complex and effective programmes for stroke prevention and management that focus on primary and secondary stroke prevention as well as on establishment of a stroke surveillance program. Due to the lack of reliable data on the determinants of stroke mortality in the CA region, there is an urgent need for individual level studies to understand this phenomenon. It is difficult to explain this high burden of stroke by differences in the prevalence of risk factors, but there might be some general patterns in the CA region related to access to health care services, or ineffective prevention or treatment strategies. However, stage of epidemiological transition and psychosocial environments should also be considered.

2.2. CVD risk factors and its characteristics in Central Asia

The levels and distribution of CVD and its risk factors are well studied in western countries. By contrast, the evidence in some other regions, including Central Asian republics of the former Soviet Union, is limited, with only sporadic publications in peer-review literature, many of which are out-dated [8, 108]. The validity of these reports is also questionable, as the design of published studies is often not well described, often of poor standard and results are difficult to compare to other studies, because inconsistent methods are used [109]. In addition, different CA countries have different healthcare and social security approaches [6, 110]. Although WHO has compiled some routine data on mortality-based indicators for major NCDs, individual level data are not available. However, in the last few years, evidence has been emerging that the trends of NCDs distribution in Central Asia are similar to western world but they may have its own peculiarities. The existing evidence is described in detail below.

2.2.1 Lifestyle and health behaviours in Central Asia

Conventional (sometimes called classical) cardiovascular risk factors include high blood pressure, high cholesterol concentrations, obesity and smoking. The risk factors overlap with risk factors for type 2 diabetes, which includes obesity (particularly central adiposity), insulin resistance, hyperglycemia, dyslipoproteinemia and hypertension. Given the fact that most of these risk factors are common for both CVD and diabetes, and diabetes itself is a risk factor for CVD, the term “cardio-metabolic” risk factors is commonly used. These conditions can occur in isolation but they often cluster within individuals, often in association with other factors, such as physical inactivity or alcohol consumption [111].

As mentioned in section 2.1.2. CVDs are the leading cause of death in Kazakhstan, and CVD mortality rates in both sexes have risen consistently the past few decades. Alcohol consumption, smoking, diets and poor detection and treatment of hypertension are considered major contributing factors to the increase in cardiovascular mortality in the region [112]. The simplest explanation is that high levels of modifiable risk factors (smoking, alcohol consumption, raised blood pressure, obesity and dyslipidaemias, physical inactivity, impaired glucose tolerance and diabetes) are the main causes for the high rates of CVDs in the former Soviet Union [27].

*Table 3*Table 3 shows the WHO estimates of the prevalence of some of these risk factors in several former Soviet countries.

Table 3. Prevalence of selected risk factors in Central Asia and in Russia

Risk factors		Males	Females	Total
Current tobacco smoking (%) (2008)	Kazakhstan	48%	12.1 %	29.8%
	Kyrgyzstan	45%	1.6%	21.8%
	Uzbekistan	20%	1.1%	10%
	Russian Fed.	59%	29%	40%
Total annual alcohol per capita consumption, in litres of pure alcohol (2010)	Kazakhstan	15.7	5.5	10.3
	Kyrgyzstan	6.7	2	4.3
	Uzbekistan	7.9	1.3	4.6
	Tajikistan	4.3	1.4	2.8
	Turkmenistan	7.6	1.3	4.3
	Russian Fed.	23.9	7.8	15.1
Obesity (BMI ≥30) (2008)	Kazakhstan	19.1%	27.6%	23.7%
	Kyrgyzstan	10.9%	19.8%	15.5%
	Uzbekistan	12.8%	17.4%	15.1%
	Tajikistan	7.2%	10%	8.6%
	Turkmenistan	12.9%	13.5%	13.2%
	Russian Fed.	18.6%	32.9%	26.5%

WHO Global Health Observatory Data Repository [29]

2.2.1.1. Diet and obesity

Over the last decades, obesity prevalence has been increasing throughout the world (WHO, 2011). Looking at the global scale, one in every nine adults was obese in 2008 [113]. Obesity prevalence has doubled between 1980 and 2014, resulting in about 600 million obese adults over 18 years old (WHO, Fact Sheet, 2015). One of the studies found that over the past four decades, the mean age-adjusted male body mass index (BMI) rose from 21.7 to 24.2 and in women from 22.1 to 24.4 [114]. Despite the common belief that obesity and overweight are less prevalent than underweight in developing countries, the data from WHO shows the opposite trend [40].

Based on aggregate data from WHO, the highest levels of obesity were observed in Kazakhstan (23.7%) and the lowest rate in Tajikistan (8.6%); Kyrgyzstan, Uzbekistan and Turkmenistan have similar prevalence of obesity (15.5%, 15.2% and 13.2% respectively) (Table 3). A large gap between genders was observed in Kazakhstan (nearly 9%) followed by Kyrgyzstan and Uzbekistan, while the gap was smallest in Turkmenistan – 1.6% (Table 3).

The available data on Central Asian region indicate that obesity has become a major public health concern, similar to high-income countries [115]. It has been estimated that overweight are among the top three leading causes of ill health burden among men in the Central Asia [116]. As obesity is strongly associated with diabetes, hypertension and other conditions, metabolic risk factors are likely to play an important role in the high CVD mortality in the region [117]. However, the current poor evidence base further underscores the need for individual level studies in the region.

Analyses of the 2002 Uzbekistan Health Examination Survey (UHES) revealed that 26% of men aged 15-29 years were overweight and 5% were obese, while among women aged 15-49 years 21% were overweight and were 7% obese [116]. The authors concluded that the proportion of overweight and obese men and women has significantly increased from 1996 to 2002. A cross-sectional pilot study on the assessment of cardio-metabolic prevalence among residents of Kyrgyzstan (n= 322) reported that ethnic Kyrgyz about 29% (but only 94 individuals) were obese and mean BMI was 27.4 30 kg/m^2 [118]. Data available on the obesity prevalence in Turkmenistan and Tajikistan is limited to WHO reports. However, surprisingly Matthys et al reported that 62% of persons in Tajikistan adults aged 45 years and over were overweight or obese [119]. In the Republic of Kazakhstan, research conducted on residents of Northern, Southern and Western regions of the country indicated that the prevalence of excessive body mass index might be as high as 36%. Among them about 23.7% were obese [120]. It should be noted that these estimates are not exactly concordant with WHO estimates but show that cardio-metabolic risk factors, specifically in middle aged and older ages, are very common in Central Asia.

There is virtually no information about the distribution of obesity within CA populations, particularly regarding social gradients in obesity. An important consideration is that the patterns of obesity in CA (and possibly other FSU countries) may not necessarily be an attribute of poverty or low socio-economic position. While in high-income countries the association between education and obesity is inverse, in the lower-income countries the social distribution of obesity is less predictable, with inconsistent findings [20]. Obesity is a complex metabolic disorder, which results from an interplay between unhealthy life style, energy intake and genetic predispositions [121].

The risk of obesity is strongly influenced by diet (high energy intake) and lifestyle (low physical activity), which have been changing dramatically as a result of economic and nutritional fluctuations in CA region. Therefore, it is important to understand the local specific determinants of obesity in these countries in order to formulate an effective policy for reducing the problem and improving the health of the population in the region.

2.2.1.2. Physical activity

Physical activity is important factor for maintaining healthy body weight (and health and functional status) of each individual. There is good evidence that physical activity is beneficial for a range of NCDs, including CVD and many cancers. [122]

Table 4 Prevalence of insufficient physical activity (age-standardized estimates)

Country	Male	Female	Both sexes
Kazakhstan	32% [12.8-66.3]	31% [12.7-65.7]	31.5% [12.1-66.0]
Russian Fed.	22.7% [8.2-54.7]	18.8% [6.7-46.1]	20.8% [7.4-52.1]
USA	33.5 [31.9-35.2]	47.4 [45.7-49.1]	40.5 [39.3-41.7]

Source: WHO Global Health Observatory Data Repository [29]

There are no reliable data from the region on the prevalence of insufficient physical activity, although some routine data for Kazakhstan and Russia exist. In these countries, the proportion of the population attaining less than 5 times for 30 minutes of moderate activity per week, or less than 3 times for 20 minutes of vigorous activity per week, or equivalent, were calculated. Kazakhstan had a much higher estimated prevalence of low physical activity than the Russian Federation (32% vs. 21%) (Table 4)

Kazakhstan had much worse level than Russian Federation (32% vs. 21%) [29]. However, it is difficult to interpret these data, because while the differences between countries are large, there is no country-specific description of how these data were collected and measured.

2.2.1.3. Smoking

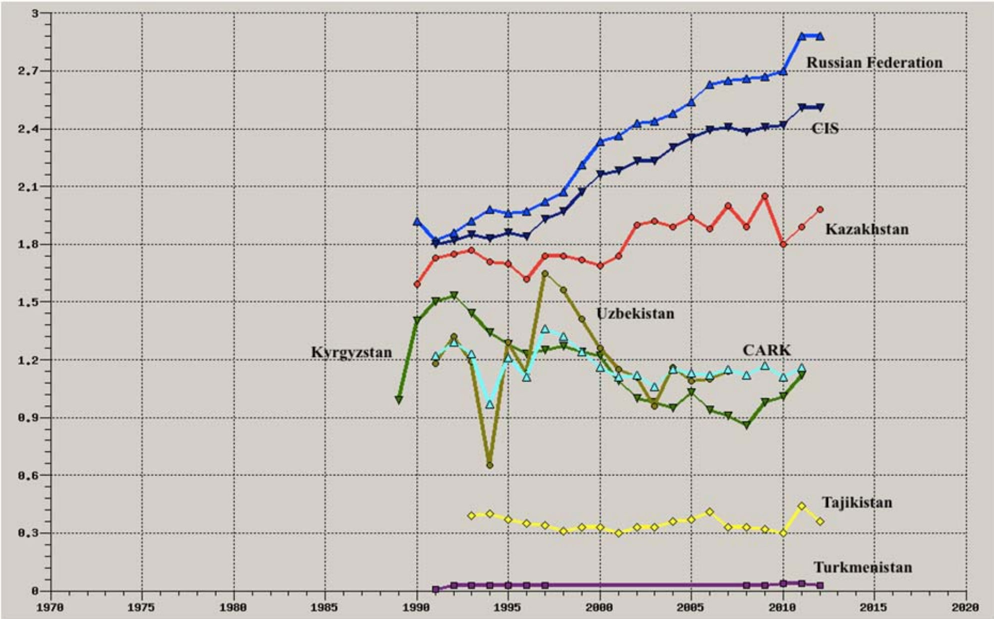
Smoking is a major risk factor for premature deaths, CVD, cancer, and a range of other diseases and conditions. The risk of death from CVD depends on the duration of smoking and number of cigarettes smoked. Passive smoking also increases the risk of CVD [123]. Smoking approximately doubles the risk of premature death (from all causes) and approximately doubles CVD mortality, while the strongest association is observed for respiratory cancers; for example, the estimates of relative risk of lung cancer in smokers (vs. never smokers) in different studies range between 10 and 20.

The prevalence of smoking in Kazakhstan has been estimated to be around 30% for both sexes combined; this is the highest rate in Central Asia according to available routine data (Table 3). The smoking rate is often underestimated due to unwillingness to reveal this information because of the stigma in some societies, such as in CA, especially among women [124]. Despite the possible underestimation, the prevalence of female smoking in Kazakhstan is approximately 10 times higher compared to Uzbekistan and Kyrgyzstan. Smoking among men is similar in Kazakhstan and Kyrgyzstan (48% and 45%), which is more than double of that reported for Uzbekistan (20%) (Table 3).

Other data from the CA region suggested that the prevalence of smoking in Kazakhstan is as high as 65% in men, which was higher than in the Russian Federation with prevalence of 60%, although among women the prevalence smoking rates were lower in Kazakhstan [125].

An alternative indirect way to approximate the scale and effect of smoking using routine data is based on the prevalence of chronic obstructive pulmonary disease (COPD), a major health outcome of smoking [126]. Kazakhstan holds the leading position for COPD in the CA region, and only the Russian Federation has a higher prevalence in the former Soviet Union. After the mid-1990s, the gap between CA countries and Kazakhstan increased and currently the gap between Kazakhstan and the other CA countries is about two-fold (Figure 12), although it is not clear whether these figures are affected by differences in detection and diagnosis.

Figure 12 Prevalence of chronic obstructive pulmonary disease (%). Source: WHO Health for all database



y- percent of cases of COPD patients, x- time period (year)

Despite the questionable accuracy of the available data, Kazakhstan and the whole CA region clearly has high rates of male smoking and this is expected to have a dramatic impact on the future burden of smoking-associated diseases. The region is undergoing huge market reforms causing the consumers to experience greater and wider availability of many goods, including cigarettes and alcohol, and regulatory measures so far have been limited [127]. As in Russia [128], the future trends may also include a dramatic rise in smoking among young women, which would further increase the burden of ill health attributed to smoking.

2.2.1.4. Alcohol

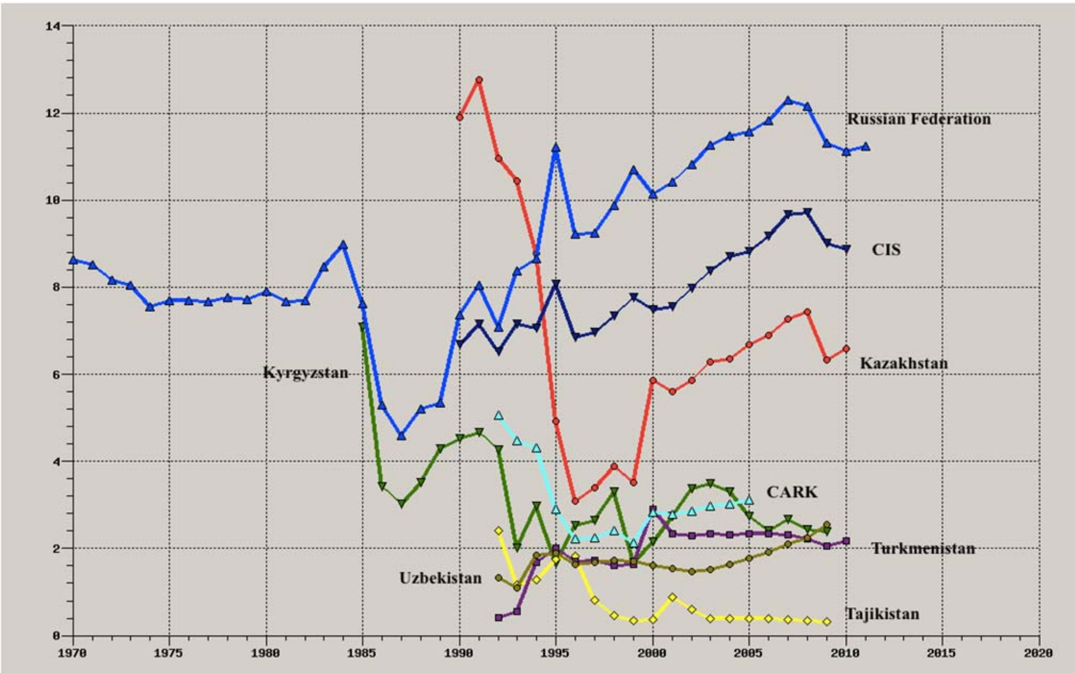
High alcohol use contributes to a range of acute and chronic health consequences, ranging from alcohol poisoning and injuries to cardiovascular disease, making it one of the leading causes of ill health globally [29]. There remains a controversy whether the cardio-protective effect of moderate alcohol intake reported in most observational studies is genuine or whether it is due to reverse causation (due to former drinkers moving to the non-drinking category), but there seems a consensus that high alcohol intake and binge drinking are associated with increased risk of CVD [129-131].

According to the WHO [29], Kazakhstan has the highest reported annual alcohol consumption in Central Asia, with 10.3 litres of pure ethanol per adult population while in Tajikistan, Turkmenistan, Kyrgyzstan and Uzbekistan the consumption levels were 2.5-3 times lower. In Kazakhstan, the consumption among men was 3 times higher than among women but in Kazakh women, the consumption estimates are 3-4 times higher compared to other CA countries (

Table 3). In addition to volume, however, many researchers also suggested that the pattern of episodic heavy drinking has independent health effects [132]. In the Living Conditions, Lifestyles and Health Study, Kazakhstan and Russia, showed the highest prevalence of episodic heavy drinking among the 8 participating countries, and, as expected, episodic heavy drinking was more frequent in males. [133]

It is has been suggested that the trends in alcohol consumption in Kazakhstan may be related to the ethnic composition of the country. Figure 13 shows a sharp fall in alcohol consumption in Kazakhstan after 1991-1992. Interestingly, the emigration of Russians from Kazakhstan coincides with changes in alcohol consumption as estimated by the WHO. Hundreds of thousands of Russians left Kazakhstan in the 1990s due the perceived lack of economic opportunities. By 1999, the number of Russians in Kazakhstan dropped by about 30%, from 6,227,549 to 4,479,618. [134]

Figure 13 Pure alcohol consumption, litres per capita, age 15+. Source: WHO Health for All database



y- litres per capita, x- time period (year)

However, since 2000 the alcohol consumption in Kazakhstan has been increasing, and it remains much higher than in other CA countries (Figure 13). This increase after 2000 seems inconsistent with the hypothesis that the consumption is mainly concentrated among ethnic Russians; instead, social and economic changes and the availability of cheap or illicit alcohol may underlie more recent trends. In addition, the methodology of estimating alcohol consumption in CA is not clear, and it is possible that changing trends may also be related to changes in the methodology.

2.2.2 Burden of cardio-metabolic risk factors: Central Asia perspective

2.2.2.1. Blood pressure and arterial hypertension

Arterial hypertension affects approximately 1 billion persons worldwide and is considered to be the leading preventable cause for cardiovascular mortality globally. It has been estimated that raised blood pressure currently kills 7.5 million people every year [135]. Therefore, timely diagnosis, treatment and control of hypertension in primary care is crucial for reducing CVD morbidity and mortality in both high and lower income countries [136]. In this respect, population data on the prevalence and awareness of high blood pressure are essential for the development and implementation of public health policies to improve identification, treatment and control of this condition.

Despite the high CVD mortality and the importance of hypertension as a cardiovascular risk factor, there are very few reliable data on hypertension in the Central Asian republics of the former Soviet Union [57]. No individual level data on hypertension prevalence in Central Asia with a clearly stated methodology could be identified. WHO has estimated that in Kazakhstan in 2008, the age-standardized prevalence of hypertension at all ages was 36%, compared to 34% in Russia and 29% in Europe (Table 5) [29]. As with other WHO estimates, it is not clear which original data were used to produce these estimates.

Table 5 Prevalence % (95% CI) of raised blood pressure (SBP≥140 OR DBP≥90)

Country or region	Males	Females	Both
Kazakhstan	40.4% [25.7-55.0]	31.8% [18.5-45.1]	35.8% [26.1-45.7]
Kyrgyzstan	38.5% [24.3-53.6]	33.4% [20.5-46.3]	36.0% [26.3-45.8]
Russian Federation	37.2% [29.0-45.8]	31.8% [24.1-39.7]	34.4% [28.8-40.3]
Tajikistan	37.4% [22.5-52.2]	34.1% [20.2-48.0]	35.7% [25.8-45.9]
Turkmenistan	38.3% [24.2-53.2]	32.8% [19.6-46.1]	35.5% [25.8-45.5]
Uzbekistan	30.5% [19.5-42.8]	26.3% [17.1-36.1]	28.4% [21.2-36.2]
Europe	33.1% [29.9-36.4]	25.6% [22.8-28.4]	29.3% [27.2-31.5]

WHO Global Health Observatory Data Repository [29]

According to these estimates, the prevalence of raised blood pressure in the adult population in Kyrgyzstan was the highest in Central Asia (Table *5*). Several potential explanations have been proposed to interpret the high levels of hypertension prevalence in the CA region, including lifestyle and diet, obesity, alcohol consumption, limited hypertension diagnosis, inadequate treatment of hypertension and/or patients' low compliance to treatment [137]. Some data has been published from Tajikistan, confirming the high prevalence of hypertension in the region: among persons aged 45 years and over, the prevalence of raised blood pressure was 46% (systolic, ≥ 140 mm Hg) and 52% (diastolic, ≥ 90 mm Hg) [119].

2.2.2.2. Diabetes

Diabetes caused 4.9 million deaths in 2014, and the global prevalence of diabetes was estimated to be 8.3% [138]. The prevalence of impaired glucose metabolism is considerably higher when the categories of “impaired fasting” and “impaired glucose tolerance” are also included. Impaired fasting glycaemia and impaired glucose tolerance are reported to be metabolically different conditions that affect different subgroups to a different degree, although there is some overlap [139]. WHO has estimated that in Kazakhstan in 2008, the age-standardized prevalence of raised fasting blood glucose was 12%, compared to 9% in Europe. (Table 6)

Table 6 Prevalence of raised fasting blood glucose (≥126 mg/dl or on medication)

Country	Males	Females	Both sexes
Kazakhstan	12.5 (5.5.-21.9)	10.8 (4.5-19.7)	11.5 (6.7-17.8)
Kyrgyzstan	11.1 (4.8-20.0)	10.4 (4.4-18.9)	10.7 (6.0-17.1)
Tajikistan	10.7 (4.5-19.5)	9.7 (4.0-18.1)	10.2 (5.7-16.1)
Turkmenistan	12.0 (5.3-21.3)	10.1 (4.1-18.6)	11.0 (6.2-17.0)
Uzbekistan	12.6 (7.0-20.0)	10.9 (5.8-17.6)	11.7 (7.8-16.4)
Russian Federation	10.5 (4.1-19.6)	10.7 (4.3-19.8)	10.6 (5.7-17.1)
Europe	9.6 (7.5-12.1)	8 (6.0-10.4)	8.8 (7.3-10.4)

WHO Global Health Observatory Data Repository [29]

Diabetes mellitus is a socially important disease with serious health and economic consequences for patients and their relatives. People with diabetes require at least 2-3 times the health care resources compared to people who do not have diabetes, and diabetes care may account for up to 15% of national healthcare budgets (depending on country) [140].

Impaired glucose tolerance and impaired fasting glycaemia predict future development of diabetes and cardiovascular disease. Persons with diabetes have an approximately two-fold increase in the risk of heart disease and stroke [141]. Numerous predictors (risk factors) associated with increased risk of diabetes have been identified, including dietary factors, obesity and psychosocial factors. In addition, socioeconomic factors, such as income and educational level, have been recognized to be powerful determinants of diabetes in western studies [142] [143]. However, no individual level data on the prevalence and predictors, and awareness, treatment and control of diabetes or impaired fasting glycaemia in Central Asia, including Kazakhstan, could be identified. According to WHO, diabetes accounted for 1,403 deaths (0.91% of total deaths) in Kazakhstan in 2011 (this excludes deaths partly attributable to diabetes, such as CVD).

2.2.2.3. Hypercholesterolemia and overall dyslipidaemias

Dyslipidaemia is an important modifiable risk factor for cardiovascular disease (CVD). Based on WHO global estimates, dyslipidaemias cause more than half of ischemic heart disease and one fifth of cerebrovascular disease and causes nearly 4.4 million deaths every year worldwide [40]. Various lipid abnormalities, such as increased total and low-density lipoprotein cholesterol, low concentrations of high-density lipoprotein cholesterol and high triglycerides concentrations, and their combinations, have been implicated as potential independent predictors of CVD [144-146] and the combination of these conditions are sometimes called atherogenic dyslipidaemia [147].

Table 7 Prevalence of raised total cholesterol (≥5.0 mmol/L)

Country	Males	Females	Both sexes
Kazakhstan	45.0 (22.0- 69.2)	45.6 (20.5-72.2)	45.7 (27.6-63.5)
Kyrgyzstan	28.3 (11.3-52.4)	31.2 (10.6-57.6)	30.1 (15.7-47.5)
Tajikistan	22.5 (8.1-44.0)	25.3 (8.0-50.5)	24.0 (11.6-39.9)
Turkmenistan	33.8 (13.9-58.7)	35.8 (13.4-62.8)	35.1 (19.0-53.2)
Uzbekistan	24.2 (12.0-40.7)	28.9 (11.3-50.9)	26.8 (15.5-40.7)
Russian Fed.	47.3 (23.3-71.3)	52.1 (25.1-75.5)	50.6 (32.3-67.9)

Source: WHO Global Health Observatory Data Repository [29]

Globally, the prevalence of raised total cholesterol (≥ 5.0 mmol/l) among adults in 2008 was 39%; the prevalence was highest in the WHO European Region (54% for both sexes), followed by the Americas (48%). According to WHO estimates, the prevalence of raised total cholesterol (≥5.0 mmol/L) in Kazakhstan was 46% (both sexes combined); this is similar to Russia and higher than in other CA countries (Table 7). If considering other cut-off points, the age-standardized the prevalence of raised total cholesterol (≥ 6.2 mmol/L) in Kazakhstan was estimated as 12%, which is similar to Russian Federation with 15% but considerably higher than in other Central Asian countries with the highest estimate for Turkmenistan with 8% and the lowest in Tajikistan with 5%, although these levels are substantially lower than in western countries (e.g. 25% in Germany and 22% in Great Britain). [29]

Unfortunately, as there have been no population-based individual level studies on dyslipidaemia in the Central Asian region, it is hard to reliably assess the magnitude of the problem. Given the rapid societal and economic changes after the breakup of the former Soviet Union, the processes of globalization and urbanization and the associated accelerated nutrition transition affecting urban centres in particular, examination of dyslipidaemias in the Central Asian republics is important for efforts aiming to reduce non-communicable diseases in the region.

2.3. Summary

In summary, the literature review suggests that while there is a wealth of information from many western populations, very little is known about the rates of CVDs, prevalence of risk factors, their socio-demographic distribution and the association between risk factors and CVDs in Central Asia.

Central Asia, a rapidly developing and populous region, with high burden of CVD, has surprisingly small evidence base on CVD (and indeed other NCDs) and its risk factors. Existing published studies are largely outdated, cover only 3 countries of the region (Kazakhstan, Kyrgyzstan and Uzbekistan), and all had the cross-sectional design. Very few studies reported on prevalence of CVDs and its risk factors. The existing studies, at best, differentiated CVD risk by ethnicity, sex and age, but details on the methodology are typically not available. There were no recent studies which reported on CVD by socioeconomic status and only limited data on urban and rural differences. Although data reported by WHO provide material for crude ecological comparisons, there are significant gaps in the evidence on CVD in Central Asia based on individual level data.

This thesis addressed some of the gaps in the knowledge on CVD and its risk factors in this region. Kazakhstan, despite being a major economic force in the region often seen as a model for successful development by other CA countries, has among the highest burden of cardiovascular disease (and all-cause mortality) in the WHO European region. While there has been an assumption that the causes of the high rates of CVD are similar to those in neighbouring Russia or some other Eastern Europe countries, the independent development of CA countries for more than two decades after the collapse of the Soviet Union may not have led to patterns identical to Russia in terms of CVD determinants (particularly as the reasons for the CVD epidemic in Russia are not well understood either). Interestingly, experience from other parts of the world suggests that policy makers prefer to draw from local reports and evidence rather than international recommendations [148]. Therefore, locally conducted research producing locally specific and applicable evidence on cardiovascular disease in Central Asia could also stimulate local governments in the region to shift their attention to more comprehensive public health preventive programmes.

CHAPTER 3

AIMS AND OBJECTIVES

The dissertation addressed the lack of evidence on risk factors for cardiovascular diseases in Kazakhstan (and indirectly in the Central Asian region). It examined: (1) the rates of cardio-metabolic and other risk factors in the Kazakh population sample; (2) the relationships between socio-demographic indicators and other risk factors; and (3) the associations between proximal (cardio-metabolic) risk factors and CVD. The detailed description of my PhD project analyses the specific research questions (hypothesis) are presented below.

The preventable nature of CVDs and their high burden of morbidity and mortality and the lack of data from the Central Asian region were the main reasons for developing the present research programme. In order to study the socioeconomic, behavioural and biological factors that determine the patterns of cardiovascular risk in Kazakhstan, the Astana Health Study (AHS) was set up as a new source of individual-level data.

3.1. Aims

The main aims of the thesis are to provide new insight into the levels and distribution of cardiovascular risk factors and to obtain evidence on the associations between a range of risk factors and CVDs in the Astana region in Kazakhstan and the Central Asian region more generally.

3.2. Objectives

In order to accomplish the overall aims, a population-based cross-sectional survey and case-control study of acute coronary syndrome and stroke was conducted in the Astana region in Kazakhstan with the following specific objectives:

1. To estimate the prevalence, awareness, treatment, and control of hypertension, diabetes and dyslipidaemias and factors associated with these parameters;
2. To estimate the prevalence and distribution of risky health behaviours such as smoking, alcohol consumption, obesity and nutrition patterns;
3. To study the association between socio-demographic factors (education, material conditions, marital status and ethnicity) and CVD risk factors.
4. To investigate the associations of socio-demographic, behavioural and biological factors with the risk of acute coronary syndrome and stroke.

3.3. Research hypotheses

It is hypothesised that:

- Objectives 1 and 2: The prevalence of the major CVD risk factors in Kazakhstan is high and that the awareness, treatment and control of the treatable conditions are low compared to western countries.
- Objective 3: Lifestyle and socioeconomic factors are associated with increased levels of cardio-metabolic risk factors (hypertension, obesity, dyslipidaemia and diabetes) in the Kazakh population, and lifestyle and biological risk factors follow a similar inverse socioeconomic gradient as in western countries;
- Objective 4:
    - Biological, social, economic and psychosocial determinants are important predictors of ACS and stroke in the Kazakh population;
    - The pattern of the associations between CVD and specific risk factors is similar to that reported in western populations.
    - Given the suspected high rates of obesity and diabetes, cardio-metabolic factors play a more prominent role (in terms of population attributable risk fraction) than in western populations;

CHAPTER 4

METHODS

This chapter describes the research approach used to achieve the proposed aims and objectives of my PhD project. This chapter covers the following major components of the methodology: study design, data collection and data management, measurement procedures and analysis of the data.

4.1. Astana Health Study

The primary source of individual-level data that was used in my work was the newly established Astana Health Study (AHS), specially developed and implemented as part of my PhD programme. The AHS was conducted in the Astana region in Kazakhstan and covered both urban and rural regions.

4.1.1. Components of the project

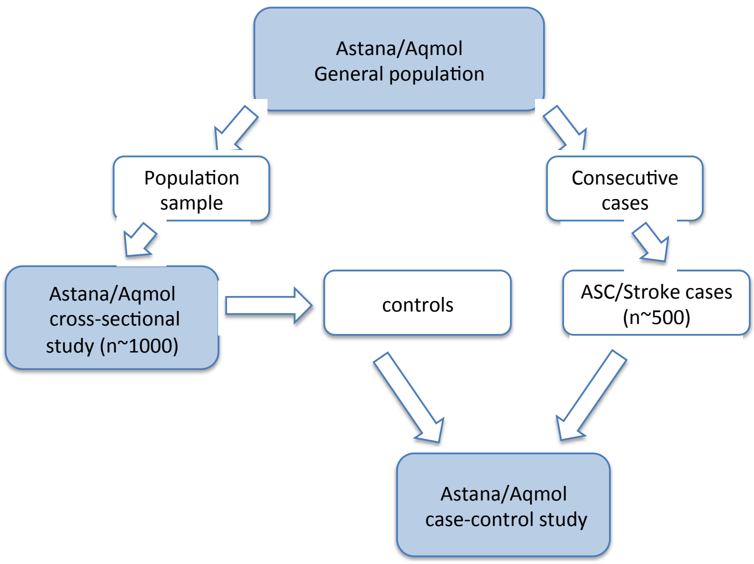
The Astana Health Study was designed as a research project with two components: (1) a cross-sectional population survey; and (2) a case-control study of all consecutive patients with acute coronary syndrome (ACS) and stroke (cases) identified during the study period. The cross-sectional study was conducted in a random population sample of Astana city (n= 493) and the Akmol settlement outside Astana city (n=484). Figure 14 shows the map of Astana city and Akmol area, located some 40-50 km away from Astana city and represent a rural population. The cross-sectional population sample was used for both cross-sectional analyses and as controls for case-control analyses. (Figure 15)

Figure 14 Map of Astana city and Akmol village

The cross-sectional study design was selected to investigate the levels and distribution of major CVD risk factors and variables associated with these risk factors. The cross-sectional study design was intentionally considered as an efficient method to assess more than one health outcome, given the nature of this type of study. This approach was practical, since CVD risk is multifactorial. Importantly, given the limited timeframe, it was not feasible to conduct a more comprehensive cohort study. Besides the initial objective to study the prevalence of CVD risk factors and its determinants, the cross-sectional sample conveniently served as population-based controls for the cases of acute coronary syndrome and stroke patients, the second part of my PhD project.

Figure 15 shows how the case-control study of acute coronary syndrome and stroke was planned simultaneously with the cross-sectional survey.

Figure 15 Astana health study graphic design



4.1.2. Ethical approval, informed consent and funding

The project protocol, including the case-control and cross-sectional studies, has been approved by the Ethical Committee at the Centre for Life Sciences, PI “National Laboratory Astana, Nazarbayev University, Astana (protocol #4, 17 April 2012, and follow-up protocol #14, 30 June 2014).

Participants were fully informed about the purpose of the research prior to the beginning of the study by the recruiting nurse and they received an information sheet (the full informed consent form is shown in Appendix 1). At the end of the medical examination, participants were again explained the nature of the study and asked explicitly if they have any questions about the research. The researchers were given the opportunity to record participants' interest if they wished to be informed about the future developments of the study (particularly about a potential follow-up). Based on the findings of the medical examination and biochemical analyses, a further information sheet explaining the examination results were provided to each participant. All information provided was treated as confidential.

This project was supported by the programme targeted funding from the Ministry of Education and Science of the Republic of Kazakhstan (Agreement #409/037-2014, March 07 2014, #089-2014, May 13 2014) and “Talap” scholarship awarded to the author by the Nazarbayev University (January 2013- June 2017). The funders had no role in the conduct of the study, analysis of the data and interpretation of the results.

4.1.3. Study population

The study population in this study is the Akmola oblast, which is a centrally located region (146,200 sq. km.) in Kazakhstan. The administrative centre of the region is Kokshetau city. The state capital, Astana, is geographically located in this region, but it is politically independent from the Akmola oblast.

According to the national statistics committee in Kazakhstan the population of Akmola oblast, as of 2015, comprised 736,605 inhabitants, with 47% living in urban and 53% in rural areas. Both urban and rural communities in Akmola oblast are largely involved in agricultural and livestock production, which are the main branches of economy in this region. The population of Akmola oblast consists mainly of Kazakhs and Russians ethnicities [134].

Astana city, with a population of 852,882 inhabitants, represents a highly urbanized setting. Indeed, Astana region, and Astana city in particular, are not representative for the whole country. Astana has much higher socioeconomic standards compared to the rest of the country, which is an important aspect, as we planned to assess the burden of CVD risk factors in this advantaged urbanised settings. Astana, as the modern capital of Kazakhstan, is important because it sets example and trends for the rest of the country, as well as for the other Central Asian countries. It is likely that current situation of Astana indicates the future of other urban settings in Central Asia. Finally, despite political independence from Akmola oblast, Astana has high influence on surrounding areas being geographically enclosed in this region.

The rural population in Akmola oblast is large and consists of many villages. We have chosen Akmol village (formerly Malinovka, until 2007), as it is located approximately 40-50 km from Astana city and this distance naturally precludes daily or frequent visits of local inhabitants to Astana city and preserves the required rural character of the study settings. At the same time, this distance was close enough to allow frequent transportation of biological samples collected in the study (the overall transportation of the samples did not exceed 4 hours) to laboratory in Astana city.

4.1.4. Data collection

The recruitment of subjects into the study was organized in several separate recruiting sites. The cross-sectional study was implemented in Astana city and

Akmol village between November 2012 and March 2015, and simultaneously the case-control study was conducted in two hospitals in Astana city between February 2013 and March 2015. The approximate timeframe of the recruiting process was established after a pilot study specially organized for testing the recruiting process. All participating staff of the project, including recruiters, doctors and nurses were trained and supervised by the author with the support of my primary PhD supervisor prior to the start of the project. Participants of the population survey were invited to a clinic (hospital or polyclinic). In the clinic, participants were interviewed by a trained general practitioner using a structured questionnaire and underwent a short physical examination, including a fasting venous blood sample.

The questionnaire (Appendix 2) covered self-rated health status, medical history, health behaviours, and socioeconomic circumstances. The questionnaire was based largely on the Health, Alcohol and Psychosocial Factors in Eastern Europe (HAPIEE) study [149]. Questions on hypertension awareness and use medication in the last two weeks were taken from the WHO MONICA Project [150]. The examination included anthropometry, blood pressure measurement and assessment of cognitive and physical functions, and the physical examination had to be completed by all study participants. All questions were translated from English into Russian and Kazakh and back translated into English to ensure accuracy and cultural appropriateness.

4.1.4.1. Cross-sectional study

Prior to project start it was decided that the optimal recruiting sites both in urban and rural location in Astana region are polyclinics. Polyclinic in Kazakhstan is an out-patient clinic that provides general (primary) and specialist care, examinations and treatments. According to Kazakh law, every citizen in Kazakhstan has to be registered (“attached”) in a polyclinic. The majority of the population prefers to be registered with (attached to) local polyclinics.

At the time of the study, there were 8 polyclinics in Astana city and only one in the Akmol village. Therefore, to generate a random population sample, the lists of “attached” population to these polyclinics, including contact information both for Astana city and Akmol village, were obtained from the Republican Centre for Healthcare Development of the Ministry of Health in Kazakhstan.

For convenience, but also to provide an incentive for participants, the well-known modern clinic at Republican Diagnostic Centre, under Nazarbayev University was chosen as the recruiting site for Astana city; the Diagnostic Centre also served as the central laboratory for the whole study (for both Astana city and Akmol village) that processed the biochemical analyses. Selection of these modern health facilities was expected to be attractive for the subjects.

In Akmol village the polyclinic of Tselinograd region was selected as recruiting site; blood samples were transported to Astana city on daily basis. To raise the awareness of the project and to encourage enrolment, the recruiting procedures included invitation to a polyclinic by landline phone calls; if telephone communication was not successful, participants were personally visited at their home by trained local staff and were invited to participate in the study.

4.1.4.2. Case-control study

All cases of ACS were admitted and treated in the city hospital #2 in Astana city. Over 90% of all acute coronary cases occurring in the Astana region (including both the Astana city and the Akmol region) are admitted to this hospital. Cases of stroke were recruited in the city hospital #1 in Astana city, this hospital covers over 70% of all stroke cases from Astana city and Akmola oblast. There are several other smaller hospitals in Astana city, which cover the remaining cases of ACS and stroke, but each of them covers only small number of cases and the logistics were too complicated, so it was decided to concentrate on only hospitals #1 and #2.

Once admitted to the participating hospital, patients were invited by one of the trained team member (cardiologist or neurologist) to participate in the study. Once the patient agreed, he signed the informed consent letter and was considered to be a study participant. Patients complete the same questionnaire as for cross-sectional study, except that most questions were amended to contain the phrase “before your current illness” (Appendix 3).

In the case-control study we were unable to stratify the cases by region (urban and rural) due to the study design peculiarities. Both participating hospitals (the case recruiting sites) tend to admit patients from Astana city and from the surrounding areas, which includes patients from Akmola region. However, the population-based controls were collected in such a way to be equally stratified by region (the planned sample size was 500 in urban and 500 in rural regions), while the cases were admitted to the appropriate hospital based on the clinical reasons, and the distribution of cases by region was therefore unconstrained.

4.2. Population-based survey

4.2.1. Subjects

The participants in the cross-sectional study were randomly selected after stratifying for sex and 5-year age groups from the lists of all residents in the age range 50-74 years who were registered at local outpatient clinics (polyclinics). The recruiting procedures included an invitation to a polyclinic by landline phone calls; if telephone communication was not successful, participants were visited at their home and invited to participate in the study. A total of 977 adults aged 50-74 years were recruited (493 in Astana city and 484 in Akmol). The overall response rate was 59% (56% in urban and 63% in rural area).

During the initial telephone contact, participants were explained the purpose and procedures of the project and were invited to participate in the study. This method of invitation was chosen in order to increase the response rate, since the previous experience with postal invitations in the clinical sub-set of the Kazakhstan Health Study (KHS) in Astana city was disappointing. The KHS used only the letter method to invite participant for a medical examination in the clinic and this produced very low response rates, particularly among older respondents. In the Akmol settlement we have also chosen the same method of invitation as in Astana city with first contact by landline telephone. However, due to a rural character of the settlement, many subjects did not have a landline; in this case, they were visited at home and were invited personally by a nurse to attend the examination in a clinic. Data were collected by face-to-face interviews conducted by trained personnel.

4.2.2. Measurements and construction of derived variables

Data were collected by trained doctors using a standardized survey protocol and paper questionnaires; the data were subsequently entered into a database. The structured questionnaire included an overall assessment of the patient's health, medical history, lifestyle and socio-economic indicators. The examination included blood pressure measurement, anthropometric measures (height, weight, waist and hip circumference) and collection of a venous blood sample.

4.2.2.1. Socio-demographic characteristics

The basic socio-demographic characteristics included age, sex and urban vs. rural area of residence. Marital status was classified as married or unmarried (widowed, divorced and single) and education was divided into primary or less, vocational/secondary, and university. As there are around 130 different ethnical groups living in Kazakhstan, ethnicity of respondents was classified into 3 primary groups: Kazakhs, Russians and others.

As reporting of income in the Kazakh population was deemed too sensitive and unreliable, ownership of selected household assets was used as to capture the economic / material situation. The assets included car, and three categories of household amenities based on the sum of items owned by the household (microwave, DVD player, TV, washing machine, dishwasher, freezer, second house ‘‘dacha’’, video camera, cable TV, land phone, mobile phone). Car ownership (yes vs. no) and material deprivation were used as markers of the economic status. Material deprivation was assessed by three questions (how often participants do not have enough money for food, clothes and paying bills for their households), and participants were classified into three categories (high, intermediate and low).

4.2.2.2. Health behaviours

Smoking status was evaluated using two questions: if subject currently smokes, and if not, did he/her smoke in the past, and accordingly individuals were categorized as ‘never smoker’, ‘ex-smoker’ or ‘current smoker’. Additionally, ex-smokers were classified into the following categories based on how long ago they gave up smoking: ‘quit within the last 5 years’, ‘quit 5–10 years ago’, ‘quit 11–20 years ago’, and ‘quit more than 20 years ago’.

Alcohol consumption was assessed by how often participant had 5+ drinks of alcohol during the last 12 months; how much alcohol (litres) do they usually drink during one week and categorized as: ‘non-drinker’, ‘rarely drinks alcohol’, ‘low-risk drinker’ (≤14 drinks per week) or ‘risky drinker’ (>14 drinks per week). (One drink was considered as 0.5 litre of beer or 2 dl glass of wine, or 5 cl of spirits.)

4.2.2.3. Anthropometric measurements and obesity

The short physical examination included measurement of height, weight, waist and hip circumference; weight of subjects with light clothing was measured by standard balanced scales to the nearest 0.1 kg, and height was measured by steel stadiometer to the nearest 0.1 cm. Waist and hip circumferences were measured with a non-stretchable standard tape measure: waist measurements were obtained over the unclothed abdomen at the narrowest point between the costal margin and iliac crest, and hip circumferences over light clothing at the level of the widest diameter around the greater trochanter area. The tape was pulled tight and measurements were taken to the nearest 0.1cm.

Two indices of obesity were derived from the objective anthropometric measurements: body mass index (BMI, kg/m2) and waist to hip ratio (WHR) to assess overall and central obesity, respectively. As recommended by WHO [151], BMI was classified as normal (BMI 18.5–24.9), overweight (BMI 25–29.9) and obese (BMI over 30 kg/m2). WHR was categorized into two groups based on WHO cut-off points: central obesity was defined as a waist to hip ratio above 0.90 for men and above 0.85 for women. [152]

4.2.2.4. Blood pressure and hypertension

Blood pressure was measured after 5 min rest three times on the right arm in the sitting position with Omron M6 (validated by the International Protocol) [149], with a 2 min interval between measurements. [153, 154] The mean of the second and third measurements was used in the analyses. Hypertension was defined as systolic blood pressure (SBP) 140 mm Hg, and/or a diastolic blood pressure (DBP) 90 mm Hg, and/or the use of antihypertensive medication [155].

Participants who reported that a doctor or another health worker ever told them they had hypertension were considered aware of their disease, and those who confirmed antihypertensive medications in the last two weeks were considered under treatment. Participants who had used antihypertensive medication in the last two weeks and who had both SBP and DBP pressure lower than 140/90 mm Hg were classified as having controlled hypertension.

4.2.2.5. Blood sample collection

Subjects were invited to visit the polyclinic in the mornings after an overnight fast. The fasting status was self-reported by participants and recorded in the questionnaire. Those who did not meet the fasting status requirements (fasting for at least 12 hour prior to examination) were invited to visit the polyclinic on another occasion.

During the medical interview in the clinic, blood sample was taken in a single venepuncture without tourniquet or after short-term ligation of the arm. In both Astana city and Akmol village, all blood samples were collected into one 7.5 ml and two 3 ml EDTA vacutainer. Vacutainers were carefully shaken, and then centrifuged. In Astana city, blood samples were processed after all participants on a given day provide blood sample, usually by noon. In Akmol village, cooled serum samples were transported to Astana city at the end of each recruitment day (usually by 11 am).

In the laboratory in Astana city, serum total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG) and fasting blood glucose concentration were measured by automatic modular analyser Cobas 8000, Roche Diagnostics (Germany) using the following reagents for the assays (reagent catalogue number: 05168538190 (TC), 05171369190 (LDL-C), 05168805190 (HDL-C), 05171407190 (TG). The maximum delay time for this biochemical analysis was 4 hours after blood collection for both Astana city and Akmol village.

Two 3 ml K2-EDTA vacutainers were not centrifuged; one vacutainer (destined for glycated haemoglobin determination) was divided into 2 aliquots × 1.5 ml. All aliquots were stored in 1.5 ml Sarstedt microtubes. The second 3 ml K2-EDTA vacutainer was for later DNA extraction and subsequent SNP analysis (Appendix 5). These microtubes were stored at -80°C for subsequent laboratory analysis. DNA has now been extracted, divided into 3 aliquots and stored at -20°C.

4.2.2.6. Glucose levels and diabetes

Diabetes was defined as fasting plasma glucose (FPG) concentration ≥7.0 mmol/l (126 mg/dl) or self-reported diabetes medication use; the questionnaire did not specify the type of diabetes (1 or 2). Diabetes awareness was assessed by the question whether the subjects had been told by a doctor that they had diabetes. Subjects taking regular hypoglycaemic medication or insulin were considered to be on treatment for diabetes. Control of diabetes among those with diabetes was defined as fasting plasma glucose <7.0 mmol/l (126 mg/dl) in persons with self-reported diabetes and medication.

4.2.2.7. Hypercholesterolemia and abnormal lipid concentrations

To study prevalence, awareness, treatment and control of hypercholesterolemia, we used two conventional cut-offs of TC concentrations. First, we used the older definition of hypercholesterolemia set as total serum cholesterol ≥6.2 mmol/l (240mg/dl) and/or current use of cholesterol lowering medication. [156] Secondly, for comparisons with other studies, we used the more recent and stricter cut-off point for hypercholesterolemia total cholesterol ≥5.0 mmol/l and/or current use of cholesterol lowering medication. [157] Awareness status was assessed by the question whether the subject had been told by a doctor that they had high level of cholesterol lipids. Subjects who reported taking regular cholesterol lowering medications were considered to be on treatment for high cholesterol. Control of hypercholesterolemia among those with self-reported high cholesterol and treatment was defined as fasting serum total cholesterol less than 6.2 mmol/l (or 5.0 mmol/l in secondary analyses).

For other lipids, we used the cut-offs recommended by the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III): raised level of low-density lipoprotein cholesterol ≥4.15 mmol/l (160 mg/dl), raised serum triglycerides levels ≥ 2.26 mmol/l (200 mg/dl) and low level of high-density lipoprotein cholesterol (calculated with the Friedewald formula) was set as < 1.04 mmol/l (40 mg/dl) for men and for women [156].

4.3. Case-control study

4.3.1. Subjects

The most critical and often controversial component of a case-control study is the selection of the controls. Our primary goal was to identify the controls that are drawn from the same population as our cases. Therefore, the Astana region was selected, both urban and rural populations.

4.3.1.1. Controls

The subjects selected for cross-sectional study, as described previously, were used as the control group. This was an unmatched case-control study, in which we enrolled controls without regard to the number or characteristics of our cases, so the number of controls was not equal to the number of cases and the distribution of controls and cases by age and sex were not similar. Subjects in the control group with previous history of MI and/or stroke events were excluded from the main analyses.

4.3.1.2. Cases

All surviving patients with their first-ever episode of acute coronary syndrome (ACS) or first-ever episode of stroke occurring in population of Astana city and nearby area in the age group 50-74 years were considered eligible. As mentioned above, the subjects were consecutive cases admitted to hospitals #1 (stroke) and #2 (ACS) in Astana city.

4.3.1.2.1. Case definition of Acute Coronary Syndrome

The diagnosis of acute coronary syndrome (ACS) applies to any group of clinical manifestations consistent with acute myocardial ischemia and refers to the range of corresponding clinical symptoms, including ST-segment elevation myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (NSTEMI) and unstable angina. The last two conditions (Unstable angina and NSTEMI) are patho-physiologically and clinically very similar, but the severity of these conditions is different. NSTEMI is diagnosed if myocardial damage results in the release of a biomarker of myocardial necrosis (such as troponin) into the circulation, while the less severe cases of unstable angina is diagnosed if such biomarker of myocardial necrosis cannot be verified. The accurate diagnosis can be established based on standard medical examination, including anamnesis, results of physical examination, electrocardiography (ECG), radiologic tests and cardiac biomarker tests [158, 159]

During the study period (since the beginning of 2013), all ACS cases were eligible for recruitment based on the described above criteria:

- ST elevation myocardial infarction (STEMI) with elevated troponin levels;
- Non-STEMI myocardial infarction (no ST elevation, elevated troponin (at least one diagnostic result); and Unstable angina cases (no ST elevation and negative troponin). [160]

For the unstable angina, the diagnosis was based on typical clinical signs as established by the cardiologists:

(1) resting angina (usually lasting >20 minutes),

(2) new-onset (<2 months previously) severe angina, and

(3) a crescendo pattern of occurrence (increasing in intensity, duration, frequency, or any combination of these factors) and positive angiography (more than a 50% reduction in luminal diameter)

4.3.1.2.2. Case definition of stroke

The conventional definition of stroke, that is currently used by WHO is “a clinical syndrome characterised by rapidly developing clinical symptoms and/or signs, and at times global, loss of cerebral function, with symptoms lasting more than 24 hours or leading to death with no apparent cause other than a vascular origin” [161]. For the present project, all non-fatal cases of stroke in the selected hospital during the selected period since the beginning of 2013 were eligible.

The hospitalised patients were diagnosed as having stroke by clinical doctors using the ICD 10 codes: I60-Nontraumatic subarachnoid haemorrhage, I61-Nontraumatic intracerebral haemorrhage, I62-Other and unspecified non-traumatic intracranial haemorrhage, I63-Cerebral infarction, I65-Occlusion and stenosis of precerebral arteries, not resulting in cerebral infarction, I66-Occlusion and stenosis of cerebral arteries, not resulting in cerebral infarction, I67-Other cerebrovascular diseases, I68-Cerebrovascular disorders in diseases classified elsewhere. Patients were eligible for the study if they presented within 5 days of symptoms onset. CT or MRI of the brain was organised only for some participants to confirm the diagnosis and it was not possible arrange a standardised assessment of the brain scans to distinguish between ischaemic and haemorrhagic strokes. The analyses therefore included all strokes without distinction of the type.

Cases in the age ranges 50-75 years admitted to hospital with first ever case of ACS or stroke were eligible for inclusion in the study. All eligible patients were approached by trained nurses. There were provided with the information about the study and invited to participate. All participants signed an informed consent. In some severe cases of stroke, the next-of-kin (who also completed the questionnaire) signed the informed consent.

4.3.2. Measurements in cases

To eligible patients who agreed to participate, a structured questionnaire, analogous to that used in the cross-sectional study (controls), was administered and physical examinations were undertaken in the same manner as it was done in controls in population-based survey. Due to severity of some cases, for participants who were unable to communicate sufficiently to respond to the project's questionnaire, proxy respondents were asked. Usually it was a spouse or next of kin relative who was living in the same household and was well informed of the participant's lifestyle, medical conditions and overall health and wellbeing situation.

4.3.2.1. Socio-demographic and behaviour characteristics

The socio-demographic characteristics included age, sex and several socioeconomic variables identical to the information collected in the cross-sectional study (see section 4.2.2. - Measurements in population-based survey).

4.3.2.2. Anthropometric measurements

The anthropometric examination of cases was limited to measurement of height and weight. Waist and hip circumference were not measured in all cases due to difficulties and mobility restrictions in many cases, particularly among stroke patients. Nevertheless, waist and hip circumference were available in most ACS cases. The measurement procedures were identical to controls. The main obesity indicator among cases was body mass index (BMI, kg/m2). Similar to cross-sectional study BMI was classified as normal (BMI 18.5–24.9), overweight (BMI 25–29.9) and obese (BMI over 30 kg/m2).

4.3.2.3. Blood pressure, diabetes and hypercholesterolemia

Once admitted to the hospital, each patient undergoes complex diagnostic and therapeutic procedures, including antihypertensive medications, blood glucose lowering and special in-hospital diet. These procedures, as well as the clinical episode itself, are likely to influence the levels blood pressure, blood glucose and blood lipids. To obtain at least some measures that are not affected by the diseases, it was decided to ask about self-reported diagnosis of hypertension, diabetes and hypercholesterolemia among cases, both ACS and stroke patients before the cardiovascular event that resulted in hospitalisation. Therefore, each participant was asked if he/she has been ever told by a doctor of having hypertension, diabetes and hypercholesterolemia prior the admission to the hospital, if the response was affirmative the participant was recorded as having the disease. Awareness, treatment and control of hypertension, high cholesterol and diabetes were not assessed in cases of ACS and stroke.

4.3.2.4. Blood samples

During the medical in-hospital examination, a blood sample was taken in a single venepuncture without tourniquet or after short-term ligation of the arm. All blood samples were collected in EDTA vacutainers. As in the cross-sectional study, venous blood was collected for analysis of total blood cholesterol, triglycerides, HDL, LDL, glycosylated haemoglobin (HbA1C), GGTP and fasting blood sugar (i.e., glucose) test (FBG).

4.4. Data management and statistical analysis

4.4.1. Data entry and management

The data collection in the Astana Health Study was conducted through traditional paper assisted personal interview process. Coding of questionnaires was conducted by the investigators. Each participant was allocated a unique 5-digit ID number at the moment of questionnaire completion; the same ID was used for medical examination form and blood sample. Upon the completion of interview, paper questionnaires and medical examination forms were transported to the archive at Nazarbayev University in Astana. Blood sample results were received electronically on a daily basis, printed and hard copies of the results were attached to the participants' documents.

All collected data during the project was computerized manually by double entry method using the Access database software. Data were validated comparing the two individual entries for inconsistency using Synkronizer Excel Compare software.

4.4.2. Missing data

Similarly to many other studies the computerised dataset had some missing values (both the in cross-sectional and case-control studies). Prior the analysis, a thorough examination of the data was conducted to identify the type and pattern of missing data. An exploratory analyses partitioning the data into those with vs. without missing values found only small differences in socio-demographic or health indicators between these groups (Appendix 4). It was therefore concluded that, as missing values were distributed across all observations in a random fashion, the complete case analyses are appropriate. This decision has a slight disadvantage that in the multivariable logistic regression analysis both in cross-sectional and case-control components a complete case analysis (listwise deletion) needs to be used which slightly reduces the number of subjects included in the analyses. However, it was deemed unnecessary to use imputation techniques or other advanced methods (simulation methods). Nevertheless, additional sensitivity analyses were conducted to compare age-sex-adjusted analyses in all subjects with non-missing data with complete case analysis. (Appendix 4 and 5)

4.4.3. Power calculations for the Astana Health Study

The sample size was largely driven by the available funding and the practical and logistical considerations, but before the study calculations were made, the statistical power of the sample size that was seen as achievable was estimated.

For the cross-sectional study, with sample size of about 1,000 persons, the statistical power was smaller than in the case-control study for binary outcomes, depending on the frequency of outcomes (Table *8*). For example, for an outcome of prevalence of 10% or lower the study would reliably detect odds ratios of about 2 or larger. However, this would be compensated by higher statistical power of analyses of continuous outcomes compared to dichotomous outcomes (e.g. blood pressure vs. hypertension or BMI vs. obesity). Overall, the size of this study was sufficient to provide precise estimates of the moderately strong associations of cardio-metabolic factors (arterial hypertension, diabetes, obesity and hypercholesterolemia) with covariates as well as the association of risk factors with CVD outcomes (ACS and stroke).

Table 8 Estimates of statistical power to demonstrate a given odds ratio in the cross-sectional survey, assuming 30% prevalence of exposure and prevalence of outcome of 10%, 20% and 30%.

Odds ratio	**Prevalence of outcome**		
	10%	**20%**	**30%**
1.5	45%	65%	73%
2.0	92%	97%	>99%
2.5	>99%	>99%	>99%

The statistical power of the case-control study was estimated for detecting given odds ratios at 95% confidence level, assuming that 15% prevalence of exposures among controls (Table *9*). Based on findings in other populations, odds ratios for most risk factors were around or higher than 1.5. The calculations show that for all CVD (i.e. ACS and stroke combined), the power to detect odds ratio of 1.5 or large would be 91%, for ACS it was 87% and for stroke 80%. The power to detect odds ratio 2.0 or larger the power would be 99% for all outcomes.

Table 9. Statistical power of the case-control study to detect the following odds ratios at 95% confidence level, assuming 15% prevalence of exposure in controls.

Odds ratios	**CVD (500 cases & 1000 controls)**	**ACS (400 cases & 1000 controls)**	**Stroke (300 cases & 1000 controls)**
1.5	91%	87%	80%
2.0	99%	99%	99%
2.5	100%	100%	99%

4.4.4. Statistical methods

The statistical methods used in the thesis will be described in reference to the specific objectives.

4.4.3.1. Cross-sectional data analysis

- **Objectives 1 and 2** (to estimate the prevalence, awareness, treatment, and control of cardio-metabolic factors, health behaviours and other variables)

Descriptive tables were used to present unadjusted frequencies of all predictor and outcome variables by urban or rural residence and by sex. Where appropriate, means and standard deviations are presented.

- **Objective 3** (to study the association between socio-demographic factors (education, material conditions, marital status and ethnicity) and cardiovascular / cardio-metabolic risk factors)

The associations between binary outcomes and covariates (socio-demographic characteristics, BMI, WHR, behaviours, cardio-metabolic risk factors) were estimated using logistic regression, after adjusting for age and sex in the first instance.

To estimate independent effects of each covariate on the prevalence of hypertension, diabetes, hypercholesterolemia and obesity, a multivariable model was built with multiple covariates entered in the logistic regression model. In some analyses (e.g. models analysing awareness, treatment and control of hypertension, diabetes and hypercholesterolemia) the numbers of subjects were too small for meaningful multivariable analyses; in such cases, only the age-sex adjusted estimates are reported.

For supplementary tables, the age-sex-adjusted means of some continuous variables (e.g. serum lipids) by all covariates were estimated, using linear regression. To account for intra-cluster correlation (within each area), robust regression (option “robust” in STATA) was used to provide more conservative estimates of statistical significance. All analyses were performed using STATA software, version 12 (College Station, Texas, USA).

4.4.3.2. Case-control data analysis

- **Objective 4** (to investigate the associations of socio-demographic, behavioural and biological factors with the risk of acute coronary syndrome and stroke)

Three outcomes were used in the case-control study: (1) an “overall” cardiovascular disease (CVD) was defined as either ACS or stroke; (2) acute coronary syndrome; and (3) stroke (diagnostic criteria of ACS and stroke are described in section 4.3.1.2). The overall CVD variable was constructed to increase the number of events and thus the statistical power; since risk factors for ACS and stroke are similar.

The case-control analyses started with simple descriptive tables presenting unadjusted frequencies of all predictor and outcome variables stratified by sex and cases vs. controls status. Additionally, missing values of each variable were presented in the descriptive table. (Table 24and Table 25) The categorisation of data by each variable was analogous to that in the cross-sectional sample (controls).

The association between the outcomes (CVD, ACS and stroke) and covariates (socio-economic and demographic characteristics, BMI, WHR, behaviours, cardio-metabolic risk factors) was estimated using logistic regression adjusted for age and sex. To estimate independent effects of each covariate in the model, a multivariable model was built, with multiple covariates entered in the logistic regression model. For the multivariable models, the covariates included all cardio-metabolic factors of interest (hypertension, diabetes, hypercholesterolemia, obesity), the two major health behaviours (smoking and alcohol consumption), and socio-demographic factors (education, ethnicity, marital status, car ownership, deprivation level and unemployment).

To maximise the statistical power, analyses were conducted on male and female subjects combined. However for each comparison a likelihood ratio test was performed to assess the statistical significance of the interaction between sex and each of the other predictors in the model, controlling for age and the main effects of each predictor and sex. When an interaction was detected (very few), sex-specific results are described in detail. All analyses were performed using STATA software, version 12 (College Station, Texas, USA).

CHAPTER 5

RESULTS

As the project described in this thesis includes a population-based cross-sectional survey and a case-control study, this chapter reports each of the two components in turn. Therefore, the results are presented in the following order:

1. Recruitment and response rates;
2. Cross-sectional study results:
    - a) Descriptive characteristics of the study population;
    - b) Arterial hypertension;
    - c) Diabetes;
    - d) Dyslipidaemia;
    - e) Obesity;
3. Case-control study results:
    - a) Descriptive characteristics of cases;
    - b) Case-control analysis;
    - c) Population attributable risk fractions

All tables and figures are numbered as per chapter and consecutive number of table. Supplemental result tables are presented in Appendices, numbered according to their appearance.

5.1. Response rates and recruitment characteristics

5.1.1. Response rate and recruitment of the cross-sectional sample (controls)

Random population samples of men and women aged 50-74 years old in Astana city (n=493) and Akmol village (n=484) were recruited. The total response rate in the cross-sectional study was 59%, as 1648 subjects were invited and 977 of them visited the recruitment centres (polyclinics). The response rate was slightly higher among rural residents (63%) compared to urban residents (56%). There were also differences in response rate by sex and age of participants. The response rate was higher in women (65%) than in men (53%) and among older participants.

Based on information obtained during telephone invitations, the reasons for non-participation in the study were largely due to a lack of interest or lack of time (>80%), sometimes subjects indicated various health or family reasons (<15%) and rarely (<5%) some subjects agreed to participate but they did not show up without a notice.

5.1.2. Response rates and recruitment of cases

Not all cases hospitalised in the participating hospitals were eligible to participate in the study analysis due to age restrictions (50-74 years) or because of their medical history; some cases were not incident (“first ever”) occurrences of ACS or stroke. Therefore, the numbers of eligible cases were lower; of a total of 404 ACS patient initially invited to participate in the study, 348 (86%) were found to be eligible, while of the 259 identified stroke cases, 235 (91%) were eligible

All 348 eligible patients with Acute Coronary Syndrome initially agreed to participate in Astana city Hospital #2, as did all 235 eligible patients with stroke that were recruited in Astana city Hospital #1. The final response rates for ACS and stroke cases were both 100%.

5.2. Cross-sectional study results

Due to the complexity of obtaining objective measurements alongside an extensive questionnaire data, there were some missing values in each category of study health outcomes. Generally, there were only few cases of missing measurements (blood pressure measurement, glucose and lipids measurements and anthropometry) for each biomarker, and the distribution of missing values between urban and rural regions were almost identical. The full list of missing values by major health outcomes in urban and rural regions are presented in Table 10. The reasons for missing measurements were either unsuccessful attempt to collect blood or refusal for blood sample collection.

Table 10 Number of observations with valid and missing values in health outcome variables used in the cross-sectional analysis by sex and urban and rural area of residence.

Astana city			
	Men	**Women**	**Total**
Total number of participants	230	263	493
Arterial Hypertension			
Valid number	229	261	490
Missing number	1	2	3
Diabetes			
Valid number	219	259	478
Missing number	11	4	15
Hypercholesterolemia			
Valid number	221	260	481
Missing number	9	3	12
Obesity and overweight			
Valid number	225	262	487
Missing number	5	1	6
Akmol village			
Total number of participants	202	282	484
Hypertension			
Valid number	197	277	474
Missing number	5	5	10
Diabetes			
Valid number	196	279	475
Missing number	6	3	9
Hypercholesterolemia			
Valid number	196	278	474
Missing number	6	4	10
Obesity and overweight			
Valid number	200	282	482
Missing number	2	0	2

5.2.1. Descriptive characteristics of the study sample

Table 11 presents the demographic and socio-economic characteristics of participants of the cross-sectional study separately for the urban vs. rural region and both ages combined. Descriptive characteristics stratified by sex are shown in Appendix 6.

Table 11 Socio-economic characteristics of study sample by urban and rural area of residence in Astana region, Kazakhstan

Variable name	**Astana city**	**Akmol village**	**Total**
Total number of participants	**493**	**484**	**977**
Sex, (%)			
Men	46.7	41.7	44.2
Women	53.4	58.3	55.8
Age, years, mean (SD)	61.2 (7.3)	60.3 (7.3)	60.7 (7.3)
Age groups, years (%)			
50-54	25.6	28.5	27.0
55-59	20.5	25.4	22.9
60-64	22.1	19.0	20.6
65-69	16.2	13.6	14.9
70-74	15.6	13.4	14.5
Marital status, (%)			
Married	73.2	73.8	73.5
Unmarried	26.8	26.2	26.5
Education, (%)			
Higher	43.6	15.2	29.6
Apprenticeship	30.2	38.1	34.1
Primary and secondary	26.2	46.7	36.3
Ethnicity, (%)			
Kazakhs	57.8	58.5	58.1
Russians	25.9	26.9	26.4
Others	16.3	14.7	15.5
Car ownership, (%)			
Yes	61.5	49.9	55.8
No	38.5	50.1	44.2
Unemployment, (%)			
Never	63.93	81.21	72.49
Less than 1 year	14.55	7.31	10.96
More than 1 year	21.52	11.48	16.55
Deprivation level, (%)			
High level	27.0	25.8	26.4
Intermediate	29.5	33.8	31.6
Low level or not	43.6	40.4	42.0
Household possessions, quartiles (%)			
Q1 lower level of possessions	16.8	32.7	24.8
Q2 medium level of possessions	21.3	36.6	29.0
Q3 higher level of possessions	34.9	27.7	31.3
Q4 highest level of possessions	26.9	3.0	15.0

The age groups were equally distributed and the majority of the respondents (74%) were married. The mean age of participants was between 61 years in urban and 60 years in rural regions. There was a large difference in marital status between male and female participants; the large proportion of unmarried women was largely due to the high percentage of widows, reflecting much higher male mortality (Appendix 7).

The overall proportion of individuals with higher education was 30%; this proportion was three times higher in urban (44%) compared to rural region (15%). Similarly, car ownership and household amenity ownership were also higher in urban vs. rural areas. The level of household amenity ownership was higher in urban (27%) vs. rural region (3%). By contrast, the proportion of ethnic groups was similar in the urban and rural region. The ethnic distribution in the cross-sectional study, with 58% of dominant Kazakhs, 26% of Russians and 16% of other ethnicities combined, which broadly reflects the national ethnic composition in Kazakhstan.

The distribution of cardio-metabolic risk factors and behavioural characteristics of the study sample is shown in Table 12. Overall, 16% of participants were smokers and 19% were past smokers; by region, there are 18% of smokers in urban vs. 14% of smokers in rural areas, and 22% of past smokers in urban vs. 17% of past smokers in rural areas. The proportion of participants reporting frequent alcohol consumption (more than 4 times per month) was small, about 5%, with 4 times higher level in rural (8%) compared to urban regions (2%); again, there were differences between men and women (Appendix 6). Both drinking and smoking were predominantly male behaviours; 30% of men were smokers vs. 4% of women, and 9% of men were frequent drinkers, compared with 2% in women (Appendix 7).

Table 12 Cardio-metabolic risk factors and behavioural characteristics of the study sample by urban and rural area of residence in Astana region, Kazakhstan

Variable name	Astana city	Akmol village	Total
Total number of participants	**493**	**484**	**977**
Behavioral factors			
Smoking status, (%)			
Non smoker	60.6	69.5	65.0
Current smoker	17.7	13.8	15.8
Past smoker	21.7	16.7	19.2
Alcohol consumption, (%)			
Never	40.3	62.1	51.1
Less 3 times a month	52.2	35.7	44.1
More 4 time a month	7.5	2.1	4.8
Blood pressure characteristics			
Systolic blood pressure, (mmHg), mean (SD)	135.0 (22.8)	138.4 (21.1)	136.7 (22.0)
Diastolic blood pressure, (mmHg), mean (SD)	87.8 (13.7)	91.8 (12.8)	89.8 (13.4)
Diabetes risk factors			
Fasting plasma glucose, mean (SD)	5.8 (2.3)	5.3 (2.0)	5.5 (2.2)
Family history of diabetes among all, (%)			
No	79.7	88.5	83.4
Yes	20.3	11.5	16.6
Blood lipids			
Total cholesterol (mmol/l), mean (SD)	5.9 (1.5)	5.4 (1.1)	5.7 (1.3)
LDL-C (mmol/l), mean (SD)	3.7 (1.0)	3.5 (1.0)	3.6 (1.0)
HDL-C (mmol/l), mean (SD)	1.3 (0.4)	1.5 (0.4)	1.4 (0.4)
TG (mmol/l), mean (SD)	1.7 (1.1)	1.5 (1.0)	1.6 (1.1)
Overweight and Obesity characteristics			
Weight, mean (SD)	79.4 (14.7)	76.6 (14.6)	78.0 (14.7)
Height, mean (SD)	163.3 (8.7)	162.1 (8.7)	162.7 (8.7)
Waist circumference, mean (SD)	98.0 (11.8)	95.0 (13.6)	96.5 (12.8)
Hip circumference, mean (SD)	106.2 (9.6)	105.6 (11.0)	105.9 (10.3)
BMI, mean (SD)	29.8 (4.9)	29.2 (5.3)	29.5 (5.1)
BMI categories, (kg/m^2) (%)			
18.50 - 24.99 (normal)	16.0	22.2	19.1
25.00 - 29.99 (pre-obese)	38.2	35.9	37.1
Over 30 (obese)	45.8	41.9	43.9
Waist–hip ratio categories, (%)			
< 0.9 in men and < 0.85 in women	18.5	38.2	28.3
≥ 0.9 in men and ≥ 0.85 in women	81.5	61.8	71.7

The levels of the main cardio-metabolic risk factors (arterial hypertension, diabetes, dyslipidaemias and obesity) in the population sample are shown in

Table 12, and more detailed analyses of these factors are presented in the subsequent section. Mean systolic blood pressure was higher in the rural (138.4 mmHg) compared to urban region (135.0 mmHg). Similarly, the mean diastolic blood pressure was higher in the rural (91.8 mmHg) than in the urban (87.8 mmHg) area. The overall mean fasting plasma glucose level was 5.5 mmol/l, and it was slightly lower in the rural area (5.3 mmol/l) compared with the urban area (5.8 mmol/l). The self-reported history of diabetes was almost twice common in the urban (20%) than in the rural (12%) region. Most of the fasting serum lipids, except HDL-C, were higher in urban than rural area. The prevalence of obesity was high; 44% of participants were obese, while there were no underweight individuals in the study, and 72% of study participants fulfilled the criterion for central obesity (Table 12).

5.2.2. Arterial hypertension

Table 13 presents the prevalence, awareness, treatment and control of arterial hypertension. The overall prevalence of hypertension (defined as SBP ≥ 140 mm Hg, and/or a DBP ≥ 90 mm Hg, and/or on antihypertensive medication) was 72%. Among hypertensive subjects, 77% were aware of their condition, 68% were taking antihypertensive medications, and 24% had controlled blood pressure (<140/90 mm Hg). Among those aware of the condition, 87% were taking medication, among those taking medication, 36% had controlled hypertension (i.e. had blood pressure below 140/90 mm Hg).

The prevalence of hypertension was slightly higher among rural residents, but the awareness, treatment and control indices were more prevalent in urban region. The biggest gap between the urban and rural regions was apparent for hypertension control; only 14% of hypertensive persons had blood pressure below the recommended cut-off, compared to 34% of urban residents. Overall, all indicators were more favourable in women than in men; for example, 92% of women aware of their condition took medication, compared with 79% of men (Figure 16).

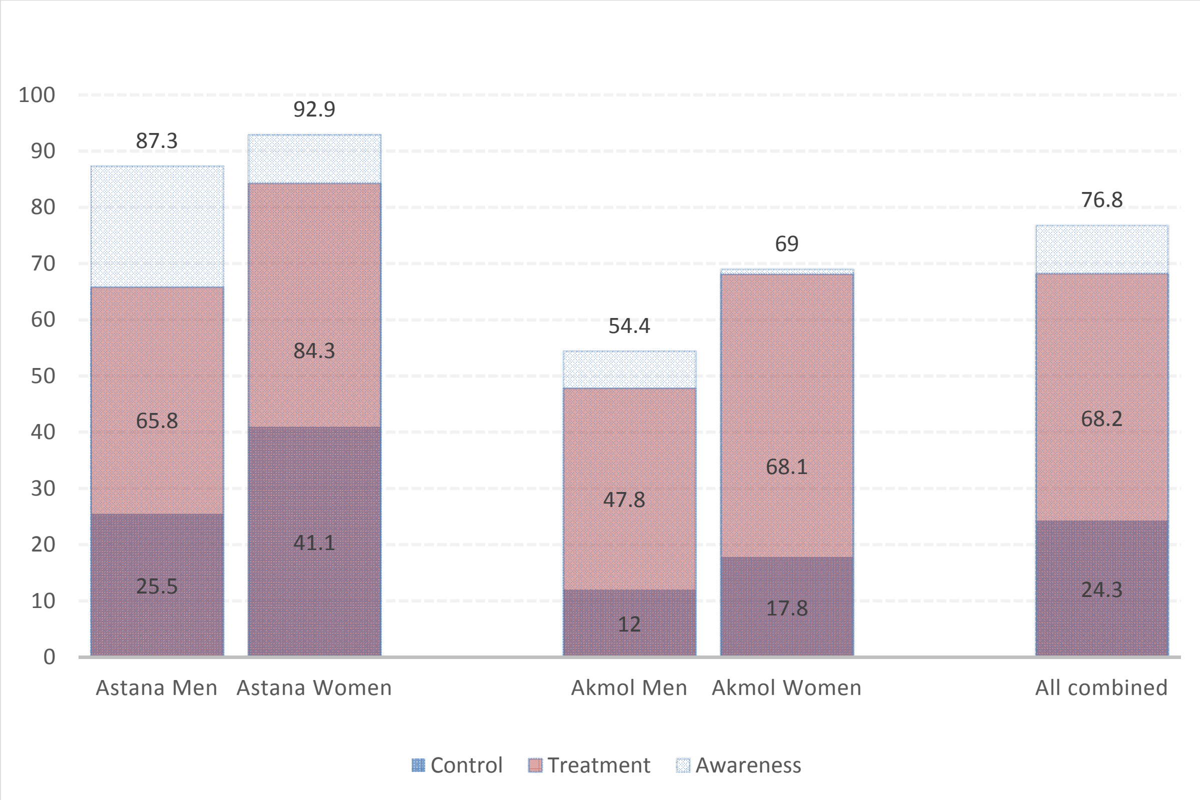
Table 14 shows the results of multiple regression analysis of the values of systolic and diastolic blood pressure measurements. Sex and age statistically significantly predicted systolic blood pressure levels, though failed to explain of the variability of diastolic blood pressure levels. Expectedly, region was a very strong predictor of both systolic and diastolic blood pressure levels, the difference between the urban and rural regions was significant in both age-sex adjusted model and fully adjusted model. The difference in cardio-metabolic risk factors levels followed an expected pattern: obesity was strongly associated with systolic and diastolic blood pressure levels, however, diabetes and hypercholesterolemia were not statistically significant as well as smoking. Ethnicity showed that there is great difference in diastolic blood pressure levels between Kazakh and Russian ethnicity groups. Socioeconomic markers, such as car and household amenity ownerships were not statistically significantly associated with blood pressure.

Table 15 shows the results of logistic regression analyses to identify correlates of hypertension prevalence, awareness, treatment and control. In the age- and sex-adjusted model, the prevalence of hypertension and awareness, treatment and control were higher in women, in persons older than 55 years, in participants with high body mass index and central obesity, as well as in participants with diabetes and hypercholesterolemia. The difference in the prevalence of hypertension between the urban vs. rural areas was small, but there was a large difference in awareness, treatment and control indices between urban and rural areas. The prevalence of awareness, treatment and control of hypertension were several times higher in the urban region.

Education was associated with awareness, treatment and control of hypertension: there were a positive gradient in the prevalence of awareness, treatment and control (indices were higher among participants with higher levels of education). The prevalence of hypertension in the Russian ethnic group was higher than in Kazakhs, while other hypertension indices were not statistically significantly associated with ethnicity. Marital status, car ownership, and smoking status were also not associated with hypertension indicators. The prevalence of hypertension appeared to be higher in more affluent groups, based on household amenity ownership, as were awareness, treatment and control; for example, the odds of awareness was four times higher in upper vs. lowest quartile of household amenities (Q1 has the lowest level of possessions).

In the multivariable model (Table 15, column 3), after controlling for all variables in the table, the associations between the prevalence of hypertension with age, sex and body mass index remained statistically significant. The difference in hypertension prevalence between rural vs. urban residents became statistical significant after adjustment, as the odds ratio increased from 1.18 to 1.66 (95% CI 1.14-2.41). By contrast, the odds ratio for Russian vs. Kazakh ethnicity decreased to 1.38 and became non-significant (95% CI 0.92-2.07). Associations with BMI, central obesity, diabetes as well as household possessions levels were all reduced after adjustment.

Figure 16 Awareness, treatment and control of hypertension among hypertensive subjects



5.2.3. Diabetes

Table *16* presents the prevalence, awareness, treatment and control of diabetes in the cross-sectional sample. From the total sample of 953 respondents from Astana city and Akmol village, 119 (12.5%) were classified as having diabetes (based on fasting glucose concentration ≥7 mmol/l; the proportion of subjects with diabetes was twice as high in Astana city than in Akmol village. Among subjects with diabetes, 72.3% were aware of their condition, 65.6% took medication, and 27.7% had fasting glucose level controlled (i.e. fasting plasma glucose <7 mmol/l). Among those who were aware of the condition, 87.2% were taking medication (only 4 persons aware of diabetes reported to be on a diet but without medication), and among those taking medication, 42.3% had controlled diabetes. Again, there were marked differences between urban and rural areas (Figure 17). The prevalence of awareness and treatment of diabetes were two times higher in urban area. Successful control of diabetes in the rural area was very low (4.9%) compared with the city (39.7%), although the difference was less dramatic among those aware of having diabetes (15.% vs. 47.7%).

Figure 17. Awareness, treatment and control of diabetes among respondents with diabetes

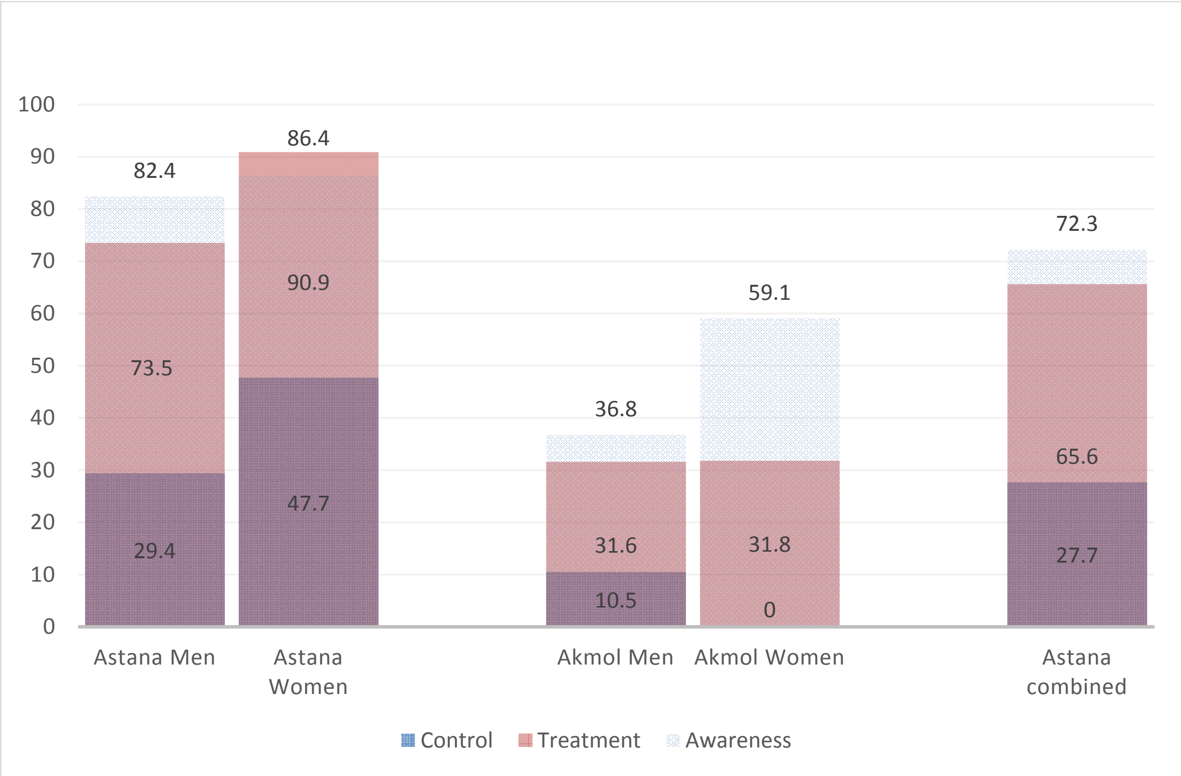


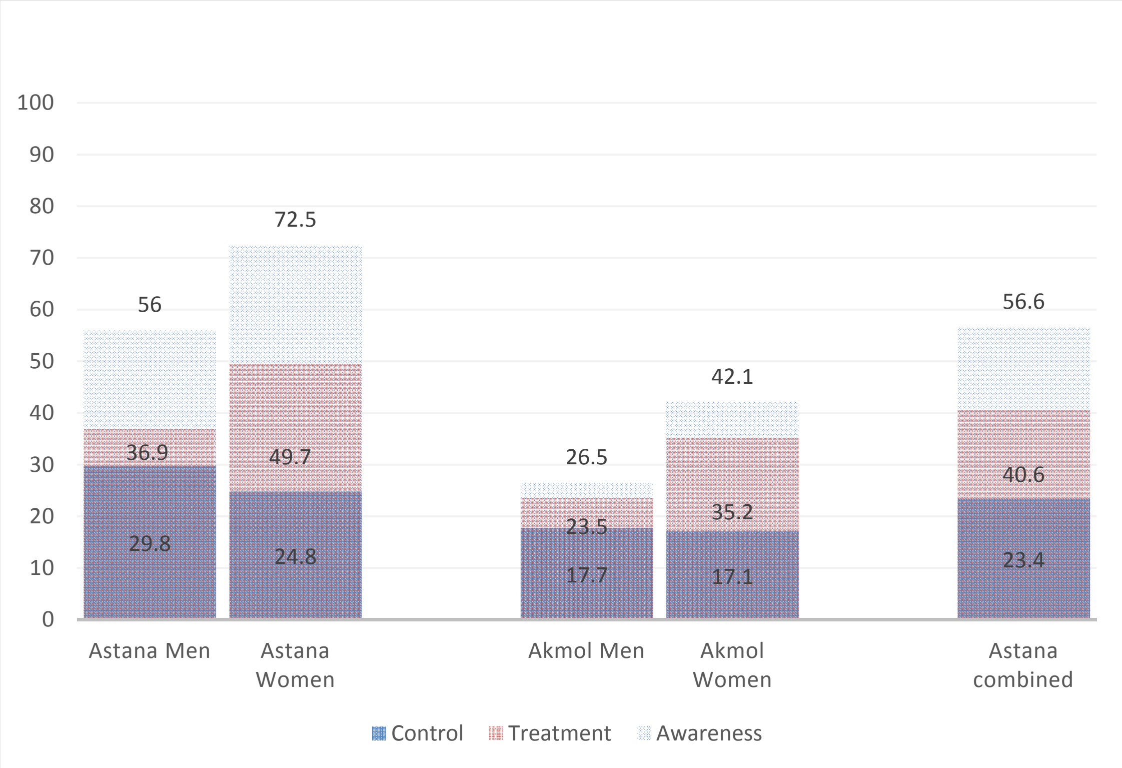
Table 17 shows age-sex-adjusted odds ratios for covariates and diabetes prevalence, awareness, treatment and control. The prevalence of diabetes was associated with higher age, increasing body mass index, central obesity and family history of diabetes. The odds of diabetes were less than half in rural Akmol compared to urban Astana city. The odds of awareness, treatment and control were also substantially lower in the rural vs. urban area. Among the socio-demographic measures, only household items were statistically significantly associated with (increased) diabetes prevalence and control of diabetes. In addition, Russian ethnicity had a marginally increased prevalence of diabetes.

Multivariable analysis was only possible for diabetes prevalence (Table 17, column 3), as the numbers of subjects were too small for multivariable analysis of awareness, treatment and control of diabetes. For diabetes prevalence, the main difference was that the odds ratio for rural vs. urban residence was attenuated (from 0.49 to 0.60), while the odds ratio for Russian vs. Kazakh ethnicity increased to 1.59 (0.99-2.57) and the association with BMI and central obesity were both reduced.

5.2.4. Dyslipidaemias

Table 18 shows the prevalence, awareness, treatment and control of hypercholesterolemia. In the total sample of 954 subjects, 37.2% were classified as having hypercholesterolemia (total cholesterol ≥6.2 mmol/l); the proportion of subjects with hypercholesterolemia was almost twice as high in the urban compared to the rural area. Among subjects with hypercholesterolemia, 56.6% were aware of their condition, 40.6% took medication, and 23.4% had total cholesterol concentrations <6.2 mmol/l (i.e. their hypercholesterolemia was controlled). Among those aware of the condition, 70.7% were taking medication, and among those taking medication, 57.6% had concentrations <6.2 mmol/l. As with hypertension and diabetes, there were pronounced differences between urban and rural areas. The prevalence of awareness, treatment and control of hypercholesterolemia were also about 1.5 times higher in the urban vs. rural area. Prevalence, awareness and treatment were about 1.5 times higher in women than men, although diabetes control was better among men than women (Figure 18).

Figure 18 Awareness, treatment and control of hypercholesterolemia (>6.2 mmol/l)



The prevalence, awareness, treatment and control of hypercholesterolemia defined by the lower cut-off of ≥ 5.0 mmol/l are shown in Table 20. Using this lower cut-off, the overall prevalence of hypercholesterolemia was 72.8%. The distribution of all characteristics is consistent with results for the condition based on 6.2 mmol cut off described above, with higher levels in urban area. However, the gap between urban and rural areas increased considerably; the prevalence of awareness and treatment of hypercholesterolemia were more than two times higher in the urban area. Overall, the prevalence of successful control of diabetes in the rural area was 1.3% compared with 7% in Astana city; among those aware of having hypercholesterolemia, the proportions with successful control was 10.3% and 25.7%, respectively. Differences between men and women were similar to those presented for the standard definition hypercholesterolemia (≥ 6.2mmol/l) (Figure 19).

Age- and sex-standardized means of serum lipids and respective odds ratios for impaired lipid concentrations by covariates are shown in Appendix 8. Impaired lipid concentrations were more common in women, obese persons and subjects with diabetes and hypertension. The odds of dyslipidemia in the rural area was about half of that in Astana city. Car ownership, deprivation levels and education were statistically significantly associated with dyslipidemia prevalence. Russian ethnicity was associated with high rates of lipid abnormalities.

Figure 19 Awareness, treatment and control of hypercholesterolemia (>5 mmol/l)

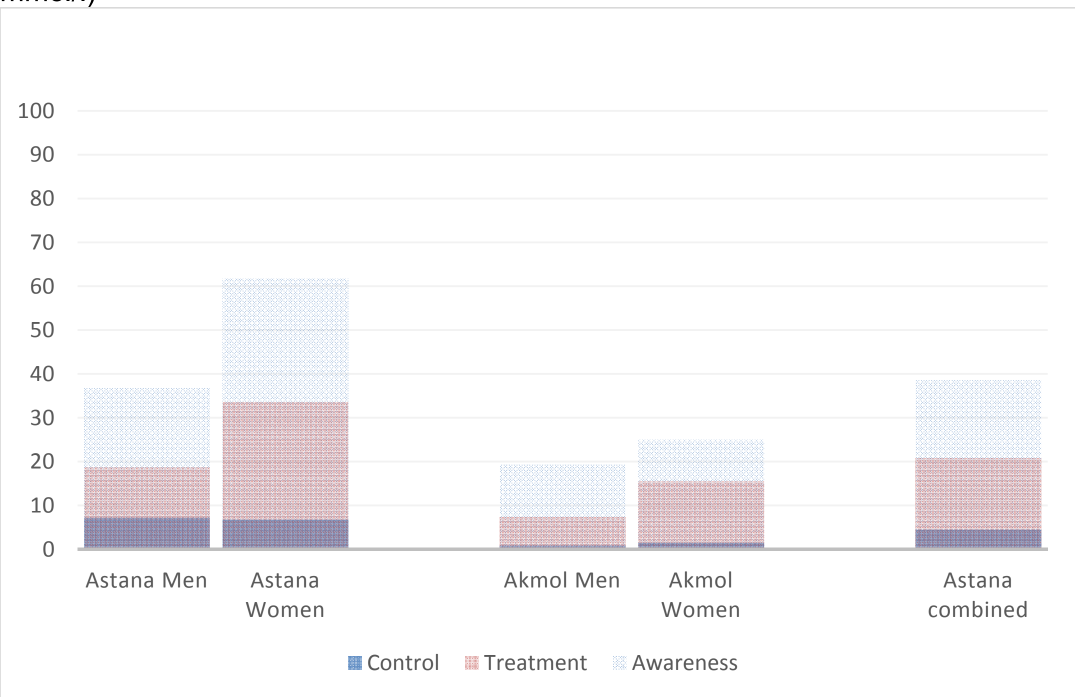


Table 19 shows the odds ratios of hypercholesterolemia prevalence, awareness, treatment and control by covariates. In the age-adjusted model, the prevalence of hypercholesterolemia was associated with female sex, older age, increasing body mass index, central obesity, diabetes and hypertension. The odds of prevalence, awareness, treatment and control were also substantially lower in the rural vs. urban area. Among the socio-demographic measures, deprivation levels and education were statistically significantly associated with (increased) hypercholesterolemia prevalence, awareness and control. As mentioned earlier, Russian ethnicity had increased prevalence of hypercholesterolemia. Multivariable analysis of hypercholesterolemia prevalence (Table 19, column 3) largely confirmed these findings, except that the association with BMI, central obesity and diabetes were reduced, mainly because these variables were strongly mutually correlated.

5.2.5. Obesity

Overall, the mean BMI of the participants was 29.5 kg/m2, and the mean was marginally higher in the urban (29.8 kg/m2) vs. rural (29.2 kg/m2) area of residence (Table 21). The mean weight of participants was 78.0 kg, and it was higher in the urban (79.4 kg) compared to the rural region (76.6 kg). There was a 3 cm difference in waist circumference between the regions (98.0 cm in urban vs. 95.0 cm in rural residents), and similarly higher mean of hip circumference in urban region.

The overall prevalence of overweight and obesity was 81% and 44%, respectively. Overweight and obesity rates were higher in women than in men: 85% of women were overweight and 52% were obese, compared with 76%

overweight and 34% obese men. Both overweight and obesity were more common among participants with other cardio-metabolic risk factors, such as diabetes, hypertension and hypercholesterolemia. In addition, the proportion of obese and overweight participants were seen among non-smokers, unmarried, Russian ethnic group and more affluent population. People with higher education were less obese as compared to undereducated groups. With regards to urban/rural distribution, both overweight and obesity were higher in urban residents.

Table 22 shows the results of multiple regression analyses of the values of body mass index and waist circumference measurements. Region was a very strong predictor of both body mass index and waist circumference, and the difference between the urban and rural regions remained significant though in fully adjusted model, although it was somewhat reduced. The difference in cardio-metabolic risk factors levels was expectedly high, diabetes, hypertension and hypercholesterolemia was strongly associated with body mass index and waist circumference, however, the effect of hypercholesterolemia was considerably attenuated in fully adjusted model. Smoking was inversely associated with body mass index. The ethnicity showed that there is great difference in body mass index and waist circumference measurements between Kazakh and Russian ethnicity groups. Socioeconomic markers, such as household amenities were statistically associated with higher levels of adiposity in wealthier groups.

Table 23 presents the odds ratios of overweight and obesity prevalence by covariates. In the age- and sex-adjusted model, the prevalence of overweight and obesity were higher in women. Women were significantly more at risk of being overweight 1.84 (95% confidence interval 1.33-2.54) or being obese 2.10 (1.62-2.74) than men. The prevalence of overweight and obesity was also strongly associated with hypertension, diabetes and hypercholesterolemia. The odds of overweight and obesity prevalence were lower in the rural vs. urban area.

The risk of being overweight or obese was also elevated in the non-Kazakh ethnic groups, with ethnic Russians and other ethnicity having significantly higher odds of obesity and overweight. Persons with higher household amenities were at a significantly increased risk of being overweight (OR 2.96, 95%CI 1.67-5.26) and obese (OR 2.01, 95%CI 1.28-3.16). Education and marital status were not significantly associated with the prevalence of overweight and obesity. Smoking was inversely associated with overweight and obesity; the odds of overweight and obesity prevalence were lower in current smokers vs. non-smoking participants.

Most of these results did not materially change in the multivariable analysis (Table 23). The strength of the associations with hypertension, diabetes and hypercholesterolemia were slightly reduced, possibly due to complex relationships of these mutually correlated covariates. For obesity prevalence, the association with education level become stronger: the odds ratio of the lowest vs. highest education increased from 1.19 to 1.57 (95% CI 1.05-2.34). The odds ratio of overweight for Russian vs. Kazakh ethnicity also became stronger (it increased from 1.86 to 2.43).

5.3. Results of the case-control study

Due to the recruitment process among cases (i.e. recruiting all consecutive incident cases hospitalised in the two main hospitals), the numbers of cases should roughly represent both rural and urban residents (see methods). However, as the numbers do not reflect the size of these populations, and the study was therefore unsuitable to investigate the regional differences in CVD risk, and the variable of urban/rural residence was not explored in the case-control analyses.

The descriptive analysis of cases and controls are presented in Table 24 (socio-demographic factors) and Table 25 (cardio-metabolic and behavioural factors). The descriptive characteristics are stratified by sex, while cases were further stratified by diagnostic group (i.e. ACS and stroke). Given the recruitment of cases (i.e. recruiting all consecutive incident cases hospitalised in the two main hospitals), the numbers of cases that should represent both rural and urban residents (see methods).

In the table, missing values were coded and shown as a separate category. Across the variables, there were only few cases of missing values in objective measurements, and similarly to cross-sectional analysis the reasons for the missing values were either unsuccessful attempt or refusal for blood sample collection.

5.3.1. Descriptive characteristics of the case-control study

The study included a total of 583 cases and 977 population-based controls. Among cases, there were 348 cases of ACS and 235 cases of stroke (Table 24). While the controls were roughly equally distributed by sex (due to sampling), the numbers of cases were almost twice higher in men than in women. This broadly reflects the incidence of most of CVD events (incidence and mortality) in the population, and is similar to reports from elsewhere. The age distribution of cases and controls was more similar; in women, cases tended to be older than controls.

The comparison of education level between cases and controls differed by sex; in men, higher level of education was observed more commonly in cases than in controls while in women the distribution of education was similar in cases and controls. Overall, there were 33% of participants with higher education level among cases vs. 30% in controls. Self-identified ethnicity among cases was similar to population controls; there were slightly more Russians (29%) among cases than among controls (26%), and this difference was larger when comparing ACS cases vs. controls. (Table 24)

The proportion of married persons was higher among population controls than among cases, both in men and women. When men and women were combined, the proportion of unmarried person was higher among controls, but this entirely driven by the larger proportion of male participants among cases combined with the huge (up to 4-fold) gender gap in marital status between men and women, most likely reflecting the sex disparity in life expectancy, leading to very high proportion of widowed women in the population (at older ages). (Table 24)

In the analysis of cardio-metabolic risk factors, one part of the investigation was based on self-reported diagnosis of hypertension, diabetes and hypercholesterolemia This approach is justified by the fact that after being admitted to hospital, cases received various treatments, including anti-hypertensive, blood sugar and cholesterol lowering medications, as well as being restricted to a special in-hospital diet. To avoid such systematic bias, we used identical questions in both cases and controls (whether they had been told by a doctor of having hypertension, diabetes and hypercholesterolemia). For overweight and obesity indices, weight and height were measured objectively in both cases and controls. (Table 25)

Using self-reported information, hypertension and diabetes were more common among cases (both in men and women) compared to controls. Stroke cases had substantially higher prevalence of self-reported hypertension and diabetes compared to controls (as well as ACS cases). By contrast, hypercholesterolemia and overweight / obesity were higher in controls than in cases. However, there were differences between men and women; for example, the prevalence of obesity among stroke cases (63%) was higher than among population controls (52%). (Table 25)

Self-reported material deprivation was used as a proxy for socio-economic position. The proportion of participants with the highest level of material deprivation was higher in the control group (26%) compared with cases (19%), and the difference was similar in gender specific analyses. However, when assessed separately by each diagnostic group, the proportion of highly materially deprived individuals among ACS cases was slightly higher than among controls in male participants. Another marker of socio-economic position was car ownership. In general, there were higher levels of reported car ownership in the household among men than among women, in both cases and controls, and moderately lower percentage of car owners in controls compared to cases. (Table 24)

The relationship between unemployment and health has been studied extensively and given its persistent adverse effect on health reported in various (mostly western) populations, this thesis explored its potential impact on CVD risk in Kazakhstan. Unemployment duration ever experienced in participants' life (i.e. never, less than a year, and one year or more) showed some differences between cases and controls. Overall, the short-term unemployment was reported by 23% of cases and 11% of controls. Men had substantially higher rate of short-term unemployment, both in cases and controls, than women. By contrast, women had higher proportion of long-term unemployment compared to men. There was almost no difference between cases and controls in the history of long-term unemployment. (Table 24)

Common health behaviours studied in this thesis included smoking and alcohol consumption. While it was common procedure of to study smoking status in various previous studies in Central Asia, alcohol consumption by standardized instrument was less often investigated in Central Asia. Considering a wide range of various indicators of alcohol consumption, the frequency of alcohol consumption during the last year (as opposed to measures of drinking volume heavy or binge drinking) was seen as the most practical way to increase the level of disclosure and minimize the missing data. (Table 25)

There was a large difference in smoking status and alcohol consumption between men and women in all groups of comparison. Indeed, few women reported to be current smokers or frequent alcohol consumers, in both cases and controls. Among men, there were 39% of current smokers among cases (37% in cases of stroke and 43% in cases of ACS) compared with 30% of current smokers in the control group. Among women, the prevalence of current smoking among cases (ACS and stroke combined) was twice higher than in controls. Frequent alcohol use (at least once a week) in men was considerable higher in cases compared to controls; in women, the reported prevalence of frequent alcohol consumption was too low for meaningful analyses. The missing data on the reported alcohol behaviour was relatively low, with 5% in cases and 3% in controls. (Table 25)

5.3.2. Logistic regression analysis of the case-control study

The associations between socio-demographic factors and CVD (i.e. ACS and stroke combined) are shown in Table 26 and the association between cardio-metabolic and behavioural risk factors with CVD are shown in Table 27. The tables shows results from two logistic regression models; model 1 shows odds ratios adjusted for age and sex, and model 2 shows results adjusted for age, sex, cardio-metabolic and behavioural factors and socio-demographic factors. The inclusion and exclusion of the covariates in the model was organized in such common way to introduce all relevant clinical, behavioural and socio-economic and demographic variables based on their significance and in order to control for potential confounding. The full list of selected variables included: sex, age, education, ethnicity and marital status, material deprivation level and unemployment, obesity, hypertension, diabetes and hypercholesterolemia and smoking and alcohol consumption.

Separate results for diagnostic subgroups of cases (ACS and stroke) are shown analogously (Table 28 and Table 29 for ACS and Table 30 and Table 31 for stroke). In order to maximise the sample size, analyses were conducted on datasets with men and women combined. However, likelihood ratio tests were performed to assess the statistical significance of the interaction of sex with each of the predictors studied; where results differed between men and women, they are described in detail.

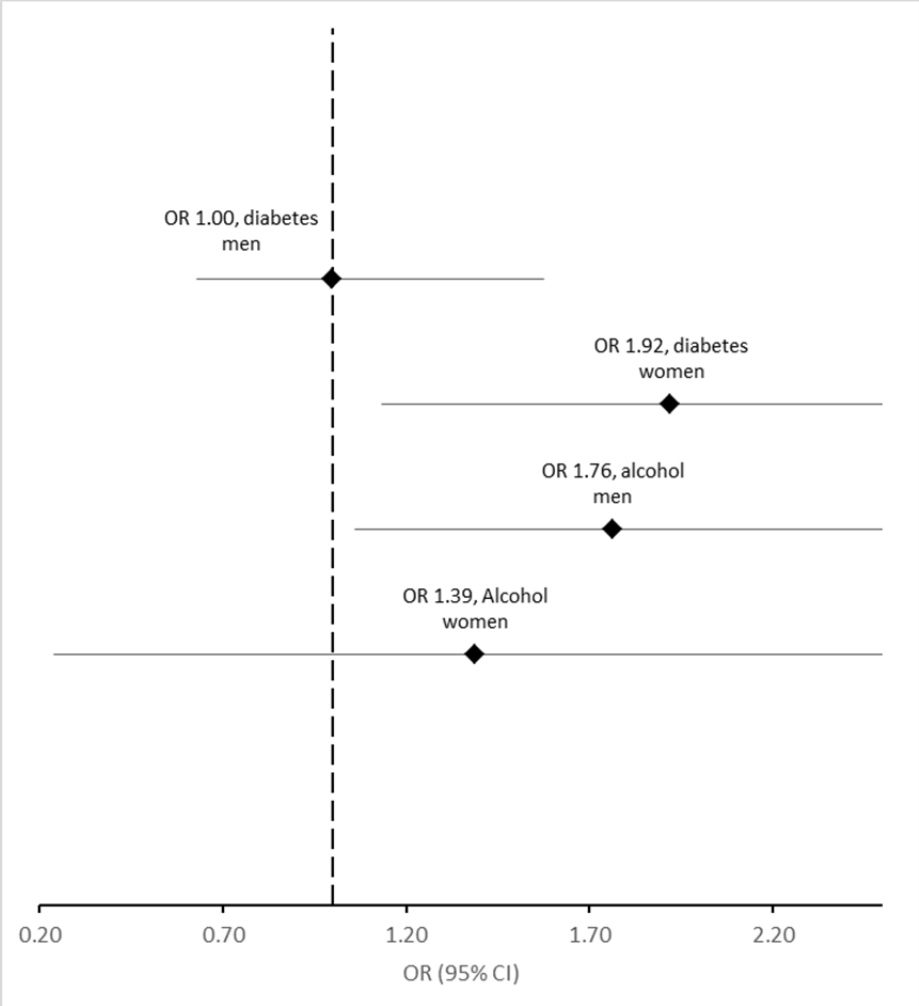
5.3.2.1. Cardio-metabolic and behavioural factors

The major objective of the current PhD project was not only to describe the levels and distribution of cardio-metabolic and behavioural factors, but also to investigate the associations of these factors with CVD event risk in the Kazakhstani population, as there is a complete lack of reliable evidence on this important public health issue in the whole Central Asian region, including Kazakhstan. The results of the analyses in many ways correspond with the reports from similar studies in other regions, although some differences were also observed. The results described below refer to tables: Table 26 and Table 27 (CVD), Table 28 and Table 29 (ACS), Table 30 and Table 31 (stroke).

In the age and sex adjusted model, participants who were told by a doctor (i.e. aware) of having arterial hypertension in the past were at significantly higher risk of CVD with OR of 1.58 (95% CI 1.24-2.02). Similar, albeit slightly weaker, CVD risk was also higher among those who reported that they have been told of having diabetes, with OR 1.31 (95% CI 0.96-1.78). By examining the risk of CVD separately for each particular diagnostic group (Table 26 and Table 27), a consistent protective pattern: risk factors such as hypertension and diabetes were favourable among those with lowered risk of ACS and stroke, with a more marked effect for stroke.

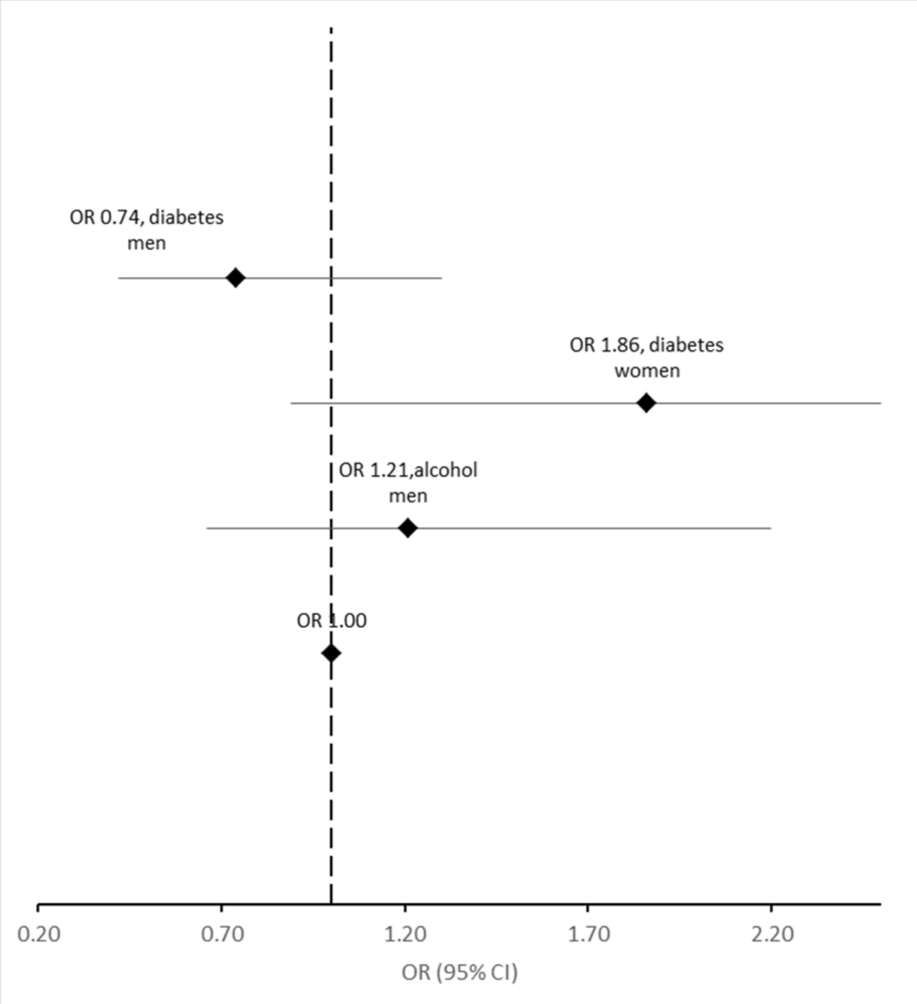
As outlined in the Methods, the significance of potential interactions between sex and each of the other predictors in the model was tested, controlling for age and the main effects of each predictor and sex. The interaction with sex was detected for alcohol consumption and diabetes. The sex-specific results are presented in forest plot format in for CVD combined (Figure 20), ACS (Figure 21) and stroke (Figure 22).

Figure 20 Sex-specific odds ratios of CVD by alcohol intake category and diabetes (case-control analysis)*



** Estimates shown as from the fully adjusted model.*

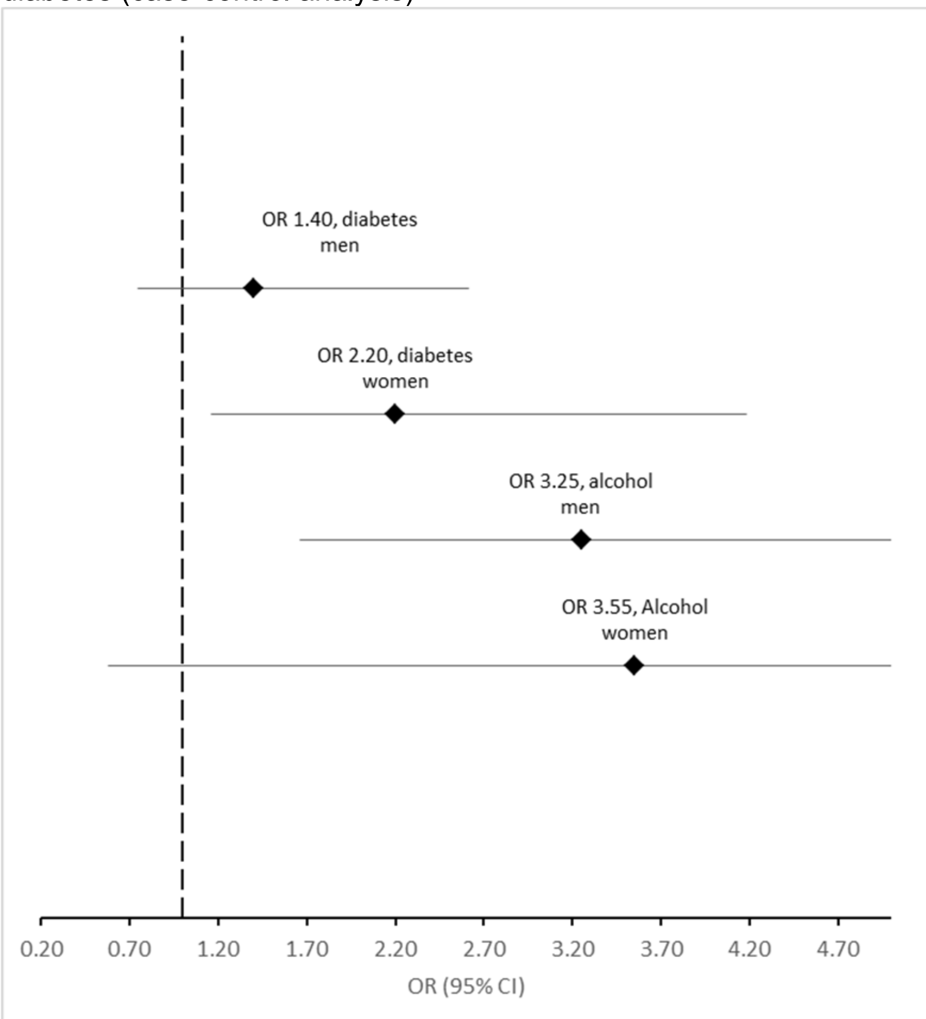
Figure 21 Sex-specific odds ratios of ACS by alcohol intake category and diabetes (case-control analysis)*



** Estimates shown as from the fully adjusted model.*

In fully adjusted model, the association of alcohol with the risk of CVD was statistically significant (OR 1.76 95% CI 1.06-2.94) in men but not in women (OR 1.39 95%CI 0.24-8.10). By contrast the association of self-reported diabetes with the risk of CVD was statistically significant in women (OR 1.92 95%CI 1.14-3.25) and for men the association was not significant (OR 1 95%CI 0.63-1.58). Interestingly, after splitting the analysis by specific CVD outcome, the effect of alcohol on ACS risk in men was diminished (OR 1.21 95%CI 0.66-2.20) and was significantly increased for stroke in men (OR 3.25 95%CI 1.66-6.36). The effect of alcohol on ACS and stroke risk in women was not significant. Similarly, the association of diabetes with ACS and stroke was not significant among men. The effect of diabetes on ACS risk in women was smaller (OR 1.86 95%CI 0.89-3.93) than the association with stroke (OR 2.2 95%CI 1.16-4.18).

Figure 22 Sex-specific odds ratios of stroke by alcohol intake category and diabetes (case-control analysis)*



** Estimates shown as from the fully adjusted model.*

As noted previously in the descriptive analyses, the differences in the distribution of hypercholesterolemia between cases vs. controls were not as expected. In age-sex adjusted model, the association of hypercholesterolemia with the risk of CVD was not statistically significant (OR 1.20). However, the association between self-reported history of high cholesterol and CVD events differed between ACS and stroke. The risk of stroke was higher among persons who were not told by a doctor to have raised cholesterol level (OR 1.51, 95% CI 1.06-2.15), but there was no association of hypercholesterolemia with ACS (OR 0.96, 95%CI 0.69-1.33).

Overweight and obesity was also not associated with the risk of CVD in our sample; the OR for CVD was 0.90 (0.66-1.22) in overweight and 0.79 (0.58-1.08) in obese individuals. Similarly, there were no associations of overweight and obesity with the risk of either ACS or stroke in separate analysis.

There were major differences in smoking between controls and cases as well as between men and women. Smoking was a strong predictor of CVD.I Individuals who reported current smoking status had 1.65 higher risk of CVD compared to non-smokers. The effect of smoking was more pronounced for ACS (OR 1.72, 95% CI 1.18-2.52) than for stroke (OR 1.53, 95% CI 1.00-2.35). Smoking in the past was not statistically significantly associated with the risk of CVD, although the odds ratio of CVD risk was marginally significant for past smokers compared to non-smokers.

The association between alcohol consumption and the risk of CVD was strong, with an almost two fold risk of CVD among frequent alcohol consumers. The effect of frequent alcohol consumption was more pronounced for stroke, with an OR of 3.32 (95% CI 2.02-5.47) compared to those who reported no alcohol use. Moderate alcohol consumption (less than 3 times per month) appeared statistically significantly protective (OR 0.70 CI 0.54-0.90) compared to those who reported no alcohol use; the protective effect remained significant in separate analyses of ACS and stroke.

5.3.2.2. Socio-economic and demographic characteristics

This project examined the associations of CVD outcomes with several socio-economic and demographic factors, as education, unemployment and material deprivation, as well as commonly used demographic indices, such as ethnicity and marital status. The results are shown in Table 26 (CVD), Table 28 (ACS), and Table 30 (stroke).

In these data, educational attainment was not associated with the risk of CVD. The multivariable adjusted odds ratio of the lowest vs. higher educational category was 0.89 (0.65-1.20). Similarly, separate analysis of each CVD diagnostic group did not reveal a significant relationship between education level and risk of ACS or stroke. In multivariable analysis, the effect of educational level was somewhat stronger, with lower odds of CVD risk among less educated individuals (OR of 0.81 for apprenticeship and OR of 0.89 for primary/secondary) but the association was not statistically significant.

Material deprivation was associated with the risk of CVD in a graded fashion; the lower the level of deprivation the higher the risk of CVD. The risk of CVD was 1.15 higher among less materially deprived (intermediate) and 1.37 higher among non-deprived individuals compared to the reference category (highest deprivation group). Interestingly, the association of deprivation with CVD differed between ACS and stroke. While there was no association between deprivation level and risk of ACS, material deprivation was strongly related to the risk of stroke, with 2.6 times higher risk of stroke among most affluent group. After adjustment for all selected variables the effect of deprivation on the risk of CVD has slightly increased, and the association between deprivation level and CVD and stroke remained insignificant in the fully-adjusted analysis. Car ownership, however, was not related to the risk of any CVD outcome; the OR of CVD in participants with a car in household was 0.88 in age- and sex-adjusted model and 0.83 in the fully adjusted model, compared with households without car ownership.

Self-reported history of short-term and long-term unemployment was associated with the increased risk of CVD in Kazakhstan, although the association did not follow a clear pattern. The risk of CVD was substantially (2.7 times) higher for short-term unemployment and 1.4 times higher for long-term unemployment experience; this difference was probably due to a large proportion of women in a group with history of long-term unemployment.

Russian ethnicity was associated with elevated risk of CVD, with OR of 1.3 (95% CI 1.00-1.71) for CVD risk compared to native Kazakhs. The risk was increased in the multivariable model (up to 1.5-fold); the association between Russian ethnicity and CVD was only seen for ACS but not for stroke.

Marital status was associated with the risk of CVD in the expected direction. The odds of CVD was approximately 30% higher among unmarried individuals, and the effect was similar in in cases of ACS and stroke. After multivariable adjustment, the associates became a slightly stronger and statistically significant for CVD and stroke.

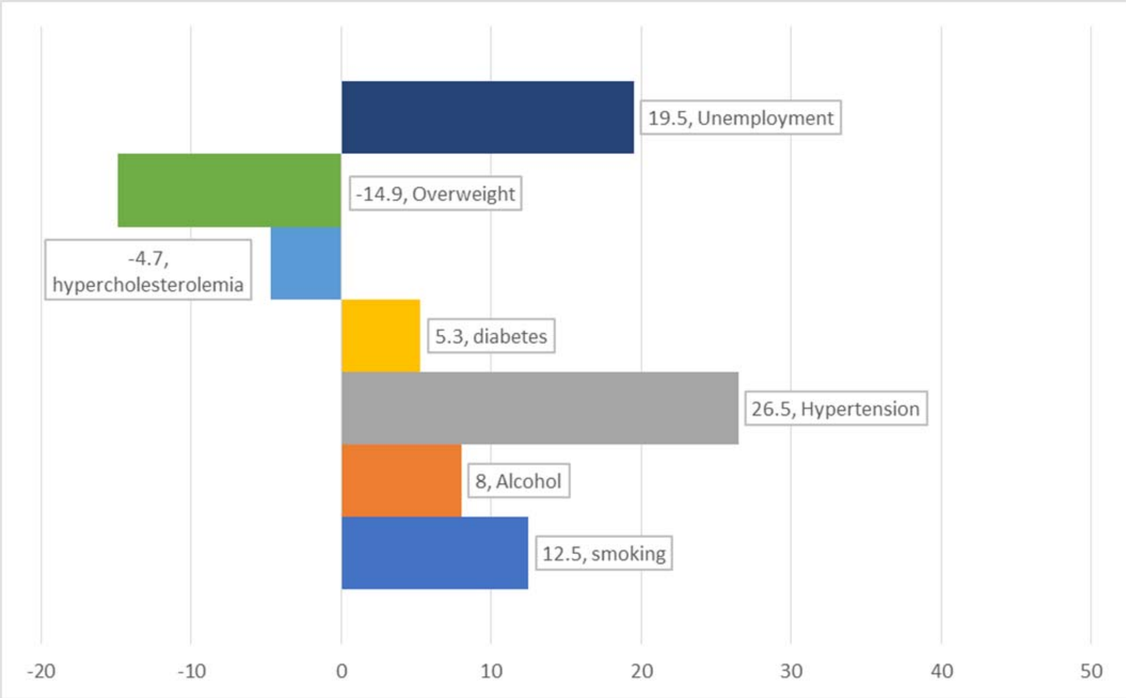
5.3.3. Population attributable risk fractions

While we are aware that there are methodological issues limiting the precision and reliability of these results, it is useful for researchers and policymakers planning public health interventions to have at least rough estimates of how much of the cardiovascular disease burden in the Kazakh population could be due to risk known factors in order to plan public health interventions. Ppopulation attributable risk fractions as serve as a guide as to proportion of CVD burden which might be eliminated (avoided) if exposure to certain risk factors were eliminated from the population.

Therefore, population attributable risk fractions (PARF) were calculated for cardio-metabolic and behavioural factors (the causality of these factors is well supported by external evidence presented in Chapter 2) and history of unemployment (as an example of socioeconomic exposure). The calculations use the prevalence of exposure among population controls and the observed odds ratio (adjusted for age and sex). (Appendix 9)

The summary of the PARF estimates is shown in Figure 23, separately for CVD, ACS and stroke. Among cardio-metabolic factors and CVD (i.e. ACS and stroke combined), the largest PARF was seen for hypertension (26.5%). Smoking was associated with 12.5% of CVD. Given the inverse association between obesity and CVD observed in the case-control study, the PARF was negative (-14.9%). History of unemployment, as example of socioeconomic variables, also appeared to have made significant contribution to the burden of CVDE, with PARF around 20%. (Figure 23)

Figure 23 Population-attributable risk proportion for various risk factors among ACS and stroke cases



5.4. Astana region cross-sectional study tables

5.4.1. Arterial hypertension tables

Table 13 Prevalence, awareness, treatment and control of Arterial Hypertension (HT) by urban and rural area of residence in Astana region, Kazakhstan

	Men (n=426)			Women (n=538)			Both sexes (n=964)		
	Prevalence	*95% CI*	*Cases/All*	*Prevalence*	*95% CI*	*Cases/All*	*Prevalence*	*95% CI*	*Cases/All*
Combined Astana city and Akmol village									
Prevalence of HT among all	66.9	62.4-71.4	285/426	76.2	72.6-79.8	410/538	72.1	69.3-74.9	695/964
Awareness among all cases of HT	71.6	66.3-76.8	204/285	80.5	76.6-84.3	330/410	76.8	73.7-80.0	534/695
Treatment among all cases of HT	57.2	51.4-63.0	163/285	75.9	71.7-80.0	311/410	68.2	64.7-71.7	474/695
Treatment among aware	79.4	73.8-85.0	330/204	92.1	89.2-95.0	304/330	87.3	84.4-90.1	466/534
Control among all cases of HT	17.5	13.1-22.0	50/285	29.0	24.6-33.4	119/410	24.3	21.1-27.5	169/695
Control among treated	30.7	23.5-37.8	50/163	38.3	32.8-43.7	119/311	35.7	31.3-40.0	169/474
Astana city									
Prevalence of HT among all	65.1	58.8-71.3	149/229	75.48	70.2-80.7	197/261	70.6	66.6-74.7	346/490
Awareness among all cases of HT	87.3	81.8-92.7	130/149	92.9	89.3-96.5	183/197	90.5	87.4-93.6	313/346
Treatment among all cases of HT	65.8	58.1-73.5	98/149	84.3	79.1-89.4	166/197	76.3	71.8-80.8	264/346
Treatment among aware	74.6	67.0-82.2	97/130	89.6	85.2-94.1	164/183	83.4	79.2-87.5	261/313
Control among all cases of HT	25.5	18.4-32.6	38/149	41.1	34.2-48.0	81/197	34.4	29.4-39.4	119/346
Control among treated	38.8	29.0-48.6	38/98	48.8	41.1-56.5	81/166	45.1	39.0-51.1	119/264
Akmol village									
Prevalence of HT among all	69.0	62.5-75.5	136/197	76.9	71.9-81.9	213/277	73.6	75.1-83.2	349/474
Awareness among all cases of HT	54.4	45.9-62.9	74/136	69.0	62.8-75.3	147/213	63.3	58.2-68.4	221/349
Treatment among all cases of HT	47.8	39.3-56.3	65/136	68.1	61.8-74.4	145/213	60.2	55.0-65.3	210/349
Treatment among aware	87.8	80.2-95.5	65/74	95.2	91.8-98.7	140/ 147	92.8	89.3-96.2	205/221
Control among all cases of HT	12.0	4.0-13.7	12/136	17.8	12.7-23.0	38/213	14.3	10.6-18.0	50/349
Control among treated	18.5	8.8-28.2	12/65	26.2	19.0-33.5	38/145	23.8	18.0-29.6	50/210

Table 14 Association of selected factors with SBP and DBP in Astana region, Kazakhstan

	Systolic blood pressure		Diastolic blood pressure	
	Model 1	**Model 2**	**Model 1**	**Model 2**
Sex				
Males	reference	reference	reference	reference
Females	-2.35 (1.47)	-5.69 (2.07) **	0.31 (0.93)	-2.66 (1.28) *
Age groups (years)				
50-54	reference	reference	reference	reference
55-59	5.32 (2.06) **	4.94 (2.03) *	1.71 (1.29)	1.37 (1.25)
60-64	8.39 (2.14) ***	8.88 (2.11) ***	1.90 (1.35)	2.18 (1.30)
65-69	10.11 (2.35) ***	9.52 (2.32) ***	0.38 (1.48)	-0.10 (1.43)
70-75	14.20 (2.37) ***	14.54 (2.48) ***	-0.26 (1.49)	-0.31 (1.53)
Urban/Rural				
Astana (urban)	reference	reference	reference	reference
Akmol (rural)	4.02 (1.46) **	4.69 (1.66) **	3.89 (0.91) ***	4.90 (1.02) ***
BMI, (kg/m2)				
18.5-24.9	reference	reference	reference	reference
25-29.9	4.09 (2.01) *	4.42 (2.14) *	2.15 (1.25)	1.91 (1.32)
≥30	11.68 (1.97) ***	11.96 (2.21) ***	8.05 (1.23) ***	7.80 (1.36) ***
WHR, obesity				
No	reference	reference	reference	reference
Yes	1.71 (1.64)	-0.97 (1.80)	1.39 (1.03)	0.26 (1.11)
Diabetes				
No	reference	reference	reference	reference
Yes	0.21 (2.18)	-1.92 (2.20)	-0.15 (1.37)	-1.73 (1.35)
Hypercholesterolemia				
No	reference	reference	reference	reference
Yes	2.77 (1.54)	3.37 (1.56) *	1.17 (0.97)	1.66 (0.96)
Smoking				
Non-smoker	reference	reference	reference	reference
Current Smoker	-4.19 (2.40)	-3.07 (2.41)	-2.86 (1.51)	-2.57 (1.49)
Ex-smoker	-2.02 (2.33)	-2.51 (2.30)	-1.30 (1.47)	-1.87 (1.42)
Marital status				
Married	reference	reference	reference	reference
Unmarried	-4.26 (1.80) *	-3.80 (1.83) *	-1.39 (1.14)	-0.72 (1.12)

	Systolic blood pressure		Diastolic blood pressure	
	Model 1	**Model 2**	**Model 1**	**Model 2**
Education				
Higher	reference	reference	reference	reference
Apprenticeship	1.23 (1.84)	0.35 (1.91)	0.60 (1.16)	-0.50 (1.18)
Primary&Secondary	3.11 (1.83)	1.86 (1.97)	1.38 (1.15)	-0.06 (1.22)
Ethnicity				
Kazakh	reference	reference	reference	reference
Russian	2.74 (1.76)	1.53 (1.78)	3.68 (1.10) **	3.00 (1.10) **
Other	1.87 (2.08)	-0.02 (2.07)	1.38 (1.30)	0.37 (1.27)
Car ownership				
Yes	reference	reference	reference	reference
No	-0.23 (1.50)	1.28 (1.63)	-0.26 (0.94)	0.60 (1.01)
Possessions				
Q1 highly deprived	reference	reference	reference	reference
Q2	2.93 (2.01)	1.96 (2.02)	2.10 (1.26)	1.42 (1.24)
Q3	2.78 (1.98)	2.44 (2.15)	2.59 (1.24) *	2.46 (1.33)
Q4 less deprived	-0.06 (2.40)	1.43 (2.80)	0.11 (1.51)	1.74 (1.72)

- < 0.05; ** <0.01 *** <0.001; Model 1Age and sex adjusted, Model 2 fully adjusted

Table 15 Association of selected factors with the prevalence, awareness, treatment and control of Arterial Hypertension in Astana region, Kazakhstan, OR (95% CI)

	Prevalence[1] OR (95% CI)	Prevalence[2] OR (95% CI)	Awareness[1]* OR (95% CI)	Treatment[1]* OR (95% CI)	Control[1]* OR (95% CI)
Sex					
Men	1	1	1	1	1
Women	1.60 (1.20-2.13)	1.14 (0.73-1.79)	1.73 (1.20-2.47)	2.52 (1.81-3.52)	1.97 (1.35-2.86)
Age groups, years					
50-54	1	1	1	1	1
55-59	1.72 (1.16-2.55)	1.61 (1.04-2.48)	1.44 (0.88-2.38)	1.79 (1.12-2.86)	1.83 (1.07-3.13)
60-64	1.77 (1.18-2.64)	1.86 (1.18-2.92)	1.80 (1.06-3.06)	2.44 (1.48-4.02)	1.80 (1.03-3.15)
65-69	2.12 (1.33-3.37)	2.05 (1.22-3.45)	2.75 (1.46-5.19)	2.39 (1.39-4.10)	1.63 (0.89-2.98)
70-75	3.13 (1.88-5.19)	2.77 (1.55-4.95)	1.46 (0.85-2.53)	1.86 (1.11-3.11)	1.75 (0.97-3.13)
Urban/Rural					
Astana city	1	1	1	1	1
Akmol village	1.18 (0.88-1.57)	1.66 (1.14-2.41)	0.17 (0.11-0.27)	0.44 (0.31-0.62)	0.30 (0.20-0.44)
BMI, kg/m^2					
18.5-24.9	1	1	1	1	1
25-29.9	1.89 (1.30-2.76)	1.48 (0.96-2.29)	2.61 (1.58-4.31)	2.14 (1.32-3.49)	1.25 (0.72-2.17)
≥30	3.44 (2.33-5.08)	2.70 (1.69-4.31)	3.71 (2.26-6.08)	2.83 (1.76-4.56)	0.82 (0.48-1.42)
WHR, obesity					
No	1	1	1	1	1
Yes	1.94 (1.42-2.66)	1.31 (0.89-1.93)	2.83 (1.89-4.25)	2.25 (1.53-3.32)	1.70 (1.09-2.67)
Diabetes					
No	1	1	1	1	1
Yes	1.52 (0.94-2.46)	1.14 (0.68-1.93)	2.10 (1.12-3.91)	2.22 (1.27-3.90)	1.50 (0.93-2.44)
Hypercholesterolemia					
No	1	1	1	1	1
Yes	1.44 (1.05-1.98)	1.46 (1.02-2.08)	1.77 (1.19-2.62)	1.81 (1.27-2.59)	1.33 (0.93-1.91)
Smoking					
Non-smoker	1	1	1	1	1
Current Smoker	0.67 (0.43-1.05)	0.72 (0.44-1.20)	0.86 (0.49-1.53)	0.86 (0.50-1.47)	1.24 (0.63-2.44)
Ex-smoker	1.04 (0.66-1.65)	0.95 (0.57-1.58)	1.47 (0.84-2.60)	1.97 (1.16-3.33)	2.06 (1.13-3.77)
Marital status					
Married	1	1	1	1	1
Unmarried	0.96 (0.66-1.38)	1.06 (0.70-1.60)	0.82 (0.52-1.28)	1.04 (0.68-1.59)	1.35 (0.89-2.03)
Education					
Higher	1	1	1	1	1
Apprenticeship	0.79 (0.55-1.15)	0.70 (0.45-1.07)	0.69 (0.43-1.12)	0.86 (0.56-1.33)	0.62 (0.40-0.95)
Primary&secondary	0.73 (0.51-1.05)	0.60 (0.39-0.94)	0.45 (0.28-0.71)	0.58 (0.38-0.88)	0.45 (0.29-0.70)
Ethnicity					
Kazakh	1	1	1	1	1
Russian	1.53 (1.07-2.20)	1.38 (0.92-2.07)	0.87 (0.57-1.31)	0.91 (0.62-1.35)	0.69 (0.45-1.06)
Other	1.28 (0.84-1.96)	1.21 (0.76-1.93)	1.51 (0.86-2.63)	1.16 (0.72-1.88)	1.04 (0.64-1.69)
Car ownership					
Yes	1	1	1	1	1
No	0.91 (0.67-1.23)	1.06 (0.74-1.52)	0.70 (0.48-1.01)	0.86 (0.61-1.22)	0.80 (0.56-1.16)
Household possessions					
Q 1	1	1	1	1	1
Q2	1.96 (1.29-2.97)	1.64 (1.04-2.58)	1.24 (0.77-2.01)	0.92 (0.58-1.47)	1.32 (0.79-2.19)
Q3	1.46 (0.99-2.16)	1.18 (0.74-1.88)	1.77 (1.07-2.92)	1.17 (0.73-1.88)	1.11 (0.65-1.88)
Q4	1.42 (0.88-2.27)	1.14 (0.62-2.10)	4.05 (1.92-8.51)	1.60 (0.88-2.91)	2.49 (1.36-4.58)

[1] age and sex adjusted, [2] fully adjusted for all variables in the table;
* Among those with Arterial hypertension

5.4.2. Diabetes tables

Table 16 Prevalence, awareness, treatment and control of diabetes by urban and rural area of residence in Astana region, Kazakhstan

	Men (n=415)			Women (n=538)			Both sexes (n=953)		
	Prevalence	*95% CI*	*Cases/All*	*Prevalence*	*95% CI*	*Cases/All*	*Prevalence*	*95% CI*	*Cases/All*
Combined Astana city and Akmol village									
Prevalence of diabetes among all	**12.8%**	9.5-16.0	53/415	**12.3%**	9.5-15.0	66/538	**12.5%**	10.4-14.6	119/953
Awareness among all cases of DM	**66.0%**	52.9-79.2	35/53	**77.3%**	66.9-87.7	51/66	**72.3%**	64.1-80.4	86/119
Treatment among all cases of DM	**58.5%**	44.8-72.2	31/53	**71.2%**	60.0-82.4	47/66	**65.6%**	56.9-74.2	78/119
Treatment among aware	**85.7%**	73.5-97.9	30/35	**88.2%**	79.1-97.4	45/51	**87.2%**	80.0-94.4	75/86
Control among all cases of DM	**22.6%**	11.0-34.3	12/53	**31.8%**	20.3-43.4	21/66	**27.7%**	19.6-35.9	33/119
Control among treated	**38.7%**	20.5-56.9	21/31	**44.7%**	29.9-59.4	21/47	**42.3%**	31.1-53.5	33/78
Astana city									
Prevalence of diabetes among all	**15.5%**	10.7-20.4	34/219	**17.0%**	12.4-21.6	44/259	**16.3%**	13.0-19.6	78/478
Awareness among all cases of DM	**82.4%**	68.9-95.9	28/34	**86.4%**	75.8-96.9	38/44	**84.6%**	76.4-92.8	66/78
Treatment among all cases of DM	**73.5%**	57.9-89.2	25/34	**90.9%**	82.1-99.8	40/44	**83.3%**	74.9-91.8	65/78
Treatment among aware	**89.3%**	77.1-101.5	25/28	**100.0%**		38/38	**95.5%**	90.3-100.4	63/66
Control among all cases of DM	**29.4%**	13.3-45.5	10/34	**47.7%**	32.4-63.1	21/44	**39.7%**	28.6-50.8	31/78
Control among treated	**40.0%**	19.4-60.6	10/25	**52.5%**	36.3-68.7	21/40	**47.7%**	35.2-60.2	31/65
Akmol village									
Prevalence of diabetes among all	**9.7%**	5.5-13.9	19/196	**7.9%**	4.7-11.1	22/279	**8.6%**	6.1-11.2	41/475
Awareness among all cases of DM	**36.8%**	13.0-60.7	7/19	**59.1%**	36.8-81.4	13/22	**48.8%**	32.8-64.8	20/41
Treatment among all cases of DM	**31.6%**	8.6-54.6	6/19	**31.8%**	10.7-53.0	7/22	**31.7%**	16.8-46.6	13/41
Treatment among aware	**71.4%**	26.3-116.6	5/7	**53.9%**	22.5-85.2	7/13	**60.0%**	36.5-83.5	12/20
Control among all cases of DM	**10.5%**	0.0-25.7	2/19	**0.0%**		0/22	**4.9%**	0.0-11.8	2/41
Control among treated	**33.3%**	0.0-87.5	2/6	**0.0%**		0/7	**15.4%**	0.0-38.1	2/13

Table 17 Association of selected factors with the prevalence, awareness, treatment and control of Diabetes in Astana region, Kazakhstan, OR (95% CI)

	Prevalence[1] OR (95% CI)	Prevalence[2] OR (95% CI)	Awareness[1]* OR (95% CI)	Treatment[1]* OR (95% CI)	Control[1]* OR (95% CI)
Sex					
Men	1	1	1	1	1
Women	0.95 (0.64-1.40)	0.63 (0.33-1.22)	2.07 (0.86-4.99)	1.82 (0.82-4.02)	1.58 (0.68-3.67)
Age groups					
50-54	1	1	1	1	1
55-59	1.69 (0.95-3.00)	1.73 (0.91-3.30)	3.74 (0.84-16.76)	2.04 (0.64-6.56)	1.37 (0.39-4.90)
60-64	1.64 (0.91-2.95)	1.35 (0.67-2.70)	0.54 (0.16-1.81)	1.37 (0.43-4.42)	1.95(0.54-6.97)
65-69	1.30 (0.66-2.56)	0.99 (0.45-2.19)	1.70 (0.36-8.08)	2.12 (0.51-8.72)	1.11 (0.24-5.07)
70-75	1.98 (1.06-3.71)	1.27 (0.57-2.82)	0.50 (0.14-1.81)	0.77 (0.23-2.60)	0.93 (0.22-3.89)
Urban/Rural					
Astana	1	1	1	1	1
Akmol	0.49 (0.32-0.73)	0.49 (0.28-0.86)	0.12 (0.05-0.34)	0.08 (0.03-0.20)	0.08 (0.02-0.34)
BMI, kg/m2					
18.5-24.9	1	1	1	1	1
25-29.9	2.65 (1.15-6.14)	1.58 (0.61-4.08)	1.71 (0.27-11.07)	0.41 (0.06-2.69)	0.58 (0.08-4.04)
≥30	6.21 (2.78-13.89)	3.42 (1.35-8.65)	1.64 (0.28-9.73)	0.53 (0.09-3.26)	0.82 (0.13-5.17)
WHR, obesity					
No	1	1	1	1	1
Yes	5.44 (2.70-10.97)	3.93 (1.70-9.09)	2.73 (0.61-12.17)	1.96 (0.47-8.20)	1.23 (0.23-6.55)
Hypertension					
No	1	1	1	1	1
Yes	1.50 (0.93-2.43)	1.11 (0.63-1.95)	0.93 (0.31-2.81)	0.75 (0.27-2.08)	0.44 (0.16-1.20)
Hypercholesterolemia					
No	1	1	1	1	1
Yes	1.72 (1.16-2.55)	1.17 (0.74-1.86)	1.79 (0.75-4.31)	1.48 (0.67-3.27)	1.60 (0.70-3.66)
Smoking					
Non-smoker	1	1	1	1	1
Current Smoker	0.65 (0.32-1.31)	0.62 (0.27-1.42)	1.18 (0.21-6.68)	0.77 (0.16-3.72)	1.28 (0.24-6.87)
Ex-smoker	1.11 (0.61-2.02)	0.86 (0.43-1.72)	0.81 (0.20-3.29)	0.57 (0.16-2.03)	0.74 (0.17-3.15)
Family history					
No	1	1	1	1	1
Yes	2.01 (1.24-3.28)	1.46 (0.85-2.53)	2.28 (0.57-9.10)	1.10 (0.38-3.17)	1.33 (0.50-3.52)
Marital status					
Married	1	1	1	1	1
Unmarried	0.98 (0.61-1.58)	1.07 (0.59-1.93)	1.80 (0.56-5.81)	2.80 (0.93-8.39)	1.91 (0.65-5.56)
Education					
Higher	1	1	1	1	1
Apprenticeship	1.09 (0.68-1.77)	1.50 (0.84-2.68)	0.50 (0.18-1.39)	0.34 (0.13-0.91)	0.65 (0.22-1.90)
Primary&secondary	0.83 (0.50-1.35)	1.34 (0.71-2.51)	2.44 (0.66-9.07)	2.34 (0.74-7.39)	1.23 (0.45-3.40)
Ethnicity					
Kazakh	1	1	1	1	1
Russian	1.48 (0.96-2.30)	1.84 (1.08-3.13)	1.28 (0.49-3.35)	0.80 (0.33-1.94)	1.74 (0.69-4.41)
Other	1.11 (0.63-1.97)	0.82 (0.42-1.62)	1.84 (0.48-7.08)	1.48 (0.44-5.01)	1.44 (0.42-4.95)
Car ownership					
Yes	1	1	1	1	1
No	0.79 (0.53-1.18)	1.03 (0.61-1.75)	0.94 (0.36-2.42)	1.03 (0.44-2.41)	1.63 (0.67-3.96)
Household possessions					
Q1	1	1	1	1	1
Q2	1.71 (0.95-3.06)	1.73 (0.87-3.44)	0.50 (0.13-2.00)	0.53 (0.15-1.79)	0.33 (0.08-1.37)
Q3	1.42 (0.79-2.58)	0.94 (0.44-1.98)	0.65 (0.16-2.68)	1.28 (0.35-4.64)	1.19 (0.32-4.37)
Q4	2.48 (1.29-4.75)	1.38 (0.58-3.26)	1.88 (0.33-10.82)	4.54 (0.87-23.61)	2.19 (0.55-8.79)

[1] age and sex adjusted, [2] fully adjusted for all variables in the table; * Among those with Diabetes

5.4.3. Dyslipidaemia tables

Table 18 Prevalence, awareness, treatment and control of Hypercholesterolemia (HC) in Astana region, Kazakhstan (total cholesterol ≥ 6.2mmol/l)

	Men (n=416)			Women (n=538)			Both sexes (n=954)		
	Prevalence	*95% CI*	*Cases/All*	*Prevalence*	*95% CI*	*Cases/All*	*Prevalence*	*95% CI*	*Cases/All*
Combined Astana city and Akmol village									
Prevalence of HC among all	**28.4%**	24.0-32.7	118/416	**44.1%**	39.8-48.3	237/538	**37.2%**	34.1-40.3	355/954
Awareness among all cases of HC	**47.5%**	38.3-56.6	56/118	**61.2%**	54.9-67.4	145/237	**56.6%**	51.4-61.8	201/355
Treatment among all cases of HC	**33.1%**	24.4-41.7	39/118	**44.3%**	37.9-50.7	105/237	**40.6%**	35.4-45.7	144/355
Treatment among aware	**67.9%**	55.2-80.5	38/56	**71.7%**	64.3-79.1	104/145	**70.7%**	64.3-77.0	142/201
Control among all cases of HC	**26.3%**	18.2-34.3	31/118	**21.9%**	16.6-27.2	52/237	**23.4%**	19.0-27.8	83/355
Control among treated	**79.5%**	66.2-92.7	31/39	**49.5%**	39.8-59.2	52/105	**57.6%**	49.5-65.8	83/144
Astana city (urban, n=480)									
Prevalence of HC among all	**38.2%**	31.7-44.7	84/220	**57.3%**	51.3-63.4	149/260	**48.5%**	44.1-53.0	233/480
Awareness among all cases of HC	**56.0%**	45.1-66.8	47/84	**72.5%**	65.2-79.7	108/149	**66.5%**	60.4-72.6	155/233
Treatment among all cases of HC	**36.9%**	26.4-47.4	31/84	**49.7%**	41.5-57.8	74/149	**45.1%**	38.6-51.5	105/233
Treatment among aware	**63.8%**	49.6-78.1	30/47	**68.5%**	59.6-77.4	74/108	**67.1%**	59.6-74.6	104/155
Control among all cases of HC	**29.8%**	19.8-39.7	25/84	**24.8%**	17.8-31.9	37/149	**26.6%**	20.9-32.3	62/233
Control among treated	**80.7%**	65.9-95.4	25/31	**50.0%**	38.3-61.7	37/74	**59.1%**	49.5-68.6	62/105
Akmol village (rural, n=474)									
Prevalence of HC among all	**17.4%**	12.0-22.7	34/196	**31.7%**	26.2-37.2	88/278	**25.7%**	21.8-29.7	122/474
Awareness among all cases of HC	**26.5%**	10.8-42.1	9/34	**42.1**%	31.5-52.6	37/88	**37.7%**	29.0-46.4	46/122
Treatment among all cases of HC	**23.5%**	8.5-38.6	8/34	**35.2%**	25.0-45.4	31/88	**32.0%**	23.6-40.4	39/122
Treatment among aware	**88.9%**	63.3-114.5	8/9	**81.1%**	67.8-94.3	30/37	**82.6%**	71.2-94.0	38/46
Control among all cases of HC	**17.7%**	4.1-31.1	6/34	**17.1%**	9.0-25.1	15/88	**17.2%**	10.4-24.0	21/122
Control among treated	**75.0%**	36.3-113.7	6/8	**48.4%**	29.8-67.0	15/31	**53.9%**	37.5-70.2	21/39

Table 19 Association of selected factors with the prevalence, awareness, treatment and control of HC (≥6.2 mmol/l) in Astana region, Kazakhstan, OR (95% CI)

	Prevalence[1] OR (95% CI)	Prevalence[2] OR (95% CI)	Awareness[1] * OR (95% CI)	Treatment[1] * OR (95% CI)	Control[1] * OR (95% CI)
Sex					
Males	1	1	1	1	1
Females	1.99 (1.51-2.61)	2.44 (1.56-3.83)	1.75 (1.11-2.74)	1.60 (1.00-2.55)	0.78 (0.47-1.31)
Age groups (years)					
50-54	1	1	1	1	1
55-59	1.55 (1.06-2.26)	1.56 (1.02-2.38)	1.32 (0.72-2.43)	1.48 (0.79-2.77)	0.98 (0.47-2.04)
60-64	1.44 (0.97-2.14)	1.27 (0.81-1.98)	1.20 (0.64-2.28)	1.55 (0.81-2.98)	1.25 (0.59-2.65)
65-69	1.32 (0.86-2.05)	1.18 (0.72-1.93)	1.45 (0.71-2.95)	1.29 (0.62-2.65)	1.47 (0.66-3.28)
70-75	1.43 (0.92-2.21)	1.07 (0.63-1.82)	1.16 (0.57-2.35)	1.24 (0.60-2.56)	1.23 (0.54-2.82)
Urban/Rural					
Astana city	1	1	1	1	1
Akmol village	0.34 (0.26-0.45)	0.39 (0.28-0.55)	0.27 (0.17-0.43)	0.53 (0.33-0.85)	0.59 (0.34-1.03)
BMI (kg/m2)					
18.5-24.9	1	1	1	1	1
25-29.9	1.74 (1.16-2.62)	1.37 (0.85-2.20)	0.90 (0.45-1.79)	0.54 (0.27-1.08)	0.72 (0.33-1.60)
≥30	1.96 (1.32-2.92)	1.35 (0.83-2.20)	1.53 (0.78-2.98)	0.82 (0.42-1.59)	0.90 (0.42-1.91)
WHR, obesity					
No	1	1	1	1	1
Yes	2.11 (1.53-2.92)	1.54 (1.05-2.26)	1.30 (0.76-2.22)	1.27 (0.73-2.19)	0.69 (0.37-1.27)
Diabetes					
No	1	1	1	1	1
Yes	1.71 (1.15-2.54)	1.18 (0.76-1.84)	2.29 (1.22-4.27)	1.83 (1.02-3.26)	2.00 (1.08-3.72)
Smoking					
Non-smoker	1	1	1	1	1
Current Smoker	1.36 (0.86-2.16)	1.26 (0.75-2.11)	0.80 (0.38-1.67)	0.91 (0.42-1.97)	0.77 (0.33-1.84)
Ex-smoker	1.42 (0.90-2.23)	1.21 (0.74-2.00)	1.82 (0.86-3.85)	1.55 (0.74-3.28)	0.78 (0.34-1.81)
Hypertension					
No	1	1	1	1	1
Yes	1.44 (1.05-1.97)	1.47 (1.03-2.09)	1.28 (0.77-2.15)	1.35 (0.79-2.29)	1.52 (0.80-2.91)
Marital status					
Married	1	1	1	1	1
Unmarried	1.12 (0.81-1.55)	1.09 (0.75-1.59)	1.02 (0.61-1.69)	0.94 (0.57-1.55)	0.55 (0.29-1.03)
Education					
Higher	1	1	1	1	1
Apprenticeship	0.70 (0.50-0.98)	0.99 (0.67-1.47)	0.51 (0.30-0.88)	0.63 (0.37-1.08)	0.85 (0.45-1.58)
Primary & secondary	0.64 (0.46-0.90)	0.98 (0.65-1.48)	0.48 (0.28-0.82)	0.65 (0.38-1.11)	1.10 (0.60-2.01)
Ethnicity					
Kazakh	1	1	1	1	1
Russian	1.39 (1.02-1.91)	1.32 (0.92-1.91)	0.80 (0.49-1.32)	1.05 (0.64-1.73)	0.95 (0.54-1.68)
Other	1.45 (0.99-2.12)	1.34 (0.88-2.04)	0.76 (0.42-1.37)	1.09 (0.60-1.98)	0.72 (0.35-1.50)
Car ownership					
Yes	1	1	1	1	1
No	0.82 (0.62-1.09)	0.95 (0.67-1.33)	0.80 (0.51-1.27)	1.15 (0.73-1.83)	1.19 (0.69-2.03)
Household possessions					
Q1	1	1	1	1	1
Q2	1.22 (0.83-1.80)	1.04 (0.68-1.61)	1.06 (0.57-1.98)	1.48 (0.78-2.84)	1.99 (0.90-4.43)
Q3	1.40 (0.95- 2.04)	0.98 (0.62-1.54)	1.27 (0.68-2.39)	1.34 (0.69-2.57)	1.80 (0.80-4.04)
Q4	2.32 (1.47-3.67)	1.21 (0.69-2.15)	2.41 (1.14-5.11)	2.17 (1.03-4.57)	2.21 (0.90-5.42)

[1] age and sex adjusted, [2] fully adjusted for all variables in the table; * Among those with hypercholesterolemia

Table 20 Prevalence, awareness, treatment and control of hypercholesterolemia (HC) in Astana region, Kazakhstan (total cholesterol ≥ 5 mmol/l)

	Men (n=416)			Women (n=538)			Both sexes (n=954)		
	Prevalence	*95% CI*	*Cases/All*	*Prevalence*	*95% CI*	*Cases/All*	*Prevalence*	*95% CI*	*Cases/All*
Combined Astana city and Akmol village									
Prevalence of HC among all	**65.9%**	61.3-70.4	274/416	**78.1%**	74.6-81.6	420/538	**72.8%**	69.9-75.6	694/954
Awareness among all cases of HC	**29.9%**	24.5-35.4	82/274	**44.3%**	39.5-49.1	186/420	**38.6%**	35.0-42.2	268/694
Treatment among all cases of HC	**14.2%**	10.1-18.4	39/274	**25.0%**	20.8-29.2	105/420	**20.8%**	17.7-23.8	144/694
Treatment among aware	**46.3%**	35.3-57.4	38/82	**55.9%**	48.7-63.1	104/186	**53.0%**	47.0-59.0	142/268
Control among all cases of HC	**4.7%**	2.2-7.3	13/274	**4.3%**	2.3-6.2	18/420	**4.5%**	2.9-6.0	31/694
Control among treated	**33.3%**	17.9-48.8	13/39	**17.1%**	9.8-24.5	18/105	**21.5%**	14.7-28.3	31/144
Astana city (urban, n=480)									
Prevalence of HC among all	**75.5%**	69.7-81.2	166/220	**84.6%**	80.2-89.0	220/260	**80.4%**	76.9-84.0	386/480
Awareness among all cases of HC	**36.8%**	29.3-44.2	61/166	**61.8%**	55.3-68.3	136/220	**51.0%**	46.0-60.5	197/386
Treatment among all cases of HC	**18.7%**	12.7-24.7	31/166	**33.6%**	27.3-39.9	74/220	**27.2%**	22.7-31.7	105/386
Treatment among aware	**49.2%**	36.3-62.1	30/61	**54.4%**	45.9-62.9	74/136	**52.8%**	45.8-59.8	104/197
Control among all cases of HC	**7.2%**	3.2-11.2	12/166	**6.8%**	3.5-10.2	15/220	**7.0%**	4.4-9.6	27/386
Control among treated	**38.7%**	20.5-56.9	12/31	**20.3%**	10.9-29.6	15/74	**25.7%**	17.2-34.2	277/105
Akmol village (rural, n=474)									
Prevalence of HC among all	**55.1%**	48.1-62.1	108/196	**71.9%**	66.6-77.3	200/278	**65.0%**	60.7-69.3	308/474
Awareness among all cases of HC	**19.4%**	11.9-27.0	21/108	**25.0%**	18.9-31.1	50/200	**23.1%**	18.3-27.8	71/308
Treatment among all cases of HC	**7.4%**	2.4-12.4	8/108	**15.5%**	10.4-20.6	31/200	**12.7**	8.9-16.4	39/308
Treatment among aware	**38.1%**	15.4-60.7	8/21	**60.0%**	45.9-74.1	30/50	**53.5%**	41.6-65.4	38/71
Control among all cases of HC	**0.9%**	0-2.8	1/108	**1.5%**	0-3.2	3/200	**1.3%**	0-2.6	4/308
Control among treated	**12.5%**	0-42.1	1/8	**9.7%**	0-20.7	3/31	**10.3%**	0.3-20.2	4/39

5.4.4. Obesity tables

Table 21 The prevalence of overweight and obesity by demographic, socio-economic, cardio-metabolic and behavioural factors in urban and rural area of residence in Astana region, Kazakhstan

	Overweight and obesity (bmi≥25)			**Obesity (bmi≥30)**		
Variable name	**Astana city**	**Akmol village**	**Total**	**Astana city**	**Akmol village**	**Total**
Total number of participants	**487**	**482**	**969**	**487**	**482**	**969**
Overall prevalence, (%)	84.0	77.8	80.9	45.8	41.9	43.9
Sex, (%)						
Men	79.6	71.0	75.5	37.3	30.0	33.9
Women	87.8	82.6	85.1	53.1	50.4	51.7
Age groups, years (%)						
50-54	84.0	75.4	79.47	48.0	45.7	46.8
55-59	81.8	82.8	82.35	41.4	42.6	42.1
60-64	80.4	71.4	76.26	44.9	37.4	41.4
65-69	89.9	77.3	84.14	49.4	47.0	48.3
70-74	85.7	83.1	84.51	45.5	33.9	40.1
Diabetes						
No	82.2	76.4	79.2	41.5	40.5	41.0
Yes	96.2	90.2	94.1	70.5	56.1	65.6
Hypertension						
No	72.7	64.0	68.7	29.4	30.4	29.9
Yes	88.6	82.5	85.5	52.5	46.6	49.5
Hypercholesterolemia						
No	81.0	74.6	77.2	40.5	40.3	40.4
Yes	87.9	86.1	87.3	51.7	45.9	49.7
Smoking status, (%)						
Non smoker	88.3	81.0	84.4	49.3	45.6	47.3
Current smoker	68.6	57.6	63.8	32.6	28.8	30.9
Past smoker	84.5	79.8	82.4	46.6	36.7	42.3

	Overweight and obesity (bmi≥25)			Obesity (bmi≥30)		
Variable name	**Astana city**	**Akmol village**	**Total**	**Astana city**	**Akmol village**	**Total**
Marital status, (%)						
Married	83.7	75.4	79.5	45.9	40.5	43.2
Unmarried	84.7	84.1	84.4	45.0	45.2	45.1
Education, (%)						
Higher	86.3	69.9	82.0	41.2	39.7	40.9
Apprenticeship	83.7	78.1	80.6	48.3	42.1	44.9
Primary and secondary	80.6	80.2	80.3	50.4	42.8	45.6
Ethnicity, (%)						
Kazakhs	81.7	71.4	76.5	41.2	36.4	38.8
Russians	87.3	87.5	87.4	50.8	46.9	48.8
Others	87.3	85.9	86.7	53.2	54.9	54.0
Car ownership, (%)						
Yes	85.7	76.1	81.4	48.6	43.2	46.2
No	82.1	79.2	80.4	40.8	39.6	40.1
Household possessions, quartiles (%)						
Q1 more deprived	77.9	68.9	71.9	36.4	31.8	33.3
Q2	86.5	79.9	82.3	46.9	44.4	45.3
Q3	85.1	83.7	84.5	50.3	48.1	49.3
Q4 less deprived	85.6	85.7	85.6	46.4	42.9	46.0

Table 22 Association of selected factors with BMI and waist circumference in Astana region, Kazakhstan

	BMI		Waist	
	Model 1 Age and sex ad	**Model 2 Fully adjusted**	**Model 1 Age and sex ad**	**Model 2 Fully adjusted**
Sex				
Males	reference	reference	reference	reference
Females	-2.16 (0.35) ***	1.88 (0.46) ***	-2.96 (0.89) **	-2.41 (1.19) *
Age groups (years)				
50-54	reference	reference	reference	reference
55-59	-0.31 (0.48)	-0.84 (0.46)	1.37 (1.24)	0.03 (1.18)
60-64	-0.34 (0.50)	-0.85 (0.47)	1.21 (1.28)	-0.14 (1.22)
65-69	0.25 (0.55)	-0.50 (0.52)	2.25 (1.41)	0.69 (1.36)
70-75	-0.02 (0.56)	-1.15 (0.56) *	3.24 (1.43) *	0.89 (1.44)
Urban/Rural				
Astana (urban)	reference	reference	reference	reference
Akmol (rural)	-0.88 (0.34) ***	-0.67 (0.37)	-3.02 (0.87) **	-2.01 (0.96) *
Diabetes				
No	reference	reference	reference	reference
Yes	3.20 (0.50) ***	2.61 (0.48) ***	7.72 (1.28) ***	6.39 (1.25) ***
Hypertension				
No	reference	reference	reference	reference
Yes	2.51 (0.38) ***	2.15 (0.37) ***	6.85 (0.96) ***	6.26 (0.95) ***
Hypercholesterolemia				
No	reference	reference	reference	reference
Yes	0.94 (0.36) **	0.29 (0.35)	3.13 (0.92) **	1.41 (0.90)
Smoking				
Non-smoker	reference	reference	reference	reference
Current Smoker	-1.07 (0.56)	-1.15 (0.53) *	-0.11 (1.44)	-0.07 (1.39)
Ex-smoker	0.82 (0.54)	0.41 (0.51)	3.14 (1.40) *	2.22 (1.33)
Marital status				
Married	reference	reference	reference	reference
Unmarried	-0.57 (0.42)	-0.37 (0.41)	-1.37 (1.09)	-1.28 (1.06)
Education				
Higher	reference	reference	reference	reference
Apprenticeship	0.12 (0.43)	0.31 (0.43)	-0.64 (1.11)	0.36 (1.11)
Primary&Secondary	0.45 (0.43)	1.17 (0.44) **	0.11 (1.10)	2.37 (1.15) *
Ethnicity				
Kazakh	reference	reference	reference	reference
Russian	1.83 (0.41) ***	1.54 (0.39) ***	2.69 (1.05) *	1.58 (1.02)
Other	2.26 (0.48) ***	2.00 (0.46) ***	4.23 (1.24) **	3.49 (1.19) **
Car ownership				
Yes	reference	reference	reference	reference
No	-0.95 (0.35) **	-0.38 (0.36)	-1.05 (0.90)	0.63 (0.95)
Possessions				
Q1 highly deprived	reference	reference	reference	reference
Q2	1.77 (0.47) ***	1.15 (0.45) *	2.94 (1.20) *	1.77 (1.17)
Q3	1.66 (0.46) ***	1.15 (0.48) *	3.74 (1.18) **	2.93 (1.24) *
Q4 less deprived	1.94 (0.56) **	1.25 (0.62) *	5.09 (1.43) ***	3.53 (1.62) *

* < 0.05; ** <0.01 *** <0.001; Model 1Age and sex adjusted, Model 2 fully adjusted

Table 23 Association of selected factors with the prevalence of overweight (bmi≥25) and obesity (bmi≥30) in Astana region, Kazakhstan, OR (95% CI)

	Overweight and obesity		Obesity	
	Prevalence [1] OR (95% CI)	Prevalence [2] OR (95% CI)	Prevalence [1] OR (95% CI)	Prevalence [2] OR (95% CI)
Sex				
Males	1	1	1	1
Females	1.84 (1.33-2.54)	1.16 (0.70-1.93)	2.10 (1.62-2.74)	2.51 (1.65-3.84)
Age groups (years)				
50-54	1	1	1	1
55-59	1.16 (0.73-1.84)	1.06 (0.62-1.79)	0.78 (0.54-1.13)	0.63 (0.41-0.95)
60-64	0.85 (0.54-1.33)	0.65 (0.39-1.08)	0.82 (0.56-1.20)	0.70 (0.45-1.07)
65-69	1.38 (0.80-2.37)	1.03 (0.56-1.91)	1.07 (0.71-1.61)	0.93 (0.58-1.48)
70-75	1.41 (0.82-2.45)	0.78 (0.41-1.48)	0.76 (0.50-1.15)	0.60 (0.36-0.99)
Urban/Rural				
Astana (urban)	1	1	1	1
Akmol (rural)	0.64 (0.46-0.89)	0.69 (0.45-1.06)	0.82 (0.63-1.06)	0.92 (0.66-1.28)
Diabetes				
No	1	1	1	1
Yes	4.32 (1.97-9.49)	3.21 (1.41-7.29)	2.97 (1.97-4.49)	2.82 (1.80-4.41)
Hypertension				
No	1	1	1	1
Yes	2.54 (1.80-3.58)	2.22 (1.51-3.26)	2.29 (1.68-3.12)	2.20 (1.56-3.09)
Hypercholesterolemia				
No	1			
Yes	1.86 (1.28-2.70)	1.54 (1.00-2.36)	1.34 (1.02-1.76)	1.16 (0.85-1.58)
Smoking				
Non-smoker	1	1	1	1
Current Smoker	0.43 (0.27-0.70)	0.36 (0.21-0.63)	0.83 (0.53-1.30)	0.91 (0.55-1.49)
Ex-smoker	1.16 (0.68-1.97)	0.89 (0.50-1.59)	1.54 (1.00-2.36)	1.48 (0.92-2.37)
Marital status				
Married	1	1	1	1
Unmarried	1.04 (0.68-1.59)	1.22 (0.75-1.98)	0.78 (0.57-1.07)	0.75 (0.52-1.09)
Education				
Higher	1	1	1	1
Apprenticeship	0.82 (0.54-1.24)	0.88 (0.53-1.45)	1.06 (0.76-1.48)	1.18 (0.80-1.73)
Primary&Secondary	0.83 (0.55-1.25)	1.14 (0.69-1.90)	1.19 (0.86-1.65)	1.57 (1.05-2.34)
Ethnicity				
Kazakh	1	1	1	1
Russian	1.95 (1.27-2.98)	2.12 (1.30-3.46)	1.45 (1.07-1.98)	1.42 (1.00-2.02)
Other	1.86 (1.11-3.11)	2.43 (1.34-4.39)	1.85 (1.28-2.69)	1.85 (1.23-2.79)
Car ownership				
Yes	1	1	1	1
No	0.81 (0.58-1.14)	1.24 (0.82-1.88)	0.70 (0.53-0.91)	0.85 (0.61-1.18)
Possessions				
Q1 highly deprived	1	1	1	1
Q2	1.88 (1.21-2.91)	1.59 (0.98-2.60)	1.62 (1.11-2.36)	1.43 (0.94-2.16)
Q3	2.42 (1.55-3.77)	2.07 (1.22-3.52)	2.08 (1.44-3.01)	1.99 (1.28-3.08)
Q4 less deprived	2.96 (1.67-5.26)	2.34 (1.13-4.85)	2.01 (1.28-3.16)	1.87 (1.06-3.30)

[1] age and sex adjusted, [2] fully adjusted for all variables in the table

5.5. Astana region case-control study tables

Table 24 Socio-demographic factors and missing values of ACS and Stroke cases vs. controls in Astana Health Study in men and women (case-control analysis) (patients with history of MI and Stroke among cases were excluded from the analysis)

	Men				Women				Both sexes			
	ACS	***Stroke***	***All cases***	***Controls***	***ACS***	***Stroke***	***All cases***	***Controls***	***ACS***	***Stroke***	***All cases***	***Controls***
Total number of participants	**254**	**139**	**393**	**432**	**94**	**96**	**190**	**545**	**348**	**235**	**583**	**977**
Age groups, years (%)												
50-54	81 (31.9%)	37 (26.6%)	118 (30.0%)	118 (27.3%)	8 (8.5%)	14 (14.6%)	22 (11.6%)	146 (26.8%)	89 (25.6%)	51 (21.7%)	140 (24.0%)	264 (27.0%)
55-59	64 (25.2%)	33 (23.7%)	97 (24.7%)	87 (20.1%)	15 (16.0%)	18 (18.8%)	33 (17.4%)	137 (25.1%)	79 (22.7%)	51 (21.7%)	130 (22.3%)	224 (22.9%)
60-64	41 (16.1%)	33 (23.7%)	74 (18.8%)	99 (22.9%)	19 (20.2%)	20 (20.8%)	39 (20.5%)	102 (18.7%)	60 (17.2%)	53 (22.6%)	113 (19.4%)	201 (20.6%)
65-69	41 (16.1%)	18 (13.0%)	59 (15.0%)	65 (15.1%)	28 (29.8%)	22 (22.9%)	50 (26.3%)	81 (14.9%)	69 (19.8%)	40 (17.0%)	109 (18.7%)	146 (14.9%)
70-75	27 (10.6%)	18 (13.0%)	45 (11.5%)	63 (14.6%)	24 (25.5%)	22 (22.9%)	46 (24.2%)	79 (14.5%)	51 (14.7%)	40 (17.0%)	91 (15.6%)	142 (14.5%)
Missing	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*
Education, (%)												
Higher	93 (36.6%)	50 (36.0%)	143 (36.4%)	150 (34.7%)	26 (27.7%)	23 (24.0%)	49 (25.8%)	138 (25.3%)	119 (34.2%)	73 (31.1%)	192 (32.9%)	288 (29.5%)
Apprenticeship	76 (29.9%)	36 (25.9%)	112 (28.5%)	120 (27.8%)	25 (26.6%)	35 (36.5%)	60 (31.6%)	212 (38.9%)	101 (29.0%)	71 (30.2%)	172 (29.5%)	332 (34.0%)
Primary/Secondary	81 (31.9%)	52 (37.4%)	133 (33.8%)	159 (36.8%)	41 (43.6%)	37 (38.5%)	78 (41.1%)	194 (35.6%)	122 (35.1%)	89 (37.9%)	211 (36.2%)	353 (36.1%)
Missing	*4 (1.6%)*	*1 (0.7%)*	*5 (1.27%)*	*3 (0.7%)*	*2 (2.1%)*	*1 (1.0%)*	*3 (1.6%)*	*1 (0.2%)*	*6 (1.7%)*	*2 (0.9%)*	*8 (1.4%)*	*4 (0.4%)*
Ethnicity, (%)												
Kazakhs	152 (59.8%)	93 (66.9%)	245 (62.3%)	276 (63.9%)	44 (46.8%)	52 (54.2%)	96 (50.5%)	290 (53.2%)	196 (56.3%)	145 (61.7%)	341 (58.5%)	566 (57.9%)
Russians	76 (29.9%)	28 (20.1%)	104 (26.5%)	90 (20.8%)	37 (39.4%)	29 (31.2%)	66 (34.7%)	167 (30.6%)	113 (32.5%)	57 (24.3%)	170 (29.2%)	257 (26.3%)
Others	23 (9.1%)	17 (12.2%)	40 (10.2%)	64 (14.8%)	11 (11.7%)	15 (15.6%)	26 (13.7%)	87 (16.0%)	34 (9.8%)	32 (13.6%)	66 (11.3%)	151 (15.5%)
Missing	*3 (1.2%)*	*1 (0.7%)*	*4 (1.0%)*	*2 (0.5%)*	*2 (2.1%)*	*0*	*2(1.1%)*	*1(0.2%)*	*5 (1.4%)*	*1 (0.4%)*	*6 (1.0%)*	*3(0.3%)*
Marital status, (%)												

	Men				Women				Both sexes			
	ACS	*Stroke*	*All cases*	*Controls*	*ACS*	*Stroke*	*All cases*	*Controls*	*ACS*	*Stroke*	*All cases*	*Controls*
Married	225 (88.6%)	123 (88.5%)	348 (88.6%)	396 (91.7%)	48 (51.1%)	49 (51.0%)	97 (51.1%)	319 (58.5%)	273 (78.5%)	172 (73.2%)	445 (76.3%)	715 (73.2%)
Unmarried	27 (10.6%)	15 (10.8%)	42 (10.7%)	35 (8.1%)	43 (45.7%)	46 (47.9%)	89 (46.8%)	223 (40.9%)	70 (20.1%)	61 (26.0%)	131 (22.5%)	258 (26.4%)
Missing	*2 (0.8%)*	*1 0.7%)*	*3 (0.8%)*	*1 (0.2%)*	*3 (3.2%)*	*1 (1.0%)*	*4 (2.1%)*	*3 (0.6%)*	*5 (1.4%)*	*2 (0.9%)*	*7 (1.2%)*	*4 (0.4%)*
Car ownership, (%)												
Yes	158 (62.2%)	87 (62.6%)	245 (62.3%)	271 (62.7%)	41 (43.6%)	52 (54.2%)	93 (49.0%)	261 (47.9%)	199 (57.2%)	139 (59.2%)	338 (58.0%)	532 (54.5%)
No	80 (31.5%)	48 (34.5%)	128 (32.6%)	150 (34.7%)	43 (45.7%)	40 (41.7%)	83 (43.7%)	272 (49.9%)	123 (35.3%)	88 (37.5%)	211 (36.2%)	422 (43.2%)
Missing	*16 (6.3%)*	*4 (2.9%)*	*20 (5.1%)*	*11 (2.6%)*	*10 (10.6%)*	*4 (4.2%)*	*14 (7.4*	*12 (2.2%)*	*26 (7.5%)*	*8 (3.4%)*	*34 (5.8%)*	*23 (2.4%)*
Deprivation level, (%)												
High	57 (22.4%)	14 (10.1%)	71 (18.07%)	83 (19.2%)	29 (30.9%)	13 (13.5%)	42 (22.1%)	173 (31.7%)	86 (24.7%)	27 (11.5%)	113 (19.4%)	256 (26.2%)
Intermediate	71 (28.0%)	51 (36.7%)	122 (31.0%)	142 (32.9%)	22 (23.4%)	29 30.2%)	51 (26.8%)	164 (30.1%)	93 (26.7%)	80 (34.0%)	173 (29.7%)	306 (31.3%)
Low	121 (47.6%)	70 (50.4%)	191 (48.6%)	202 (47.8%)	40 (42.6%)	51 (53.1%)	91 (47.9%)	205 (37.6%)	161 (46.3%)	121 (51.5%)	282 (48.4%)	407 (42.7%)
Missing	*5 (2.0%)*	*4 (2.9%)*	*9 (2.3%)*	*5 (1.2%)*	*3 (3.2%)*	*3 (3.1%)*	*6 (3.2%)*	*3 (0.6%)*	*8 (2.3%)*	*7 (3.0%)*	*15 (2.6%)*	*8 (0.8%)*
Unemployment, (%)												
Never	153 (60.2%)	72 (51.8%)	225 (57.3%)	303 (70.1%)	52 (55.3%)	55 (57.3%)	107 (56.3%)	398 (73.0%)	205 (58.9%)	127 (54.0%)	332 (57.0%)	701 (71.8%)
Less 1 year	60 (23.6%)	44 (31.7%)	104 (26.5%)	60 (13.9%)	16 (17.0%)	16 (16.7%)	32 (16.8%)	46 (8.4%)	76 (21.8%)	60 (25.5%)	136 (23.3%)	106 (10.9%)
More 1 year	35 (13.8%)	17 (12.2%)	52 (13.2%)	66 (15.3%)	20 (21.3%)	16 (16.7%)	36 (19.0%)	94 (17.3%)	55 (15.8%)	33 (14.0%)	88 (15.1%)	160 (16.4%)
Missing	*6 (2.4%)*	*6 (4.3%)*	*12 (3.1%)*	*3 (0.7%)*	*6 (6.4%)*	*9 (9.4%)*	*15 (7.9%)*	*7 (1.2%)*	*12 (3.5%)*	*15 (6.4%)*	*27 (4.6%)*	*10 (1.0%)*

Table 25 Cardio-metabolic factors and missing values of ACS and Stroke cases vs. controls in Astana Health Study in men and women (case-control analysis) (patients with history of MI and Stroke among cases were excluded from the analysis)

	Men				**Women**				**Both sexes**			
	ACS	***Stroke***	***All cases***	***Controls***	***ACS***	***Stroke***	***All cases***	***Controls***	***ACS***	***Stroke***	***All cases***	***Controls***
BMI (kg/m^2), (%)												
18.5-24.9	68 (26.8%)	39 (28.1%)	107 (27.2%)	104 (24.1%)	22 (23.4%)	9 (9.4%)	31 (16.3%)	81 (14.9%)	90 (25.9%)	48 (20.4%)	138 (23.7%)	185 (18.9%)
25-29.9	116 (45.7%)	61 (43.9%)	177 (45.0%)	177 (41.0%)	33 (35.1%)	26 (27.1%)	59 (31.1%)	182 (33.4%)	149 (42.8%)	87 (37.0%)	236 (40.5%)	359 (36.8%)
≥30	58 (22.8%)	37 (26.6%)	95 (24.2%)	144 (33.3%)	38 (40.4%)	60 (62.5%)	98 (51.6%)	281 (51.6%)	96 (27.6%)	97 (41.3%)	193 (33.1%)	425 (43.5%)
Missing	*12 (4.7%)*	*2 (1.4%)*	*14 (3.6%)*	*7 (1.6%)*	*1 (1.1%)*	*1 (1.0%)*	*2 (1.1%)*	*1 (0.2%)*	*13 (3.7%)*	*3 (1.3%)*	*16 (2.7%)*	*8 (0.8%)*
Hypertension (told), (%)												
No	102 (40.2%)	38 (27.3%)	140 (35.6%)	199 (46.1%)	19 (20.2%)	21 (21.9%)	40 (21.1%)	195 (35.8%)	121 (34.8%)	59 (25.1%)	180 (30.9%)	394 (40.3%)
Yes	149 (58.7%)	95 (68.4%)	244 (62.1%)	231 (53.5%)	73 (77.7%)	75 (78.1%)	148 (77.9%)	350 (64.2%)	222 (63.8%)	170 (72.3%)	392 (67.2%)	581 (59.5%)
Missing	*3 (1.2%)*	*6 (4.3%)*	*9 (2.3%)*	*2 (0.5%)*	*2 (2.1%)*	*0*	*2 (1.05%)*	*0*	*5 (1.4%)*	*6 (2.6%)*	*11 (1.9%)*	*2 (0.2%)*
Diabetes (told), (%)												
No	220 (86.6%)	113 (81.3%)	333 (84.7%)	370 (85.7%)	72 (76.6%)	69 (71.9%)	141 (74.2%)	472 (86.6%)	292 (83.9%)	182 (77.5%)	474 (81.3%)	842 (86.2%)
Yes	33 (13.0%)	24 (17.3%)	57 (14.5%)	61 (14.1%)	20 (21.3%)	27 (28.1%)	47 (24.7%)	73 (13.4%)	53 (15.2%)	51 (21.7%)	104 (17.8%)	134 (13.7%)
Missing	*1 (0.4%)*	*2 (1.4%)*	*3 (0.8%)*	*1 (0.2%)*	*2 (2.1%)*	*0*	*2 (1.1%)*	*0*	*3 (0.9%)*	*2 (0.9%)*	*5 (0.9%)*	*1 (0.1%)*
Hypercholesterolemia (told), (%)												
No	197 (77.6%)	115 (82.7%)	312 (79.4%)	340 (78.7%)	59 (62.8%)	69 (71.9%)	128 (67.4%)	345 (63.3%)	256 (73.6%)	184 (78.3%)	440 (75.5%)	685 (70.1%)
Yes	55 (21.7%)	22 (15.8%)	77 (19.6%)	92 (21.3%)	31 (33.0%)	26 (27.1%)	57 (30.0%)	200 (36.7%)	86 (24.7%)	48 (20.4%)	134 (23.0%)	292 (29.9%)
Missing	*2 (0.8%)*	*2 (1.4%)*	*4 (1.0%)*	*0*	*4 (4.3%)*	*1 (1.0%)*	*5 (2.6%)*	*0*	*6 (1.7%)*	*3 (1.3%)*	*9 (1.5%)*	*0*
Smoking status, (%)												
Non-smoker	60 (23.6%)	38 (27.3%)	98 (24.9%)	130 (30.1%)	81 (86.2%)	90 (93.8%)	171 (90.0%)	496 (91.0%)	141 (40.5%)	128 (54.5%)	269 (46.1%)	626 (64.1%)
Current smoker	95 (37.4%)	60 (43.2%)	155 (39.4%)	128 (29.6%)	3 (3.2%)	3 (3.1%)	6 (3.2%)	24 (4.4%)	98 (28.2%)	63 (26.8%)	161 (27.6%)	152 (15.6%)

	Men				**Women**				**Both sexes**			
	ACS	***Stroke***	***All cases***	***Controls***	***ACS***	***Stroke***	***All cases***	***Controls***	***ACS***	***Stroke***	***All cases***	***Controls***
Past smoker	91 (35.8%)	37 (26.6%)	128 (32.6%)	170 (39.4%)	7 (7.5%)	3 (3.1%)	10 (5.3%)	15 (2.8%)	98 (28.2%)	40 (17.0%)	138 (23.7%)	185 (18.9%)
Missing	*8 (3.2%)*	*4 (2.9%)*	*12 (3.1%)*	*4 (0.9%)*	*3 (3.2%)*	*0*	*3 (1.6%)*	*10 (1.8%)*	*11 (3.2%)*	*4 (1.7%)*	*15 (2.6%)*	*14 (1.4%)*
Alcohol consumption, (%)												
Never	110 (43.3%)	46 (33.1%)	156 (39.7%)	192 (44.4%)	68 (72.3%)	71 (74.0%)	139 (73.2%)	294 (53.9%)	178 (51.2%)	117 (49.8%)	295 (50.6%)	486 (49.7%)
Less 3 a month	94 (37.0%)	54 (38.9%)	148 (37.7%)	198 (45.8%)	16 (17.0%)	21 (21.9%)	37 (19.5%)	221 (40.6%)	110 (31.6%)	75 (31.9%)	185 (31.7%)	419 (42.9%)
At least 1 a week	34 (13.4%)	37 (26.6%)	71 (18.1%)	37 (8.7%)	1 (1.1%)	3 (3.1%)	4 (2.1%)	9 (1.7%)	35 (10.1%)	40 (17.0%)	75 (12.9%)	46 (4.7%)
Missing	16 (6.3%)	2 (1.4%)	*18 (4.6%)*	*5 (1.2%)*	9 (9.6%)	1 (1.0%)	*10 (5.3%)*	*21 (3.9%)*	25 (7.2%)	3 (1.3%)	*28 (4.8%)*	*26 (2.7%)*

Table 26 Associations of socio-economic risk factors with risk of CVD (both ACS and Stroke) in Astana Health Study (case-control analysis) in men and women (missing values were excluded)

	Cases ACS &Stroke	Controls	Model 1 OR (95% CI)	Model 2 OR (95% CI)	P value* lrtest
Education					
Higher	192 (33.4%)	288 (29.6%)	1	1	0.270
Apprenticeship	172 (29.9%)	332 (34.1%)	0.85 (0.63-1.13)	0.81 (0.59-1.11)	
Primary/Secondary	211 (36.7%)	353 (36.3%)	0.91 (0.69-1.20)	0.89 (0.65-1.20)	
Ethnicity					
Kazakhs	341 (59.1%)	566 (58.1%)	1	1	0.673
Russians	170 (29.5%)	257 (26.4%)	1.31 (1.00-1.71)	1.48 (1.10-1.98)	
Others	66 (11.4%)	151 (15.5%)	0.78 (0.55-1.12)	0.86 (0.59-1.26)	
Marital status					
Married	445 (77.3%)	715 (73.5%)	1	1	0.775
Unmarried	131 (22.7%)	258 (26.5%)	1.37 (1.01-1.86)	1.41 (1.01-1.95)	
Car ownership					
Yes	338 (61.6%)	532 (55.8%)	1	1	0.695
No	211 (38.4%)	422 (44.2%)	0.87 (0.69-1.11)	0.83 (0.63-1.08)	
Deprivation level					
High level (poor)	113 (19.9%)	256 (26.4%)	1	1	0.226
Intermediate level	173 (30.5%)	306 (31.6%)	1.16 (0.84-1.61)	1.19 (0.85-1.69)	
Low level	282 (49.7%)	407 (42.0%)	1.38 (1.02-1.87)	1.51 (1.09-2.10)	
Unemployment					
Never	332 (59.7%)	701 (72.5%)	1	1	0.639
Less 1 year	136 (24.5%)	106 (11.0%)	2.65 (1.92-3.65)	2.78 (1.98-3.91)	
More 1 year	88 (15.8%)	160 (16.6%)	1.24 (0.89-1.73)	1.24 (0.88-1.77)	

Model 1 – age and sex adjusted; Model 2 – fully adjusted for all variables in the table

Table 27 Association of cardio-metabolic risk factors with risk of CVD (both ACS and stroke) in Astana Health Study (case-control analysis) in men and women (missing values were excluded)

	Cases ACS &Stroke	Controls	Model 1 OR (95% CI)	Model 2 OR (95% CI)	P value* lrtest
BMI (kg/m^2)					
18.5-24.9	138 (24.3%)	185 (19.1%)	1	1	0.168
25-29.9	236 (41.6%)	359 (37.1%)	0.90 (0.66-1.22)	0.89 (0.64-1.23)	
≥30	193 (34.0%)	425 (43.9%)	0.79 (0.58-1.08)	0.71 (0.50-1.01)	
Hypertension (told)					
Yes	392 (68.5%)	581 (59.6%)	1	1	0.198
No	180 (31.5%)	394 (40.4%)	1.58 (1.24-2.02)	1.77 (1.35-2.32)	
Diabetes (told)					
Yes	104 (18.0%)	134 (13.7%)	1	1	0.013
No	474 (82.0%)	842 (86.3%)	1.31 (0.96-1.78)	1.28 (0.91-1.80)	
Hypercholesterolemia					
Yes	134 (23.3%)	292 (29.9%)	1	1	0.435
No	440 (76.7%)	685 (70.1%)	0.83 (0.63-1.08)	0.71 (0.53-0.96)	
Smoking					
Non-smoker	269 (47.4%)	626 (65.0%)	1	1	0.082
Current smoker	161 (28.4%)	152 (15.8%)	1.63 (1.15-2.30)	1.48 (1.02-2.16)	
Past smoker	138 (24.3%)	185 (19.2%)	1.05 (0.74-1.47)	0.97 (0.68-1.39)	
Alcohol					
Never	295 (53.2%)	486 (51.1%)	1	1	<0.000
Less 3 a month	185 (33.3%)	419 (44.1%)	0.70 (0.54-0.90)	0.58 (0.44-0.76)	
At least 1 a week	75 (13.5%)	46 (4.8%)	2.16 (1.38-3.36)	1.57 (0.97-2.52)	

Model 1 – age and sex adjusted; Model 2 – fully adjusted for all variables in the table

Table 28 Effect of socio-economic risk factors on risk of ACS in Astana Health Study (case-control analysis) in men and women (missing values were excluded)

	Cases ACS	Controls	Model 1 OR (95% CI)	Model 2 OR (95% CI)	P value* lrtest
Education					
Higher	119 (34.8%)	288 (29.6%)	1	1	0.078
Apprenticeship	101 (29.5%)	332 (34.1%)	0.81 (0.57-1.16)	0.74 (0.50-1.09)	
Primary/Secondary	122 (35.7%)	353 (36.3%)	0.89 (0.63-1.25)	0.82 (0.57-1.20)	
Ethnicity					
Kazakhs	196 (57.1%)	566 (58.1%)	1	1	0.817
Russians	113 (32.9%)	257 (26.4%)	1.60 (1.16-2.20)	1.93 (1.36-2.74)	
Others	34 (9.9%)	151 (15.5%)	0.77 (0.49-1.22)	0.95 (0.59-1.53)	
Marital status					
Married	273 (79.6%)	715 (73.5%)	1	1	0.803
Unmarried	70 (20.4%)	258 (26.5%)	1.38 (0.93-2.05)	1.34 (0.89-2.03)	
Car ownership					
Yes	199 (61.8%)	532 (55.8%)	1	1	0.704
No	123 (38.2%)	422 (44.2%)	0.93 (0.69-1.25)	0.84 (0.61-1.17)	
Deprivation level					
High level (poor)	86 (25.3%)	256 (26.4%)	1	1	0.734
Intermediate level	93 (27.4%)	306 (31.6%)	0.80 (0.54-1.18)	0.81 (0.54-1.23)	
Low level	161 (47.4%)	407 (42.0%)	0.99 (0.70-1.41)	1.06 (0.73-1.55)	
Unemployment					
Never	205 (61.0%)	701 (72.5%)	1	1	0.437
Less 1 year	76 (22.6%)	106 (11.0%)	2.32 (1.57-3.42)	2.36 (1.57-3.57)	
More 1 year	55 (16.4%)	160 (16.6%)	1.29 (0.87-1.93)	1.27 (0.83-1.93)	

Model 1 – age and sex adjusted; Model 2 – fully adjusted for all variables in the table

Table 29 Effect of cardio-metabolic risk factors on risk of ACS in Astana health Study (case-control analysis) in men and women (missing value were excluded)

	Cases ACS	Controls	Model 1 OR (95% CI)	Model 2 OR (95% CI)	P value* lrtest
BMI group, (kg/m^2)					
18.5-24.9	90 (26.9%)	185 (19.1%)	1	1	0.501
25-29.9	149 (44.5%)	359 (37.1%)	0.87 (0.61-1.24)	0.86 (0.59-1.27)	
≥30	96 (28.7%)	425 (43.9%)	0.63 (0.43-0.92)	0.59 (0.39-0.90)	
Hypertension (told)					
Yes	222 (64.7%)	581 (59.6%)	1	1	0.082
No	121 (35.3%)	394 (40.4%)	1.34 (1.00-1.80)	1.58 (1.14-2.19)	
Diabetes (told)					
Yes	53 (15.4%)	134 (13.7%)	1	1	0.057
No	292 (84.6%)	842 (86.3%)	1.00 (0.67-1.50)	0.93 (0.60-1.44)	
Hypercholesterolemia					
Yes	86 (25.2%)	292 (29.9%)	1	1	0.616
No	256 (74.9%)	685 (70.1%)	0.96 (0.69-1.33)	0.89 (0.62-1.27)	
Smoking					
Non-smoker	141 (41.8%)	626 (65.0%)	1	1	0.1158
Current smoker	98 (29.1%)	152 (15.8%)	1.80 (1.19-2.71)	1.60 (1.03-2.49)	
Past smoker	98 (29.1%)	185 (19.2%)	1.31 (0.88-1.96)	1.19 (0.78-1.80)	
Alcohol					
Never	178 (55.1%)	486 (51.1%)	1	1	0.009
Less 3 a month	110 (34.1%)	419 (44.1%)	0.68 (0.50-0.93)	0.54 (0.39-0.76)	
At least 1 a week	35 (10.8%)	46 (4.8%)	1.50 (0.88-2.56)	1.03 (0.58-1.83)	

Model 1 – age and sex adjusted; Model 2 – fully adjusted for all variables in the table

Table 30 Effect of socio-economic risk factors on risk of Stroke in Astana Health Study (case-control analysis) in men and women (complete case analysis)

	Cases Stroke	Controls	Model 1 OR (95% CI)	Model 2 OR (95% CI)	P value* lrtest
Education					
Higher	73 (31.3%)	288 (29.6%)	1	1	0.948
Apprenticeship	71 (30.5%)	332 (34.1%)	0.90 (0.61-1.32)	0.97 (0.63-1.49)	
Primary/Secondary	89 (38.2%)	353 (36.3%)	0.94 (0.65-1.36)	1.02 (0.67-1.55)	
Ethnicity					
Kazakhs	145 (62.0%)	566 (58.1%)	1	1	0.905
Russians	57 (24.4%)	257 (26.4%)	0.99 (0.68-1.43)	1.06 (0.70-1.61)	
Others	32 (13.7%)	151 (15.5%)	0.78 (0.49-1.25)	0.79 (0.47-1.31)	
Marital status					
Married	172 (73.8%)	715 (73.5%)	1	1	0.840
Unmarried	61 (26.2%)	258 (26.5%)	1.39 (0.94-2.07)	1.62 (1.04-2.52)	
Car ownership					
Yes	139 (61.2%)	532 (55.8%)	1	1	0.323
No	88 (38.8%)	422 (44.2%)	0.81 (0.58-1.11)	0.79 (0.55-1.14)	
Deprivation level					
High level (poor)	27 (11.8%)	256 (26.4%)	1	1	0.412
Intermediate level	80 (35.1%)	306 (31.6%)	2.08 (1.28-3.39)	2.47 (1.46-4.17)	
Low level	121 (53.1%)	407 (42.0%)	2.32 (1.46-3.69)	2.92 (1.75-4.85)	
Unemployment					
Never	127 (57.7%)	701 (72.5%)	1	1	0.810
Less 1 year	60 (27.3%)	106 (11.0%)	3.26 (2.17-4.89)	3.67 (2.35-5.74)	
More 1 year	33 (15.0%)	160 (16.6%)	1.17 (0.73-1.86)	1.18 (0.71-1.95)	

Model 1 – age and sex adjusted; Model 2 – fully adjusted for all variables in the table

Table 31 Effect of cardio-metabolic risk factors on risk of Stroke in Astana Health Study (case-control analysis) in men and women (complete case analysis)

	Cases Stroke	Controls	Model 1 OR (95% CI)	Model 2 OR (95% CI)	P value* lrtest
BMI (kg/m^2)					
18.5-24.9	48 (20.7%)	185 (19.1%)	1	1	0.042
25-29.9	87 (37.5%)	359 (37.1%)	0.92 (0.61-1.41)	0.83 (0.52-1.34)	
≥30	97 (41.8%)	425 (43.9%)	0.99 (0.65-1.52)	0.83 (0.51-1.37)	
Hypertension (told)					
Yes	170 (74.2%)	581 (59.6%)	1	1	0.831
No	59 (25.8%)	394 (40.4%)	1.95 (1.38-2.76)	2.10 (1.42-3.11)	
Diabetes (told)					
Yes	51 (21.9%)	134 (13.7%)	1	1	0.083
No	182 (78.1%)	842 (86.3%)	1.66 (1.13-2.44)	1.71 (1.11-2.65)	
Hypercholesterolemia					
Yes	48 (20.7%)	292 (29.9%)	1	1	0.734
No	184 (79.3%)	685 (70.1%)	0.67 (0.46-0.97)	0.52 (0.34-0.79)	
Smoking					
Non-smoker	128 (55.4%)	626 (65.0%)	1	1	0.349
Current smoker	63 (27.3%)	152 (15.8%)	1.42 (0.91-2.24)	1.21 (0.71-2.04)	
Past smoker	40 (17.3%)	185 (19.2%)	0.72 (0.45-1.17)	0.64 (0.38-1.07)	
Alcohol					
Never	117 (50.4%)	486 (51.1%)	1	1	0.005
Less 3 a month	75 (32.3%)	419 (44.1%)	0.75 (0.53-1.07)	0.66 (0.45-0.97)	
At least 1 a week	40 (17.2%)	46 (4.8%)	3.54 (2.08-6.03)	2.97 (1.63-5.40)	

Model 1 – age and sex adjusted; Model 2 – fully adjusted for all variables in the table

CHAPTER 6

DISCUSSION

This chapter is structured as follows. First, it summarises the main results of the project. Second, the strengths and limitation of the study are discussed. Finally, the project findings are interpreted in the context of international literature and existing evidence.

6.1. Summary of the main findings

This population-based study had two main components. First, a cross-sectional survey was set up to investigate the population levels and distribution of four major cardio-metabolic risk factors (hypertension, diabetes, dyslipidaemia and obesity) in the Astana region of Kazakhstan. Secondly, a population-based case-control study examined the association of socioeconomic, behavioural and cardio-metabolic factors with acute coronary syndrome (ACS) and stroke in Astana.

The cross-sectional study found a high prevalence of all four cardio-metabolic risk factors in the study population. There were differences in the prevalence of risk factors by virtually all socioeconomic and demographic characteristics available, including urban vs. rural area of residence. Awareness, treatment and control of hypertension, diabetes and dyslipidaemias were significantly lower in the rural area. Russian ethnicity, unmarried status and deprivation levels were also associated with less favourable profile of cardio-metabolic risk factors but not all of these associations were consistent.

The case-control study identified considerable differences between cases and controls in the exposures to cardio-metabolic risk factors, health behaviours and socioeconomic factors. Cardio-metabolic risk factors (except obesity) and smoking and alcohol consumption were associated with increased risk of CVD. Socioeconomic risk factors were also associated with CVD risk but the relationships were more complex. Russian ethnicity, unmarried status and unemployment were associated with higher CVD risk but, paradoxically, participants with higher levels of material deprivation appeared to have lower CVD risk.

6.2. Main strengths and limitations of the project

This section discusses the general weaknesses and strengths of the study, largely in relation to the cross-section and case-control study design. Issues specific to particular risk factors or outcomes will be discussed in the subsequent sections.

6.2.1. Population-based cross-sectional survey

6.2.1.1 Limitations

When interpreting the results of the cross-sectional study, a number of limitations should be kept in mind.

Firstly, the cross-sectional design is not well suited to establish the temporal direction of some associations between exposure and disease, because data on each participant was recorded only at one point in time, and it is difficult to infer the temporality of the observed associations between risk factors and outcomes. The uncertainty about temporality differs by factor. On the one hand, education is generally completed in early life and is unlikely to be modified by health outcomes; similarly, ethnicity is unlikely to change during life. On the other hand, we are less sure about deprivation, car ownership and health behaviours, which can change relatively quickly, potentially reflecting poor health status (reverse causation).

Second, cross-sectional studies aiming to estimate the prevalence of risk factors in the population are sensitive to non-response bias. Evidence from elsewhere suggests that responders tend to differ from non-responders [162-166], which may ultimately affect the representativeness of the sample for the study population and limit the generalization of these results to the general population in Astana city and Astana region [167].

The response rate was modest but similar to most recent studies in Europe and elsewhere. The real response may have been higher, as we may speculate that some selected subjects may not have received the invitation to participate in the study due to inaccurate information in the polyclinic registers. It has been suggested that a response rate of 60% or so is satisfactory [168] and response rates similar to our study are common for recent studies in Europe and elsewhere but some at least selection bias is likely. and response rates similar to our study are common for recent studies in more advanced settings but at least some degree of selection bias is likely. Typically, participants in epidemiological studies tend to have a higher socio-economic status and better health than non-participants [169]. It is also possible that a study based in polyclinics may have attracted less healthy patients with higher perceived needs for medical care. Therefore, the lower response rates may lead to both under- and overestimation of prevalence of CVD and its risk factors. Since response rates were higher in women and in older age groups, some overestimation of the diabetes prevalence is also possible.

The response rates were slightly higher in Astana but the difference was not large enough to introduce serious selection bias. Response rates are usually positively associated with socioeconomic status, as reflected in high education and car ownership in the study sample. It has been reported that respondents in epidemiological surveys are not only more healthy, but also more health conscious than non-respondents [162-166]. These factors are likely to affect the results, although they are aware that the bias can affect the results either way. In comparison to the national population, participants in this study were more affluent and had a better access to health care, and this may explain their high rates of awareness, treatment and control of all cardiometabolic risk factors, especially in urban areas. Although the calculated response rates may be under-estimates, as the sampling frame did not cover recent out- and in-migration, the sample may not be completely representative for the Astana population.

On the other hand, internal validity of results (i.e. association between variables) is less sensitive to non-response than estimation of absolute rates [164]. It is unlikely that nonresponse and potentially incomplete sampling frame substantially affected the relationships (or lack of it) between risk factors indices and covariates.

Third, the wider representativeness of the study sample needs to be considered. The study is clearly not representative for the whole country. Astana is a new capital; over the past 15 years, its population has increased about 5-fold, and its growth has attracted well-educated persons from throughout the country who were employed in large civil service and thriving private business. For this reasons, Astana population is considerably more affluent, and healthier (or perhaps less health), than the national average. In addition, although registration with a polyclinic is mandatory in Kazakhstan, more affluent persons may be more likely to adhere to this rule.

The rural and urban areas in this study were intentionally chosen to assess urban-rural differences. Astana, as a very young capital city, has a high proportion of civil servants and businessmen who are more affluent and relatively better-educated than the rest of the population. Akmol is a rural area, proximal to Astana but it is remote enough to have a stable population with low level of migration and not many residents who commute to Astana city for work. Nevertheless, it is likely that more distant areas, or other regions in Kazakhstan, would present even larger differences in socio-demographic and health indicators compared to Astana city.

Finally, the survey had a relatively small sample size and therefore low statistical power. The sample size was based partly on logistical and financial reasons (mainly because there was no specific funding available) but sample size calculations were also conducted to ensure that meaningful differences can be detected. Nevertheless, given the modest sample size, it is possible that some associations were not detected.

The PhD project was established in challenging low-resource settings, so there was no opportunity to conduct additional objective measurements and examinations. However, all the fieldwork was performed by specially trained staff and supervised directly by the author. The geographical location and regional environments were chosen intentionally, the capital city and its surrounding area to assess the potential effects of different stages of the of urbanization processes. Since the completion of the work described in this thesis, we have expanded this project for two other regions in Kazakhstan (East and South of Kazakhstan) to confirm the findings. The work is currently underway and hence it is not included in the thesis.

6.2.1.2. Strengths

Despite these limitations, the chosen design has major advantages. A major advantage is that the cross-sectional design is relatively quick and inexpensive way to perform this exploratory study and to estimate the prevalence of major CVD risk factors. A relatively short-term survey is easier to implement in low resource settings, compared to a longitudinal study. Conveniently, there would be no loss to follow-up as the participants were interviewed only once.

An obvious strength is the Central Asian setting of the study. Given the almost complete lack of individual-level data on cardiovascular disease from the Central Asian countries of the former Soviet Union, the survey provides useful evidence on an important public health issue. The countries in this region have a high burden of CVD and followed heterogeneous patterns of socioeconomic development after the dissolution of the former Soviet Union, with different countries choosing different health or social systems [6, 170]. However, many uniform challenges remain, including rising social inequalities, westernization, urbanization and nutrition transition processes [171, 172].

Although, as stated above, Astana city is atypical of the whole country, there are several reasons why this study is useful, even if it is not fully representative for the whole country. First, to the author's best knowledge, there are no published individual level data from Kazakhstan. Second, the Astana region has higher income and socioeconomic standards than the rest of the country, and it is important to see the burden and management of cardiovascular disease and its risk factors in this economically advantaged setting (as it is hoped that the whole country will advance in terms of economic and social developments). Third, Astana, as the capital of Kazakhstan, is important because it sets example and trends for the rest of the country; it is likely that the current situation of Astana is the future of other urbanised centres in Central Asia.

6.2.2. Case-control study

6.2.2.1. Limitations

Many limitations of the case-control study as similar to those described in the context of the cross-sectional study. Particularly pertinent are the well-known issues of temporality (and reverse causation) and non-response, potentially leading to systematic differences between controls and cases (selection bias), and generalizability to the national population. Regarding reverse causation, an important issue is the fact that many biological and laboratory parameters are likely to change after the clinical event and after being hospitalised (and treated); this was the main reason that some of these factors (e.g. objectively measured blood pressure) could not be used in the analyses.

As in most case-control studies, it is difficult to exclude the possibility of selection bias. While controls were population based (with the caveat of modest response rates), cases were identified and recruited in hospitals. The rationale is that these are major hospitals caring for the vast majority of cases occurring in the study area. However, if cases of ACS and stroke, which were treated in other hospitals, or not treated at all, differed substantially from cases included in the study, the results may be biased. There is no practical way to assess this possibility but given that, to our best knowledge, cases recruited to the study account for over 90% of all hospitalised cases of ACS (and slightly lower proportion of strokes) in Astana, any potential bias is likely to be too small to materially affect the results.

An Additional (and related) limitation is that fact that the study included only non-fatal cases of CVD, i.e. participants who have survived ACS or stroke. This can introduce further selection bias. It is possible that non-fatal cases differ from fatal cases in the severity of the condition, although it is less likely that they also differ in aetiology, and it is possible that the associations of risk factors with less severe condition are weaker than with more severe (e.g. fatal) disease. If this were the case, it may be more difficult to establish a relationship between exposures and non-fatal CVD.

A related potential consideration is the classification of outcome. It is theoretically possible that reliability of the diagnosis of ACS and/or stroke differs between fatal and non-fatal events. However, a major bias due to disease misclassification is unlikely, as we used well-defined and internationally accepted clinical diagnostic criteria. There remains, however, one potentially important weakness – given the current clinical practice in Astana hospitals, we were unable to distinguish specific subtypes of ischemic strokes, such as embolic, thrombotic, and of small vessels. As the effects of some risk factors depend on the specific type of stroke, the overall observed association with any stroke depends on the mixture of clinical subtypes, and the mix of the types of stroke can therefore affect the observed associations.

Another potential problem is that both the cases and the interviewers knew the disease status at the time of the data collection. It is thus possible that respondents or interviewers may have been more likely to identify the presence of one of the risk factors at the time of interview than were the healthy population controls. There is little direct evidence in this study concerning this source of bias, although the possibility cannot be excluded that either patients or interviewers suspected that, for example, smoking or hypertension are risk factors for their condition. To minimise such recall / reporting bias, data collection was standardized between cases and control, using virtually identical questionnaires and procedures.

On the other hand, as mentioned above, the prevalence of risk factors in cases may have been under-estimated due to the hospital care after admission. For example, blood pressure could not be measured before the occurrence of stroke, and high blood pressure could have been treated and controlled after admission. If such high blood pressure was not previously diagnosed and cases were not aware of it, this would lead to underestimation of the contribution of hypertension.

6.2.2.2. Strengths

As commented in the context of the cross-sectional study, the case-control also had a number of important strengths. First, this was, in principle, a population-based case-control study, in which both cases and controls were selected from the general population in Astana. Despite the caveats discussed above, population-based case-control studies are generally considered more reliable than hospital-based studies, particularly for socioeconomic exposures.

The restriction of the cases to incident (first ever) episode of ACS or stroke reduces the possibility that individuals with previous cardiovascular disease might have substantially altered their lifestyles or risk factor levels before this event. An important support for the validity of the study comes from the observation that most odds ratios associated with all major risk factors, such as smoking, lipids, diabetes and hypertension, were similar to that reported in cohort studies in western populations.

6.3. Interpretation of the study results

The interpretation of the study results is described in the order as reported in Chapter 5. The cross-sectional results on CVD risk factors are discussed first, followed by discussion of results of the case-control study.

6.3.1. Population-based survey

6.3.1.1. Arterial Hypertension

This part of the study aimed to fill the gap on the evidence on hypertension in the Central Asian republics of the former Soviet Union. In this population sample, the prevalence of hypertension was similar to other populations while the levels of awareness, treatment and control were relatively high, and were positively associated with female sex, older age and high BMI.

The association with obesity was expected, since both obesity and hypertension tend to cluster within individuals (and both are part of the metabolic syndrome). However, apart from obesity, only a few covariates were related to hypertension indices in this study. It is possible that this lack of associations is due to changes in behaviour or socio-economic status among subjects who have been previously diagnosed with hypertension. However, it is not likely that this bias played a major role in the results. The diagnosis of hypertension may be inaccurate, as blood pressure levels were based on readings taken during one visit to the policlinic. In addition, the automated blood pressure monitor, used in this study, is not common in Kazakhstan. This may potentially lead to overestimation of the prevalence of hypertension, because of the white coat effect [173], and because the diagnosis of hypertension could not be based on persistent high blood pressure established in several occasions.

To our best knowledge, this is the first report attempting to estimate prevalence, awareness, treatment and control of hypertension in a Kazakh population sample, and it is likely to be one of the first studies using a standard and internationally comparable methodology in any Central Asian republic of the former Soviet Union.

All hypertension indices were less favourable compared to results published in the literature from many lower-income countries, and they were comparable to reports from high-income countries. For example, in the US in 1990-2000s, the levels of awareness, treatment and control were around 70%, 59% and 34% [155]; a more recent study reported the proportion of controlled hypertension as 27% in England, 53% in the US and 66% in Canada [174]. In the Czech Republic, results were very similar to those found in this study [175]. By contrast, recently published data from the SAGE study in six lower- and middle-income countries have shown prevalence of awareness ranging between 23% in Ghana to 72% in Russia, and prevalence of controlled hypertension between 4% in Ghana to 14% in India [176]. An earlier study in Krasnodar, Russia, reported the awareness, treatment and control of hypertension of 78%, 71% and 4%, respectively [177].

By contrast, an early study from Uzbekistan (from the 1980s) estimated awareness of 40% and control of 4% before a hypertension control programme [108]. Our results are therefore more similar to high-income countries than to lower income countries, and – perhaps as expected – to be similar to other former Soviet countries, such as Russia and Uzbekistan. On the other hand, as a recent multi-country study in eight post-Soviet countries found much lower levels of regular antihypertensive treatment use (27%) in Kazakhstan [178]; however, differences in methodology make direct comparison difficult.

In the SAGE study, the associations between hypertension indices and socio-economic circumstances were inconsistent between the low- and middle-income countries examined [176]. Awareness and control of hypertension were often but not always higher in subjects with higher education and higher income. In Russia, a country historically close to Kazakhstan, awareness of hypertension was positively associated with both education and higher material status while hypertension control was positively associated with higher material status but not with education. It is not clear why the consistent social gradients in hypertension indices in the data were not found. This could be due to high access to health services in this study sample (particularly in Astana city). It is also possible that, given the modest response rate, self-selection of participants may have resulted in a very health conscious sample with high levels of treatment in all socio-economic groups. Alternatively, the Kazakh population may still be at an earlier stage of the epidemiological transition and the western-type of socio-economic gradient has not yet been established.

There were pronounced differences in the all indices of hypertension between the urban and rural areas. Generally, the rural residence showed much less favourable pattern, with higher prevalence (particularly when controlling for covariates) and lower awareness, treatment and control. The most likely explanation is the worse access to (and perhaps lower quality of) medical care. However, it is not possible to exclude some contribution of selection bias (e.g. health conscious respondents in Astana may have been over-represented in the urban sample).

In conclusion, high levels of awareness and treatment were found, and the proportion of controlled hypertensive subjects was higher than in most low- and middle-income countries, including Eastern Europe and Central Asia, possibly due to the high levels of education and a large proportion of civil servants in this population sample. Although the study suggested good access to health services and treatment, the levels of hypertension control were lower than those achieved in some high-income countries, potentially suggesting less effective use of medication.

Given the very high prevalence of hypertension in this sample, and since Astana is not nationally representative, there is urgent need for a nationwide study, or at least surveys including rural areas, to understand the burden of hypertension, and to design an appropriate strategy to monitor and control hypertension in Kazakhstan. It is important to obtain reliable and internationally comparable estimates of the prevalence, awareness and treatment of hypertension in different sections of the Kazakh population, particularly in rural areas and in lower socio-economic groups. Finally, the results from Astana suggest that, even in affluent populations with high levels of treatment, achieving successful control is difficult; adoption of and adherence to modern management guidelines in primary care will be essential

6.3.1.2. Diabetes

The overall prevalence of diabetes was 12.5%, which is very close to the WHO estimate of 13.2% (based on uncertain data source) [29]. We also detected marked, almost two-fold differences between urban and rural areas, as all outcome measures were higher in urban residents. As expected, diabetes prevalence was also positively associated with older age, higher BMI and WHR and family history of diabetes. There was also a suggestion that diabetes prevalence was higher among Russians.

The diagnosis of diabetes used in the study may be imprecise, as only one measurement of fasting blood glucose was used; for logistic and financial reasons, other markers used to diagnose diabetes in clinical practice and epidemiological studies (such as oral glucose tolerance test and glycated haemoglobin) were not measured. However, fasting blood glucose is a widely recognized as an acceptable screening tool for diabetes and a good measure of diabetes control [179, 180]. On the other hand, it is reassuring that high BMI, high WHR and family history of diabetes were associated with diabetes, in a manner consistent with published studies [181, 182]. This supports the validity of the diabetes classification in this study and generally suggests a good quality of the data.

To our best knowledge, there were no previously published studies on the awareness, treatment and control of diabetes in Kazakhstan, and there is only limited evidence in other Central Asian republics. [183, 184] The high levels of awareness, treatment and control of diabetes in Astana city residents are similar to previously described levels of these indices for hypertension discussed in the previous section. This pattern of high awareness and treatment are likely to reflect the affluent and better educated population in Astana city with good access to health care. Similarly, the low levels observed in Akmol village may indicate poor access to adequate health care.

The high levels of diabetes indices in our study are similar to recently published estimates for other low- and middle-income countries. [185, 186] For example, data from India suggest a prevalence of diabetes among older persons of 16%, and levels of awareness, treatment and control of 72%, 54%, and 40%, respectively. [187] In the US, as an example from a high-income country, the estimates in elderly population were even higher, with a prevalence of 21% and awareness, treatment and control reported as 71%, 51% and 50%, respectively [188].

The inclusion of the rural Akmol village in this study revealed a huge gap between two populations. All diabetes indices were several times lower in Akmol village than in the capital city. Interestingly, awareness was very low and there were very few cases of controlled diabetes in the rural area. Although there are no reliable data on levels and distribution of lifestyle factors in Kazakhstan, the high prevalence of diabetes, obesity and hypertension in Astana city may reflect the urbanised and affluent life style, with easily available elements of westernised diet and high density to fast food outlets is consistent with higher rates of different non-communicable diseases in urban vs. rural areas reported from other Asian populations in lower and middle income countries [60, 189]. In addition, the type of employment is likely to differ between urban and rural areas, with more manual (and physically active) jobs in the rural area. Although obesity was common in both urban and rural areas in our study, the mean BMI and the prevalence of obesity were higher in Astana than in the rural area. It is possible that rapid urbanization, the introduction of western life style and economic development in Kazakhstan are associated with a particularly obesogenic environment and an accelerated nutrition transition, as seen in other rapidly “westernised” populations [190].

Regarding the social, demographic and economic determinants of diabetes indices, residence in an urban or rural setting exerted the greatest influence. Surprisingly, we found only modest differences in diabetes prevalence by education and car ownership; in addition, in age-sex-adjusted analyses, higher household item ownership was associated with increased odds of prevalent diabetes. This pattern may potentially reflect the current position of Kazakhstan in terms of epidemiological and nutritional transition. There is evidence that the social gradient in obesity changes with affluence and development; at earlier stages of transition, obesity shows a positive association with socioeconomic status but at later stages the gradient becomes inverse [20].

The higher prevalence of diabetes in ethnic Russians is analogous to previously reported lower self-rated health in the Russian vs. Kazakh ethnicity [23, 66], although the difference for diabetes prevalence was only marginally statistically significant. While the increased risk in Russians may be related to life style of socioeconomic status, it was not attenuated in the fully adjusted model. Persons with high education had a clear advantage in terms of awareness, treatment and control of diabetes; this pattern most likely reflects the better access to health care or, potential, better health literacy.

In summary, this study found relatively high prevalence of diabetes in this Kazakh population sample, and large differences in all diabetes indices were observed between urban and rural areas. These results require confirmation in a larger study, preferably using a large number of more diverse urban and rural areas. If confirmed, the urban/rural differences suggest a need for a diabetes screening and management programme, focusing on access to health care in rural areas and on prevention in the cities.

6.3.1.3. Dyslipidaemia

In this population-based study in the Astana region of Kazakhstan, we found an overall prevalence of hypercholesterolemia of 37.2% using the ≥6.2 mmol/l cut-off and 72.8% using the ≥5 mmol/l cut-off. There were large differences between urban and rural settings, with almost all lipid indicators being less favourable among urban residents. Most associations of hypercholesterolemia with covariates were in the expected direction. The prevalence of lipid abnormalities were higher among ethnic Russians and in more economically advantaged groups.

The urban-rural differences in dyslipidemias are consistent with the distribution of other variables, such as obesity or diabetes. The validity of our findings is supported by the fact that being female, higher BMI and WHR, diabetes and hypertension were also positively significantly associated with dyslipidemia, similarly to other published studies [191, 192].

The literature review did not identify any previously published studies on the awareness, treatment and control of hypercholesterolemia or determinants of any other lipid abnormalities in Kazakhstan and other Central Asian countries. Despite the strong association of dyslipidemia with cardiovascular risk, with a few exceptions [193], there is an inexplicable lack of evidence of this important aspect of cardiovascular health in the Central Asian region. The available information is largely limited to WHO reports on cardiovascular disease risk factors, where the source of data for this region are sometimes uncertain or perhaps are based on extrapolations from other regions [7, 194].

Studies in low and middle-income countries frequently reported high prevalence of dyslipidemia in urban areas and low prevalence of awareness, treatment and control levels in rural settings [195, 196]. We found large disparities in hypercholesterolemia prevalence between the two locations. All hypercholesterolemia indices were lower in Akmol village than in the capital city. However, using lower TC cut-off point (≥5.0 mmol/l) revealed even a more marked difference between urban and rural populations regarding awareness and treatment of disease, and extremely low proportion of controlled cases of hypercholesterolemia in the rural area.

The relatively high levels of awareness, treatment and control in this study could be attributed to wealthier and better educated population in Astana city; these indices were lower in the rural area. The high prevalence of lipid abnormalities, as well as high levels of dyslipidemias, diabetes and obesity in Astana city may point towards large-scale globalization and urbanization processes. The pattern may indicate rapid epidemiological and nutrition transition where easy access to fast food industry and sedentary lifestyle are commonplace. This is consistent with reported findings from other developing Asian populations with higher rates of various health outcomes of non-communicable diseases in urban vs. rural areas [60].

Several recent studies have examined the distribution of dyslipidemia in various populations. In China, the prevalence of dyslipidemias were much lower compared to our study (12% had TC ≥6.2 mmol/l, 18% had high LDL-C, 12% had low HDL-C and 15% had high TG); similarly, the levels of awareness, treatment and control indices (22%, 10% and 4% respectively) were much lower. However, this discrepancy may be explained by the fact that the Chinese study population study included younger subjects (18-79 years) who would have lower cholesterol levels [197]. A study in Turkish population (age 20-83 years) showed much higher prevalence of dyslipidemias (43% had TC ≥5.0 mmol/l, 42% had low HDL-C, 36% had high LDL-C, and 36% had high TG) [198]. Compared to similar aged population groups, our results were relatively similar to Italy with 78.2% of subjects with hypercholesterolemia (using the cut off ≥5.0 mmol/l) [199]. Internationally, lipid abnormalities tend to be more common in more affluent countries [200], and this pattern may be analogous to our finding of higher prevalence of dyslipidemia in the urban vs. rural populations.

Our findings confirm the association of lipid abnormalities with the cardio-metabolic risk factors, obesity, diabetes and hypertension [201]. Behavioural differences, including smoking, were also reported to be associated with hypercholesterolemia and other dyslipidemias [202, 203]. We found only small differences in abnormal lipid prevalence by education and car ownership, and deprivation levels were inversely associated with increased odds of dyslipidemias. The higher prevalence of dyslipidemia in ethnic Russians in Kazakhstan may be related to differences in life style and nutrition [63], but we do not have data on this interesting question.

In conclusion, this study found relatively high prevalence of dyslipidemia in the Kazakhstan population, and the lipid profile was much less favourable in the urban area. These pronounced urban vs. rural differences raise questions about both the potential distal and proximal causes of dyslipidemias in such middle income settings, and they suggest that a screening and treatment of hypercholesterolemia needs to cover the whole country, rather than urban setting, if Kazakhstan and other Central Asian countries want to succeed in preventing the higher burden of cardiovascular diseases in this region.

6.3.1.4. Obesity

In the population-based study in the Astana region of Kazakhstan, we found an overall prevalence of overweight (BMI >25) of 81% and prevalence of obesity (BMI >30) of 44%. This is very high. For both overweight and obesity, there were large differences between men and women and between urban and rural residents, with overweight and obesity being more prevalent among women and in urban residents. As expected, overweight and obesity were strongly associated with diabetes, hypertension and hypercholesterolemia. In addition, the prevalence of both overweight and obesity were also found among non-smokers, ethnic Russians and among more affluent groups. The prevalence of overweight and obesity was very high in both urban and rural areas in our study, although the mean BMI and , waist circumference nd the binary prevalence of overweight and obesity were marginally higher in Astana city compared to rural area in both sexes. In women, almost 90% of female participants in Astana city were classified as overweight and over half were categorized as obese.

There is a large level of heterogeneity between men and women in overweight and obesity prevalence in the world. In western Europe, men are more likely to be obese than women [204] while in the US, the obesity rates were slightly higher among women [205]. Interestingly, several studies from Eastern Europe and Russia have shown higher prevalence rates of both overweight and obesity in men than men [20, 206]. In the HAPIEE Study, obesity was more common in women than in men in 3 populations of Russia, Czech Republic and Poland: it ranged from 21% in Russia up to 30% in the Czech Republic in men and from 32% in the Czech Republic up to 47% in Russia in women; in addition, more than 70% of that study population were overweight (BMI over 25) [20]. In our study, in a similar age group, 52% of women and 34% of men were obese and 85% of women and 76% of men were overweight. Internationally, the gender differences in the prevalence of overweight and obesity are generally higher in lower income countries and the gap usually increases with decreasing levels of per capita income. Internationally, the gender differences in the prevalence of overweight and obesity are generally higher in lower income countries and the gap usually increases with decreasing levels of per capita income [20, 207], which might explain these gender gaps in Central Asia and Kazakhstan in particular. It also has to be noted that the risk of obesity increases with age in both men and women in all countries [208, 209].

Research on the association between various socioeconomic factors and health outcomes, like overweight and obesity remains scarce in the Central Asian region. Our study adds value to this research field for several reasons. First, this study aimed to fill the gap on evidence on overweight and obesity in the Central Asian republics of the former Soviet Union. To our knowledge, there were no similar studies of the determinants of the overweight and obesity in Central Asia over the last decades. This is also the first attempt to use standard measurement procedures for cardio-metabolic variables, including objective anthropometry using based a standard internationally comparable protocol.

There are numerous studies on the levels and distribution of obesity by urban and rural region and the data vary considerably between populations. For example, obesity was reported to be markedly higher among adults in rural versus urban areas in the United States [210], while no differences in the prevalence of overweight and obesity was found between rural and urban areas in 10 European countries [211]. A more recent study in 20 European countries has shown that rural residents were significantly more overweight and obese than those who lived in urban areas [212]. As previously discussed it is highly possible that rapid urbanization, introduction of western life style, as well as the economic transformation in Kazakhstan might be associated with accelerated nutrition transition, as seen in other populations [190].

Our study results suggest that current smokers are less overweight and obese than non-smokers, which is consistent with several other studies [213, 214]. In addition, past smokers often tend to be more overweight or obese compared to both current and non-smokers as weight gain usually follows smoking cessation [213-215]. In our study, this association with past smoking was only marginally significant in the analysis of obesity (BMI over 30) and non-significant in the analysis of overweight (BMI over 25). Given the low self-reported ex-smoking status in women (3%) we were not able to clearly identify the effect of smoking cessation on the overweight and obesity prevalence in women.

We found only marginal differences in overweight and obesity by education, marital status and car ownership; in the fully adjusted model of obesity, participants with lowest level of education (primary or secondary) had significantly higher risk of being obese (OR 1.57, 95% confidence interval 1.05-2.34). Our results are consistent with other studies, which reported significant educational gradient in obesity; often, these gradients were more pronounced effect in women than in men [20, 216]. One of the conventional explanations of the educational gradient in obesity is that unhealthy diets and lower level of physical activity are more common in in subjects with lower socioeconomic status [217].

The ownership of household amenities in this study were strongly associated with increased odds of overweight and obesity in dose response fashion, but the association was in the unexpected direction: participants with higher household amenity ownership were at significantly higher at risk of being overweight (OR 2.96, 95% confidence interval 1.67-5.26) and obese (OR 2.01, 95% confidence interval 1.28-3.16). By contrast, in most developed countries, the obesity is widely considered a condition that affects people of lower socioeconomic status. It was argued that for some selected household devices, including TV, computer and car, the effect on obesity might be mediated by its effects on reduced physical activity, more sedentary lifestyle time and higher dietary energy intake [78]. However, in our study we used the set of various household amenities in the total amenity score, and we did not observe any particular association of obesity with specific items.

There are several reasons that might explain the positive relation between socioeconomic status and obesity. Low/moderate food intake and high energy expenditure are more likely to be seen among the poorer people, while access to excess food supply and lower physical activity is more likely among the more affluent groups. In addition, there are certain cultural values in Central Asia that might associate the dense (i.e. larger) physique with wealth, as is often observed at the early stage of socioeconomic development [218, 219].

The higher prevalence of overweight and obesity in ethnic Russians in Kazakhstan may also be related to differences in life style and nutrition [25], but we do not have data to explore this important consideration. Overall, however, consumption of healthy foods, such as fruit and vegetable, in the former Soviet Union seems inadequate, particularly among lower socio-economic groups [220].

In conclusion, the obesity pattern observed in this study are alarming, with over 80% of the study participants being overweight or obese. There is a huge gap in overweight and obesity prevalence between men and women and some differences between urban and rural areas, and there seems to be a positive (rather than inverse) social gradient in overweight and obesity. The prevention of obesity should become an important feature of the public health agenda Central Asia.

6.3.2. Case-control study

Overall, the results of the case-control study largely confirmed the patterns of association between risk factors and CVD risk observed in other populations.

6.3.2.1. Cardio-metabolic risk factors

6.3.2.1.1. Hypertension

Self-reported history of doctor-diagnosed hypertension was significantly associated with the risk of CVD. The association was seen for both ACS and stroke cases, but it was stronger for stroke. This is as expected, since the diagnostic category of stroke includes haemorrhagic cerebrovascular events which are strongly associated with blood pressure. The effect of hypertension remained significant even after adjustment for all covariates in the reported model. Overall, the finding of an independent effect of hypertension on increased risk of CVD is well consistent with the literature.

As discussed above, because of the possible changes in blood pressure after clinical event and after hospitalisation, the case-control study had to rely on self-reported history of doctor-diagnosed hypertension. This is not the optimal measure; for example, history of doctor diagnosed hypertension was reported by 60% of controls, but the more comprehensive definition of hypertension, which included objective blood pressure measurement, yielded a higher prevalence of hypertension (72%). However, self-reported hypertension is an accepted and reasonably reliable measure that has been used for surveillance of hypertension in many countries [221]. Given the relatively poor measure of hypertension in the case-control study, it is difficult to compare our results quantitatively with previous studies. The important finding is that the direction of the association was consistent with existing evidence

6.3.2.1.2. Diabetes

Diabetic individuals, in general, have higher levels of cardiovascular risk factors than those without the disease. This is to a large extent due to the direct effects of diabetes on CVD risk, but there is also a strong association of diabetes with a higher level of other atherogenic traits (e.g. components of the metabolic syndrome, as seen in the cross-sectional results), which also contribute to increased CVD risk.

As with hypertension, self-report of doctor diagnosed disease was used to define diabetes mellitus. The effect of diabetes on the risk of CVD was observed in both age-sex-adjusted analyses and in the fully adjusted models. The strongest effect of diabetes was demonstrated among cases of stroke. Similar to the seminal Framingham Study, the relative impact of diabetes was greater in women than in men [222, 223]. However, our study detected only a weak association between diabetes and ACS. The lack of an association between these two could be related to the fact that patients with the more severe or fatal cases were excluded from our study (because they may have had ACS event in the past or because they may have a fatal event). There is also some possibility that the accuracy of ACS diagnosis is less than optimal; this would also partly explain why the association of diabetes was stronger with stroke.

6.3.2.1.3. Hypercholesterolemia

High total cholesterol is well established risk factor for CVD [224] and cholesterol lowering therapy is part of many national and international recommendations [156]. This study did not detect an unequivocal strong association of high total cholesterol with increased risk of CVD or ACS; however, there was relatively strong association with stroke in the multivariable adjusted model.

It is not certain what explains the lack of the expected association between high total cholesterol concentrations and ACS. One possible explanation is the decline in cholesterol concentrations that have been observed after acute coronary event [225]. However, there is also some evidence from more recent cohorts that total cholesterol is less consistently associated with ACS than in historically older cohorts, although the explanation for this heterogeneity in the effects of cholesterol remains unclear [203].

As with hypertension and diabetes, the case-control study relied on self-reported doctor diagnosed hypercholesterolemia, and this is likely to have introduced some misclassification, which, in turn, would lead to the underestimation of the association between cholesterol and CVD outcomes. The lack of an overall association between hypercholesterolemia in this study is more likely to be a false negative finding rather than a genuine lack of association.

6.3.2.1.4. Obesity

Obesity is considered a risk factor for CVD, particularly as it is associated with diabetes and the components of the metabolic syndrome, all of which are associated with increased CVD risk. For example, a recent meta-analysis of 10 large cohorts in United States reported that life time risk of CVD was about 75% higher among obese subjects than among normal weight subjects [226]. Similar findings were reported from East and South Asians [227]. On the other hand, there is also some evidence that obesity is associate with lower mortality among CVD patients [228].

In our study, we observed an unexpected inverse association between BMI categories and CVD, with obese subjects having about 30% lower odds of CVD after adjustment for covariates compared with those with normal weight. This association was driven entirely by ACS (the odds of ACS among obese vs. normal weight was 0.59), while there was no association with stroke. It is unclear how to explain the “protective” association for ACS. It is unlikely it is due to a confounding by socio-demographic variables, since the association persisted after adjustment for covariates. Since body weight and height is easy to measure, a measurement bias is unlikely, although different personnel conducted anthropometric measurements in the cross-sectional survey and in cases. As a genuine protective effect is very unlikely, the most likely possibility that this is a spurious observation possibly due to a selection bias in the recruitment of cases and controls.

6.3.2.2. Behavioural risk factors

In the thesis, it was possible to assess only two major behavioural determinants of CVD risk – smoking and alcohol consumption. These risk factors will be discussed in turn.

6.3.2.2.1. Smoking

The results of our study have confirmed the general pattern of association of the tobacco use with cardiovascular disease. [229] Cigarettes smoking was significantly statistically associated with the increased risk of CVD, both in ACS and Stroke cases. As might be expected, the risk was slightly higher in ACS cases compared to stroke cases; in the fully adjusted model, the odds ratio in current smokers was 1.48 for CVD, 1.60 for ACS and 1.21 for stroke. This is likely to reflect the differential importance of smoking in the aetiology of ischaemic heart disease and stroke The results are consistent with previously published data both from developed and developing countries [230].

The proportion of former smokers is a good indicator of smoking cessation patterns at a population level. In our study, we observed 33% in cases and 39% of former smokers in controls in men. Although former smokers had higher risk of CVD, particularly ACS, compared to non-smokers, the difference was not statistically significant. In high-income countries, the proportion of ex-smokers has been increasing and it currently exceeds 30% of population among men, while in low income countries the proportion of former smokers is lower (between 2% in China and 10% in Vietnam) [231] [232] Unfortunately, we were unable to collect the information on time after quitting smoking and the number of cigarettes smoked to verify the time and number effect of smoking on CVD risk.

There was a large gap in the prevalence of smoking between men and women and the risk of CVD was greater in men compared to women (supplemental tables). In high-income countries the differences between men and women are much narrower. [231] Given the high rates of westernization processes in the region and increase in overall wealth of the Central Asian societies we may expect the increased smoking rates in women in near future, and accordingly CVD rates are also likely to increase noticeably, especially in women population.

Our estimate of the population attributable risk fraction of (unadjusted figure 27%, Appendix 9) is consistent with the other estimates of the proportion of deaths from all causes attributable to cigarette smoking [230]. This clearly indicates a very high public health impact, the harmful effects of tobacco are not limited to CVD. A recent estimation of the proportion of cancer deaths attributable to smoking and alcohol in three eastern European countries, including Russia, have also suggested a marked contribution of tobacco: 43% of all cancer deaths in Russia were estimated to be attributable to smoking [233].

6.3.2.2.2. Alcohol consumption

The presented analysis of association between alcohol consumption and risk of cardiovascular disease used simplified approach to explore the role of alcohol use in our study population, focusing on drinking frequency. Given the low overall frequency of reported alcohol consumption, the cut off for “frequent” drinking was set as drinking at least once a week. This may not be an ideal measure of exposure. Nevertheless, there was a large difference of frequent alcohol consumption between cases (13% for both ACS and stroke) and population controls (5%). While the difference between cases and controls was similar in men and women, the absolute frequency of alcohol consumption in men was much higher.

The frequency of alcohol consumption was statistically significantly associated with CVD risk in a “J-shaped” fashion. Frequent alcohol consumption increased the risk of CVD while less frequent alcohol consumption had a “protective” effect both in age-sex-adjusted models and in fully adjusted models. In our study we found only modest effect of frequent consumption on the risk of ACS. The effect on the risk of stroke was much more pronounced; in the fully adjusted model frequent alcohol intake was associated with approximately 3-fold increase risk. We could not differentiate between stroke types; however, it has been suggested, that frequent alcohol consumption may increase the risk of any type of stroke, while light or moderate alcohol consumption could have a protective in ischemic stroke cases [234].

The effect of moderate alcohol consumption on cardiovascular disease has been extensively studied, and there are numerous reports that light to moderate alcohol consumption is associated with reduced risk of various cardiovascular outcomes. [129] However, there has been extensive criticism of the observation studies reporting the beneficial effect of moderated alcohol consumption on the risk of CVD, mainly on the grounds that non-drinkers are an inappropriate reference group, because they also include former drinkers who quit drinking because of their poor health (associated with their past drinking).

For this reason, conclusions and any general recommendations on alcohol intake for health promotion made on the basis of reasons should be given only cautiously, as alcohol may cause substantially more harm than good, [235] especially in such transitional societies like Central Asia.

As the study was not designed specifically to study alcohol intake, we did not measure the amount of alcohol consumed. Therefore, the study has only a limited ability to provide evidence on the role of alcohol consumption in cardiovascular risk. Binge drinking could be a potentially important factor for explaining the suspected role of alcohol in central Asian countries, as it appears to be in Russia. [236]

There are concerns about the reliability of the alcohol measurement in the study. About half of the participants, both among cases and controls, reported that they have not drunk any alcohol type within the last year (this proportion was much higher among women than among men). We did not specify in our questionnaire the reasons why participants have chosen not to drink; these reasons may include moral or religious motivations or alcohol intolerance issues. We can speculate that religion influences in the Central populations may be particularly important, as as the majority of our study population were Kazakhs and other Central Asian ethnical groups who usually identify to belong to Islam religion. Nevertheless, the overall level of drinking in the study was suspiciously low, even among ethnic Russians. It is likely that alcohol was substantially under-reported, for various reasons, including the social stigma association with drinking, particularly among women.

6.3.2.3. Socioeconomic risk factors

Consistently with recent findings [237], our results suggest considerable socioeconomic differentials in Kazakhstan. In crude analyses, differences in most risk factors and in CVD were present by most socioeconomic characteristics available in the present analysis. However, in multivariable analyses some of the associations changed, sometimes considerably. The discussion below is organized by major findings on each group of socioeconomic predictors.

The findings were less consistent when comparing the results with the developed countries. We found inconsistent differences of CVD risk factors between socioeconomic groups, while in most studies from high income countries these associations followed the social gradient. The inconsistent or indeed positive gradients were seen with prevalence of obesity (i.e. persons with higher household amenities had higher increased risk of being overweight) as well with CVD risk in the case-control analyses (the risk of CVD was higher in participants with lower levels of deprivation). Indeed, these positive relationships between socioeconomic measures and cardiovascular risk have been reported from other lower income settings; in particular, obesity and other cardiometabolic outcomes appear to be more common in more affluent groups [219, 238, 239]. There are hypotheses regarding this shift in the burden towards the wealthier groups, especially in middle-income countries, which may be only temporary and partially linked to rapid urbanization [219].

6.3.2.3.1. Education

While education has been found to be one of the most robust and consistent predictors of health outcomes in many epidemiological studies, in this study educational levels did not differ between cases and controls in crude or in multivariable analysis. However, this may partially be driven by the disproportionate distribution of urban and rural participants in cases and controls, as was mentioned previously. There is large difference between the education levels in urban vs rural areas, with almost 3 times more higher education among urban residents (and the proportion of women with higher education levels was by almost 10% lower among women compared to men in both cases and controls). The way controls were sampled and cases recruited may have obscured an association, if it indeed existed.

When a national health survey in Kazakhstan was analysed, there was a strong association between education and self-rated health [23], consistent with findings in most populations with available data. The lack of association between education and CVD in the case-control study remains puzzling.

6.3.2.3.2. Marital status

We found that marital status was associated with CVD in both men and women. Married individuals had lower risk of both ACS and stroke in both age-sex-adjusted models and in fully adjusted models. A wide variety of published research has shown that lower morbidity rates occur for married persons when compared with unmarried groups and that, generally, this impact is more pronounced in men than in women.

In our study, we observed a large gap between men and women in marital status; while only around 10% of men reported to be unmarried, this proportion was close to one half among women. This indirectly suggest the high mortality rates among men in Kazakhstan and other Central Asian and post-Soviet countries, where the gap between life-expectancy is almost 10 years between men and women [240].

6.3.2.3.3. Ethnicity

This study revealed that in this study population the risk of CVD was associated with ethnicity. The Russian ethnicity was associated with increased risk of CVD, both ACS and stroke; the association was only marginally statistically significant in the age-sex adjusted models but after the full adjustment the association became stronger. In separate analysis of ACS and stroke, there was a strong association of increased risk of ACS (but not stroke) with Russian ethnicity.

These results are consistent with recent studies on the ethnic disparities in health status in post-soviet countries. For example, in Kazakhstan and Estonia, ethnic Russians showed a lower health status compared to the titular ethnic groups population [65]. This does not seem to be the case regarding other ethnic groups in our analysis, as there were no statistically significant associations between CVD risk and ethnicity other than Russian (compared to Kazakhs). This is consistent with the analyses of self-rated health in the national health survey in Kazakhstan which found that participants reporting Russian ethnicity had moderately increased risk of poor self-rated health [23, 66]. This pattern may reflect either genuinely worse health status of the Russian minorities, consistent, for example, with higher mortality of Russians in census-linked analyses in Lithuania [241] or unlinked data from Kyrgyzstan [242]. On the other hand, we cannot exclude the possibility of differential reporting of self-rated health in Kazakh Russians compared to other Kazakh ethnicities.

One potential explanation for the less favourable risk profile associated with Russian ethnicity is that ethnic Russians have lower socioeconomic status, which may mediate (or confound) the association. However, bivariate cross-tabulations do not suggest large differences between Russians and Kazakhs in terms of their socioeconomic status, and adjustment for socioeconomic and demographic variables did not considerably attenuate the associations. It is therefore unlikely that socioeconomic status explains the ethnic differences in health outcomes.

Our study seems to confirm that ethnic disparities in health status are persistent in Central Asia countries. Sharygin and Guillot suggested that there might be influence by the degree of russification processes in these societies whereby non-Russian groups may replicate the patterns of alcohol consumption commonly seen in Russia [68].In their study, Sharygin and Guillot found that mortality rates among Kazakhs were lower compared to Russians but higher compared to Kyrgyzes. This is intriguing, as higher socioeconomic status of Kazakhs was not associated with better health compared to Kyrgyz [68].

It is worth noting that in Central Asian states, there are other ethnic minorities that probably were better adapted to the new transformation processes that evolved after the dissolution of USSR compared to ethnic Russians; for example, easier adaptation to new official languages and other cultural features of the titular ethnic groups. These are the so-called “old minorities” of Turkic ethnic origin (Uzbek, Uyghur, Tatar, Kyrgyz, Turkish, Azerbaijani, Tajik etc). This possibility gives rise to further research questions; for example, could ethnic disparities be attributed to behavioural changes defined by religious or cultural characteristics of the minorities, or does the lack of capacity to adapt to new cultural and linguistic transformations disconnect new minorities from the society? Both these mechanisms could potentially increase health inequalities.

6.3.2.3.4. Deprivation levels

We found only modest differences in CVD risk by socioeconomic status defined by material deprivation. However, the direction of the association was unexpected. In both age-sex-adjusted and multivariable analyses, higher socioeconomic position (less deprivation) was associated with increased odds of CVD. On the other hand, car ownership showed opposite association, although this was not statistically significant.

Analogous to cross-sectional analyses, this paradoxical pattern may potentially reflect the current position of Kazakhstan in terms of epidemiological and nutritional transitions. For example, there is evidence that the social gradient in obesity changes with affluence and development; at earlier stages of transition, obesity shows a positive association with socioeconomic status but at later stages the gradient becomes inverse. Despite the universal coverage model of healthcare in Kazakhstan and equal access to healthcare facilities, especially in emergency cases, we may argue that more affluent population would consume more healthcare services due to their higher level of awareness, better ability to seek medical care and also better social connections. This has been shown previously in our cross-sectional analysis that awareness treatment and controls levels of cardio-metabolic risk factors were significantly higher in more affluent urban population in Astana city.

There may be a difference between these two markers of material condition. In Kazakhstan, car ownership may have a particular significance, potentially being a visible marker of socioeconomic position or a measure of wealth and may have an implication for own self-perceived standing in the social hierarchy. Also, car ownership is measured more easily and more precisely in population-based studies, and it may be a more practical measure of material conditions for population studies in the region. Household amenities, on the other hand, are less visible, may not be as important for people's perception of own social status, and may also be more complex and difficult to measure.

6.3.2.3.5. Unemployment

The primary observation of this study is that the unemployment status had a strong positive relationship on CVD risk, including both ACS and stroke. This is consistent to what has been reported in other studies in various populations [243, 244]. The risks associated with unemployment was of similar magnitude or even greater as classical CVD risk factors, such as smoking, diabetes and hypertension. Surprisingly, the more pronounced effect was observed among those who had been exposed to a shorter period of unemployment (less than one year of unemployment) while the risk of long-term unemployment was smaller.

Strully et al. reported that unemployment was linked to a significant increase of acute myocardial infarction and, is consistent to our results, the risk in their study was highest in the first year of unemployment [245]. Similarly, using data from the Russian Longitudinal Monitoring Survey, Perlman and Bobak found that the increase in mortality was largest during the first year of unemployment, while the risk associated with a longer term unemployment was less pronounced [87]. In addition, the proportion of persons who reported unemployed longer more than one year was mostly much higher among women, whereas the proportion on unemployed less than a year were higher among men. This could partially explain such a strong effect of short-term unemployment status on CVD risk. [246-248]

Although unemployment is a stressful life event, the mechanisms of its association with CVD remain unclear. One of the theories of the mechanisms of job loss effect on heart disease and stroke relates to the traditional perspective of the “stress” concept [249] and stress induced depression, which may also operate via behavioural responses. Irrespective of the mechanism, unemployment should be considered a strong health-risk health factor. The unadjusted calculations of population attributable risk fraction for unemployment suggest that almost 20% of CVD might be attributable to unemployment. While this is only a very crude estimate, this study suggests that unemployment may pose a considerable health risk.

CHAPTER 7

CONCLUSIONS AND IMPLICATIONS

7.1. Conclusions

Based on data from the Astana Health Study it can be concluded that there are considerable differentials in cardio-metabolic risk and behavioural factors by several socioeconomic and demographic factors characteristics. In particular, there seem to be considerable differences in the levels of risk factors between rural and urban areas, between Kazakh and Russian ethnic groups, and, less consistently, between population groups characterised by various indicators of socioeconomic position. The case-control study found associations between cardio-metabolic risk factors and risk of CVD, which are broadly consistent with studies in western populations and in other eastern European countries, while the association of CVD risk with sociodemographic factors were also present, but sometimes less consistent.

While the associations of CVD with cardio-metabolic risk factors are consistent with the international literature and follow the relatively well-understood biological mechanisms, the pattern of risk factors and CVD risk distribution by socioeconomic factors are more complex and more difficult to interpret. It is likely that the differences between urban and rural areas are connected with the process of globalisation, westernisation and epidemiological and nutritional transition. It is also likely that the differences between the Russian and Kazakh ethnicity are driven by social, economic and cultural factors, which were not captured by the measurements in the study. The increased risk of CVD associated with short-term unemployment may reflect acute, possibly psychosocial, negative consequences of losing employment. However, some of the conflicting findings regarding socioeconomic gradient in risk factors and CVD are difficult to reconcile. Some of them may genuinely reflect the locally specific meanings of various socioeconomic measures, but it is also possible that some of these inconsistent finding reflect the limitations of the measurements, which may have been inaccurate and potentially taping into concepts which are culturally distant to the Kazakh population and therefore not well understood.

7.2. Implications of this research

Perhaps most important impact of this research is the fact that it provides the first individual-level evidence on cardiovascular diseases (CVD) in Central Asia, obtained in a clearly described population sample and by using internationally comparable methodology. As CVD remain the most important cause of high total mortality in the region, examination of the prevalence of a wide range of risk factors and their associations with CVD is of a great importance for the region. Such a study is the first step to consider options for serious deliberations on effective prevention and curative strategy. So far, such data on CVD have not been available. It is hoped that the information presented in this thesis (and the resulting publications) will be important for governmental officials and policy makers.

The second implication relates to the general view of the importance and amenability of CVD diseases within Central Asian countries. CVD remained to be considered to be the domain of clinicians and hardly amenable to preventive activities. There have been few efforts to design public health measures to control CVD and other non-communicable diseases. The thesis presents convincing evidence that environmental factors play a major role in determination of CVD risk and they need to be taken into account. With the emergence of evidence-based medicine and evidence-based public health, these locally specific data from Kazakhstan will provide a major impetus to consider evidence in clinical and preventive deliberations.

There is no simple solution to the challenges posed by CVD to society and the healthcare system, especially given the complexity of cardiovascular diseases, local peculiarities and practical and financial constraints of Central Asian countries. Nevertheless, given that a common set of CVD risk factors affects the disease risk in various populations worldwide, similar strategies, related to both management and prevention of CVD, are expected to be effective.

It has been suggested that as much as 90% of the CVD burden is attributable to modifiable risk factors, with over 75% of them being due to behavioural factors such as smoking, adverse dietary patterns and sedentary lifestyles [250]. These estimates may imply that controlling these behavioural risk factors would make a major contribution to reducing CVD rates. Ideally, these behavioural interventions should be addressed at all stages of the life course, since CVD results from risks accumulated throughout life.

The population-wide strategies, including the development, or at least the adoption of such policies and regulations that are related to food and tobacco control, may effectively alter the behavioural patterns of populations in both developed and developing countries, and have a great potential in Central Asian settings. Specifically, the taxation and regulation of tobacco products, as well as regulation of food marketing strategies could be potentially successful, given the relatively low income in Central Asia, although it is recommended that the regulatory changes should be sustainable, economically feasible and incremental. Additionally, international guidelines suggest that population-level interventions with support of NGOs and mass media further raise the awareness levels of CVD risk [251] through health education, improved health literacy and behavioural change towards a healthier lifestyle. Good examples of such programmes are the Act FAST and KNOW STROKE campaigns in western countries [252]. These population wide strategies need to take into account the distribution of risk factors by social and demographic factors. In the case of Kazakhstan, our results suggest important variation by urban / rural residence and ethnicity and, to a less degree, socioeconomic status, and the population-based approaches may need to be modified to take into account these differences.

Along with population-based approaches, it is equally important to strengthen the health system, in order to deliver high quality and accessible health care for the prevention and management of CVD. This includes improving the healthcare financing mechanisms, workforce capacity building programs and infrastructure development [8], as well as increasing access to essential medication [253]. Health system policies may not be as effective or immediate, as their theoretical prediction and political expectations are sometimes rather imbalanced. With Central Asian countries being increasingly affluent, an excessive focus on high-risk prevention strategies has emerged, which in turn might have led to limited focus on primary care and population-based CVD prevention. There is an urgent need to emphasize the role of primary care in achieving better health outcomes and the reorientation of primary health care towards CVD prevention. For example, the redistribution of the work undertaken by general practice staff to support the patients (health coaching service) in health behaviour change might be effectively implemented in Central Asia settings [254]. Also, the ongoing surveillance and evaluation processes of implemented activities should always accompany the primary health care initiatives.

Therefore, comprehensive strategies addressing the full range of complex and wider determinants of CVD would have the highest potential for CVD prevention in Central Asia region [255]. In addition, the context is highly important for the planning and implementation of CVD prevention strategies. While there are common needs and priorities for every state, each country in the CA region has its own specific needs and circumstances. Thereby, local knowledge is required to design and implement these interventions in Central Asian settings.

The third implication is connected to the fact that the study has included and examined a wide range of socio-economic and demographic factors as potential determinants of CVD. Although not all the results show consistent strong association with all socio-economic measures, the introduction of social determinants into the study of non-communicable diseases is novel in Central Asia (and other parts of former Soviet Union), and it is hoped that this project will contribute to the recognition that these factors are perhaps the most powerful determinants of health.

Finally, this research may have an impact on academia and research. Epidemiology of non-communicable diseases has not been well developed in most post-Soviet countries. Traditionally, epidemiology focused on communicable diseases and public health was concerned with industrial hygiene. As a result, non-communicable diseases have been largely neglected and considered too complex for interventions. This population-based study provides an example that it is feasible to conduct high quality epidemiological studies of a non-communicable disease in Central Asian settings. It is hoped that this will provide a motivation to improve academic teaching and training in research methods, introduce modern methods in teaching and training curricula, and eventually lead to expansion of academic research into non-communicable diseases, leading to more effective policies and interventions.

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Appendices

Appendix 1. Informed Consent

INFORMATION FORM FOR PATIENT

AND INFORMED CONSENT FOR PARTICIPATION IN RESEARCH

You are invited to participate in a scientific study. It is important that before your decision, you understand why this study is being conducted and what it is about. Please read carefully the information below, and if you do not understand something, or you want to receive additional information, ask the doctor responsible for the study.

If you choose to participate in the study, you will be asked to complete, sign and date this form of patient information and informed consent to participate in the study.

We invite you to participate in a survey developed within the framework of the research project "Study of the determinants of CVD and metabolic syndrome in elderly population in Kazakhstan", The survey and examination will be held in the Republican Diagnostic Center, UMC, located in Astana, Sagynak #2.

Currently, the health status of the population of the republic is characterized by the growth of non-communicable diseases, specifically cardiovascular disease and metabolic syndrome. In this regard, the purpose of this survey is to monitor the health of the people, and to study the main risk factors for cardiovascular disease and metabolic syndrome.

Personnel of the Center for Life Sciences at Nazarbayev University within the framework of the project "Study of the determinants of CVD and metabolic syndrome in elderly population in Kazakhstan” will conduct a survey to assess your health and possible risk of developing cardiovascular disease and metabolic syndrome. The examination will help to understand the causes of the development of cardiovascular disease and metabolic syndrome in the population of the Republic of Kazakhstan, as well as their relationship to lifestyle, social and economic factors.

During the examination, your blood pressure and anthropometry will be measured; you will be asked to answer a number of questions concerning your lifestyle and behavior (social stress, smoking, economic conditions, etc.); you will also have a series of tests to determine the blood lipids (fat) and glucose concentrations. All examinations are free of charge. Based on the results of the examination, a medical report will be prepared for you and preventive and therapeutic recommendations will be given.

The survey timeframe is planned between 2013 - 2015. Examination will take no more than 1-1,5 hours. If the visit to the clinic coincides with your working time, you will be issued a document for the provision in your workplace.

• Information regarding your lifestyle (smoking, alcohol consumption, economic conditions) and health status is strictly confidential, i.e. will not be given and told to anyone and will only be used for processing in a unidentified form.

- Blood sampling for analysis is performed with a one-time sterile instrument and by qualified medical personnel,
- Your blood will NOT be used for other purposes not related to this program,
- You can withdraw from this study at any time and any stage of the project.

If you have any other questions, you can contact the responsible Principal Investigator at the Center for Life Sciences, Nazarbayev University, Dr. Adil Supiyev.

I, the undersigned (s)

(FULL NAME.)
____,

Resident, the address ____ I give my voluntary consent to participate in the study: "Study of the determinants of metabolic syndrome in elderly population in Kazakhstan". After due consideration, I agree to cooperate with the doctor
____ who is in charge of the study and, if necessary, with all persons authorized by him.

I understand that I can refuse to participate in the study at any time if I want to, and this under no circumstances will affect the quality of medical care that I receive.

Patient

Date: ______________________

Signature: __________

Doctor/interviewer

FULL NAME: ____

Date: ________________________
Signature: _________________

Appendix 2. The Astana Health Study Questionnaire (population-based survey)

Date of questionnaire filled

Day	Month	Year

Astana Health Study

Questionnaire

Name: .... Surname: ....

: Second **name**………………………………..

Date of birth

Day	Month	Year

Study ID

Address (street____________________) (House number____) (Flat number_____)
(Phone number_____________________)

1. Place of birth (city, oblast): ____

2. Sex:

1. Male
2. Female

3. What is your highest completed level of education?

1. Incomplete primary or no formal education
2. Primary
3. Vocational (apprenticeship)
4. Secondary
5. University (degree)

4. What is your marital status?

1. Single
2. Married
3. Cohabiting
4. Divorced / Separated
5. Widowed

About your health

5. Over the last 12 months, would you say your health has been:

1. Very good
2. Good
3. Average
4. Poor
5. Very poor

6. Have any of the following diseases ever been diagnosed in you by a doctor and have you ever been hospitalised for this disease?

	Yes, diagnosed and hospitalised	***Yes, diagnosed, never hospitalised***	***No or do not know***
heart attack / acute myocardial infarction	☐ 1	☐ 2	☐ 3
angina / ischaemic heart disease	☐ 1	☐ 2	☐ 3
stroke	☐ 1	☐ 2	☐ 3
chronic respiratory disease	☐ 1	☐ 2	☐ 3
cancer	☐ 1	☐ 2	☐ 3

7. (a) Do you have any long-standing illness or health problem? By longstanding I mean illnesses or health problems which have lasted, or are expected to last, for 6 months or more.

1. Yes (Go to Question 7b)
2. No (Go to question 8)

(b) If yes: For at least the past 6 months, to what extent have you been limited because of a health problem in activities that people usually do? Would you say you have been …

1. Severely limited
2. Limited but not severely,
3. Not limited

8. We need to understand the difficulties people may have with various activities because of a health, physical, mental, emotional or memory problem. Please tell me whether you have any difficulty doing each of the following everyday activities. Exclude any difficulties that you expect to last less than three months. Because of a health, physical, mental, emotional or memory problem, do you have difficulty with...?

Activity	***Yes***	***No***
Walking 100 meters	☐	☐
Climbing several flights of stairs without resting	☐	☐
Climbing one flight of stairs without resting	☐	☐
Stooping, kneeling or crouching	☐	☐
Pulling or pushing large objects like a living room chair	☐	☐
Lifting/carrying weights over 5 kilograms, like a heavy bag or groceries	☐	☐
Picking up a small coin from a table	☐	☐

Here are a few more activities. Because of a health, physical, mental, emotional or memory problem, do you have difficulty with...?

Activity	***Yes***	***No***
Dressing, including putting on shoes and socks	☐	☐
Walking across a room	☐	☐
Bathing or showering	☐	☐
Eating, such as cutting up your food	☐	☐
Getting in or out of bed	☐	☐
Using the toilet, including getting up or down	☐	☐
Preparing a hot meal	☐	☐
Shopping for groceries	☐	☐
Making telephone calls	☐	☐
Taking medications	☐	☐
Doing work around the house or garden	☐	☐
Managing money, such as paying bills and keeping track of expenses	☐	☐

9. Have you ever been told by a doctor that you have **high blood pressure**?

1. Yes
2. No

If **YES**, have you been taking drugs for high blood pressure in the last 2 weeks?

1. Yes
2. No
3. Don't know

10. Have you every been told by a doctor that you have **diabetes**?

1. Yes
2. No

If YES, at what age: __

If **YES**, how are you treated?

1. Only by diet
2. By diet and insulin
3. By diet and tablets
4. By diet, tablets and insulin
5. No treatment

11. Have you ever been told by a doctor that you have **high blood cholesterol**?

1. Yes
2. No

If **YES**, how are you treated?

1. Only by diet
2. By diet and tablets
3. Tablets only
4. No treatment

12. Are you under **long-term treatment or medical care** for any medical condition, except for high blood pressure, high cholesterol or diabetes?

1. Yes
2. No

If **YES**, please give details: ______________________________

13. Do you have a disability?

1 = Yes
2 = No → [SKIP TO 17]
99 = Refuse to answer → [SKIP TO 17]

14. What is the class of your disability?

1 = Class 1
2 = Class 2
3 = Class 3
4 = Not registered as disabled
98 = Don't know
99 = Refuse to answer

15. Do you take any **vitamins or mineral supplements**?

1. Yes (regularly, at least 3 times per week)
2. Yes (irregularly, less than 3 times per week)
2. No

16. (a)Did you lose **more than 5kg of weight** during the last 12 months?

1. Yes (go to question 17(b))
□ No (go to question 18)

16 (b) If yes, please indicate if this was

□ On purpose (i.e. by diet)
□ Unintended (i.e. not by diet)

17. Did any of your **parents or siblings suffer** from any of the **following diseases?**

	Did parents or siblings suffer from disease?		**IF YES**, did a parent or sibling have onset before the age of 60?	
	Yes	No	Yes	No
Heart disease (infarction, angina)	☐ 1	☐ 2	☐ 1	☐ 2
Stroke	☐ 1	☐ 2	☐ 1	☐ 2
Diabetes	☐ 1	☐ 2	☐ 1	☐ 2

18. Have you ever had any pain or discomfort in your chest?

1. Yes
2. No

If no, please, **women** proceed to **Question 25**, **men** proceed to **Question 31**.

19. Do you get it when you walk uphill or hurry or do physically demanding work?

1. Yes
2. No
3. Never hurries or walks uphill or does physically demanding work

20. Do you get it when you walk at an ordinary pace on the level?

1. Yes
2. No

21. What do you do if you get it while you are walking?

1. Stop or slow down
2. Carry on at the same pace
3. Take nitroglycerine

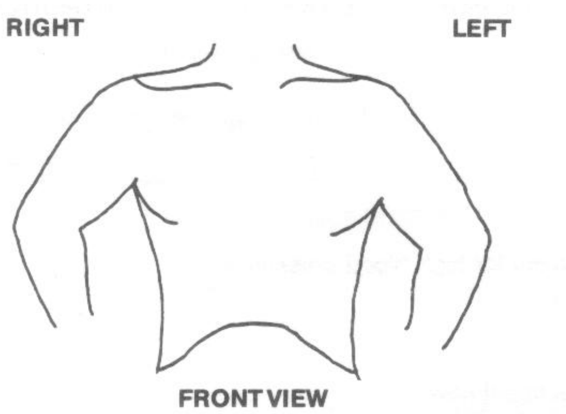
22. If you stand still, what happens to it?

1. Relieved
2. Not relieved

23. If relieved, how soon?

1. 10 minutes or less
2. More than 10 minutes

24. Can you specify where such pain or discomfort appeared? (*Please mark all appropriate sites by cross)*



Only for women

25. Do you still have periods?

1. Yes, regularly
2. Yes, irregularly **If YES**, go to question 32.
3. No

26. How old were you when the periods stopped? [ ][ ] Years

27. What was the cause of the menopause?

1. Natural
2. Surgical (operation)
3. Other (e.g. hormonal dysfunction)

28. Have you ever used hormonal contraception?

1. No, never
2. Yes, but I no longer use it
3. Yes and I still use it

20. Have you ever had hormonal replacement therapy?

1. Yes
2. No

30. If YES, are you still taking hormonal replacement therapy?

1. Yes
2. No

Health behaviours

31. How many hours during a typical week, <u>except when at work</u>, do you engage in physically demanding activities, such as housework, gardening, maintenance of the house (DIY) etc? [ ][ ][ ]

32. How many hours during a typical week do you engage in sports, games or hiking? | | |

33 How would you describe the **physical demands of your work**?

1. Sedentary work
2. Some physical activity at work
3. Heavy physical work
4. I am not working

34. Do you smoke cigarettes?

1. Yes, regularly, at least one cigarette a day on average
2. Yes, occasionally, less than one cigarette a day
3. No, I smoked in the past but I stopped
4. No, I have never smoked

35. For current and past smokers: How many cigarettes a day do you smoke now (or you used to smoke, if you stopped)? | | |

36. For current and past smokers: How old were you when you started smoking? | | | Years

37. For past smokers: How old were you when you stopped smoking? | | | Years

38. For past smokers: When did you stop smoking? | | | | | Calendar year

39. During the **last 12 months**, how often did you drink alcohol?

1. every day or at least 5 times a week
2. about 2-4 times a week
3. about once a week
4. about 1-3 times a month
5. less than once a month
6. never in the past year

40. The next few questions are about how much wine, beer and spirits you may have had during the last 12 months. When we say one drink, we mean 0.5 litre of beer, 2 dl glass of wine, or 5 cl of spirits. Please answer each question below - ie. cross a square **in each row -** to indicate how often you had that amount of alcohol during one day.
Here is an example how to calculate correct amount of alcohol on a single occasion: if you had 0.7 l bottle of wine AND two 5cl measures of spirit in a single occasion you had 3.5 drinks of wine and 2 drinks of spirit which is a total of 5.5 drinks. Then you need to choose correct column to indicate how often in the last year you had such amount of alcohol.

	Every day or almost every day	***3-4 per week***	***1-2 per week***	***2-3 per month***	***About once a month***	***6-11 in past year***	***3-5 in past year***	***1-2 in past year***	***Never in past year***

1. **For man.** How often in the last year did you have 5 or more drinks during one occasion?

5+ drinks (5+ x 0.5 l of beer or 5+ x 2 dl of wine or 5+ x 5 cl of spirits)	☐	☐	☐		☐	☐	☐	☐	☐

2. **For women.** How often in the last year did you have 3 or more drinks during one occasion?

3+ drinks (3+ x 0.5 l of beer or 3+ x 2 dl of wine or 3+ x 5 cl of spirits)	☐	☐	☐	☐	☐	☐	☐	☐	☐

41. How much beer (litres) do you usually drink during one week? ☐☐

42. How much wine (decilitres) do you usually drink during one week? ☐☐

43. How much spirits (decilitres) do you usually drink during one week? ☐☐

44. What was the largest amount of alcohol you had **on a single occasion** during <u>the last 4 weeks</u>?

☐☐☐☐ 0.5 L bottles or glasses of beer AND

☐☐☐☐ 2 dl glasses of wine AND

☐☐☐☐ 5 cl glasses of spirits (double shots)

45. During the **last 12 months**, how often did you drink enough to feel drunk?

1. every day or at least 5 times a week
2. about 1-4 times a week
3. about 1-3 times a month
4. 3-11 times a year
5. once or twice a year
6. never in the past year

46A. In the past, did you used to drink alcohol more often than you did during the last year?
1. No (if No move to question 47)
2. Yes –

46B. Why did you cut down on your drinking or stop drinking?
1. because of ill health
2. because of work
3. family
4. other reason

47. In the **last 12 months**, did you have any of the following experiences?

Please cross appropriate box in each row:	Yes	No
Have you ever felt you should cut down on your drinking?	☐ 1	☐ 2
Have people ever annoyed you by criticising your drinking?	☐ 1	☐ 2
Have you ever felt bad or guilty about your drinking?	☐	☐
Have you ever had a drink first thing in the morning to steady your nerves or get rid of a hangover?	☐ 1	☐ 2

48. How do the following factors influence human health?

Please cross appropriate box in each row:	Improve		No effect	Make It Worse	
	Strongly	Slightly		Slightly	Strongly
Eating meat	☐ 1	☐ 2	☐ 3-4	☐ 5	☐ 6
Eating fruit and vegetables	☐ 1	☐ 2	☐ 3-4	☐ 5	☐ 6
Lack of physical activity	☐ 1	☐ 2	☐ 3-4	☐ 5	☐ 6
Obesity	☐ 1	☐ 2	☐ 3-4	☐ 5	☐ 6
Smoking	☐ 1	☐ 2	☐ 3-4	☐ 5	☐ 6
Drinking alcohol	☐ 1	☐ 2	☐ 3-4	☐ 5	☐ 6
Passive smoking	☐ 1	☐ 2	☐ 3-4	☐ 5	☐ 6
Environmental pollution	☐ 1	☐ 2	☐ 3-4	☐ 5	☐ 6

Lack of money	☐ 1	☐ 2	☐ 3-4	☐ 5	☐ 6
Stress	☐ 1	☐ 2	☐ 3-4	☐ 5	☐ 6
Exercise	☐ 1	☐ 2	☐ 3-4	☐ 5	☐ 6

49. Below is a list of the ways you might have felt or behaved during **the last week**.
For each of the following statements, please indicate how often you felt that way:

During the past week:	*Less than one day*	*1-2 days*	*3-4 days*	*5-7 days*
a) I was bothered by things that usually do not bother me	☐ 1	☐ 2	☐ 3	☐ 4
b) I did not feel like eating, my appetite was poor	☐ 1	☐ 2	☐ 3	☐ 4
c) I felt that I could not shake off the blues even with help from my family and friends	☐ 1	☐ 2	☐ 3	☐ 4
d) I felt that I was just as good as other people	☐ 1	☐ 2	☐ 3	☐ 4
e) I had trouble keeping my mind on what I was doing	☐ 1	☐ 2	☐ 3	☐ 4
f) I felt depressed.	☐ 1	☐ 2	☐ 3	☐ 4
g) I felt that everything I did was an effort	☐ 1	☐ 2	☐ 3	☐ 4
h) I felt hopeful about the future	☐ 1	☐ 2	☐ 3	☐ 4
i) I thought my life had been a failure	☐ 1	☐ 2	☐ 3	☐ 4
j) I felt fearful	☐ 1	☐ 2	☐ 3	☐ 4
k) My sleep was restless	☐ 1	☐ 2	☐ 3	☐ 4
l) I was happy	☐ 1	☐ 2	☐ 3	☐ 4
m) I talked less than usual	☐ 1	☐ 2	☐ 3	☐ 4
n) I felt lonely	☐ 1	☐ 2	☐ 3	☐ 4
o) People were unfriendly	☐ 1	☐ 2	☐ 3	☐ 4
p) I enjoyed life	☐ 1	☐ 2	☐ 3	☐ 4
q) I had crying spells	☐ 1	☐ 2	☐ 3	☐ 4
r) I felt sad	☐ 1	☐ 2	☐ 3	☐ 4
s) I felt people dislike me	☐ 1	☐ 2	☐ 3	☐ 4
t) I could not get going	☐ 1	☐ 2	☐ 3	☐ 4

50**. Here is a list of statements that people have used to describe their lives or how they feel. We would like to know how often, if at all, you think they apply to you.**

	Often	Sometimes	Not often	Never	Don't know	Refused to answer	Missing
My age prevents me from doing the things I would like to	☐1	☐2	☐3	☐4	☐5	☐6	☐9
I feel that what happens to me is out of my control	☐1	☐2	☐3	☐4	☐5	☐6	☐9
I feel left out of things	☐1	☐2	☐3	☐4	☐5	☐6	☐9
I can do the things that I want to do	☐1	☐2	☐3	☐4	☐5	☐6	☐9
Family responsibilities prevent me from doing what I want to do	☐1	☐2	☐3	☐4	☐5	☐6	☐9
Shortage of money stops me from doing the things that I want to do	☐1	☐2	☐3	☐4	☐5	☐6	☐9
I look forward to each day	☐1	☐2	☐3	☐4	☐5	☐6	☐9
I feel that my life has meaning	☐1	☐2	☐3	☐4	☐5	☐6	☐9
On balance, I look back on my life with a sense of happiness	☐1	☐2	☐3	☐4	☐5	☐6	☐9
I feel full of energy these days	☐1	☐2	☐3	☐4	☐5	☐6	☐9
I feel that life is full of opportunities	☐1	☐2	☐3	☐4	☐5	☐6	☐9
I feel that the future looks good for me	☐1	☐2	☐3	☐4	☐5	☐6	☐9

Social and economic conditions

51. How often does it happen that you do not have enough **money for food** which you and your family need? And how often did this happen before 1990? **We would reword it in Russian**

…enough money to buy food …

at present

☐ 1. all the time
☐ 2. often
☐ 3. sometimes
☐ 4. rarely
☐ 5. never

52. How often does it happen that you do not have enough **money for clothing** which you and your family need? And how often did this happen before 1990?

at present
- [ ] 1. all the time
- [ ] 2. often
- [ ] 3. sometimes
- [ ] 4. rarely
- [ ] 5. never ________________

53. Do you have difficulties with **paying bills** (for housing, electricity, heating etc)? And what was the situation before 1990?

at present
- [ ] 1. all the time
- [ ] 2. often
- [ ] 3. sometimes
- [ ] 4. rarely
- [ ] 5. never ________________

54. Are you in receipt of any of the following benefits at the moment? *Choose all that apply. ?*

1. Child benefit
2. Unemployment benefit
3. Care allowance (care for invalid)
4. Widow(er)'s pension
5. Social assistance (e.g. with food, fuel, clothes or medication)
6. Others – please specify: ________________
7. Do not receive any state benefits

55. How many **rooms** does your house/flat have **(excluding kitchen and bathrooms)**? [|]

56. How many **adults** (18 years or older) live in your house/flat? [|]

57. How many **children** (under 18 years old) live in your house/flat? [|]

58. What is your current economic activity?

1. Employed
2. Entrepreneur (owner of a company)
3. Self-employed / freelance
4. Housewife
5. **Farmer**
6. Pensioner, still employed
7. Pensioner, not employed. At what age did you retire ? …… [|] years old
8. Unemployed

59. What was your main life-time occupation? _

____

60. Have you ever experienced unemployment?

1. No
2. Yes, for up to 3 months in total
3. Yes, for 3 months to 1 year
4. Yes, for more than one year

61. If you are <u>out of work and not retired</u>, do you look for a job?

1. Yes
2. No, no hope
3. No, I choose not to work
4. No, I am too ill to work
5. No, I am retired
6. No, other reason: please specify ____________________

62. Now, would you tell us about your household? Below is a list of various items, which of the following do you have in your household?

	Yes	No, I do not want it	No, I can not afford it
Microwave	☐1	☐2	☐3
DVD player	☐1	☐2	☐3
Television	☐1	☐2	☐3
Washing machine	☐1	☐2	☐3
Dishwasher	☐1	☐2	☐3
Car	☐1	☐2	☐3
Freezer	☐1	☐2	☐3
Cottage (for holidays / weekends etc.)	☐1	☐2	☐3
Videocamera / camcorder	☐1	☐2	☐3
Satellite / cable TV	☐1	☐2	☐3
Telephone	☐1	☐2	☐3
Mobile phone	☐1	☐2	☐3
Internet at home	☐1	☐2	☐3
Bank account	☐1	☐2	☐3
Debit card	☐1	☐2	☐3
Credit card	☐1	☐2	☐3

63A What religious denomination do you refer yourself to?

1 = None → [SKIP TO]
2 = Muslim (Islam)
3 = Buddhist (Lamaism)
4 = Jewish
5 = Orthodox
6 = Armenian-Gregorian
10 = Other (specify):____________________
99 = Refused to answer

63B Do you follow the ceremonies and rules prescribed by your religion?

1 = yes, regularly
2 = yes, from time to time
3 = no

98 = Do not know
99 = Refusal

64 What nationality do you consider yourself to be? –

.

1 = Kazakh
2 = Russian
3 = Other, specify __________

65 How many children they have?

THANK YOU VERY MUCH FOR YOUR COOPERATION!

THANK YOU FOR COMPLETING THE QUESTIONNAIRE

We would like to contact you from time to time and ask you a few short questions about your health. If this is alright, would you please write your area code and telephone number in the box

Area code	Telephone number

Appendix 3. The Astana Health Study Questionnaire (case-control study)

The case-control questionnaire was identical to that used in the cross-sectional study, except that questions on medical history and risk factors were asked with the phrase *"before your current illness".*

Appendix 4. Comparison of selected characteristics between subjects with complete and incomplete data (cross-sectional sample)

Variable name	Complete data	Incomplete data *	P value
Total number of participants	**867**	**110**	
Sex, (%)			
Men	43.5	50.0	
Women	56.5	50.0	0.195
Age, years, mean (SD)	60.7 (7.3)	61.3 (7.4)	0.397
Age groups, years (%)			
50-54	27.2	25.5	
55-59	23.3	20.0	
60-64	20.2	23.6	
65-69	14.9	15.5	
70-74	14.4	15.5	0.872
Marital status, (%)			
Married	74.2	67.9	
Unmarried	25.8	32.1	0.170
BMI, mean (SD)	29.5 (5.1)	29.8 (5.0)	0.498
SBP, mean (SD)	136.2 (22.0)	140.5 (22.2)	0.072
DBP, mean (SD)	89.6 (13.5)	91.1 (12.8)	0.302
Cholesterol, mean (SD)	5.7 (1.2)	5.7 (2.1)	0.755
Ldl, mean (SD)	3.6 (0.03)	3.5 (0.1)	0.362
Hdl, mean (SD)	1.4 (0.01)	1.3 (0.05)	0.047
Triglycerides, mean (SD)	1.6 (0.04)	1.6 (0.2)	0.564
Weight, mean (SD)	78.0 (0.5)	78.1 (1.3)	0.978
Waist, mean (SD)	96.4 (0.4)	97.5 (1.1)	0.417
Hip, mean (SD)	105.8 (0.4)	106.7 (1.0)	0.392
Education, (%)			
Higher	29.8	28.3	
Apprenticeship	34.5	31.1	
Primary and secondary	35.8	40.6	0.612
Ethnicity, (%)			
Kazakhs	58.5	55.1	
Russians	25.6	32.7	
Others	15.9	12.2	0.237
Car ownership, (%)			
Yes	54.9	64.4	
No	45.1	35.6	0.090
Household possessions, quartiles (%)			
Q1 lower level of possessions	25.1	19.4	
Q2 medium level of possessions	28.5	35.5	
Q3 higher level of possessions	30.9	37.1	
Q4 highest level of possessions	15.5	8.1	0.205

*** missing in at least one characteristic in analysis**

Appendix 5. Comparison of age-sex-adjusted analyses in all subjects with complete case analysis (cross-sectional sample)

	Incomplete Age and sex adjusted	Complete Age and sex adjusted	Complete Multivariate
PREVALENCE HT	N=964	N=867	N=867
Education			
Higher	1	1	1
Apprenticeship	0.79 (0.55-1.15)	0.82 (0.56-1.20)	0.70 (0.45-1.07)
Primary&Secondary	0.73 (0.51-1.05)	0.73 (0.50-1.07)	0.60 (0.39-0.94)
Car ownership			
Yes	1	1	1
No	0.91 (0.67-1.23)	0.92 (0.68-1.26)	1.06 (0.74-1.52)
Possessions			
Q1 highly deprived	1	1	1
Q2	1.96 (1.29-2.97)	1.85 (1.21-2.82)	1.64 (1.04-2.58)
Q3	1.46 (0.99-2.16)	1.42 (0.95-2.11)	1.18 (0.74-1.88)
Q4 less deprived	1.42 (0.88-2.27)	1.39 (0.86-2.25)	1.14 (0.62-2.10)
PREVALENCE DM	953	745	
Education			
Higher	1	1	1
Apprenticeship	1.09 (0.68-1.77)	1.06 (0.63-1.77)	1.50 (0.84-2.68)
Primary&Secondary	0.83 (0.50-1.35)	0.88 (0.51-1.50)	1.34 (0.71-2.51)
Car ownership			
Yes	1	1	1
No	0.79 (0.53-1.18)	0.77 (0.49-1.19)	1.03 (0.61-1.75)
Possessions			
Q1 highly deprived	1		1
Q2	1.71 (0.95-3.06)	2.0 (1.06-3.76)	1.73 (0.87-3.44)
Q3	1.42 (0.79-2.58)	1.43 (0.75-2.72)	0.94 (0.44-1.98)
Q4 less deprived	2.48 (1.29-4.75)	2.47 (1.24-4.91)	1.38 (0.58-3.26)
PREVALENCE HC		867	
Education			
Higher	1	1	1
Apprenticeship	0.70 (0.50-0.98)	0.75 (0.53-1.07)	0.99 (0.67-1.47)
Primary&Secondary	0.64 (0.46-0.90)	0.65 (0.46-0.93)	0.98 (0.65-1.48)
Car ownership			
Yes	1		1
No	0.82 (0.62-1.09)	0.82 (0.61-1.09)	0.95 (0.67-1.33)
Possessions			
Q1 highly deprived	1		1
Q2	1.22 (0.83-1.80)	1.19 (0.80-1.77)	1.04 (0.68-1.61)
Q3	1.40 (0.95- 2.04)	1.35 (0.93-2.03)	0.98 (0.62-1.54)
Q4 less deprived	2.32 (1.47-3.67)	2.34 (1.50-3.81)	1.21 (0.69-2.15)
PREVALENCE OB	N=947	N=870	N=870
Education			
Higher	1	1	1
Apprenticeship	1.06 (0.76-1.48)	1.03 (0.73-1.46)	1.18 (0.80-1.73)
Primary&Secondary	1.19 (0.86-1.65)	1.12 (0.79-1.57)	1.57 (1.05-2.34)

	Incomplete Age and sex adjusted	Complete Age and sex adjusted	Complete Multivariate
Car ownership			
Yes	1		1
No	0.70 (0.53-0.91)	0.66 (0.50-0.88)	0.85 (0.61-1.18)
Possessions			
Q1 highly deprived	1	1	
Q2	1.62 (1.11-2.36)	1.72 (1.17-2.53)	1.43 (0.94-2.16)
Q3	2.08 (1.44-3.01)	2.19 (1.50-3.21)	1.99 (1.28-3.08)
Q4 less deprived	2.01 (1.28-3.16)	2.16 (1.36-3.42)	1.87 (1.06-3.30)

Appendix 6. Socio-economic characteristics of the study sample by urban and rural area of residence in Astana region in men and women

	Astana			Akmol		
Variable name	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**
Total number of participants	**230**	**263**	**493**	**202**	**282**	**484**
Age, years, mean (SD)	60.7 (7.3)	61.6 (7.3)	61.2 (7.3)	60.8 (7.5)	59.9 (7.1)	60.3 (7.3)
Age groups, years (%)						
50-54	27.0	24.3	25.6	27.7	29.1	28.5
55-59	20.9	20.2	20.5	19.3	29.8	25.4
60-64	22.6	21.7	22.1	23.3	16.0	19.0
65-69	15.7	16.7	16.2	14.4	13.1	13.6
70-74	13.9	17.1	15.6	15.4	12.1	13.4
Marital status, (%)						
Married	92.6	56.3	73.2	91.1	61.3	73.8
Unmarried	7.4	43.7	26.8	8.9	38.7	26.2
Education, (%)						
Higher	51.3	36.9	43.6	16.1	14.6	15.2
Apprenticeship	25.7	34.2	30.2	30.7	43.4	38.1
Primary and secondary	23.0	28.9	26.2	53.3	42.0	46.7
Ethnicity, (%)						
Kazakhs	64.9	51.5	57.8	63.4	55.0	58.5
Russians	19.3	31.7	25.9	22.8	29.8	26.9
Others	15.8	16.8	16.3	13.9	15.3	14.7
Car ownership, (%)						
Yes	69.2	54.7	61.5	58.8	43.7	49.9
No	30.8	45.3	38.5	41.2	56.3	50.1

	Astana			Akmol		
Variable name	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**
Unemployment, (%)						
Never	60.1	67.3	63.9	82.6	80.2	81.2
Less than 1 year	21.1	8.9	14.6	6.0	8.3	7.3
More than 1 year	18.9	23.9	21.5	11.4	11.5	11.5
Deprivation level, (%)						
High level	19.7	33.3	27.0	19.1	30.6	25.8
Intermediate	31.6	27.6	29.5	35.2	32.7	33.8
Low level or not	48.7	39.1	43.6	45.7	36.7	40.4
Household possessions, quartiles (%)						
Q1 lower level of possessions	12.4	20.7	16.8	35.4	30.8	32.7
Q2 medium level of possessions	17.9	24.4	21.3	32.3	39.6	36.6
Q3 higher level of possessions	35.8	34.2	34.9	28.7	27.1	27.7
Q4 highest level of possessions	33.9	20.7	26.9	3.7	2.6	3.0

Appendix 7. Cardio-metabolic risk factors and behavioral characteristics of the study sample by urban and rural area of residence in Astana region

	Astana city			Akmol village		
Variable name	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**
Total number of participants	**230**	**263**	**493**	**202**	**282**	**484**
Behavioral factors						
Smoking status, (%)						
Non smoker	24.7	92.3	60.6	36.8	93.1	69.5
Current smoker	32.6	4.7	17.7	26.9	4.3	13.8
Past smoker	42.7	3.1	21.7	36.3	2.5	16.7
Alcohol consumption, (%)						
Never	35.0	45.1	40.3	56.2	66.5	62.1
Less 3 times a month	51.8	52.6	52.2	40.3	32.3	35.7
More 4 time a month	13.3	2.4	7.5	3.5	1.1	2.1
Blood pressure characteristics						
Systolic blood pressure, (mmHg), mean (SD)	136.2 (22.9)	134.0 (22.7)	135.0 (22.8)	139.9 (21.1)	137.3 (21.0)	138.4 (21.1)
Diastolic blood pressure, (mmHg), mean (SD)	87.5 (13.6)	88.0 (13.8)	87.8 (13.7)	91.6 (12.8)	91.9 (12.8)	91.8 (12.8)
Diabetes risk factors						
Fasting plasma glucose, mean (SD)	5.9 (2.3)	5.7 (2.2)	5.8 (2.3)	5.1 (2.2)	5.4 (1.9)	5.3 (2.0)
Family history of diabetes among all, (%)						
No	79.7	79.2	79.7	87.8	88.1	88.5
Yes	20.3	20.9	20.3	12.2	11.9	11.5
Blood lipids						
Total cholesterol (mmol/l), mean (SD)	5.6 (1.2)	6.1 (1.7)	5.9 (1.5)	5.1 (1.0)	5.7 (1.1)	5.4 (1.1)
LDL-C (mmol/l), mean (SD)	3.6 (0.9)	3.8 (1.0)	3.7 (1.0)	3.3 (0.9)	3.6 (1.0)	3.5 (1.0)
HDL-C (mmol/l), mean (SD)	1.2 (0.3)	1.4 (0.4)	1.3 (0.4)	1.4 (0.4)	1.5 (0.4)	1.5 (0.4)
TG (mmol/l), mean (SD)	1.8 (1.3)	1.6 (0.9)	1.7 (1.1)	1.5 (1.3)	1.5 (0.8)	1.5 (1.0)

	Astana city			Akmol village		
Variable name	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**
Overweight and Obesity characteristics						
Weight, mean (SD)	83.1 (14.8)	76.2 (13.9)	79.4 (14.7)	78.6 (14.6)	75.2 (14.4)	76.6 (14.6)
Height, mean (SD)	169.9 (6.4)	157.6 (5.9)	163.3 (8.7)	168.2 (6.9)	157.7 (7.1)	162.1 (8.7)
Waist circumference, mean (SD)	100.6 (12.2)	95.9 (11.0)	98.0 (11.8)	95.6 (13.2)	94.6 (13.8)	95.0 (13.6)
Hip circumference, mean (SD)	103.9 (9.3)	108.1 (9.4)	106.2 (9.6)	101.5 (9.2)	108.5 (11.3)	105.6 (11.0)
BMI, mean (SD)	28.7 (4.5)	30.7 (5.1)	29.8 (4.9)	27.7 (4.6)	30.3 (5.5)	29.2 (5.3)
BMI categories, (kg/m^2) (%)						
18.50 - 24.99 (normal)	20.4	12.2	16.0	29.0	17.4	22.2
25.00 - 29.99 (pre-obese)	42.2	34.7	38.2	41.0	32.3	35.9
Over 30 (obese)	37.3	53.1	45.8	30.0	50.4	41.9
Waist–hip ratio categories, (%)						
< 0.9 in men and < 0.85 in women	12.2	23.8	18.5	31.0	43.3	38.2
≥ 0.9 in men and ≥ 0.85 in women	87.8	76.3	81.5	69.0	56.7	61.8

Appendix 8. Associations between independent variables and serum cholesterols in Astana region, OR (95% CI)

	TC Mean (SE)*	Raised TC Prevalence[1] OR (95% CI)	LDL mean (SE)*	Raised LDL Prevalence[1] OR (95% CI)	HDL mean (SE)*	Low HDL Prevalence[1] OR (95% CI)	TG mean (SE)*	Raised TG Prevalence[1] OR (95% CI)
Sex								
Males	5.12 (0.04)	1	3.47 (0.05)	1	1.29 (0.02)	1	1.67 (0.07)	1
Females	5.70 (0.05)	1.84 (1.38-2.46)	3.73 (0.04)	1.82 (1.35-2.45)	1.45 (0.02)	0.30 (0.21-0.42)	1.54 (0.04)	0.83 (0.59-1.18)
P value	<0.001		<0.001		<0.001		0.093	
Age groups (years)								
50-54	5.36 (0.06)	1	3.57 (0.07)	1	1.36 (0.03)	1	1.65 (0.10)	1
55-59	5.48 (0.06)	1.18 (0.78-1.77)	3.63 (0.07)	1.40 (0.94-2.10)	1.39 (0.03)	1.03 (0.63-1.67)	1.75 (0.11)	1.20 (0.74-1.95)
60-64	5.35 (0.06)	1.19 (0.78-1.81)	3.62 (0.06)	1.24 (0.82-1.90)	1.39 (0.03)	0.82 (0.49-1.36)	1.58 (0.06)	1.25 (0.76-2.05)
65-69	5.40 (0.08)	1.02 (0.65-1.61)	3.53 (0.08)	0.90 (0.56-1.46)	1.33 (0.03)	0.91 (0.52-1.58)	1.51 (0.06)	0.79 (0.43-1.45)
70-75	5.39 (0.10)	1.21 (0.75-1.94)	3.60 (0.08)	1.01 (0.62-1.64)	1.36 (0.03)	0.94 (0.54-1.66)	1.47 (0.08)	0.94 (0.53-1.70)
P value	0.643		0.721		0.501		0.339	
Urban/Rural								
Astana (urban)	5.85 (0.06)	1	3.70 (0.04)	1	1.29 (0.02)	1	1.68 (0.05)	1
Akmol (rural)	5.40 (0.05)	0.43 (0.32-0.58)	3.48 (0.04)	0.67 (0.50-0.89)	1.45 (0.02)	0.52 (0.36-0.74)	1.54 (0.06)	0.78 (0.55-1.10)
P value	<0.001		0.001		0.001		0.036	
BMI, (kg/m^2)								
18.5-24.9	5.46 (0.11)	1	3.41 (0.07)	1	1.57 (0.04)	1	1.16 (0.05)	1
25-29.9	5.63 (0.06)	1.71 (1.15-2.56)	3.61 (0.05)	1.27 (0.81-1.98)	1.37 (0.02)	1.67 (0.95-2.93)	1.58 (0.07)	3.34 (1.55-7.21)
≥30	5.68 (0.07)	1.62 (1.09-2.41)	3.63 (0.05)	1.39 (0.90-2.16)	1.28 (0.02)	2.38 (1.36-4.16)	1.86 (0.07)	5.75 (2.70-12.24)
P value	0.291		0.051		0.001		0.001	
WHR, obesity								
No	5.32 (0.07)	1	3.34 (0.06)	1	1.53 (0.03)	1	1.15 (0.03)	1
Yes	5.74 (0.05)	1.97 (1.43-2.71)	3.70 (0.04)	2.07 (1.45-2.95)	1.31 (0.01)	1.84 (1.18-2.88)	1.77 (0.05)	4.81 (2.71-8.55)
P value	<0.001		0.001		0.001		0.001	
Diabetes								
No	5.60 (0.04)	1	3.58 (0.03)	1	1.39 (0.01)	1	1.52 (0.04)	1
Yes	5.78 (0.14)	1.39 (0.87-2.21)	3.66 (0.09)	1.10 (0.71-1.68)	1.21 (0.03)	2.17 (1.36-3.44)	2.24 (0.16)	3.09 (2.00-4.77)
P value	0.080		0.355		0.001		0.001	

Hypertension								
No	5.69 (0.14)	1	3.54 (0.06)	1	1.41 (0.03)	1	1.49 (0.07)	1
Yes	5.64 (0.05)	1.07 (0.77-1.48)	3.61 (0.04)	1.12 (0.80-1.56)	1.34 (0.02)	1.01 (0.69-1.50)	1.68 (0.06)	1.79 (1.15-2.78)
P value	0.801		0.341		0.040		0.041	
Smoking								
Current smoker	5.84 (0.17)	1	3.71 (0.08)	1	1.29 (0.03)	1	1.68 (0.10)	1
Past smoker	5.85 (0.13)	1.14 (0.71-1.83)	3.83 (0.13)	0.70 (0.42-1.17)	1.35 (0.04)	0.76 (0.46-1.24)	1.74 (0.10)	0.90 (0.51-1.58)
Non-smoker	5.55 (0.06)	0.95 (0.60-1.51)	3.51 (0.05)	0.52 (0.31-0.85)	1.41 (0.02)	0.47 (0.29-0.77)	1.55 (0.06)	0.65 (0.37-1.14)
P value	0.088		0.049		0.024		0.311	
Marital status								
Unmarried	5.49 (0.14)	1	3.33 (0.10)	1	1.37 (0.07)	1	1.67 (0.27)	1
Married	5.61 (0.05)	1.22 (0.84-1.75)	3.58 (0.04)	0.96 (0.68-1.36)	1.37 (0.02)	0.67 (0.42-1.07)	1.61 (0.04)	1.32 (0.84-2.08)
P value	0.729		0.749		0.668		0.967	
Education								
Primary	5.68 (0.08)	1	3.62 (0.06)	1	1.39 (0.02)	1	1.59 (0.07)	1
Vocational	5.48 (0.07)	0.95 (0.68-1.34)	3.47 (0.05)	0.80 (0.56-1.15)	1.38 (0.03)	1.22 (0.80-1.86)	1.65 (0.09)	1.10 (0.72-1.69)
Higher	5.76 (0.07)	1.89 (1.29-2.78)	3.70 (0.06)	1.24 (0.87-1.76)	1.32 (0.02)	1.11 (0.71-1.71)	1.61 (0.06)	1.21 (0.79-1.86)
P value	0.022		0.026		0.145		0.729	
Ethnicity								
Kazakh	5.56 (0.07)	1	3.49 (0.04)	1	1.41 (0.02)	1	1.53 (0.04)	1
Russian	5.68 (0.08)	1.35 (0.95-1.92)	3.68 (0.06)	1.44 (1.03-2.03)	1.29 (0.02)	2.43 (1.62-3.63)	1.77 (0.12)	1.36 (0.90-2.05)
Other	5.79 (0.10)	1.39 (0.91-2.14)	3.76 (0.08)	2.11 (1.42-3.14)	1.30 (0.03)	1.34 (0.80-2.26)	1.74 (0.12)	1.65 (1.03-2.65)
P value	0.039		0.001		0.001		0.023	
Car ownership								
No	5.56 (0.05)	1	3.55 (0.05)	1	1.42 (0.02)	1	1.55 (0.07)	1
Yes	5.62 (0.05)	0.92 (0.68-1.24)	3.60 (0.04)	1.22 (0.91-1.65)	1.34 (0.02)	1.48 (1.02-2.14)	1.64 (0.05)	1.06 (0.74-1.52)
P value	0.596		0.546		0.005		0.443	
Deprivation								
High level	5.55 (0.10)	1	3.53 (0.06)	1	1.38 (0.03)	1	1.46 (0.06)	1
Intermediate	5.62 (0.06)	1.41 (0.97-2.06)	3.59 (0.06)	1.19 (0.81-1.75)	1.39 (0.02)	0.60 (0.37-0.97)	1.61 (0.07)	1.44 (0.89-2.33)
Low level	5.66 (0.06)	1.53 (1.07-2.19)	3.62 (0.05)	1.30 (0.90-1.87)	1.34 (0.02)	0.89 (0.58-1.36)	1.69 (0.07)	1.44 (0.91-2.28)
P value	0.863		0.616		0.372		0.162	

* Age and sex standardized means of serum lipids; [1] Age and sex adjusted prevalence of raised TC ≥ 5 mmol/l (200 mg/dl) or on treatment,
[2] Age and sex adjusted prevalence of serum lipids: raised LDL ≥ 4.15 mmol/l (160 mg/dl), low HDL < 1.04 mmol/l (40 mg/dl), raised TG ≥ 2.26 mmol/l (200 mg/dl)

Appendix 9. Population-attributable risk proportion for various risk factors among ACS and Stroke cases

	Prevalence Controls	Prevalence Cases	OR[1] (95% CI)	PAR[1]% (95% CI)	OR[2] (95% CI)	PAR[2]% (95% CI)
BOTH ACS AND STROKE						
Current and former smoking (all smokers vs never)	35.0%	52.6%	2.06 (1.67-2.55)	27.1 (19.6-34.0)	1.32 (1.00-1.74)	12.5 (0.5-23.0)
Frequent Alcohol intake	4.8%	13.5%	3.07 (2.09-4.51)	9.1 (5.8-12.3)	2.43(1.65-3.59)	8.0 (4.4-11.4)
History of Hypertension	59.6%	68.5%	1.48 (1.19-1.84)	22.1 (10.2-32.5)	1.63 (1.30-2.04)	26.5 (15.0-36.4)
History of diabetes	13.7%	18.0%	1.38 (1.04-1.82)	4.9 (0.5-9.2)	1.42 (1.05-1.91)	5.3 (0.7-9.7)
History of hypercholesterolemia	29.9%	23.3%	0.71 (0.56-0.91)	-9.3 (-16.2 to -2.9)	0.83 (0.65-1.06)	-4.7 (-11.3-1.5)
Overweight	80.9%	75.7%	0.73 (0.57-0.94)	-27.5 (-54.9 to -4.9)	0.84 (0.65-1.08)	-14.9 (-40.1-5.9)
Unemployment	27.5%	40.3%	1.78 (1.43-2.22)	17.6 (10.9-23.9)	1.94 (1.53-2.46)	19.5 (12.7-.25.8)
ACS						
	Prevalence Controls	**Prevalence Cases**	**OR[1] (95% CI)**	**PAR[1]% (95% CI)**	**OR[2] (95% CI)**	**PAR[2]% (95% CI)**
Current and former smoking (all smokers vs never)	35.0%	58.2%	2.58 (2.00-3.33)	35.6 (26.4-43.7)	1.48 (1.06-2.05)	18.8 (3.4-31.8)
Frequent Alcohol intake	4.8%	10.8%	2.39 (1.51-3.78)	6.3 (2.4-10.0)	1.74 (1.09-2.76)	4.6 (0.4-8.6)
History of Hypertension	59.6%	64.7%	1.24 (0.96-1.61)	12.7 (-2.7-.25.8)	1.42 (1.09-1.85)	19.1 (4.5-31.4)
History of diabetes	13.7%	15.4%	1.14 (0.81-1.61)	1.9 (-3.3-6.8)	1.14 (0.79-1.65)	1.9 (-3.6-7.1)
History of hypercholesterolemia	29.9%	25.2%	0.79 (0.60-1.04)	-6.8 (-14.9-0.8)	0.98 (0.73-1.31)	-0.6 (-8.4-6.6)
Overweight & Obesity (BMI>30)	80.9%	73.1%	0.64 (0.48-0.86)	-40.7 (-75.2 to -13.0)	0.73 (0.54-0.99)	-27.2 (-60.0 to -1.1)
Central obesity	71.7%	87.5%	2.78 (1.94-3.96)	56.0 (40.4-67.5)	2.36 (1.64-3.40)	50.5 (32.4-63.7)
Unemployment	27.5%	39.0%	1.68 (1.30-2.19)	15.8 (7.5-23.4)	1.80 (1.35-2.41)	17.3 (8.7-25.2)

	Prevalence Controls	Prevalence Cases	OR[1] (95% CI)	PAR[1]% (95% CI)	OR[2] (95% CI)	PAR[2]% (95% CI)
STROKE						
Current and former smoking (all smokers vs never)	35.0%	44.6%	1.49 (1.12-2.00)	14.8 (3.4-24.7)	1.08 (0.74-1.58)	3.4 (-13.9-18.0)
Frequent Alcohol intake	4.8%	17.2%	4.10 (2.61-6.44)	13.0 (7.6-18.1)	3.86 (2.41-6.19)	12.8 (7.3-17.9)
History of Hypertension	59.6%	74.2%	1.95 (1.42-2.70)	36.2 (19.5-49.5)	2.03 (1.45-2.82)	37.6 (20.9-50.8)
History of diabetes	13.7%	21.9%	1.76 (1.23-2.52)	9.46 (2.7-15.8)	1.76 (1.21-2.54)	9.4 (2.5-15.8)
History of hypercholesterolemia	29.9%	20.7%	0.61 (0.43-0.87)	-13.1(-.22.2 to -4.7)	0.66 (0.47-0.94)	-10.5 (-19.6 to -2.2)
Overweight & Obesity (BMI>30)	80.9%	79.3%	0.90 (0.63-1.29)	-8.4 (-43.9-18.4)	1.00 (0.70-1.43)	-0.2 (-33.0-24.6)
Unemployment	27.5%	42.3%	1.93 (1.43-2.61)	20.4 (10.3-29.3)	2.19 (1.58-3.05)	23.0 (12.9-31.9)

1 unadjusted, 2 adjusted for age and sex

Appendix 10. Published studies on CVD and cardiovascular risk factors in Central Asia identified by the systematic review.

	Author	Year	Country (language)	Outcome	Area of residence	Comments
1	Nasyrov MM et al	1985	Uzbekistan (Russian)	Ischemic heart disease	Rural	IHD prevalence was approximately 9%.
2	Makhmudov BKh et al	1986	Uzbekistan (Russian)	Ischemic heart disease	Urban	IHD prevalence was 10.8% in total population and 9.5% among Uzbeks ethnicity.
3	Salakhitdinov AS et al	1989	Uzbekistan (Russian)	Arterial hypertension	Rural	Intervention in a rural community seemed to improve awareness, treatment and control of arterial hypertension.
4	Mishra V et al	2006	Uzbekistan (English)	Obesity and hypertension	Urban/Rural	Description of Uzbekistan Health Examination Survey in 2002 to study cardio-metabolic risk factors; no specific results were shown.
5	Madaminov IK et al	1987	Kyrgyzstan (Russian)	Ischemic heart disease	Urban	IHD prevalence 13.9% among Kyrgyzes, 12.8% in Russians and 8.3% in other central Asian nationalities.
6	Young JH et al	2005	Kyrgyzstan (English)	Hypertension	Rural	High prevalence of hypertension in Kyrgyzstan and forecast an epidemic of cardiovascular disease in Central Asia.
7	Mirrakhimov EM et al	2014	Kyrgyzstan (English)	Dyslipidemia and obesity	Urban/Rural	High prevalence of obesity (29%) in Kyrgyz population.
8	Matthys B et al	2014	Tajikistan (English)	Cardiometabolic risk factors	Urban/Rural	21.2% of the participants had diabetes, 61.5% had BMI ≥ 25, 45.6% had hypertension.
9	Abzhanov EA et al	1977	Kazakhstan (Russian)	Ischemic heart disease	Rural	Differences in IHD prevalence between office workers and labourers. Overall IHD was found in 4.1%, with 47.2% cases being newly diagnosed.
10	Kadyrova RKh et al	1990	Kazakhstan (Russian)	Obesity	Urban	Prevalence of overweight was 36%, obesity 24%. Obesity was higher in urban than in rural region among women, the opposite was seen in men.
11	Kulkayeva G et al	2012	Kazakhstan (English)	CVD risk factors	Rural	Prevalence of CVD risk factors were high but the level of awareness was very low.
12	Abikulova AK et al	2013	Kazakhstan (English)	NCDs	Urban/Rural	High levels of inequalities in SRH. Ethnic Russians and unmarried participants had greater odds for poor vs. good health.

	Author	Year	Country (language)	Outcome	Area of residence	Comments
13	Shinbolatova A et al	2014	Kazakhstan (English)	Arterial Hypertension	Urban/Rural	Prevalence of hypertension was higher among urban residents but rural citizens had more complications and lower level of control.
14	Davletov K et al	2015	Kazakhstan (English)	Cardiovascular mortality	Urban/Rural	CVD mortality rates were the highest in Northeastern region in Kazakhstan with predominant Russian population. Self-reported alcohol drinking was higher among ethnic Russians.
15	Davletov K et al	2016	Kazakhstan (English)	All-cause mortality	Urban/Rural	All-cause mortality rates were higher among ethnic Russians, also higher rates of alcohol consumption and smoking among ethnic Russians.
16	Akimbaeva Z et al	2017	Kazakhstan (English)	Myocardial infarction	Urban/Rural	Hospital mortality among STEMI patients was 9.0%. Various predictors of hospital deaths in STEMI patients were studied.
17	Glasunov IS et al	1988	Central Asia (Russian)	Ischaemic heart disease		Screening examination among 12,191 students found high prevalences of CVD risk factors in CA.
18	Balabanova D et al	2004	Central Asia, FSU (English)	CVD	Urban/Rural	Low levels of access to health services in the region.
19	Pomerleau J et al	2004	Central Asia, FSU (English)	Smoking	Urban/Rural	Smoking presented as major public health issue in the FSU. High-risk groups are socially vulnerable men and young women in urbanized areas.
20	Pomerleau J et al	2008	Central Asia, FSU (English)	Alcohol drinking	Urban/Rural	Heavy episodic alcohol drinking is common in men throughout the region and relatively rare in women.
21	Groenewold WG et al	2011	Central Asia, FSU (English)	CVD	Urban/Rural	Differences in health status between ethnic Russians and the majority population in Kazakhstan.
22	A. Nikishin et al	2011	Central Asia, FSU (English)	Acute coronary syndrome	Urban/Rural	Women with ACS in Central Asia were less likely to adhere to the treatment, more obese, and have significantly longer arrival time to the hospital compared to men.
23	Roberts B et al	2012	Central Asia, FSU (English)	Smoking	Urban/Rural	Smoking prevalence in FSU have stabilized in 2001-2010 but remain high among men, especially in lower socioeconomic groups.