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Classical Risk Factors of Cardiovascular Diseases (CVDs) in Arkhangelsk: Have They Changed over the Years?

Comparison of Cross-sectional Studies: Arkhangelsk Study 2000 and Arkhangelsk Part of Know Your Heart Study 2015-17.

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Abbreviations

AUDIT	Alcohol Use Disorder Identification Test
Ark.2000	Arkhangelsk study 2000
BMI	Body mass index
BP/BPs	Blood pressure(s)
CAGE	The CAGE questionnaire
CHD	Coronary heart disease
CV	Analytic coefficient of variation
CVD/CVDs	Cardiovascular disease(s)
GDP/GDPs	Gross domestic product(s)
GGT	Gamma-glutamyl transferase
HALE	Healthy life expectancy
HDL	High-density lipoprotein
IPCDR	International Project on Cardiovascular Diseases in Russia
KYH	Know Your Heart study
LDL	Low-density lipoprotein
LE/LEs	Life expectancy at birth/Life expectancies at birth
MI/MIs	Myocardial infarction(s)
NCD/NCDs	Non-communicable disease(s)
RHR	Resting heart rates
RLMS	Russian Longitudinal Monitoring Survey
WHO	World Health Organization

Units Used

Cholesterols	mmol/L (KYH) mg/dL (Framingham risk score)
Blood pressures (BPs)	mmHg
Resting heart rates (RHR)	beats per minute
Body mass index (BMI)	kg/m^2
Gamma-glutamyl transferase (GGT)	U/L
Alcohol consumption (table 17)	dL

Abstract

Background:

According to the World Health Organization, 31% of all deaths worldwide result from cardiovascular diseases (CVDs), mostly in low- and middle-income countries. Even though Russia, an upper-middle income country, still have higher CVD mortality compared to the neighboring countries such as Finland and Norway, it has seen a reduction in CVD mortality since the turn of the millennium. Investigating how risk factors have changed over the years might be beneficial to the explanation of the recent downward of CVD mortality in Russia.

Objectives:

The objective of this thesis was to see if there have been any changes in the classical risk factors of CVDs since the year 2000 in a north-western city of Arkhangelsk in Russia.

Subjects & Methods:

A cross-sectional study on CVDs called Arkhangelsk study 2000 (Ark.2000) was performed in Arkhangelsk in 2000. 15 years later, another cross-sectional study called Know Your Heart (KYH) was carried out in Arkhangelsk and Novosibirsk as a part of the International Project on Cardiovascular Disease in Russia (IPCDR). Changes in the classical CVD risk factors since 2000 were investigated by descriptive statistics by comparing these two studies.

For the comparison purpose, participants above 40 years of age were included for the analyses in this thesis. 2132 participants (1087 men) from Ark.2000, recruited at a polyclinic while attending annual health checks, and 2222 participants (930 men) from the Arkhangelsk part of KYH, randomly selected from the general population, were included. Raw data was available from KYH, but not from Ark.2000. Therefore, descriptive statistics published from Ark.2000 and raw data from KYH were used for the comparison. Some of the classical risk factors that were comparable between the studies were included. Those were total and high-density lipoprotein (HDL) cholesterol, systolic and diastolic blood pressures (BPs), resting heart rates (RHRs), body mass index (BMI), education, physical activity at work, smoking, alcohol consumption measured by gamma-glutamyl transferase (GGT), Alcohol Use Disorder Identification Test (AUDIT), and the CAGE questionnaire (CAGE). Using those risk factors, Ten-year risk of developing coronary heart disease (CHD) was calculated by Framingham risk scores.

Results:

For men, total and HDL-cholesterol, systolic BP, GGT, AUDIT, and smoking have improved while diastolic BP, RHR, BMI, physical activity at work, and CAGE have shown opposite trends. Although most of the variables related to alcohol such as GGT and AUDIT decreased, GGT remained still high in all age groups (40-49, 50-59, above 60). Improvements in some of the risk factors improved the risk scores for developing CHD for ages above 60.

For women, total and HDL-cholesterol, systolic BP, GGT, AUDIT, CAGE, education, and physical activity at work have shown improvements. However, diastolic BP, RHR, and smoking showed unfavorable trends, and BMI remained similar over the years. Improvements in ten-year risk scores for developing CHD were seen in all age groups, and they were lower for women compared to men.

Conclusion:

Some of the classical risk factors have shown improvements over the years for both men and women, which has led to improvements in the ten-year risk scores of CHD development. However, those changes are still small, and the factors which have not been improved may be hindering a further reduction in CVD prevalence. For further reduction in risk factors, control of alcohol consumption for men and BMI and smoking for women would be necessary. In order to understand the reasons behind the recent reduction in CVD mortality in Russia, conducting longitudinal studies will be important. In addition, communicating the results of the studies to the general public in Arkhangelsk would be beneficial for the prevention of CVDs.

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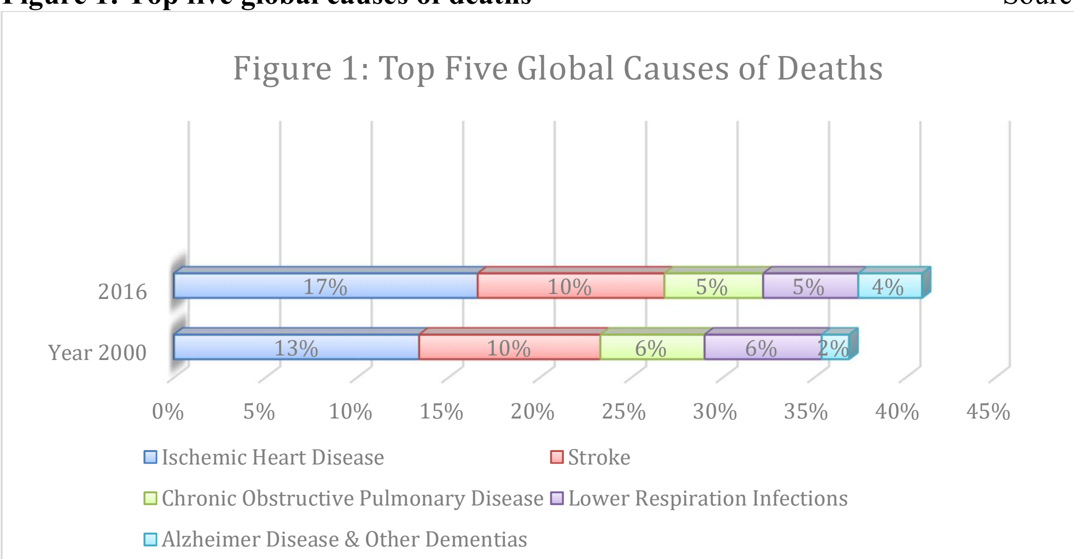
1 Introduction & Background

1.1 CVDs Worldwide

According to the World Health Organization (WHO), 17.9 million people worldwide died from cardiovascular diseases (CVDs) in 2016 (1). This is 31.4 percent (%) of all deaths in the world (2). Figure 1 shows the top five causes of deaths worldwide between 2000 and 2016 (2,3) Two of the highest global cause of deaths are ischemic heart disease and stroke, which account for 26.8%, 15.2 million, of deaths in 2016 globally (2,3). These two diseases account for 85% of the CVD deaths, and more than 80% of the world's CVDs occur in low- and middle-income countries (1)

Figure 1: Top five global causes of deaths Source: (2)



1.2 CVDs in Russia

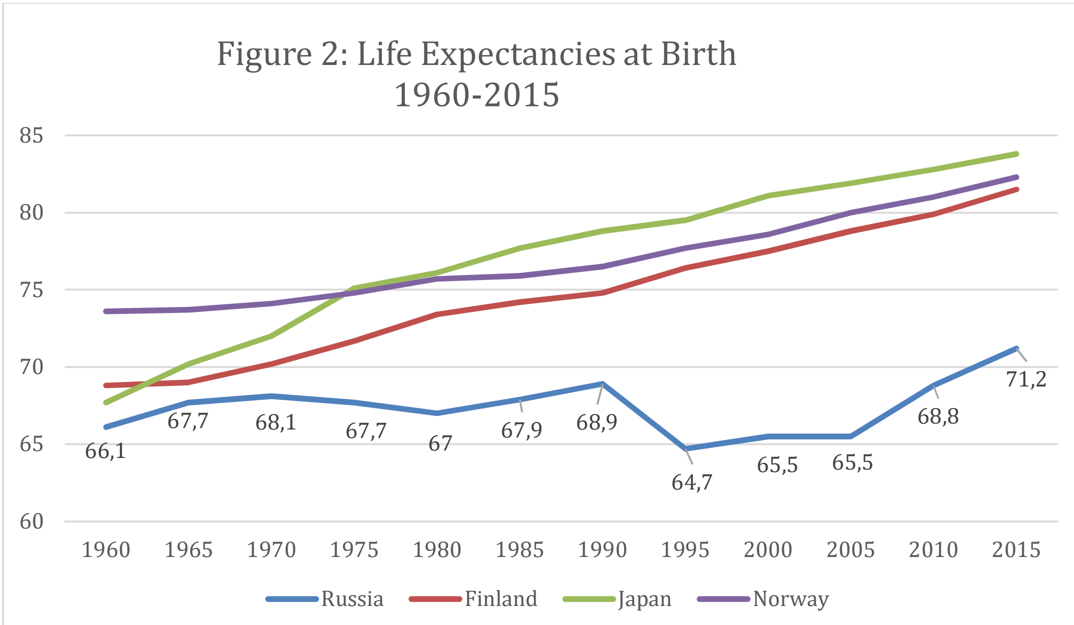
1.2.1 Life Expectancy and CVDs in Russia, Comparison with the Neighboring Countries

Although the life expectancy at birth (LE) including both men and women in Russia has been increasing since 2003, it had fluctuated between the 1970s and 2000s (4). With the decline in the number of deaths from infectious diseases, the LE including both genders in the former

Soviet Union in the 1960s were similar to Finland and Japan (4–7). Figure 2 shows the LE including both genders in four countries between 1960 and 2015 (4,6–8).

Figure 2: Life expectancies at birth: Russia, Finland, Norway, and Japan 1960-2015

Source (4,6–8)



Improvements in the LE were shown in the former Soviet Union until 1970; however, inadequate response to the epidemiological transition from infectious diseases to non-communicable diseases (NCDs) such as CVDs started to affect the LE in the 1970s (5). The LE improved during the 1980s from Gorbachev's anti-alcohol campaign; however, the removal of all restrictions on the alcohol sales and the stress from political and socioeconomic transitions including the financial crisis in Russia during the 1990s increased CVD deaths and lowered life expectancies at birth (5,9,10). The difference in the total life expectancy at birth between Russia and the average of the other three countries was 13.6 years in 2000 (4,6–8). Since 2000, CVDs remain to be the leading causes of mortality and account for more than half of deaths in Russia (11). Table 1 shows the percent of total deaths due to CVDs between 2000 and 2016 for Russia, Finland, Norway, and Japan (2). Even though the amount of CVD deaths is declining in Russia since 2010, the rate of declining is slow compared to those other countries. The amounts of

CVD deaths between 2000 and 2016 have decreased by 13.6%, 7.3%, and 3.5% in Norway, Finland, and Japan, respectively (2). However, it was only 0.6% for Russia (2). CVD deaths still account for more than half of all-cause deaths, 54.7%, as of 2016. The difference in the LE between Russia and the average of those three countries is still 11.3 years in 2015 (4,6–8). Improvements in CVD mortality might improve life expectancy further in Russia. According to the 2004 World Bank report, matching the European Union's CVD mortality rate would enable Russia to gain 6.7 years in life expectancy (10).

	Russia	Finland	Norway	Japan
2000	55.3%	43.1%	42.0%	30.9%
2010	56.2%	40.0%	32.5%	29.0 %
2015	54.7%	37.0%	29.2%	27.6%
2016	54.7%	35.8%	28.4%	27.4%

Table 1: The percent of total deaths due to CVDs in Russia, Finland, Norway, and Japan

Source: (2)

Russia experiences not only high CVD mortality but also lower healthy life expectancy (HALE). HALE takes into account mortality and morbidity, adjusted based on the severity of illnesses and considered to be the length of a life lived without disability (10). According to the WHO, the HALE at birth was 63.3 years worldwide in 2016 (12). Table 2 shows the HALE at birth in Russia, Finland, Norway, and Japan in 2016. Although the HALE at birth in Russia was above the global average in 2016, differences in HALE at birth between Russia and the average of the three countries were 9.6 years (13).

Table 2: HALE at birth in Russia, Finland, Norway, and Japan in 2016 Source: (13)

	Russia	Finland	Norway	Japan
HALE at birth in 2016 (years old)	63.5	71.7	73.0	74.8

Comparing to the countries such as Finland, Norway, and Japan, Russia has both lower LE and HALE due to the strong influence of NCD mortality and morbidity including CVDs (10).

1.2.2 Comparison between Russia and European Countries with Lower GDP per capita than Russia

Based on the gross domestic product (GDP) per capita data provided by the World Bank, 15 countries in Europe had a lower GDP per capita than Russia in 2016 (14). Table 3 shows the GDP per capita (constant 2010 US $), the LE, and age-adjusted CVD mortality rates of some of the countries. The age-adjustment was performed using the European standard population of 2013 (15).

Table 3: GDP per capita, LE, age-adjusted CVD mortality rates of Russia and some European countries with lower income than that of Russia

	GDP per capita (constant 2010 US$)	LE (years old)	Age-Adjusted CVD Mortality Rate (per 100,000 population)
Russia	11,279.6	71.6	957.9
Romania	10,236.9	75.0	835.3
Bulgaria	7,966.9	74.6	949.0
Montenegro	7,487.4	77.1	829.8
Albania	4,683.5	78.3	757.5
Kosovo	3,925.3	71.6	-
Ukraine	2,909.6	71.5	1075.0
Moldova	2,070.6	71.6	-

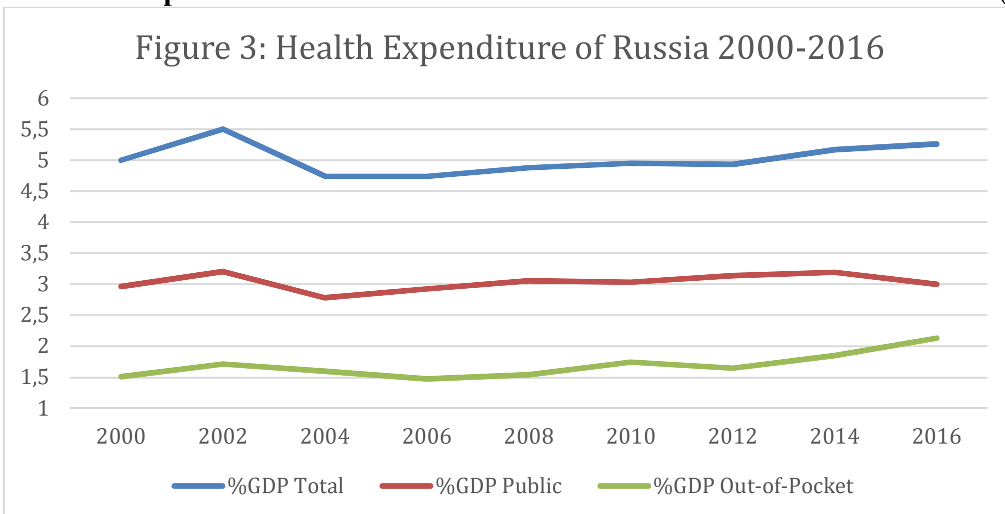
Source: (2,14,15)

Of those European countries, Ukraine was the only country that had a lower LE and a higher age-adjusted CVD mortality than Russia, 71.5 and 71.6 years and 1075.0 and 957.9 per 100,000 population, respectively (14). The highest LE was of Albania, 78.3 years (14). There were two European Union countries with lower GDP per capita than Russia: Romania and Bulgaria. Both of them had a higher LE than Russia, 75.0 and 74.6 years, respectively (14). For the age-adjusted CVD mortality rates, all the countries except Ukraine had a lower rate than Russia (2,15). These results suggest that the LEs and the age-adjusted CVD mortality rates are not solely dependent on the GDP per capita (5). The recent study by Shkolnikov et al. discovered high mortality from external causes for working ages and from CVDs for older ages when comparing Russia with countries with similar GDP per capita (16).

1.2.3 Health Expenditure Trend and Cost of CVDs in Russia

Russian public expenditures on health have fluctuated over the years, similar to its LE. Figure 3 shows the percentage of GDP that current health expenditure of Russia accounts for since 2000 (17).

Figure 3: Health expenditure of Russia 2000-2016 Source: (17)



Although the global trends in health expenditure show an increase in public sources and a decrease in out-of-pocket payments, public spending on health has been decreasing since 2014 in Russia and out-of-pocket payments have been increasing since 2012 (17,18). In 2016, Russia spent 5.26% of GDP for total health expenditure with 3.00% as public spending and 2.13% as out-of-pocket, suggesting roughly 40% of health expenditure comes from out-of-pocket, making it hard to access healthcare for people with lower socioeconomic status (17).

Of the health expenditure, CVDs were estimated to cost RUB 836.1 billion (€24,517.8 million) in 2006 and RUB 1076 billion (€24,400.4 million) in 2009, including both direct (healthcare costs) and indirect costs (non-healthcare costs) (19). Those amounts were estimated to account 3.1% and 2.8% of GDPs in 2006 and 2009, respectively (19). Since the total healthcare expenditure of Russia was 4.74% of GDP in 2006 and 5.61% of GDP in 2009, 65.4% and 49.9% of the total healthcare expenditure went to CVDs (17,19). There is an estimate that controlling hypertension by antihypertensive treatment can significantly reduce CVD mortality, diagnoses, and CVD healthcare costs (20). Comparing to the current rate, achieving 40% and 60% of systolic blood pressure (BP) control rates were estimated to reduce 1.0 million and 2.4 million 10-year total number of CVD deaths, 1.2 million and 2.7 million stroke or myocardial infarction (MI) diagnoses, and US$1.1billion and US$2.6 billion direct costs, respectively (20). It was also estimated that achieving these hypertension control rates would increase 1.21 and 2.72 years of LE in the working-age population, respectively (20).

1.2.4 CVD trends in Russia since 2000 and Disparities within the Country

With the increase in the LE, CVD mortality has been declining since 2000 in Russia. Table 4 shows the estimated population and the number of CVD deaths by WHO for 2000, 2010, 2015, and 2016.

Table 4: Estimated population and the number of CVD deaths in Russia (thousands)

Year	Total Population	Total CVD deaths	Male Population	Male CVD deaths	Female Population	Female CVD deaths
2000	146,397	1246.5	68,509	547.6	77,887	698.8
2010	143,154	1142.8	66,389	511.1	76,765	631.7
2015	143,888	1027.0	66,848	451.3	77,040	575.7
2016	143,965	1022.8	66,899	448.1	77,066	574.7

Source: (2)

Both male and female CVD deaths have decreased, which lead to a reduction in total CVD mortality (2). Between 2000 and 2016, the total CVD deaths have fallen from 1246,500 to 1022,800 with the reduction rate of 17.9% (2). During the same period, CVD deaths decreased from 547,600 to 448,100 with 18.2% reduction rate for male and from 698,800 to 574,700 with 17.8% reduction for female (2).

Although the reduction rates for the total, male, and female population seem similar, there are disparities in CVD mortality rates between genders. Age-specific CVD mortality rates and age-adjusted CVD mortality rates for the total population, male, and female are shown in table 5. For age-adjusted CVD mortality rates, the European Standard Population of 2013 was used for the calculation (15).

Although age-specific CVD mortality rates for the age 0-4 and 5-14 are similar between genders, the difference in CVD mortality becomes larger starting at age 15. Especially the groups that are in the working-age, 15 to 64 years of age, male CVD mortality rates were 2.8-4.0 times higher than those of female (2,15). Furthermore, age-adjusted CVD mortality rates were 957.9, 1165.4, and 826. 5 per 100,000 population for total, male, and female, respectively (2,15). These results show higher male CVD mortality is raising the total CVD mortality rates. These differences in CVD mortality between male and female correspond with the differences in the LEs, 66.5 and 76.9 years for male and female, respectively (21,22). Some studies suggest that the differences in CVD mortality between genders can be explained by psychological and behavioral factors: gender differences in care-seeking, alcohol consumption, smoking, educational levels, and socioeconomic status (10).

Table 5: Age-specific CVD mortality rates and age-adjusted CVD mortality rates (per 100,000 population) in Russia in 2016 Source: (2,15)

	Age-Specific CVD Mortality Rates (per 100,000 population)		
Age	Total	Male	Female
0-4	1.17	1.27	1.07
5-14	0.54	0.55	0.52
15-29	12.8	18.8	6.45
30-49	104.5	169.2	42.3
50-59	413.6	690.1	185.0
60-69	987.6	1598.6	568.5
70+	5410.3	5988.5	5166.4
Age-Adjusted CVD Mortality Rates (per 100,000 population)	957.9	1165.4	826.5

Another disparity in mortality and LEs can be seen among different regions due to socioeconomic and health level differences (10). Mortality rates of economically active male population ranged from 3.8 to 17.8 deaths per 100,000 population among regions (10). Alcohol consumption also differs among regions with higher consumption and mortality in rural areas (10). Reduction in coronary heart disease (CHD) mortality rates between 2005 and 2013 were different among regions: Moscow with the highest reduction, 1.3 times higher than that of St. Petersburg, 2.6 times higher than in the Moscow region, and 1.5 times higher than the country as a whole (23). The highest CVD mortality rates in 2009 were found in the Northwest regions of the country such as Tver and Pskov regions while the lowest CVD mortality was seen in the Southern Federal District such as Chechnya and Ingushetia (5). Between 2012 and 2016, the total circulatory disease mortality for 35-69 years old in urban Novosibirsk region was lower than that of the national average while that was higher for the urban Arkhangelsk region (24).

1.2.5 Preventive Interventions in Russia

Although the CVD mortality in Russia is still high, the government has started programs to prioritize health. "Prevention and Treatment of Arterial Hypertension in the Russian Federation" between 2002 and 2008 had focused on one of the CVD risk factors, hypertension (10). "National Priority Project Health" started in 2005 increased availability of modern treatments and interventions for CVDs with special focus on primary prevention of CVDs (23,25). Multidisciplinary and inter-sectorial document "Strategy for Prevention and Control of Non-communicable Diseases and Injuries in the Russian Federation" was also developed in 2008 by focusing on policy development, health care systems, personnel training, public education, risk factor monitoring systems, and international cooperation (5). In 2013, the program "Dispanserization" started to improve screening as well as risk factor counseling and management (23,25).

1.3 Risk Factors of CVDs

O'Donnell defines risk factors as "a measurable element or characteristic that is causally associated with an increased rate of a disease and that is an independent and significant predictor of the risk of presenting a disease" (26). Risk factors of CVDs can be categorized into non-modifiable risk factors and modifiable risk factors. Non-modifiable risk factors include age, gender, and family history of CVDs (27). Modifiable risk factors include a raised level of blood cholesterol and triglycerides, low-density lipoprotein (LDL)-cholesterol, high-density lipoprotein (HDL)-cholesterol, high BP, diabetes, smoking, unhealthy diet, obesity and overweight, physical inactivity, and an excessive amount of alcohol, socioeconomic factors, and stress (1,27). For alcohol use, the Alcohol Use Disorder Identification Test (AUDIT) and the CAGE questionnaire (CAGE) are used to identify hazardous alcohol consumption patterns. AUDIT has 10 questions including three sections to identify hazardous use, dependence, and harmful use (28). The cutoff points are eight for AUDIT and two for CAGE with a total of four questions for CAGE (28,29).

These classical risk factors have been studied extensively through Framingham Heart Study since 1948 (26). In 1957, high BP and cholesterol levels were found to increase the risk of heart disease (26). In the 1960s, the association between smoking and heart diseases was found followed by the association between heart diseases and sedentary lifestyles including obesity (26). Since 1970, more CVD risk factors and underlying diseases have been identified through the study: high BP and risk of stroke in 1970, diabetes with CVDs in 1974, triglycerides and lipoproteins with heart diseases in 1977, atrial fibrillation with stroke in 1978 (26). In the 1980s, the direct association of isolated systolic BP and heart diseases was found while HDL-cholesterol was found to be inversely associated with mortality (26). In the 1990s, risk factors of atrial fibrillation were described followed by the description of the progression of hypertension to heart failure and the development of the new method of predicting coronary disease risk (26).

1.3.1 Changes in Risk Factors in Other Countries

Some of the levels of these risk factors have declined over the years and have contributed to the decline of CVDs in the western world. In the United States, the Framingham Heart Study showed a lower serum cholesterol level, a lower systolic BP, reduced level of cigarette smoking, and better management of hypertension contributing to the decline in CVDs (30).

Due to its geographical location close to northern Russia, CVD researches from northern Norway are worth mentioning. In northern Norway, more than 40 years of cardiovascular research through the Tromsø Studies between 1974 and 2016 showed a reduction in total cholesterol, BP, and smoking corresponded to reduced CHD deaths (31). The mean total cholesterol decreased between 1979 and 2016 in both men and women in all age groups (32) Total cholesterol increased with age with a peak around middle age followed by a decline, and total cholesterol declined based on age: the younger, the lower (32). Lipid-lowering drug treatment for above 50 years old was associated with 21% and 28% of total cholesterol decline in women and men, respectively (32). Moreover, the Tromsø Studies showed that the decline in mean systolic and diastolic BPs from 1979 to 2008 in both genders for the ages of 30 to 89 years (33). The decrease in systolic BP for the age group of 40 to 49 years was more than twice as high in women compared to men (33). Systolic BP increased in both genders born between 1920 and 1949, but younger participants had a decrease or flattening of the curve (33). For ischemic stroke, systolic BP accounted for 26% of the decline (34). The reduced level of smoking in the same study accounted for 17% of the decline in ischemic stroke (34). In addition, the reduction in resting heart rates (RHR) has attributed to favorable changes in other risk factors of CVDs in the Tromsø Studies especially for those participants whose BP, total and HDL-cholesterol, triglycerides, body mass index (BMI), smoking, and physical activity changed from adverse to favorable values and those who started BP treatment (35,36)

The Tromsø Studies also showed a 3.0 % decline in acute CHD between 1994 and 2010, and the changes in CHD risk factors accounted for 66% of the decline (37). The severity and the case fatality rates of MIs declined in both genders; however, the age-adjusted incidence of MIs in the age group 35-79 showed a decline in men but an increase in women (38).

1.3.2 Risk Factors of CVDs in Russia

Some of the classical risk factors seem to attribute significantly to CVDs in Russia. The important factors include high alcohol intake, smoking, eating habits, hypertension, physical inactivity and obesity, psychological stress, and dyslipidemia (5). However, special attention should be given to alcohol, smoking, hypertension, and obesity due to the high prevalence of these risk factors in Russia.

Alcohol consumption remains high for the past few decades in Russia, 10-15 liters per person per year (5). Current alcohol consumption in Russia is 11.7 liters; however, it is still higher compared to the neighboring countries such as Norway and Finland, 7.5 and 10.7 liters per person per year according to WHO World Health Statistics 2018 (39). In 2004, 70% of men, 47% of women, 30% of teenagers consumed alcohol with 70% of the population preferred drinking strong alcoholic beverages (5,10). For Karelia population in Pitkäranta region of Russia, a study using biomarkers indicated alcohol abuse (>20g/day) in 37% of men and 18% of women (5). These values were more than twice as high compared to those in Finland, 9.6% for men and 9.4% for women (5). Some studies suggested that 21.4% of CVD deaths in Russia were attributed to alcohol, and one-liter increase in per capita consumption showed an increase in CHD mortality: 3.6% in male and 4.5% in age 30-54 (9). This relationship of an increase in alcohol consumption and an increase in mortality was found for CHD, stroke, and hypertension as well: 41.1% of male and 30.7% female CHD deaths, 26.8% of male and 18.4% of female deaths from stroke, and 57.5% of male and 48.6% of female deaths due to hypertension were attributed to alcohol consumption (9). In the study of alcohol-related deaths, acute ischemic heart disease except MIs was the third highest in Russia (40). Binge drinking is found to be strongly associated with CVD mortality (10,41,42).

Tobacco smoking is also crucial. According to WHO, the prevalence of smoking for men and women above 15 years of age in 2015 were 59.3 and 19.3 for Russia and 22.1 and 21.2 for Norway, respectively (43). There were regional differences as well. The proportions of smokers were different among regions: 56-60.3% in men and 19.6-3.7% in women in Moscow, Tver, and St. Petersburg, according to the Russian Longitudinal Monitoring Survey (RLMS) (5). In addition, 29% of CVD deaths in Russia were found to be attributed to smoking (5).

High prevalence of hypertension has been a problem in Russia as uncontrolled hypertension has 3-4 times higher risk of developing CHD (10). In the Izhevsk Family Study II between 2008 and 2009, the prevalence of hypertension and hyperlipidemia was 61 and 49%, respectively (44). Of those found to have hypertension, 44% were unaware of the diagnosis (44). Another study from Pitkäranta region of Russia found that 39% and 42% of CVDs, 41% and 34% of CHD, 81% and 73% of stroke were attributable to hypertension for men aged 40-50 and women aged 30-69, respectively (5). In addition, Russian men and women with hypertension are estimated to live 12.2 and 6.0 years shorter than those without hypertension, respectively (5).

High prevalence of overweight and obesity in Russia was estimated by WHO with 2008 data (45). For those above 20 years of age, 56.2 and 62.8% of men and women were estimated to be overweight while obese was 18.6 and 32.9%, respectively (45). BMI was used to estimate overweight and obesity for the estimation. BMI is calculated by weight divided by the square of height (weight/$[height]_2$), and overweight is defined by BMI between 25 to 29.9 while BMI of above 30 is considered obese (10). Diet, physical inactivity, and obesity are associated with elevated BP, high cholesterol levels and type two diabetes as well as a complication from type two diabetes causing cardiovascular problems (5,10).

1.3.3 Arkhangelsk Study 2000 & Know Your Heart Study 2015-2018

Arkhangelsk study 2000 (Ark.2000) is a cross-sectional health survey combined with a physical examination and blood tests, held in the northwestern region of Russia, Arkhangelsk, between 1999-2000 to investigate the reasons behind the high CVD mortality in Russia (46). 15 years later, another cross-sectional study called Know Your Heart study (KYH) was conducted in Arkhangelsk and Novosibirsk, between 2015 and 2018 as a part of the International Project on Cardiovascular Disease in Russia (IPCDR) (24). Although these studies were not designed in the same ways, some of the classical risk factors were comparable.

2 Objectives

The objective of this thesis is to investigate if there have been any changes in the classical CVD risk factors over the years by comparing data from Ark.2000 and the Arkhangelsk part of the KYH. The results of this comparison may add up to the explanations of the recent downward trends in CVD mortality in Russia.

As CVD mortality has been falling in Russia, it would be reasonable to think that there has been an improvement in risk factors such as a decrease in the amount of binge drinking or smoking. However, many risk factors are related to human behaviors, which are difficult to change. Therefore, there might not be any change in risk factors of CVDs in Arkhangelsk.

3 Methods

3.1 Study Design & Settings

Both Arkhangelsk Study 2000 and Know Your Heart Study 2015-2018 are cross-sectional studies conducted in Arkhangelsk, Russia, which is an administrative center of the Arkhangelsk region. Arkhangelsk is located in the north of Severnaya (North) Dvina River, 40 km from the White Sea (47). The area of Arkhangelsk is 2994.4 square kilometers (km^2) with a population of approximately 351,000 in 2015 and 367,000 in 1999 with 46% men and 54% women (47,48). In 2015, 0.24% of the total population of Russia was in Arkhangelsk (2,47). Arkhangelsk has a temperate climate with a long cold winter and a short cool summer (47). The average temperature is -12.8 degree Celsius (°C) in January and +16.3°C in July (47). In terms of the economy, Arkhangelsk has historically been an important seaport, many residents engaged in fisheries, aquaculture, fish processing as well as dock works, shipbuilding and repairing (49). It is a scientific and industrial city with its major industries in woodworking, timber-chemical, and pulp and paper (47).

3.2 Arkhangelsk Study 2000

3.2.1 Recruitment of Participants

The recruitment of participants was carried out at Semashko polyclinic, one of the largest polyclinics in Arkhangelsk for providing voluntary screening medical examinations of the general population for the purpose of prevention and early diagnosis as well as compulsory annual medical examinations for sailors (48). Participants who came to the clinic for annual medical examinations were recruited between 8:00 and noon on certain days of the week for a year between 1999 and 2000 (48). In addition, some of the workplaces and educational institutions were actively contacted and recruited for annual medical examinations such as students, pensioners, and teachers (48,50). Four nurses and two physicians were responsible for daily registration, examination, and blood tests (48). At the point of registration, attendees were informed about the project and asked to participate (48). 40 attendees, which is one percent of the attendees, refused to participate (48). The sample size was determined to be 4000 (48,50). In order to have participants of similar sex and age groups, recruitment of groups with enough participants was stopped earlier than the rest of the groups (48).

3.2.2 Eligibility Criteria

All males and females aged above 18 who underwent the health check in a certain period were invited to participate and all of them who agreed were considered eligible for the study (48). The total of 4129 attendees was invited to participate, of which 40 refused to participate (48,50). Of 4089 who agreed to participate, 43 did not return the questionnaire and five did not provide blood (48,50). All the blood samples were analyzed in both Arkhangelsk and Tromsø, but two of serum were missing in Arkhangelsk, and three were missing in Tromsø (48,50). Of the 4036 participants, those younger than 18 years old were excluded from the study; hence, 3705 attendees participated at the end (48). For the purpose of comparison in this thesis, ages above 40 were included (2132 participants, 1087 males and 1045 females) (50).

3.2.3 Ethics

At the time of the study, there were no centralized ethical committee in Russia as well as no ethical committee in the Arkhangelsk region (48). However, this study was approved by the regional ethical committee in Norway (48). In addition, verbal informed consent was obtained from all the participants (48). However, the use of raw data from the Arkhangelsk 2000 was not approved for this thesis; therefore, already published data are used for the comparison with KYH study.

3.2.4 Procedures: Data Collection & Examination

There were four stages in the survey procedure: registration, questionnaire, BP and heart rate, and blood samples (48,50). First, information about the study was provided (48,50). For those agreed to participate, their names are registered, and a personal participant number was given (48). Anthropometrical measures such as height, weight, waist-hip circumferences were measured by a trained nurse (48,50). Weight measurement was performed without clothes and shoes by an electronic device, which was adjusted every morning (48,50). Both height and weight were read to the lowest whole centimeters (cm) and kilogram (kg) (50).

Questionnaire (See Appendix):

At the second stage, each participant filled out a questionnaire in a separate room (48). The questionnaire was developed in English using the Tromsø, the Finnmark, and Svalbard studies, and then translated to Russian, followed by re-translation by different translators for quality assurance (48,50). Participants filled out a Russian version of the questionnaire, which has six pages, consisting of 111 questions, with the assistance of a trained nurse (48,50). The nurse checked if all the questionnaires were completed (48,50).

Blood Pressure & Heart Rate:

At the third stage, participants provided BP and heart rate measurements in another quiet room (48,50). Both measurements were taken three times on the right upper arm in a sitting position with intervals of two minutes using an automatic BP monitor (DINAMAP-R, Critikon, Tampa, Florida) (48,50). Both measurements were taken and recorded by a trained nurse (48).

Blood Samples:

At the fourth stage, participants were invited to a different room separately for blood sampling (48). Although participants were not told to fast for the study, most of the participants fasted as it was required for the annual medical examination (48,50). 25 milliliters (ml) of blood samples were obtained from the cubital vein by a trained nurse and centrifuged at the Semashko polyclinic laboratory within 15-25 minutes (48,50). On the same day, GGT and lipids were analyzed at the polyclinic laboratory (48,50). Four containers of serum and one container of full blood from each patient were frozen down to -20 degree Celsius (°C) immediately for later analyses (48,50). These samples were stored at -20°C for 3-4 weeks and transported to Tromsø by a five-hour flight in boxes with freezing elements (48).

Laboratory Analyses:

Blood analyses were performed in both Arkhangelsk and Tromsø (50). All kits including a new spectrophotometer were purchased in the United States and transported to Arkhangelsk via Tromsø (50). Due to the laboratory capacity, the spectrophotometer was switched back to older Kobas analyzer after two months, and all the work performed on the spectrophotometer were analyzed on the Kobas analyzer (50). When the results from Arkhangelsk and Tromsø did not agree, the results from Tromsø were used for further analyses (50).

Laboratory Analyses in Tromsø:

Enzymatic colorimetric method (cholesterol esterase and cholesterol oxidase) was used to analyze serum total cholesterol using a Hitachi 737 assay machine with an analytic coefficient of variation (CV) of five percent (48,50). Homogeneous enzymatic colorimetric test (PEG cholesterol esterase and PEG cholesterol oxidase) was used to analyze HDL-cholesterol using a Hitachi 737 assay machine with a CV of three percent (48,50). LDL-cholesterol was measured differently based on the serum triglyceride level (50). When triglyceride levels were lower than four millimoles per liter (<4mmol/l), Friedwald's formula (LDL cholesterol = total cholesterol HDL cholesterol – (triglycerides * 0.46)) was used for determination of LDL-cholesterol while the measurement of LDL-cholesterol was done directly at higher triglyceride levels with enzymatic colorimetric test (Roche, selective inhibition of VLDL-, chylomicron-, HDL-cholesterol) using a Hitachi 737 device with a three percent CV(48,50). For GGT, an enzymatic colorimetric assay (Roche) was used to measure the formation of free 5-amino-2-nitrobenzoate formation, proportional to GGT activity, using Hitachi 917 device with a 2.5% CV(48,50).

3.3 Know Your Heart 2015-2018

3.3.1 Recruitment of Participants

The sample size was calculated to be 4500 (2250 for Arkhangelsk) to have enough power for comparisons with other population-based studies and for investigation of associations of interest within KYH study (24). Four districts in Arkhangelsk (Lomonosovsky, Maymaksansky, Mayskaya Gorka, and Oktyabrsky) were selected for the recruitment of participants to represent socio-demographic and mortality range (24). Within each district, individuals were contacted randomly based on the age, sex, and address without individual names provided by the regional health insurance funds in order to have an equal number of participants and in each sex and each age group (five-year range) (24). Trained interviewers from a local commercial survey company visited the randomly selected home addresses for recruitment (24). An address was visited up to five times in order to reach potential participants at home and make the invitation (24). After successful interviews, participants were invited for health examination at a polyclinic with online calendar appointments upon their agreement (24). There was a total of 5089 participants in ages from 35 to 68 in both Arkhangelsk and Novosibirsk (24). Of those, the total of 4542 participants attended health check in both cities (24). In Arkhangelsk, there were 2381 participants with a median age of 54 with 41.5% male (24). The total response rate and the response rate for men and women in Arkhangelsk were 68.2, 60.4, and 75.2% with the type three response, which includes all the addresses with people with expected age and sex were found (24). To see if there is any sampling bias due to non-response, the educational distribution of the participants were compared to that of the city from the 2010 census after indirect standardization for age and sex (24). The overall ratio for completion of the questionnaire and that of attending the health examination were 0.98 and 0.99, respectively (24).

3.3.2 Eligibility Criteria

Of those participated in the baseline sociological interview (5089 participants), 4542 participants completed health check (24). Of those who completed health check, those living in Arkhangelsk were 2381 (24). For the purpose of this thesis, those only above 40 years of age were included in the following analyses for the comparison with Ark.2000 (2222 participants with 930 males and 1292 females).

3.3.3 Ethics

Ethical approvals for the study were obtained from the ethics committees of the London School of Hygiene & Tropical Medicine (approval number 8808) and Northern State Medical University, Arkhangelsk (approval number 01/01-15) (24).

3.3.4 Funding

IPCDR project was funded by a Wellcome Trust Strategic Award (100217) as well as UiT the Arctic University of Norway, Norwegian Institute of Public Health, and the Norwegian Ministry of Health and Social Affairs (24). The study design, data collection, analyses, and publication were independent of the funding sources (24).

3.3.5 Procedures: Data Collection & Examination

There were two stages for data collection: baseline interview and health check (24). Baseline interviews were conducted at home to obtain information on socio-demographic characteristics and cardiovascular risk factors, and health check at a primary care clinic (polyclinic) examined the cardiovascular system including providing blood samples (24).

Baseline Interviews:

A trained interviewer filled out the questionnaire with the computer-assisted personal interviewing device on a tablet with an automatic time recording system for completing each question (24). It took a median of 36 minutes to complete the questionnaire with a series of questions with detailed questions on alcohol use (24). Some of the sections related to the purpose of this thesis include socio-demographic factors, physical activity, smoking status, disease history, and CAGE score for detection of problem drinking. For CAGE questions, time reference used in KYH was "past 12 months" rather than "ever", which was used in the original questionnaires as well as Ark.2000 (24).

Health Check Examination:

Health check included both a questionnaire and a physical examination (24). The questionnaire regarded past medical history, and it was administered by either a nurse or a cardiologist. It took three hours for the whole health check, and all the aspects followed the standard operating procedures. The use of medication was also measured by asking questions covering up to seven medications, and participants were asked to bring all medications to the health check. Assessment of hazardous alcohol use was made by AUDIT score, and questions on smoking from baseline interview were repeated. Some of the physical examination measurement related for the purpose of this thesis were: BPs, heart rates, anthropometry (BMI), lipids (total, HDL- and LDL-cholesterol), GGT and AUDIT. Due to the length of the health check, participants were asked to fast for 4 hours before the health check. Times of the last meal, drinks, and alcohol consumption within 24 hours were recorded at the arrival.

Anthropometry:

Weight was measured by TANITA BC418 body composition analyzer (TANITA Europe GmbH), and 98.1% of the participants for the health check completed with body composition data (24). Height was measured twice using Seca® 217 portable stadiometer (Seca Limited), and the completion rate was 99.9% (24).

Blood Pressure & Heart Rate:

BP and pulse measurements were taken three times in a sitting position with an interval of two minutes using OMRON 705 IT automatic BP monitors (OMRON Healthcare) (24). 98.9% of the participants for the health check completed the measurements (24).

Blood Samples:

Blood samples were collected and centrifuged at 4°C for 15 minutes (24). Serum was transferred to barcoded 1.8 ml cryovials and frozen at -80°C within two hours after venipuncture (24). This was confirmed for 100% of the samples in Arkhangelsk by time stamps and uniquely identified bar-code labels (24). The analyses of the samples were performed at the end of the study (24).

Laboratory Analyses:

All the samples were analyzed in Moscow. Total and HDL-cholesterol from serum were analyzed by the enzymatic color test using AU 680 Chemistry System Beckman Coulter, and LDL-cholesterol from serum was analyzed by the immuno-inhibition enzymatic color test with AU 680 Chemistry System Beckman Coulter (24). GGT from serum was analyzed by kinetic color test (IFCC) with AU 680 Chemistry System Beckman Coulter (24).

3.4 Comparison of the Studies

Table 6 shows the comparisons of the two studies based on recruitment, participants, period, diagnostic criteria, measurement of each variable. The number of participants listed was those included in this thesis.

Table 6: Comparison of study designs of Ark.2000 and KYH Source: (24,48,50)

	Ark.2000	KYH
Recruitment	Population attending annual medical exam at Semashko polyclinic Some workplaces and educational institutions	General population (four districts, individual addresses randomly selected)
Participants	2132 participants (1087 males and 1045 females)	2222 participants (930 males and 1292 females)
Period	May 15, 2000 – Nov. 17, 2001	Nov. 2, 2015 – Oct. 30, 2017
Measurement: Devices Used		
Cholesterols	Total & HDL: enzymatic color test by Hitachi 917 LDL: for low triglycerides (<4 mmol/l), the Friedwald's formula was used for calculation. For >4 mmol/l, enzymatic colorimetric test by Hitachi 737	Total & HDL: enzymatic color test LDL: immune-inhibition enzymatic color test AU 680 Chemistry System Beckman Coulter for all tests
BPs & RHR	DINAMAP-R	OMRON705 IT automatic BP monitors
BMI	-	Height: Seca 217 portable stadiometer Weight: TANITA BC 418 body composition analyzer
GGT	Enzymatic colorimetric assay by Hitachi 917	Kinetic color test by AU 680 Chemistry System Beckman Coulter

3.5 Statistical Analyses

For analyses, participants above the age of 40 in Arkhangelsk were included from ARK.2000 (2132 total) and KYH (2222 total). For Ark.2000, descriptive statistics data were published and available although raw data were not available (48,50). For classical risk factors which were comparable between the studies, descriptive statistics including means, standard deviations, medians for GGT were performed using data published from Ark.2000 (48,50) and SPSS Statistics 25 for KYH. Those risk factors include total-, HDL-, and LDL-cholesterol, systolic and diastolic BP, RHR, BMI, GGT, AUDIT and CAGE scores, education, physical activity at work, and smoking. To account for confounders, each risk factor was stratified by age and sex. Participants were classified into groups with 10-year age using the nearest lower whole number.

For statistical significance, two-sample t-tests were performed using an online calculator (51) on the differences between the studies of continuous variables using means, standard deviations, and sample sizes. Cholesterols, BPs, RHR, BMI, GGT, and AUDIT were treated as continuous variables as they were reported as continuous variables in Ark.2000 (50). For categorical variables such as education, physical activity at work, and smoking, the proportion of participants for each category was reported. Using those proportions and sample sizes, chi-square tests were performed with an online calculator (52) to see the significance in differences between the studies. For CAGE, means and standard deviations were not available for each age group from Ark.2000 as the proportion of participants in each CAGE score was reported.

Categories from each categorical variable were different between the studies; hence, they were recategorized to make them comparable. Recategorizations of categorical variables are listed in table 7.

The ten-year risk scores for CHD development calculated using the Framingham risk score were available from Ark.2000. Therefore, those scores from KYH were calculated using Excel and SPSS Statistics 25. Variables used to calculate Framingham scores include age, total- and HDL-cholesterol, systolic BP, and smoking status. The points for each variable were assigned using the tables provided in the Framingham Heart Study website (53). For cholesterols, the unit was given in mg/dL in the Framingham risk score tables; however, the unit was given in mmol/L in KYH data. Therefore, cholesterol values from KYH were multiplied by 38.67 to convert them to mg/dL based on the literature (54).

Table 7: Recategorization of categorical variables of Ark.2000 and KYH Source:(24,50)

This thesis	Arkhangelsk 2000	KYH
Education		
Primary	Primary school	Incomplete secondary or lower
		Professional school without secondary, PTU
Secondary	Secondary school	Complete secondary
Professional	Secondary professional school	Professional school with secondary
	Some college	Specialized secondary
		Incomplete higher
Higher	Graduated from college	Higher
Physical Activity at Work		
Sedentary occupation	Mostly sedentary work (e.g. office work etc.)	Sedentary occupation (most of your time sitting such as in an office)
Standing occupation	Work that requires a lot of walking (e.g. shop-assistant, waiter, etc.)	Standing occupation (most of your time standing or walking. E.g. shop assistant, hairdresser, guard, etc.)
Physical work	Work that requires a lot of walking and lifting (e.g. postman, construction, etc.)	Physical work (some physical effort including handling of heavy objects and use of tools. E.g. plumer, cleaner, nurse, sports instructor, electrician, carpenter, etc.)
	Heavy manual work (e.g. farmer, forestry, etc.)	Heavy manual work (vigorous physical activity including handling of very heavy objects. E.g. docker, miner, bricklayer, construction worker, etc.)
Smoking		
Never	No, never smoked	Never smoked
Former	Smoked previously	No, ex-smoker
Current	Sometimes	Yes, I smoke but less than 1 cigarette a day
	Yes, every day	Yes, a regular smoker

4 Results

4.1 Study population

The numbers of eligible participants from both studies as well as those for each age group are listed in table 8 below. The total of 2132 and 2222 participants from Ark.2000 and KYH, respectively, were included in the analyses.

Table 8: Study population – the number of participants included for analyses

		Ark.2000	KYH
Eligible - **Above 40** - **Arkhangelsk**	Total	2132	2222
	Male	1087	930
	Female	1045	1292
Age: 40-49	Male	447	280
	Female	420	411
Age: 50-59	Male	308	324
	Female	305	422
Age: 60+	Male	332	326
	Female	320	459

4.2 Main findings

4.2.1 Continuous Variables (Biomarkers, BPs, RHR, BMI)

The following tables 9-10 show the means, the standard deviations, the number of valid entries, and the p-values for the differences between the studies for the continuous variables such as biomarkers (total and HDL-cholesterol), systolic and diastolic BPs, RHR, and BMI.

For men, total cholesterol and systolic BP have slightly decreased while diastolic BP, RHR, and BMI have slightly increased for all the age groups. HDL-cholesterol improved for all groups. For age 40-49, significant differences were observed in diastolic BP, RHR, and BMI while total cholesterol, HDL-cholesterol, diastolic BP, and RHR were significant for age 50-59. For those above 60 years of age, the increase in HDL-cholesterol, diastolic BPs, and BMI and the decrease in systolic BP were significant. Standard deviations for both cholesterols were narrow in both studies, suggesting lesser individual differences.

Table 9: Comparison of continuous variables and their means, standard deviations, valid numbers, differences of means (p-values) for men age 40-49, 50-59, and 60+

Men	Age 40-49		Age 50-59		Age 60+	
	Ark. 2000	KYH	Ark. 2000	KYH	Ark. 2000	KYH
Total cholesterol	5.4 (1.1) N=446	5.29 (1.05) N=266	5.5 (1.1) N=308	5.33 (1.02) N=313	5.3 (1.1) N=332	5.18 (1.12) N=312
	p=0.185		p=0.046		p=0.171	
HDL-cholesterol	1.3 (0.4) N=446	1.31 (0.32) N=266	1.2 (0.4) N=308	1.32 (0.34) N=313	1.2 (0.4) N=332	1.33 (0.35) N=312
	p=0.714		p<0.001		p<0.001	
Systolic BP	132.9 (16.3) N=447	132.0 (17.6) N=266	139.4 (18.3) N=308	137.9 (18.5) N=311	149.8 (22.3) N=332	144.8 (20.6) N=311
	p=0.498		p=0.311		p=0.003	
Diastolic BP	80.6 (11.9) N=447	86.0 (11.9) N=266	83.1 (11.5) N=308	87.9 (10.7) N=311	83.5 (11.3) N=332	87.0 (11.2) N=311
	p<0.001		p<0.001		p<0.001	
RHR	70.6 (10.9) N=447	72.8 (12.7) N=267	71.2 (8.9) N=308	74.1 (11.6) N=311	72.0 (9.9) N=332	72.9 (12.7) N=311
	p=0.019		p<0.001		p=0.344	
BMI	26.1 (4.0) N=447	27.5 (4.54) N=267	26.9 (3.7) N=308	27.5 (4.90) N=313	26.5 (3.3) N=332	27.6 (4.57) N=312
	p<0.001		p=0.085		p<0.001	

For women, total cholesterol has slightly and systolic BP has greatly decreased while diastolic BP and RHR have increased. An improvement in HDL-cholesterol was seen, but BMI remained similar between the studies. For age 40-49 and 50-59, HDL-cholesterol, systolic and diastolic BPs, and RHR were significant while the significant differences were seen in total- and HDL-cholesterol, systolic BP, and BMI for ages above 60. Standard deviations for both cholesterols in both studies were narrow, implying there is small variation within individuals in the population.

Table 10: Comparison of continuous variables and their means, standard deviations, valid numbers, differences of means (p-values) for women age 40-49, 50-59, and 60+

Women	Age 40-49		Age 50-59		Age 60+	
	Ark. 2000	KYH	Ark. 2000	KYH	Ark. 2000	KYH
Total cholesterol	5.2 (1.1) N=419	5.25 (0.98) N=391	5.9 (1.1) N=305	5.78 (1.11) N=401	6.0 (1.3) N=320	5.73 (1.25) N=445
	p=0.494		p=0.153		p=0.004	
HDL-cholesterol	1.4 (0.4) N=419	1.56 (0.36) N=391	1.3 (0.4) N=305	1.56 (0.38) N=401	1.3 (0.3) N=320	1.51 (0.34) N=445
	P<0.001		p<0.001		p<0.001	
Systolic BP	127.6 (19.7) N=420	120.6 (15.8) N=389	138.6 (21.5) N=305	128.9 (18.3) N=403	150.5 (24.5) N=320	137.3 (21.1) N=444
	p<0.001		p<0.001		p<0.001	
Diastolic BP	74.5 (12.7) N=420	78.7 (11.1) N=389	79.6 (11.7) N=305	82.9 (10.9) N=403	82.7 (13.9) N=320	82.8 (11.1) N=444
	p<0.001		p<0.001		p=0.915	
RHR	70.2 (9.1) N=420	73.5 (9.9) N=388	71.2 (9.2) N=305	72.8 (10.9) N=402	72.1 (10.3) N=320	72.6 (11.0) N=444
	p<0.001		p=0.035		p=0.072	
BMI	27.0 (5.0) N=420	26.5 (5.59) N=392	28.8 (7.9) N=305	28.7 (5.93) N=404	28.0 (4.8) N=320	29.9 (5.70) N=446
	p=0.181		p=0.853		p<0.001	

Source: (50)

4.2.2 Categorical Variables

The following tables 11-12 show the proportion (%) of each category for other characteristics such as education, physical activity, and smoking for men and women. For men, both educational attainment and smoking improved for all age groups. However, the proportion of physical work has declined for ages 40-49 and 50-59 while it has increased for ages above 60.

For women, educational attainment increased as well as the proportion of physical work, especially for higher ages. However, the proportion of never smoker decreased while former and current smokers increased for all age groups.

Table 11: Risk factors with categorical variables (education, physical activity at work, and smoking) for men Source:(50)

Men	Age 40-49		Age 50-59		Age 60+	
	Ark. 2000	KYH	Ark. 2000	KYH	Ark. 2000	KYH
Education (%)						
Valid number	N=447	N=280	N=308	N=324	N=332	N=326
Primary	4.7	7.9	6.2	5.6	19.0	14.7
Secondary	22.8	8.6	15.3	10.2	18.7	12.3
Professional	51.2	47.1	53.0	54.6	43.1	40.8
Higher	21.3	36.4	25.6	29.6	19.3	32.2
Difference	p<0.001		p=0.231		p<0.001	
Physical Activity at Work (%)						
Valid number	N=447	N=249	N=308	N=240	N=332	N=120
Sedentary occupation	22.6	46.2	30.2	48.3	50.3	41.7
Standing occupation	23.3	17.7	27.6	17.9	33.7	22.5
Physical Work	54.1	36.1	42.2	33.8	15.9	35.8
Difference	p<0.001		p<0.001		p<0.001	
Smoking (%)						
Valid number	N=447	N=267	N=308	N=312	N=332	N=311
Never	28.2	28.1	17.9	24.0	25.3	25.7
Former	17.7	35.6	22.4	37.8	34.9	44.4
Current	54.1	36.3	59.8	38.1	39.7	29.9
Difference	p<0.001		p<0.001		p=0.018	

Table 12: Risk factors with categorical variables (education, physical activity at work, and smoking) for women Source:(50)

Women	Age 40-49		Age 50-59		Age 60+	
	Ark. 2000	KYH	Ark. 2000	KYH	Ark. 2000	KYH
Education (%)						
Valid number	N=420	N=411	N=305	N=422	N=320	N=459
Primary	2.9	3.9	4.9	4.8	32.5	10.7
Secondary	13.8	3.4	16.1	6.2	23.8	10.0
Professional	51.6	44.0	46.2	55.4	28.1	54.7
Higher	31.7	48.7	32.8	33.6	15.6	24.6
Difference	p<0.001		p<0.001		p<0.001	
Physical Activity at Work (%)						
Valid number	N=420	N=365	N=305	N=297	N=320	N=134
Sedentary occupation	53.1	53.7	52.5	56.2	65.6	47.0
Standing occupation	35.7	29.0	35.4	22.2	29.1	26.9
Physical Work	11.2	17.3	12.1	21.6	5.3	26.1
Difference	p=0.020		p<0.001		p<0.001	
Smoking (%)						
Valid number	N=420	N=391	N=305	N=403	N=330	N=446
Never	69.0	57.0	86.6	65.0	96.6	83.9
Former	6.9	23.3	4.6	15.9	2.2	9.6
Current	24.0	19.7	8.8	19.1	1.2	6.5
Difference	p<0.001		p<0.001		p<0.001	

4.2.3 Alcohol-Related Values

The following tables 13-14 show factors related to alcohol. Those include GGT, total AUDIT scores, proportions of AUDIT scores of above eight, proportions of each CAGE score, and the number of alcohol units consumed per capita. Values for GGT, total AUDIT scores, and alcohol units consumed include means, standard deviations, valid numbers, medians, and p-values for differences between the studies. The information on the frequency of alcohol drinking was not available for Ark.2000 due to how it was reported in the publications. Also, the amount of alcohol consumed in alcohol units was per week for Ark.2000 and per day for KYH. Due to the differences in the period, p-values were not reported for the amount of alcohol consumed.

Table 13: Alcohol-related variables (GGT, AUDIT, CAGE, and consumption) for men

Men		Age 40-49		Age 50-59		Age 60+	
		Ark. 2000	KYH	Ark. 2000	KYH	Ark. 2000	KYH
GGT	Mean	51.5 (77.0) N=446	50.0 (52.1) N=266	57.5 (78.9) N=308	50.4 (58.1) N=313	45.9 (68.7) N=332	43.1 (84.8) N=312
	Median	34.0	32.1	38.0	33.4	30.0	28.7
	Difference Mean	p=0.757		p=0.203		p=0.647	
Total AUDIT	Mean	7.6 (4.7) N=446	6.77 (5.11) N=266	8.0 (4.8) N=308	5.84 (4.76) N=312	6.1 (4.4) N=332	4.29 (3.88) N=311
	Difference	p=0.031		p<0.001		p<0.001	
AUDIT≥8 (%)		45.0	38.0	49.5	32.2	29.4	17.7
AUDIT≥13(%)		14.8	11.7	14.7	9.3	9.2	3.9
CAGE score (%)							
Valid number		N=400	N=280	N=279	N=324	N=238	N=326
CAGE 0		55.8	50.4	49.1	63.3	63.0	68.1
CAGE 1		23.5	19.6	24.4	12.0	22.3	12.0
CAGE 2		11.0	16.1	14.7	11.7	9.2	10.1
CAGE 3		7.8	9.3	8.6	9.0	4.6	7.7
CAGE 4		2.0	4.6	3.2	4.0	0.8	2.1
	Difference	p=0.051		p<0.001		p=0.011	
Amount consumed (alcohol units)*		9.7 (9.5) N=400	2.83 (1.33) N=244	8.0 (8.7) N=279	2.68 (1.38) N=274	4.8 (6.0) N=238	2.20 (1.22) N=260

*Ark. 2000 per week, KYH per day — Source: (48,50)

For men, GGT has slightly decreased, but the values are still high for all the groups. The standard deviation for each age group was large, suggesting large individual differences in alcohol consumption. The mean total AUDIT score and the proportion of participants with the total AUDIT score of eight or higher also decreased. The proportion of those with a CAGE score of two or higher has decreased only in the age 50-59. For those above the score of three increased for all the age groups. These differences in CAGE scores suggest there might have been underreporting of alcohol drinking in Ark.2000 as well as KYH. Although alcohol consumption in Arkhangelsk seems declined over the years, it still remains high.

Table 14: Alcohol-related variables (GGT, AUDIT, CAGE, & consumption) for women

Women		Age 40-49		Age 50-59		Age 60+	
		Ark. 2000	KYH	Ark. 2000	KYH	Ark. 2000	KYH
GGT	Mean	32.9 (58.4) N=419	25.3 (29.7) N=391	31.1 (32.3) N=305	36.2 (56.7) N=401	35.9 (43.0) N=320	32.5 (46.4) N=445
	Median	20.0	17.8	23.0	21.8	24.0	22.4
	Difference Mean	p=0.019		p=0.148		p=0.297	
Total AUDIT score		3.6 (3.3) N=419	2.78 (2.33) N=391	3.0 (2.2) N=305	2.18 (2.02) N=403	2.2 (1.5) N=320	1.50 (1.29) N=446
	Difference	p<0.001		p<0.001		p<0.001	
AUDIT≥8 (%)		9.0	4.1	5.9	2.5	2.0	0.2
AUDIT≥13(%)		2.3	0.7	0.0	0.5	0.0	0.0
CAGE score (%)							
Valid number		N=345	N=411	N=219	N=422	N=99	N=459
CAGE 0		70.1	83.9	77.6	88.6	91.9	93.0
CAGE 1		18.8	8.8	17.8	5.5	7.1	4.4
CAGE 2		9.0	5.4	3.2	3.6	1.0	2.6
CAGE 3		1.7	1.5	1.4	1.9	0.0	0.0
CAGE 4		0.3	0.5	0.0	0.5	0.0	0.0
	Difference	p<0.001		p<0.001		p=0.341	
Amount consumed (alcohol units)*		2.6 (2.3) N=345	1.62 (0.77) N=363	2.8 (5.7) N=219	1.51 (0.83) N=360	2.1 (3.2) N=99	1.30 (0.59) N=378

*Ark. 2000 per week, KYH per day Source: (48,50)

For women, the mean GGT slightly decreased except for age 50-59 while the median decreased for all the groups, suggesting a decline in alcohol consumption although the individual difference seems to be large. The decline in the mean total AUDIT score was significant for all the age groups, and the proportion of participants with an AUDIT score of eight or higher decreased at all the groups whereas the proportion of those above 13 increased for age 50-59. The proportions of participants with lower CAGE score (below one) increased for all age groups except age 40-49 while those of higher CAGE score (two to four) decreased except for ages above 60.

4.2.4 Ten-Year Risk Scores for CHD Development

The following table 15 shows ten-year risk scores of developing CHD for men and women for groups of five-year age range above 40 with means, standard deviations, and valid numbers. For Ark.2000, valid numbers were available only for the ten-year age range. For men, each age group below 60 had an increased score while that of above 60 had a decreased score. As the age group goes higher, the larger the decrease of the scores between the studies was (7.6 lower for age 70-74). For women, the risk scores decreased drastically over the years with the highest decrease of 8.74 for the age 60-64.

Table 15: Ten-year risk scores of developing CHD for men and women (means, standard deviations, and valid numbers) Source (46,50)

Age	Men				Women			
	Ark.2000		KYH		Ark.2000		KYH	
		Valid		Valid		Valid		Valid
40-44	5	447	5.37 (5.07)	27	2	420	0.86 (1.51)	37
45-49	8		9.36 (7.28)	36	4		3.00 (5.02)	43
50-54	10	308	10.55 (5.62)	55	8	305	3.02 (2.98)	63
55-59	13		16.06 (6.73)	68	10		4.72 (4.44)	110
60-64	18	332	15.11 (4.11)	83	13	320	4.26 (2.60)	133
65-69	25		18.72 (5.59)	93	13		6.87 (4.54)	167
70-74	28		20.40 (4.51)	5	13		8.80 (4.63)	15

5 Discussion

5.1 Main findings

For men, total- and HDL-cholesterol, systolic BP, GGT, total AUDIT, and smoking have improved over the years while diastolic BP, RHR, BMI, physical activity at work, and CAGE have increased. Although most of the variables related to alcohol decreased and suggest a reduction in alcohol consumption, GGT remains high for all the age groups. Reduction in some of the risk factors has improved the risk scores for developing CHD. However, a further decrease in risk factors would be necessary for a reduction in CVD prevalence. For women, total and HDL-cholesterol, systolic BP, GGT, total AUDIT, CAGE, education, physical activity at work improved while diastolic BP, RHR, and smoking increased. BMI remained similar between the studies. There were larger declines in ten-year risk scores for CHD development for women compared to men. For further reduction in risk factors, control of BMI and prevention of increasing smoking prevalence would be necessary.

5.1.1 Total cholesterol & HDL-cholesterol

For men, changes in the mean total cholesterol were not significant except for age 50-59. Changes in the mean HDL-cholesterol were significant for above 50 years old. For women, the mean total cholesterol values were similar for age 40-49 and 50-59, but the differences were larger and significant for above 60 years old. Differences in the mean HDL-cholesterols were significant at all age groups.

Cholesterol is a lipid found in blood, and it can be deposited, creating plaque when in high abundance. Sudden breakage of those clots can cause a heart attack or stroke (55). HDL-cholesterol is considered to be the good cholesterol as it transports excess cholesterol back to the liver (55). Genetics and age play roles in high cholesterol; however, unhealthy lifestyle choices such as unhealthy diet, smoking as well as sedentary lifestyle affect cholesterol as well

(55). Reduction in total cholesterol in men aged 50-59 and women above 50 years old and increase in HDL-cholesterol in men above 50 and women of all age groups could suggest improvements in these modifiable risk factors for cholesterol in all age groups in both genders. However, it is likely that there are differences in improvements among different age groups and between genders, suggesting older age groups and women were more health-conscious.

5.1.2 Systolic & Diastolic Blood Pressures and Pulse Pressure

For men, the decreases in the systolic BP were significant only for participants above 60 years of age. However, the increases in the diastolic BP were significant for all age groups. For women, the decreases in the systolic BPs were significant for all ages. The increases of diastolic BPs were significant for age 40-49 and 50-59.

BPs are determined by the amount of blood pumped by the heart and the arterial resistance (56). Systolic BP is the arterial pressure from ventricular contraction pushing blood from the heart, typically around 120 mmHg while diastolic BP is from ventricular relaxation, typically around 80 mmHg (57). The risk factors of high BP include age, race, family history, chronic conditions, obesity, physical inactivity, smoking, high sodium and low potassium in diet, alcohol, and stress (56). BPs can also be modified by medications. Decreases in systolic BPs in both genders could suggest improvements in the modifiable risk factors of hypertension or high BP as well as medication use. There was also a gender difference in improvement in systolic BP. The decrease in systolic BP was larger in women compared to men. The largest reduction was observed in women over 60 years of age with 13.2 mmHg, 8.8% reduction. This could be due to the higher tendency of women seeking healthcare compared to men; thus higher number of women using medication to control BPs (10).

Although systolic BPs in both genders improved, diastolic BP has increased in both genders. This could be due to the differences in the devices used for measurements in the studies. There were several validation studies for both DINAMAP and OMRON705 IT. OMRON705 IT was tested on participants with different BP groups including children and adolescents and satisfied both the British Hypertension Society criteria (A-very good) and the Association for the Advancement of Medical Instrumentation SP10 Standard less than ±5 (with a standard deviation of 8) mmHg (58,59).

However, there were contradicting results for DINAMAP. One study measured ankle systolic BP on adults using DINAMAP1846 SX and Doppler and concluded DINAMAP as a more precise and useful tool for epidemiological studies (60). Another study compared DINAMAP and the conventional auscultatory method to measure BP in infants and children and concluded DINAMAP as more preferred method compared to the conventional auscultatory method as the mean error was smaller and reflected the direct radial artery pressure well (61).

Yet another study recognized DINAMAP disregarding certain systolic BP values in three epidemiological studies due to the algorithm used to improve the precision of the device (62). There were also other articles that question the accuracy of the DINAMAP model 8100 for measuring diastolic BP. It was found that the device achieved a grade B for systolic BP measurements and a D (poor) for diastolic BP based on the British Hypertension Society criteria (63,64). Both the accuracy and inaccuracy of DINAMAP devices were reported on different devices from the ones that were used in Ark.2000 study. The company that produced DINAMAP-R was acquired by another healthcare company in 2000 (65). The validation of DINAMAP-R could not be found since the DINAMAP website no longer exists.

Another possible explanation for systolic and diastolic BPs moving to different directions might be due to pulse pressure change between Ark.2000 and KYH. Pulse pressure is the differences between systolic and diastolic BPs (66). For those above 60 years of age, a pulse pressure of above 60 is an indicator of CVDs and suggests losses in elasticity in aorta leading to leaky heart valves (valve regurgitation) (66). Pulse pressure of lower than 40 also indicates poor cardiovascular function (66). Elevated pulse pressure indicates aortic stiffness from high BP, damages of arterial walls from plaque, and lack of elasticity in blood vessels (atherosclerosis) (66). Pulse pressure was lower in KYH than Ark.2000 at all age groups for both genders. This suggests an improvement in cardiovascular functions. Although diastolic BP increased over the years, the improvement seen in both systolic BP and pulse pressure suggests recent positive trends in improvement of CVD risk factors as well as CVD mortality.

5.1.3 Resting heart rate

RHRs for both men and women increased in all age groups with a significance for those aged 40-49 and 50-59 for men and women. Normal heart rates range between 60 and 100 beats per minute with lower RHRs indicating efficient cardiovascular functions (67). Factors for an increase in heart rate include age, physical inactivity, smoking, disease history (having CVDs, high cholesterol, or diabetes), air temperature, emotions, body size, and use of medications (67). Although there was a decrease in smoking prevalence in men, a decrease in physical activity at work might have increased resting heart rate as it is another risk factor. An increase in RHR in women might have been affected by the increase in the prevalence of smoking in women.

5.1.4 Body Mass Index, Physical Activity at Work, and Education

For men, BMI has increased between 2000 and 2017. The differences in BMI were significant for age 40-49 and above 60. This might be due to different sample populations with different proportion of physical work occupations as BMI is a measure of obesity and physical inactivity. For the age groups 40-49 and 50-59, sedentary occupation increased whereas physical work including heavy manual work decreased. For those above 60 years of age, sedentary and standing occupation decreased while physical and heavy manual work increased.

In fact, the proportion of sailors in Ark.2000 was higher compared to that of KYH (50). Sample population representing the general population in KYH might have given the impression of a decrease in the proportion of participants with physical work for younger age groups.

These changes in the proportion of different occupations could also be related to educational attainment. The proportion of higher education increased for all age groups in KYH. However, this could also be thought of the sample population in KYH representing the general population well as sailors do not require to have higher education. Thus, those with higher education were underrepresented in Ark.2000. In addition, misclassification of education groups might have occurred as the questions on educational attainment were formulated differently between the studies. Nevertheless, it is also possible that the educational attainment has increased over the years as the youngest age group (40-49) has the highest higher education attainment.

The information on physical activity at leisure time was not available; however, these age groups are working-age groups and spend a great amount of time at work. Therefore, physical activity at work is an important factor to control BMI. One study looked at BMI and workplace characteristics such as decision making, job flexibility and workplace harassment (68). They found out that greater decision making and job flexibility increased physical activity (68). Therefore, increasing physical activity at work is possible even with sedentary occupations. In fact, there are multiple studies and policy guidelines recommending to increase workplace physical activity as workplace physical activity can lead to higher productivity, lesser sick leaves, and lower healthcare costs (69,70).

For women, BMI was similar in both studies for ages 40-49 and 50-59. For those above 60, BMI has increased with significance. With social changes in female occupations, sedentary and standing occupation decreased while physical and heavy manual work increased at all age groups. However, misclassification could also be a possible explanation for the increase in physical work as the occupation questions were formulated differently between the studies. Despite the increase in physical work at all age groups, BMI increased in the age group above 60. This might have been related to the educational attainment. Even though higher educational attainment was achieved at all age groups, the proportion of the participants with higher education was lowest for the group above 60. The association of higher educational levels and lower BMI was found in several studies (71,72). Those participants with higher educational attainment might have cared about their health by increasing physical activity and had access to healthier food due to the tendency to have higher income with higher educational attainment.

5.1.5 Smoking & Education

For men, never and former smokers increased while current smokers decreased for all age groups. This reduction in current smokers might be influenced by educational attainment. A study of Australian twins found nine months of reduction in smoking duration as the educational attainment increases by one year (73).

For women, the comparison of Ark.2000 and KYH showed the opposite trend. The proportion of never smoker decreased while former and current smoker increased except for current smokers of age 40-49. Although the proportion of women with higher education increased, there was also an increase in the number of current smokers. This might be due to the thought of losing weight from smoking. In fact, this idea has started around the 1930s from an advertisement to recommend women smoking: "reach for a cigarette instead of a sweet"(74). Some smokers think weight gain as a drawback of smoking cessation (74).

The research which looked at consequences of smoking on body weight concluded that smoking can reduce appetite and body weight by nicotine increasing expenditure of energy in the short term (75). However, those who smoke do not seem to know about the long-term effect of smoking on body weight. The addictive effect of nicotine is well known (76,77). Heavy smoking is associated with weight gain compared to light smoking and non-smoking as it is related to other risk factors such as physical inactivity and poor diet (75). The authors also concluded that smoking increases the risk of metabolic syndrome, diabetes, and CVDs (75). Therefore, increasing awareness of the negative effect of smoking on body weight and offering support for smoking cessation will be important for CVD prevention. This is especially essential for women to stop the current trend of an increase in smoking.

5.1.6 GGT, CAGE, AUDIT & Alcohol Consumption

For men, both the mean and the median of GGT decreased over the years for all the age groups although they were not statistically significant. For women, both the mean and the median of GGT decreased for all the age groups except for the mean GGT for age 50-59. The reduction in GGT was significant for age 40-49.

GGT is an enzyme primarily found in kidney, liver, and pancreas to transport peptides and amino acids to cells (78,79). An elevated level of GGT suggests alcohol abuse and is associated with CVDs due to its involvement in atherosclerosis (78,80). The reference levels of GGT for adult men and women are 8-61 and 5-36 U/L but vary between studies (79). One study categorized GGT for men and women as normal low (<14 and <9U/L), normal high (14-27 and 9-17 U/L), moderately elevated (28-41 and 18-26 U/L), increased (42-55 and 27-35 U/L), and highly elevated (≥56 and ≥36 U/L, respectively) (80). With this categorization, the current GGT levels for all the age groups in men are at an increased level while those are moderately elevated, highly elevated, and increased for women aged 40-49, 50-59, and above 60. These GGT levels indicate high alcohol consumption in Arkhangelsk population. Even though the levels have been decreasing, there is a concern that GGT has a large number of false negatives (78). Hence, the use of AUDIT and CAGE would be beneficial in addition to GGT.

Even though both AUDIT and CAGE are self-reporting questionnaires, both have been validated for its sensitivity and specificity (28,81–83). Some researchers found AUDIT more reliable than CAGE as CAGE has only four questions; however, adjusting the number of item criteria to two or three instead of four (88, 83, 81, 94% for sensitivity and specificity of two and three positive response, respectively), CAGE was considered to satisfy the validity (81,82).

From Ark.2000 to KYH, the mean of the total AUDIT scores have been significantly decreased for all the age groups in both genders. The proportion of AUDIT scores of equal or above eight, indicating hazardous drinking, also decreased for both gender and all age groups.

On the other hand, the CAGE score indicated the opposite results for men and women. For men, the proportion of men having a CAGE score of 0 and 1 decreased except for CAGE score 0 for age 50-59. Higher CAGE scores increased for all the age groups. For women, CAGE scores were similar between the studies for all the age groups except age 40-49. For this group, the positive trend of having lower scores was seen. Reduction of CAGE scores in women but not men suggests underreporting in Ark.2000. Underreporting of alcohol consumption is also possible in KYH as well.

Nevertheless, the decline in GGT levels and AUDIT scores for both genders and CAGE score for women could suggest a positive trend of reduction in alcohol consumption in Arkhangelsk. The following table 17 shows the consumption of total alcohol and different types of alcohol consumed in dL in Arkhangelsk (Arkhangelsk oblast – Nenets autonomous okrug) between 2010 and 2017 as 2000 data was only available for the whole Arkhangelsk region (84).

The total consumption of alcohol in dL decreased by 436,500dL between 2010 and 2017 (84). Not only the consumption of alcohol but also the types of alcohol consumed have changed over the years. The consumption of vodka and cognac decreased while beer consumption increased (84). As vodka and cognac have higher alcohol content than beer, it might have had an effect to lower GGT and lead to the reduction of total AUDIT scores.

Table 16: Yearly alcohol consumption in dL in Arkhangelsk Source: (84)

Year	Vodka & Liquor	Cognac	Wine	Sparkling wines	Beer	Total
2010	1,902,000	143,300	1,431,200	219,600	4,815,800	8,511,900
2016	1,376,300	105,600	940,900	205,000	5,808,900	8,436,700
2017	1,235,300	103,900	1,006,900	169,800	5,559,500	8,075,400

5.1.7 Ten-year risk of developing CHD

Although the ten-year risk of developing CHD has increased for ages between 40 and 59 in men, it has decreased significantly in women of all age groups. The largest reduction was found in women aged 60-64. However, the sample sizes were smaller in KYH compared to Ark.2000, which might have affected the result. In addition, some of the risk factors such as GGT, AUDIT, CAGE, education, physical activity at work were not included in the calculation of ten-year risk of developing CHD. Since the reduction in alcohol consumption in men was not included in the calculation, it might have led to the large gender difference in the ten-year risk of developing CHD.

Nevertheless, these factors that were not included in the calculation might have affected other risk factors that were in the calculation as these factors were interconnected. The improvements in CVD risk factors such as reductions in total cholesterol, systolic BP, pulse pressure, smoking, GGT, and AUDIT as well as increases in HDL-cholesterol and educational attainment suggest the reduction in ten-year risk of CHD development for ages above 60 in men. For ages below 60, slight increases in BMI and RHR and still high consumption of alcohol seen from GGT, AUDIT, and CAGE might have hindered the benefits of improvements in other risk factors. For women, a slight reduction in total cholesterol, systolic BP, GGT, and AUDIT, as well as increases in HDL-cholesterol, physical activity at work, and educational attainment seemed to favor a reduction in the ten-year risk of CHD development especially in ages above the age of 60.

5.2 Limitations & Strength

5.2.1 Study population

The total number of participants included for the analyses were similar in both Ark.2000 and KYH. However, the ways participants were recruited differed in the two studies. For Ark. 2000, although some workplaces and educational institutions were invited, most of the participants were recruited at a polyclinic while attending annual medical examinations. Since it was a mandatory annual health check for sailors, the proportion of sailors were overrepresented in Ark.2000. However, participants were recruited from the general population for KYH by randomly selecting individual addresses. Since those two study populations were recruited differently, it is important to consider selection bias in each study. According to Henderson, "Selection bias in epidemiological studies occurs when there is a systematic difference between the characteristics of those selected for the study and those who are not" (85).

For Ark.2000, participants attended annual medical examinations through workplaces and educational institutions, which means they were healthy enough to work or study. This indicates healthy worker effect, which is defined by Last as "a phenomenon initially observed in studies of occupational diseases: Workers usually exhibit lower overall death rates than the general population because the severely ill and chronically disabled are ordinarily excluded from employment" (86). In fact, the proportions of sailors and fishermen in men who are 40-59 in the study population were large compared to other occupations due to the polyclinic used to serve mainly sailors, fishermen, and their families (50). Participants with manual labor jobs including fishery would have to be healthier to perform manual labor jobs. Therefore, there might have been an underestimation of CVDs due to participants being healthy. In addition, the proportion of the male unemployed population was underrepresented in the study as most people go to annual medical examinations through workplaces (46,48).

Moreover, the study population was more educated than the general Arkhangelsk region population. Manual labor jobs, which include sailors and fishermen, are unlikely to require higher education. Therefore, even with the higher proportion of younger males being sailors and fishermen, the sample population of Ark.2000 represented somewhat general population in terms of educational attainment. However, the higher educational attainment of the sample population is likely to be due to urban-rural differences that there are more educated people working in an urban setting (48). In fact, the Programme for International Student Assessment (PISA) scores for secondary students in Russia were higher in urban areas compared to rural areas between 2000 and 2009 (87). This was explained by the socioeconomic differences of students, urban schools having a significantly higher proportion of students whose parents have higher education (87). Even though the male unemployed population was underrepresented, age distributions of the study sample and the general Arkhangelsk population were relatively similar (48).

Furthermore, non-response bias arising from having a large number of non-responders can be disregarded for this study as they have recruited participants who were already at the polyclinic. Hence, the response rate for the study was 98% (40 non-participants and 43 without questionnaires out of 4129 recruited for the study), which was a strength of Ark.2000 (50).

For KYH, random addresses from four districts with different socio-demographic characteristics were selected to represent the general Arkhangelsk population; therefore, it is likely that the study population represented the general population. However, there could be non-response bias as the response rates calculated based on the addresses matching expected and observed age and sex of occupants were lower for the younger male and higher for the older female with an overall response rate of 68.2% in Arkhangelsk (24). There were general tendencies of non-responders being younger male with lower educational level without regular paid employment and responders with a history of CVDs with a high attendance of medical examination except for those with previous stroke (24). In addition, participants living far from the clinic were also less likely to complete the medical examinations (24). However, the proportion of baseline questionnaire responders who attended medical examinations for all ages were 96% in Arkhangelsk (24).

In order to rule out selection bias due to non-response, Cook et al compared the educational attainment of the sample population and the general Arkhangelsk population from the Russian census 2010 (24). Although higher education attainment was higher for younger age and lower for older age in the sample population compared to the general Arkhangelsk population, the overall ratios of observed to expected for those completed baseline survey and health check were 0.98 and 0.99, showing the sample population representing the general Arkhangelsk population (24).

Even though the study populations were collected differently, both studies are likely to be comparable. The representation of the general Arkhangelsk population was seen in KYH. Although there seems to be an overrepresentation of sailors and fishermen for younger male age groups inArk.2000, the sample population seems to be representing the general population in terms of educational attainment and age distribution.

5.2.2 Data collection & Analyses

There are also possibilities of information biases, specifically misclassification bias, recall bias, self-reporting bias and social desirability bias and measurement error bias.

Kesmodel describes information bias as inaccurate measurement and or recording of any information used in a study (88).

A possible source of misclassification would be altering categories of variables. For the purpose of the comparison between the two studies in this thesis, some of the categories were reclassified. However, these changes were carefully made by comparing the description of each category from both studies, and some comparisons were dropped when questions were formulated differently to avoid further misclassification.

Recall bias occurs due to participants who have experienced CVDs previously might recall exposure to risk factors better than those who have not experienced CVDs. This would lead to over-reporting of exposures in those who have experienced CVDs but underreporting in those who have not experienced CVDs. Underreporting reduces the effect of a dose-response relationship (88).

Underreporting is closely related to self-reporting and social desirability bias. Social desirability bias occurs when private or sensitive information such as dietary intake and substance use are collected (89). For questionnaires and surveys, participants might choose categories that are preferred or approved by society since it is self-reported. This leads to underreporting of alcohol consumption and smoking. In order to reduce self-reporting and social desirability bias, validation of self-reporting questionnaires are important (89). In both Arkhangelsk 2000 and KYH, alcohol consumption was measured using validated questions such as AUDIT and CAGE. The use of the same tests in both studies enabled the direct comparison of alcohol consumption in this thesis, which is one of the strengths.

Another bias that needs to be considered is measurement error bias. Measurement error bias occurs due to the inaccuracy of devices used to measure outcomes, conditions of laboratories, and self-reported measurements (89). In order to avoid observer bias caused by differences in measurements among diverse observers, health examinations and baseline questionnaires were carried out by trained professionals in both studies (24,48). Questionnaires from both studies were also double translated (forward and backward between English and Russian) to avoid the bias (24,48). These attempts were strengths of the studies.

Some of the variables in Ark.2000 and KYH such as biomarkers and anthropometry were measured differently using different devices, which might have affected the results. To avoid measurement error bias from devices, frequent calibration of devices, controlling environment, and validations of devices used in the studies are essential. In both studies, BP measurements were performed in a different room with only one participant at a time (24,48). Even though validation and frequent calibrations of devices were performed in each study, there was no validation or calibration between the studies. Therefore, it is possible that the results might be affected by measurement error. In addition, participants knowing that they are part of a study or being nervous at health checks could lead to a measurement error. For example, BPs could fluctuate by participants being at a polyclinic. For this reason, the means of second and third measurements of systolic and diastolic BPs from both studies were used for the analyses.

Furthermore, confounding is another factor that needs to be considered when analyzing multiple variables. Aronson and Delgado-Rodriguez describe a confounder as a variable which is a risk factor for an effect and modifies the association between the exposure and the outcome (90,91). Since raw data was not available from Ark.2000, adjustment for age or other factors was not performed on KYH data. However, the descriptive statistics published from Ark.2000 was stratified by age and sex, so KYH data were also stratified by age and sex to control for confounding. Nevertheless, there might be other confounders that were not adjusted due to the unavailability of raw data from Ark.2000.

5.2.3 Strengths

Strengths of the studies were the locations of the polyclinics in both studies. Being in or close to the city center made it easier for participants to attend health checks (24,48). In addition, data collection in KYH was done electronically for both baseline questionnaires and health checks, which eliminated recording errors (24). Moreover, this thesis was the first to compare CVD risk factor changes in Arkhangelsk to the knowledge of the author. Sampled populations in both Ark.2000 and KYH relatively represented the general Arkhangelsk population. Since Russia is a larger country with a lot of diversity, it might be difficult to generalize the result of this thesis. However, the results would be beneficial to understand the recent downward in CVD deaths in similar population-sized cities in Russia.

5.3 Further Research

The accuracy of the comparisons provided in this thesis could be improved by conducting longitudinal studies on the same population. Cohort study and time trend analysis would be possible by conducting the same study again on the same individuals. The use of the same questionnaires, protocols, and measuring devices would reduce biases and would provide more reliable results. More accurate and reliable results would help to explain the recent decline in CVD mortality in Russia and be beneficial for future preventive strategies. Communicating the knowledge gained through these studies to the general public in Arkhangelsk would be beneficial for future preventive strategies.

6 Conclusion

Although some of the changes were small, total- and HDL-cholesterol, systolic BP, GGT, total AUDIT, and education improved for both genders between Ark.2000 and KYH. Smoking for men, CAGE and physical activity at work for women have also improved between the studies. The decline in the ten-year CHD risk scores was larger for women compared to men.

This might be due to the reduction in the important risk factor for Russian male, alcohol consumption, not included in the calculation. Nevertheless, the reduction in alcohol consumption could modify other risk factors that were included in the calculation and could contribute to CHD reduction. Controlling alcohol consumption in men and smoking and BMI in women would be beneficial for further reduction of CVD risk factors as well as its prevalence. Conducting longitudinal studies and communicating the results to the general public in Arkhangelsk would be necessary and beneficial for the prevention of CVDs and a further reduction in its mortality in Arkhangelsk as well as Russia.

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8 Appendix

Questionnaire Arkhangelsk 2000

(only those questions included in the thesis are listed)

1. Personal information

1.1. **SEX:** male □□female □□
1.2. **AGE:** □□□years

2. Occupational activity and social conditions

2.1. **EDUCATION:**

primary school □
secondary school □
secondary professional school □
some college □
graduated from college □

3. Heredity and disease history

3.2. **DO YOU NOW HAVE OR HAVE YOU EVER HAD:** Yes No Don't know

myocardial infarction □□□
angina pectoris □□□
cerebral stroke or brain haemorrhage (insult) □□□
sugar diabetes □□□
high blood pressure (hypertensive disease) □□□
pancreatitis □□□
hepatitis or cirrhosis of the liver □□□
nephritis □□□
stomach bleeding □□□
dyspepsia (digestive trouble) □□□
stomach or duodenal ulcer □□□
brain concussion □□□
trauma to the extremities or to the spine □□□

5. Physical activity

5.2. **PLEASE ESTIMATE YOUR LEVEL OF PHYSICAL ACTIVITY IN THE WORK PLACE:**

During the last year you have had:
mostly sedentary work (e.g. office work, etc.) □
work that requires a lot of walking (e.g. shop-assistant, waiter, etc.) □
work that requires a lot of walking and lifting (e.g. postman, construction, etc.) □
heavy manual work (e.g. farmer, forestry, etc.) □

7. Smoking

7.4. **DO YOU SMOKE:**

yes, every day □
sometimes □
no, never smoked □
smoked previously □

8. Alcohol

8.1. **DO YOU DRINK ALCOHOLIC BEVERAGES:**

yes □ no □

We provide an explanation of the term ALCOHOL UNIT. One alcohol unit corresponds to *(illustration in Russian questionnaire)*:
1 bottle (0.33 l) of strong beer or 2 bottles (0.33 l) of light beer
1 ordinary glass of table wine (120 ml)
1 glass fortified wine (80 ml)
1 shot of liquor (40%, 40 ml)
This means that for instance, 0.5 l strong beer or 1 l light beer = 1.5 alc. units; 1 bottle of table wine = 5 alc. units; 1 bottle of fortified wine = 8 alc. units; 1 bottle of liquor = 15 alc. units.

8.2. **HOW MANY ALC. UNITS DO YOU DRINK PER WEEK:**

beer □□
table wine □□
fortified wine □□
liquor □□
in total □□

8.5. **DO YOU EVER HAVE THOUGHTS ABOUT THE NECESSITY TO GIVE**

UP DRINKING ALCOHOL:
yes no

8.6. **DOES CRITICISM OF YOUR DRINKING FROM THE SUR-ROUNDINGS EVER BOTHER YOU:**
yes no

8.7. **DO YOU EVER HAVE WORRIES OR A SENSE OF GUILT REGARDING YOUR DRINKING:**
yes no

8.8. **DOES IT EVER HAPPEN IN THE MORNINGS THAT YOU FIRST OF ALL START DRINKING IN ORDER TO CALM DOWN OR GET RID OF A HANGOVER:**
yes no

8.9. **HOW OFTEN DO YOU DRINK ALCOHOLIC BEVERAGES:**
never
once a month or less
2-4 times a month
2-3 times a week
4 or more times a week

8.10. **HOW MANY ALC. UN. DO YOU USUALLY DRINK ON ONE OCCASION:**
1-2
3-4
5-6
7-9
10 or more alc. units

8.11. **HOW OFTEN DO YOU DRINK 6 OR MORE ALC. UN. ON ONE OCCASION:**
never
less than once a month
once a month
once a week
daily or almost daily

8.12. **HOW OFTEN DURING THE LAST YEAR DID YOU FEEL THAT YOU COULD NOT STOP DRINKING ONCE YOU HAVE STARTED:**
never
less than once a month
once a month
once a week
daily or almost daily

8.13. **HOW OFTEN DURING THE LAST YEAR SHOULD YOU HAVE FULFIL-LED OR DONE SOMETHING, WHICH YOU WERE NOT ABLE TO DO BE-CAUSE OF ALCOHOLCONSUMPTION:**
never
less than once a month
once a month
once a week
daily or almost daily

8.14. **HOW OFTEN DURING THE LAST YEAR DID YOU HAVE TO DRINK AL-COHOL IN THE MORNING IN ORDER TO COME ROUND AFTER HEAVY AL-COHOL INTAKE THE DAY BEFORE:**
never
less than once a month
once a month
once a week
daily or almost daily

8.15. **HOW OFTEN DURING THE LAST YEAR WERE YOU UNABLE TO RE-CALL WHAT HAPPENED IN THE EVENING OF THE DAY BEFORE BE-CAUSE OF ALCOHOL CONSUMPTION:**
never
less than once a month
once a month
once a week
daily or almost daily

8.16. **HAVE YOU OR ANYBODY ELSE EVER HAD TRAUMA AS A RESULT OF YOUR ALCOHOL CONSUMPTION:**
no
yes, but not in this year
yes, in this year

8.17. **HAVE ANY OF YOUR RELATIVES, FRIENDS OR PERSONS IN THE HEALTH SERVICE EVER EXPRES-SED ANXIETY REGARDING YOUR HARD DRINKING AND SUGGESTED THAT YOU BETTER CUT DOWN THE ALCOHOL CONSUMPTION:**
no
yes, but not in this year
yes, in this year

8.18. **HOW OFTEN DURING THE LAST YEAR HAVE YOU FELT GUILT BECAUSE OF YOUR DRINKING:**

never □
less than once a month □
once a month □
once a week □
daily or almost daily □

THIS PART WILL BE FILLED IN BY MED. PERSONELL □

10. Anthropometry

10.1. **WEIGHT:** □□kg
10.2. **HEIGHT:** □□cm
10.5. **SYSTOLIC BLOOD PRESSURE:**
1 □ 2 □ 3 □

10.6. **DIASTOLIC BLOOD PRESSURE:**
1 □ 2 □ 3 □
10.7. **PULSE RATE:**
1 □ 2 □ 3 □

11. Laboratory parameters

11.2**. CHOLESTEROL** □
11.3. **HIGH-DENSITY LIPOPROTEIN**
11.4. **LOW-DENSITY LIPOPROTEIN** □
11.7. **GGT** □

Know Your Heart: Questionnaires

(only those questions included in the thesis are listed)

Baseline Questionnaire		
Module A: Socio-demographic Factors		
A1. How old are you?	______Years	
	97	Difficult to answer
	98	Refuse to answer
A3. Interviewer: Please mark the gender of the respondent.	1	Male
	2	Female
A9. What is your level of education? SHOW CARD 1. Please choose the single most appropriate answer.	1	Incomplete secondary or lower
	2	Complete secondary
	3	Professional school (without secondary degree, PTU)
	4	Professional school and secondary (e.g. PTU and secondary education)
	5	Specialised secondary (e.g. medical, pedagogical college, technicum)
	6	Incomplete higher
	7	Higher
	97	Difficult to answer
	98	Refuse to answer
A12. Are you in regular paid work?	1	Yes
	2	No Go to A 14
	97	Difficult to answer
	98	Refuse to answer

A14. Are you…Ask only those who are not in regular paid work (A12-NO)	1	In irregular paid work
	2	Unemployed, seeking work
	3	Unemployed, not seeking work
	4	Housewife
	5	Other
	5a	Other. Specify:
	6	None of the above
	97	Difficult to answer
	98	Refuse to answer

Module B: Physical Activity

Next questions will be related to your physical activity.

We would like to know the type and amount of physical activity involved in your work (only asked those who worked in the past 12 months)

B1. Please choose what best corresponds to your present activities from the following four possibilities. SHOW CARD 3.	1	**Sedentary occupation** - You spend most of your time sitting (such as in an office)
	2	**Standing occupation -** You spend most of your time standing or walking. However, your work does not require intense physical effort (e.g. shop assistant, hairdresser,guard, etc.)
	3	**Physical work -** This involves some physical effort including handling of heavy objects and use of tools (e.g. plumber, cleaner, nurse, sports instructor, electrician, carpenter, etc.)
	4	**Heavy manual work -** This involves very vigorous physical activity including handling of very heavy objects (e.g. docker, miner, bricklayer, construction worker, etc.)
	97	Difficult to answer
	98	Refuse to answer

Module D: Use of Health Care Services

This module contains questions about use of medical services, presence of some diseases and use of medications.

D10. Have you ever been told by a doctor (been diagnosed) that you have:

Arterial hypertension (high blood pressure). *For women "except during pregnancy"*	1: Yes 2: No 97: Difficult to answer 98: Refuse to answer
High cholesterol level	1: Yes 2: No 97: Difficult to answer

	98: Refuse to answer
Myocardial Infarction/Heart attack	1: Yes 2: No 97: Difficult to answer 98: Refuse to answer
Heart failure	1: Yes 2: No 97: Difficult to answer 98: Refuse to answer
Atrial fibrillation	1: Yes 2: No 97: Difficult to answer 98: Refuse to answer
Angina	1: Yes 2: No 97: Difficult to answer 98: Refuse to answer
Stroke	1: Yes 2: No 97: Difficult to answer 98: Refuse to answer
Diabetes	1: Yes 2: No 97: Difficult to answer 98: Refuse to answer
Module G: Alcohol Consumption	
G1-5: For each type of drink listed in the left hand column, please indicate how often each was usually drunk in the last 12 months. SHOW CRAD 6.	
G1. Any alcohol	1. Every day or more often 2. Nearly every day 3. 3-4 times per week 4. Once or twice a week 5. 1-3 times a month 6. A few times a year 7. Never or almost never 97. Difficult to answer 98. Refuse to answer
G2: Beer	1. Every day or more often 2. Nearly every day 3. 3-4 times per week 4. Once or twice a week 5. 1-3 times a month 6. A few times a year 7. Never or almost never 97. Difficult to answer 98. Refuse to answer
G3: Wine (not home produced)	1. Every day or more often 2. Nearly every day 3. 3-4 times per week 4. Once or twice a week

	5. 1-3 times a month 6. A few times a year 7. Never or almost never 97. Difficult to answer 98. Refuse to answer
G4: Fortified wine (e.g. port wine)	1. Every day or more often 2. Nearly every day 3. 3-4 times per week 4. Once or twice a week 5. 1-3 times a month 6. A few times a year 7. Never or almost never 97. Difficult to answer 98. Refuse to answer
G5: Spirits (vodka, cognac, whisky, gin, rum, etc.)	1. Every day or more often 2. Nearly every day 3. 3-4 times per week 4. Once or twice a week 5. 1-3 times a month 6. A few times a year 7. Never or almost never 97. Difficult to answer 98. Refuse to answer
CAGE Score	
G11. During last 12 months how much beer did you usually drink on one occasion? ('occasion' means a single continuous period of drinking). *Please choose the single most appropriate answer.*	1. Never drink beer 2. 1 bottle (0.5l) or less 3. 2-4 bottles 4. 5-6 bottles 5. More than 6 bottles 97. Difficult to answer 98. Refuse to answer
G12. During last 12 months how much wine did you usually drink on one occasion? *Please choose the single most appropriate answer.*	1. Never drink wine 2. Up to 200g 3. Between 200-400g 4. Between 400-600g 5. Between 600-1000g 6. More than 1L 97. Difficult to answer 98. Refuse to answer
G13. During last 12 months how much spirits, such as vodka or other spirits, do you usually drink on one occasion? *Please choose the single most appropriate answer.*	1. Never drink spirits 2. Up to 50g 3. Between 50-100g 4. Between 100-200g 5. Between 200-300g 6. Between 300-400g 7. Between 400-500g 8. More than 500g 97. Difficult to answer 98. Refuse to answer

G14. During last 12 months what was the maximum quantity of beer ever drunk on one occasion? *Please choose the single most appropriate answer.*	1. Never drink beer 2. 1 bottle (0.5l) or less 3. 2-4 bottles 4. 5-6 bottles 5. More than 6 bottles 97. Difficult to answer 98. Refuse to answer
Module H: Smoking	
H1. Are you a current smoker? Please choose most appropriate answer.	1. Never smoked 2. No, ex-smoker 3. Yes, a current-smoker 97. Difficult to answer 98. Refused to answer
Health Examination Questionnaire	
Alcohol Use Disorder Identification Test	
Systolic & Diastolic BPs	
Resting Heart Rate	
BMI	
Total, HDL- and LDL- cholesterol	
GGT	